in the assessment and treatment of T1DM. Whether hope is valuable for risk prediction models of future HbA1c remains to be determined.

Supported by: KU Diabetes Institute

2320-PO

Patterns of Complementary Therapy Use Among Rural Older Adults With Diabetes

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Previous studies on complementary therapy (CT) use among adults with diabetes have been limited by crude measures of current use across broad CT categories, and by a lack of specificity of CT use for treating diabetes. Data for the current analysis are drawn from a study of CT use among rural African American and white older (age ≥65) adults in southeastern North Carolina. Among the 200 study participants, 71 (35.6%) reported having been told by a doctor that they have diabetes. Baseline and repeated three-day assessments (n=52) of use of six categories of CTs for treating diabetes symptoms were conducted monthly by trained interviewers over a six-month period. At baseline, the most commonly used CTs included prayer (88.7%), food or beverages (50.7%), herbs (11.3%) and home remedies (9.9%). Over-the-counter therapies and CT professionals were used by less than 1% of participants. In repeated measures representing 1131 interviews, prayer was used on 57.2% of days, followed by food or beverages (12.7%), herbs (3.4%) and home remedies (2.7%). Over half (56.3%) of those using prayer did so in at least five of the six reporting periods, whereas use of other CTs was more sporadic. These data show, with the exception of prayer and food and beverages, fairly limited use of CTs for diabetes treatment among rural older adults, and less consistent use for most CTs except prayer. Further research is needed to more fully understand the motivations and patterns of CT use in this population.

CT Use at Baseline and in Repeated Assessments among Rural Older Adults with Diabetes

Therapy	Baseline (N=71)	Six-Month Follow-Up (n=52)	
	N, % of Total	N, % of Days Used	N, % of Use at Least 5 of 6 Months
Prayer	63 (88.7%)	531 (57.2%)	27 (56.3%)
Food or Beverage	36 (50.7%)	119 (12.7%)	2 (7.4%)
Over-the-Counter Remedies	1 (1.4%)	—	—
Herbs	8 (11.3%)	32 (3.4%)	1 (14.3%)
Home Remedies	7 (9.9%)	25 (2.7%)	0
Complementary Health Professionals	3 (4.2%)	3 (0.3%)	0

Supported by: National Center for Complementary and Alternative Medicine (R01 AT003635)

2321-PO

Recruiting Lower-Income African American Women into a Diabetes Medical Nutritional Therapy Intervention

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This research describes the recruitment of lower-income African American (AA) women into a diabetes medical nutritional therapy intervention as part of an academic research institution (ARI)/managed care organization (MCO) partnership. The MCO partners mailed out 331 invitation letters to AA women enrolled in their diabetes management program. The letter described the ARI-facilitated diabetes medical nutritional therapy intervention and provided an ARI contact number. The ARI partners used a paper and electronic tracking system to monitor responses to the invitation letter and follow-up communications. One hundred thirty-eight women responded to the letter or follow-up calls (25 called the ARI to request additional information; the ARI partners contacted 113 by phone after receiving no responses to the letter). The ARI partners left voice mails for forty-five women for which no return calls were received. Seventy-three had disconnected phones or numbers not receiving incoming calls. Eighty-five women had no phone number listed in the MCO database. Of the 138 women that responded to the letter or follow-up calls, 42 were screened by phone, met non-clinical study criteria, and scheduled a clinical in-person screening visit. Ninety-six either failed the phone screening or were not interested due to reasons such as family responsibilities and other chronic health conditions. Of the 42 women that scheduled a clinical in-person screening visit, 28 kept appointments. Seventeen met all study criteria and were enrolled into the study. Traditional methods to recruit lower income AA women into diabetes self-care interventions may be challenging due to the transient nature of the population and women's competing life and medical priorities. Finding ways to help women manage these priorities as part of the recruitment process as well as employing non-traditional recruitment methods, such as face-to-face recruitment in community settings, may yield better recruitment results.

2322-PO

The Effect of Diabetes and its Control on Susceptibility to Learned Helplessness in Streptozotocin-Induced Diabetes Rats

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AIMS: In order to examine the mechanism linking diabetes to depression, hyper and hypoglycemia are different at risk of affective disorder. METHODS: Using the streptzotocin rats, totally 37 rats, were divided into 4 types of glycemic control groups, Group A (good), B (hypo-hyper) ,C (untreated), D (controls). The bodyweight, the blood glucose concentration and HbA1c were measured. And all animals were placed in a learned helplessness paradigm, Forced swimming test : the scorer would rate immobility and another action. We examined the differences in the length of immobility (a key marker of learned helplessness) with the analysis using Tukey-Kramer multiple comparison. RESULTS: Glycemic control: Group A had nearly kept smaller change of blood glucose throughout the day. Group B of blood glucose showed a very steep fall from 475.8 ± 193.2 (mean ± SD) mg/dl to 42.8 ± 22.6 mg/dl within three hours after the insulin injection. Mean HbA1c of Group C significantly increased from 5.9 ± 1.3 to 8.7 ± 4.0 % ($p < 0.0001$). In A and B group the level of HbA1c decreased from 5.6 ± 1.0 to 3.8 ± 0.6 % and 6.4 ± 1.7 to 3.7 ± 0.5 % respectively. The bodyweight in A and B groups was not significantly different compared with that in non diabetic control group (P = 0.001, 0.001). Group C is significantly low compared with that in Group D (< 0.0001). FST: There were trends for counts of immobility to be higher in all 3 diabetic groups compared to Group D, especially in Group B, the mean count of immobility is significantly high compared with Group D (< 0.001). There is no significant difference in the mean counts of swimming. The climbing was significantly low in Group C compared to Group D (< 0.001). CONCLUSION: These investigations are thought to be interesting to examine the relationship between diabetes and depression, and suggested that acute varieties in glycemic control could be the mechanism of susceptibility to affective disorder.

CLINICAL THERAPEUTICS/NEW TECHNOLOGY—GLUCOSE MONITORING AND SENSING

2323-PO

Assessment of Hematocrit Interference of Blood Glucose Meters in a Comprehensive Laboratory Setting

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Primary objective of this study was to investigate the susceptibility of four blood glucose meters to hematocrit (HCT) interference in a laboratory setting. Three different strip lots were used for each of the following devices: BG*Star and iBG*Star (both Sanofi), Breeze 2 (Bayer), OneTouch Verio Pro (Lifescan), and YSI analyzer (reference method). Heparinized blood was manipulated to contain 6 different blood glucose levels in a range from 30 mg/dL to 600 mg/dL and 9 hematocrit concentrations (20 % to 60 %, in 5 % increments), resulting in 54 individual samples. In order to eliminate disturbing systematic external factors, all measurements were carried out in triplicate and in parallel within 20 min for all meter/strips combinations by 12 experienced investigators after confirmation of a physiological oxygen pressure in each freshly prepared sample (468 readings per device&strip lot combination). For the analysis, values at 45 % hematocrit were set to 100 %. For benchmarking, maximally observed mean deviations from this value in both directions were added to determine the hematocrit interference factor (HIF). Based on clinical considerations, an HIF > 10 % was arbitrarily defined to present relevant hematocrit interference. Accuracy was determined by calculating the mean absolute percent deviation from the reference method (MARD). As indicated by HIF/MARD-values of 4.6%/4.8% for BG*Star, 3.0%/4.9% for iBG*Star, and 1.7/4.6 % for OneTouch Verio Pro, these devices showed to have a high accuracy at all HCT concentrations. This was not the case for Breeze 2 (42.6%/15.9%), which showed too high reading at low HCT levels and vice versa. In this comprehensive laboratory investigation, the technologies of BG*Star, iBG*Star and OneTouch Verio Pro showed to be not affected by hematocrit and to be very accurate in comparison to the reference method even under these artificial laboratory conditions.

Supported by: sanofi-aventis

2324-PO

Consistent Performance of Dexcom G4 When Calibrated at Different Rates-of-Change (ROC)

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Continuous Glucose Monitors (CGM) measure glucose in the interstitial fluid (IF), but are calibrated with blood glucose (BG) from capillary fingersticks. During rapid change, glucose concentrations in the blood and IF may not be in equilibrium; and as a result, some CGM devices suggest, or require, calibration only during periods of stable glucose. In a home use setting, this limitation can hinder patient compliance and CGM usage. This analysis shows the effect of ROC at calibration on CGM accuracy based on clinical trial data of the Dexcom G4 CGM system. CGM data was collected at 1 US center from 21 adult subjects (n=19 type 1, n=2 type 2). The data was generated from 40 sensors. Each sensor was worn for 7 days and calibrated twice per day with a BG meter. Each subject was required to complete a tracking study on Day 1, 4 or 7 of sensor use where BG values were collected every 15 minutes for 10 hours. On non-tracking study days, subjects were instructed to take a minimum of 7 BG values per day for accuracy comparison. At each calibration, glucose ROC was estimated using the previous 20 minutes of CGM trend data (provided the data did not exceed the CGM's criteria for noise). The Mean Absolute Relative Difference (MARD) and the percentage of points within 20 mg/dl (BG $\leq$ 80 mg/dl) or 20% (BG > 80 mg/dl) (%20/20) was calculated for the paired sensor and BG values collected between calibrations. The MARD and %20/20 were then placed into a corresponding Absolute ROC (AROC) bin: 0 to 1, 1 to 2 and > 2 mg/dl/min. Accuracy, across the different ROC at the time of calibration, is shown below. When calibrated at different ROC, the accuracy of the Dexcom G4 remains consistent:

AROC (mg/dl/min.)	AROC $\leq$ 1	1 < AROC $\leq$ 2	AROC > 2
Mean MARD (95% Confidence Interval)	13.6 (12.7, 14.5)	14.1 (12.2, 15.9)	13.5 (11.2, 15.8)
Median MARD	12.0	11.5	12.3
Mean %20/20	82.0	79.2	81.4
No. of Calibrations	346	102	25

2325-PO

Comparative Investigation of Basal Insulin Glargine versus Metformin as First Line Drug in Patients With Type 2 Diabetes

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Metformin (MET) as first line drug fails to prevent disease progression. Early use of insulin might be able to preserve beta cell function. We compared effect on B-Cell and endothelial function and cardiovascular risk factors. Open-label, randomized, prospective 36-wk study. 75 eligible drug naive patients (45/30 m/f, age 60.7±9.2 yr), HbA1c between 6.5 & 8.5% were allocated to MET 1000 mg b.i.d. (n=36) or insulin glargine (GLA) at bedtime (n=39). GLA dose was adjusted to target fasting plasma glucose (FPG) <5.6 mmol/l. At baseline and study end proinsulin and C-peptide levels, glucose homeostasis by CGMS, insulin secretion, endothelial function and cardiovascular (CV) risk factors were measured. GLA treatment compared to MET resulted in a more pronounced reduction of FPG (Δ: 3.1±2.5 vs.1.4±1.5 mmol/L; p<0.001), decrease of mean interstitial glucose (IG) level during CGM (Δ: 2.4±1.8 vs. 1.4±1.8mmol/l; p=0.02) and overall IG-area under the curve (AUC Δ: 671.2±507.9 vs. 416.1±537.6 mmol/L min; p=0.04). 2-h pp PG after test meal as well as IG-AUC differences after test meal and HbA1c were not significantly different between treatment groups. A significant reduction of proinsulin to Cpeptide ratio compared to baseline was found for both interventions however insulin treatment resulted in a significantly better improvement in proinsulin/Cpeptide ratio than MET. Diastolic blood pressure was significantly reduced with GLA (Δ: -4.4±6.7 mmHg) but remained constant with MET. No significant differences were observed for effects on blood lipids, albumin/creatinine ratio and hsCRP. Endothelial dysfunction measured with Laser Doppler Velocimetry (O2C) was only significantly improved by MET treatment. Early GLA insulin treatment in T2D patients showed better control of FPG and overall glycemic load than MET. This was associated with improved B-cell function. MET improved endothelial function whereas GLA improved diastolic blood pressure.

2326-PO

Use of Glucolysis Inhibitors in Blood Drawing Tubes Shall not Prevent Diagnostic Errors

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Blood glucose is an important test to identify and evaluate diabetic patients. *In vitro* utilization of blood glucose by erythrocytes is a potential source of error in the determination of glucose and relates to the time elapsed from sample drawing to analysis. The use of tubes with glucolysis inhibitors (GI) has been proposed as a solution but the impact of this recommendation has not been properly evaluated. In order to know the utility of GI we obtained venous blood with three types of tubes to draw samples -plain (P), serum separating gel (SST®) and sodium fluoride glucolysis inhibition (SFGI) tubes-, and measured glucose by the hexokinase method within 30 minutes, and 120 and 240 minutes after venipucture. We compared glucose levels among the three tubes, and the three results in each tube. Subjects (16 men and 19 women) were randomly accrued in the study, their ages ranged from 17 to 86 years (median 40.5 years) Mean glucose concentration decreased by -1.37% in P tubes, -1.02% in SST tubes and -1.08% in SFGI tubes after 120 minutes; similarly glucose levels decreased -3.99% in P tubes, -1.69% in SST tubes, and -2.09% in SFGI tubes at 240 minutes. Glucose diminished significantly from baseline to 240 minutes in all tubes (p<0.05), decrease in the P, SST and SFGI tubes was 3.97±1.55, 1.72±1.46 and 2.19±1.06 mg/dL, respectively. The change in glucose was statistically significant between P and each of the other 2 tubes, but not between SST and SFGI tubes No statistical differences were seen in blood glucose levels amongst the three types of tubes in any of the determinations. Three patients tagged as having "abnormal fasting glucose levels" turned to "normal" after 240 minutes in the P tubes. The same occurred in two subjects at 120 minutes in each the SST and the SFGI tube SFGI tubes offers no advantages in the preservation of glucose when compared to the SST tubes, but might have some utility as compared with the P tubes. The risk of misclassification of subjects is present despite the type of tube.

2327-PO

Short-Term Psychosocial Impact of Sensor-Augmented Pump Therapy Within Three Months of Diagnosis of Type 1 Diabetes

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Sensor-augmented pumps (SAP) have been shown to improve glycemic control of type 1 diabetes (T1D). However, the psychosocial impact of intensive therapy with SAP at onset of diabetes is unknown. This study presents short-term psychosocial data on a subset of subjects randomized to the treatment arm of a 2-year study evaluating the effect of closed-loop control plus SAP vs standard MDI and routine glucose monitoring on residual beta cell function. Psychosocial measures of anxiety (State-Trait Anxiety Inventory, STAI); depression (Children's Depression Inventory-2, CDI-2; Center for Epidemiological Study of Depression-Revised, CESD-R); perceived parental burden (Pediatric Assessment in Diabetes-Parent, PAID-P); and fear of hypoglycemia (Hypoglycemia Fear Survey-Parent (HFS-P) were completed by children and their parents at diagnosis of T1D prior to randomization (Mean age: 11.7±3.1 y; 9M, 2F) and 3 months later. As compared to published reference group means, child and parent state anxiety and depressive symptoms were not elevated at baseline, and anxiety scores remained stable at 3 months. PAID and HFS scores do not reflect high perceived parental burden or fear of hypoglycemia at 3 months. These preliminary data suggest children and parents adapt well to use of SAP from diagnosis, but follow-up is needed to monitor adjustment and burden of care with longer-term use.

		Diagnosis (n=11)	3 months (n=8)	Reference Group
Child	STAI-Y (Trait[1]/ State)	29.9±6.8 / 29.6±9.5	— / 28.1±11.8	36.7±6.3 / 31.0±5.7
	CDI-2[1]	2.8±2.9	—	2.6±2.9
Parent	STAI (Trait[1]/ State)	31.0±9.1 / 35.7±9.0	— / 32.4±12.4	34.8±9.2 / 35.2±10.6
	CESD-R[1]	4.6±5.0	—	10.7±9.9
	PAID-P[2,3]	—	73.4±14.2	47.8±16.6
	HFS-P (Behavior / Worry)[2]	— / —	21.8±8.6 / 11.5±6.4	27.8±5.8 / 31.7±10.6

[1]not repeated at 3 months; [2]not applicable at diagnosis; [3]unlike all other measures higher score indicates less burden

For author disclosure information, see page 797.

ADA-Funded Research

2328-PO

Encouraging Adherence and Compliance With Self-Monitoring of Blood Glucose—The Non-Invasive Approach

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Over the last years, a consensus advocating the performance of self-monitoring of blood glucose (SMBG) for people with diabetes has been reached. Moreover, the benefits and contribution of SMBG to metabolic control are enhanced with increased frequency and appropriate timing of SMBG performed in a structured way. Nevertheless, SMBG is still underutilized, especially by non-insulin treated type 2 individuals. Apparently, lack of glucose monitoring education isn't the main obstacle for following proper SMBG routine. Other commonly suggested barriers to efficient SMBG utilization are pain, inconvenience and cost, associated with the invasive nature of conventional SMBG methods. Painless and low cost methods may overcome these barriers. GlucoTrack® is a Non-Invasive (NI) home use intended device, which allows real time spot SMBG. Its primary advantages include pain-free and inexpensive use (due to lack of expendables), without the need to be continuously worn. GlucoTrack performances were evaluated in a variety of clinical trials for all groups of gender, BMI and diabetes type adult (> 18 year old) subjects. In addition, feedback regarding usability of the device was analyzed. Clarke Error Grid pulled data analysis of 121 subjects (2850 points) shows 96% of the points in the clinically accepted zones A+B, of which 58% in zone A. Mean Absolute Relative Difference of all subjects is 23.0%. 86% of the responders declared they'll use the device more frequently than the invasive one. Though the proposed NI device is still less accurate in comparison with existing invasive devices, it offers a plausible alternative for invasive SMBG. A trade-off between less accurate NI device, which leads to frequent and contributive utilization on one hand, and more accurate invasive glucose monitor, which is less utilized, on the other hand, should be individually considered. We believe that in many cases, the alternative that encourages better adherence and compliance will gain priority.

2329-PO

Correlation Between Self-Monitoring Blood Glucose And Glycated Albumin In Pregnant Women With Diabetes

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Hemoglobin A1c(HbA1c) is reliable and objective parameter for 12 weeks glycemic control. In gestational diabetes(GDM), HbA1c is inadequate for glycemic control parameter because screening and confirmation test were carried out at 24-28 weeks of gestation, only 12-16 weeks is left from diagnosis to delivery. Glycated albumin(glycoalbumin, GA) is useful to reflect short-term glycemic control status. We investigated relation between mean self-monitoring blood glucose, target glucose achievement ratio and GA in pregnant women with diabetes. This study enrolled 49 pregnant women with diabetes(45 GDM and 4 type 2 diabetes). Self-monitoring blood glucose was measured every day, mean glucose and target glucose achievement ratio during 2 weeks was calculated. GA was measured every 2 weeks. We can find correlations between GA and mean fasting glucose(p=0.044), mean postprandial glucose(p=0.004), mean overall glucose(p=0.008), target postprandial glucose achievement ratio(p=0.029) and target overall glucose achievement ratio(p=0.029). mean postprandial glucose and postprandial glucose achievement ratio has moderate Pearson correlation coefficient(r) 0.386 and -0.310 respectively. That suggest GA is potential parameter for short-term glycemic control in pregnant women with diabetes. Further study will be needed whether GA can substitute for self-monitoring blood glucose.

Supported by: Handok Pharmaceuticals Co., Ltd.

2330-PO

Simple Simulation Models of Continuous Glucose Monitoring Data

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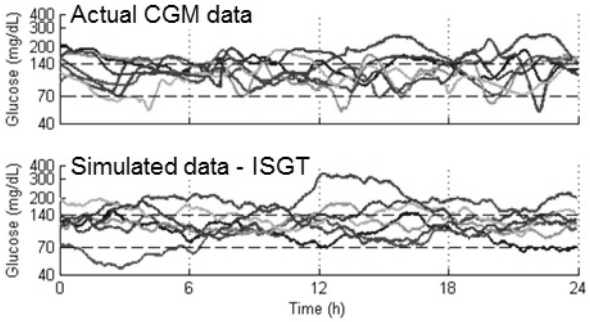
To accelerate development of future products and services, two simple simulation models of glycemia in people with type 1 diabetes were developed (Medtronic MiniMed, Inc). The Population Static Glucose Distribution (PSGD) and Individual Subject Glucose Trend (ISGT) models were parameterized on random samples drawn from over 4000 subject-months of continuous glucose monitoring (CGM) data in the Medtronic CareLink database. Both models assume a log-normal blood glucose distribution and have been extensively validated. The PSGD was modeled using a bivariate log-normal probability distribution with just 5 parameters. The ISGT was modeled using a second order autoregressive time series driven by independent, identically distributed, white Gaussian noise. The series is first log-transformed and mean-centered. Its 4 parameters provide simulated CGM tracings that closely resemble actual patient data (Figure). The PSGD model has been used to estimate population glycemic variability and hypoglycemia risk, to evaluate and develop glycemia metrics, and to design "virtual clinical trials" in the artificial pancreas project. Individual "virtual subjects" created using the ISGT model have been used to design user interfaces and develop artificial pancreas control and prediction algorithms. The PSGD and ISGT models have enabled model based development, rapid prototyping, concept engineering, and robust design. These models allow for more exploration of algorithms in a shorter time than traditional techniques, and can be used to accelerate innovation in diabetes technologies and treatments.



Supported by: Medtronic, Inc.

2331-PO

Continuous Glucose Monitoring Improves Glycemic Control in Subjects With Type 2 Diabetes on Basal Insulin

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Continuous glucose monitoring (CGM) is currently recommended for patients using MDI or CSII to improve glucose management. Whether patients with T2DM on basal insulin ± oral agents (OADs) benefit from CGM has not been studied. This open-label, uncontrolled, single-center, investigator initiated, pilot study was designed to examine the effectiveness of real-time (rt) CGM, with minimal device training, to improve glucose control in subjects with T2DM using basal insulin. A subset of older subjects (age ≥ 65y) was included. Thirty adults (age 58±12.4y) on basal insulin only ± OADs with baseline A1C (8.9±1.5%) were enrolled and used rt DexCom™ 7 ®Plus CGM device continuously for 6 months (26 subjects completed). A1C values were obtained at 3 and 6 months and compared to baseline values. Subjects were allowed to meet with an Investigator or Diabetes Educator to make therapeutic changes based on CGM data at their discretion. CGM was not the primary resource for self-treatment decisions (patients relied on SMBG data), but trend data was used by subjects to make lifestyle changes. Glycemic control improved significantly after 6 months of real-time CGM use with 58% of subjects reaching an A1C of ≤ 7%. The data (see table) suggest that patients of all adult ages with type 2 diabetes on basal insulin can successfully use CGM data to modify behavior; additional improvement in A1C is realized when CGM is used in conjunction with diabetes education and adjustments to diabetes therapy. Future randomized controlled trials are required to further assess the benefits of CGM in patients with T2DM.

Table 1. Mean Change in A1C from Baseline at 6 Months

Group	Decrease in A1C	n	P
All Subjects	1.9±1.4%	26	<.001
Subjects ≥ 65 years of age	1.6±.5%	10	<.001
Subjects < 65 years of age	2.1±1.8%	16	<.001
Subjects Receiving Diabetes Education	2.1±1.5%	18	<.001
Subjects Receiving no Diabetes Education	1.4±1.1%	8	<.01
Subjects with no New Medications Added	1.5±1.0%	9	.001
Subjects with OADs or Prandial Insulin Added	2.1±1.6%	17	<.001
Subjects with Added Prandial Insulin	2.1±1.7%	12	<.001
Subjects on Basal Insulin only ± OADs	1.8±1.2%	14	<.001
Subjects with Baseline A1C ≥ 9	3.5±.8%	8	<.001
Subjects with Baseline A1C < 9	1.2±1.0%	18	<.001

Table 1. Shows mean decrease in A1C at 6 months from baseline in subjects from various groupings within the study population.

2332-PO

Dexcom G4, A Next Generation Continuous Glucose Monitoring (CGM) System, Demonstrates a Strong Correlation to Self-Monitored Blood Glucose (SMBG)

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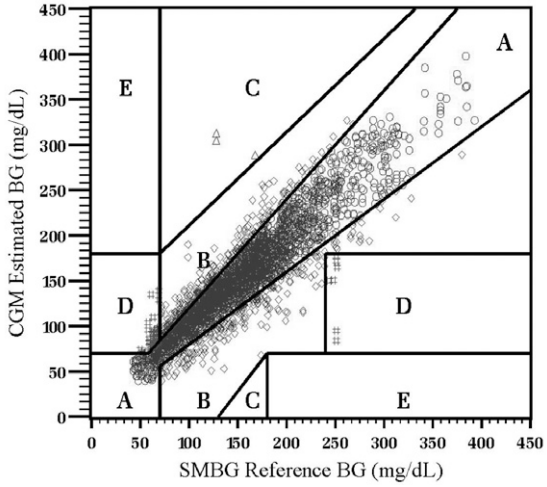
Persistent CGM use is associated with improved outcomes. However, perceived inaccuracy by some patients, because of differences between glucose values obtained from CGM and SMBG, causes them to discontinue CGM use. The Dexcom G4 was designed for improved performance and initial performance data was obtained from 21 subjects at one US center. Subjects: all White; age 44 ± 13 years old; 10 M; duration of diabetes 21 ±13 years; 19 with T1DM, 2 with insulin-requiring T2DM; baseline A1C 7.5 ± 1.2 %; and BMI 27.3 ± 3.6 kg/m^2. Subjects self-inserted sensors after device training, wore 2 sensors (1 was un-blinded during home use) for 7 days, calibrated sensors once every 12 hours, and participated in one 10-hour in-clinic session (CGM was blinded) with SMBG obtained every 15 minutes on study day 1, 4, or 7. CGM glucose values were compared to SMBG to emulate the patient experience. The overall mean system bias to SMBG was -0.04 ± 24 mg/dl, and the Pearson correlation coefficient was 0.917 with a 95% CI of (0.91, 0.92). The Mean Absolute Relative Difference was 12.6%, the % 20/20 was 83%, and 82% of values were in the Clark Error Grid A Zone (Figure). 93% of the sensors lasted until day 7, and on average, subjects experienced more than 95% of anticipated glucose readings. Coefficient of variations was 6% from two concurrently worn systems. The Dexcom G4 demonstrates improved accuracy, precision, and sensor life compared to currently marketed devices. The enhanced precision and negligible bias to SMBG should provide greater confidence to patients using CGM as part of their clinical decision making.



2333-PO

Nateglinide has Comparable Effectiveness With Acarbose in Reducing Postprandial Glucose Excursions in Chinese Anti-hyperglycemic Agent Naïve Subjects With Type 2 Diabetes Mellitus

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This was a multi-center, open-label, randomized, active-control, parallel-group study which compared the effects of nateglinide paralleled with those of acarbose on postprandial glucose excursions in Chinese anti-hyperglycemic agent naïve subjects with type 2 diabetes mellitus by continuous glucose monitoring system (CGMS). A total of 103 anti-hyperglycemic agent naïve subjects with type 2 diabetes mellitus [age: 53.5±9.81 yrs, duration of diabetes: 0.1 (0.8) yrs] from four hospitals in China were randomized (1:1) to nateglinide 120mg TID or acarbose 50mg TID groups. After 14 days treatment, compared with baseline, both nateglinide and acarbose reduced the area under curve of 0-4 hours postprandial glucose (AUCpp) significantly (P<0.001).Whereas no significant differences were found between two groups (P= 0.6908). The mean blood glucose (MBG), mean amplitude glycemic excursions (MAGE) and standardized difference of daily blood glucose excursion (SDBG) decreased significantly in both groups (all P<0.001). No significant differences were found between two groups in reductions of MBG, MAGE, SDBG after treatment. Both the two agents had comparable effects on reducing glycated albumin [2.0 (2.5) % and 1.0 (1.6) %, P<0.0001].The rates of adverse events (AE) and AE related to trial products were significantly higher in acarbose group than nateglinide group (P<0.05). No serious AE was noted. The rates of hypoglycemic episodes were comparable in two groupsThere was no severe hypoglycemic episode being noted in either group. Our study suggests that nateglinide was well tolerated among patients recruited in this study. It showed that natiglinide had comparable effectiveness with acarbose in reducing postprandial glucose excursions in Chinese anti-hyperglycemic agent naïve subjects with type 2 diabetes mellitus.

2334-PO

Usability and Performance of a Pattern Detection Glucose Meter

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The automated detection of dysglycemic patterns offers the potential to alert users and healthcare providers (HCPs) to initiate clinical interventions and improve glycemic control in people with diabetes. The OneTouch® Verio™IQ meter with PatternAlert™ Technology uses an algorithm to detect glycemic patterns by analyzing blood glucose (BG) readings in the meter memory and alerting users with a message when a pattern is identified. A high pattern is defined as a minimum of 1 result tagged 'Before Meal' that is above a Before Meal High limit on 3 separate days out of the last 5 days, all within a 3-hour period. A low pattern is defined as a minimum of 1 result below a Low limit on 2 separate days out of the last 5 days, all within a 3-hour period. The OneTouch VerioIQ meter with PatternAlert was tested in a clinical study by 185 people with diabetes (47 % Type 1 and 53% Type 2). At BG <75 mg/dL, 100% (31/31) of test results were within ±10 mg/dL of reference values. At BG ≥75 mg/dL, 99.2% (243/245) were within ±15% of reference values. Appreciation of the PatternAlert Technology was assessed by questionnaire. The PatternAlert was considered easy to set up by 99.5% of participants and 97.8% of participants considered the messages easy to understand. Additionally, 99.5% of participants liked that the PatternAlert automatically identified new patterns and 98.9% found it easier to find patterns using PatternAlert on the OneTouch VerioIQ than with a paper logbook. HCPs reported that lay users were able to correctly use the OneTouch VerioIQ meter with PatternAlert Technology, with a success rate of >98% (183/185). The Figure below shows an example of the Pattern Alert tool in action.

2335-PO

Evaluation of Continuous Glucose Monitoring (CGM) On Gestational Diabetes Mellitus In China

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To evaluate the effects of the Continuous Glucose Monitoring (CGM) on Gestational Diabetes Mellitus (GDM). From February 2010 to October 2011, pregnant women underwent GDM screen tests. We used retrospective Continuous Glucose Monitoring system, according to China Association of gestational diabetes diagnostic criteria; one hundred twenty-eight women were diagnosed with GDM, and were randomly divided into two groups; the test group, with 68 cases, and the control group, with 60 cases. The test group wore the Continuous Glucose Monitor for 72 hours. The control group tested the capillary blood glucose with a single spot blood glucose meter, 7 times a day. There were no records of conscious hypoglycemic symptoms or hypoglycemia during the monitoring period. The CGMS data showed that the percentage record of hyperglycemia was (17.9±2.8%). The percentage of hypoglycemia was (2.4±0.9%), which was significantly higher than those of the control group [(14.9±2.8)% and(1.0±0.3)%, respectively]. We recommend that pregnant women with GDM monitor their blood glucose level using CGMS regularly. It will help them systematically evaluate their real glucose condition, and ensure the health of both themselves and their babies.

Supported by: America-Asia Diabetes Research Foundation

For author disclosure information, see page 797.

2336-PO

An Improved Approach to Measuring Blood Glucose Concentration from Metabolic Heat: Application and Clinical Data

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Diabetes afflicts 24 million people in the U.S. and is the seventh leading cause of death by disease. Frequent monitoring of blood glucose is crucial for effective treatment of diabetes. Due to the well-known drawbacks of invasive blood glucose meters, development of noninvasive approaches is ongoing, with accuracy, reliability and cost as main obstacles to commercialization. The correlation between glucose metabolism and body heat production is the basis for the metabolic heat conformation method. In principle, glucose utilization increases production of body heat. Hence, blood glucose levels can be determined by measuring the body's metabolic heat, usually from ambient and skin temperatures. Accurate measurement of heat production due to glucose metabolism, however, is impacted by the environment and the body's changing baseline metabolic heat. The former is important in selecting temperature measurement sites while the latter is evident from innate core body temperature rhythms. Our approach accounts for these factors in two empirically derived equations: one for determining body metabolic heat, and the other for relating metabolic heat to blood glucose level. To minimize environmental effects, skin and core body temperatures are measured in the ear canal and oral cavity, respectively. Both sites are minimally affected by brain activity and not directly exposed to the environment. We developed a microprocessor-controlled device with temperature probes and a customizable core body temperature function, then conducted a clinical trial of 45 subjects to compare our instrument to an invasive approach (blood sample from fingertip) using a biochemical analyzer. Compared with test results obtained from the biochemical analyzer, the correlation coefficient of the data from our device is 0.975, indicating that the device and method is accurate and reliable. The project is now in the commercialization phase.

2337-PO

Analysis of Blood Glucose Pattern Management Practices by Healthcare Providers (HCPs)

GILL TEFT, LAWRENCE W. CESNIK, *Inverness, United Kingdom, Milpitas, CA*

Self-monitoring of blood glucose (BG) is a common way for individuals with diabetes to assess glycemic control at home and make appropriate treatment and lifestyle changes. Systematic BG testing allows BG patterns to be identified and acted upon. A qualitative pilot study was conducted to assess the use of software tools in pattern management activities by HCPs. A series of 3-day online bulletin boards were conducted, 1 each for certified diabetes educators (CDEs; n = 12), endocrinologists (n = 12), pharmacists (n = 12), and primary care physicians (PCPs; n = 14). HCPs were asked to identify who reviews patterns of BG results, how frequently, and how these were used. The 4 groups of HCPs reviewed the data differently (Table 1) and for different reasons (Table 2). HCPs considered pattern management most important for patients who use intensive insulin therapy/pumps, are titrating medication, are prone to hypoglycemia, or have a high A1C. Pattern management was used as a teaching tool to show patients how BG values correlate with behaviors. HCPs felt that pattern self-management empowered patients. Home BG testing was considered more important than A1C assessment because of the ability to get immediate feedback on therapy changes.

Table 1: Method of reviewing

	CDE	Endocrinologist	PCP	Pharmacist
Use log books	Every time	Every time	Every time	Rarely
Use custom log books	Sometimes	Rarely	Never	NA
Use downloads	Sometimes	Sometimes	Never	NA
Use patient memory	Rarely	Rarely	Rarely	NA
Emails from patients	NA	NA	Sometimes	NA
Scroll through meters	Sometimes	Sometimes	Sometimes	Sometimes

NA: not applicable.

Table 2: Reasons for reviewing

	CDE	Endocrinologist	PCP	Pharmacist
Look for out of range patterns/trends	Every time	Every time	Every time	NA
Look for hypoglycemia	Every time	Every time	Every time	Sometimes
As a teaching tool	Every time	Sometimes	NA	NA
Make or recommend therapy changes	Sometimes	Every time	Every time	NA
Spot discrepancies between BG results and A1C	NA	NA	Every time	NA
Encourage compliance	Every time	Sometimes	NA	Sometimes
Patient asks	NA	NA	NA	Every time

2338-PO

Factors Affecting Insulin Dosing Accuracy

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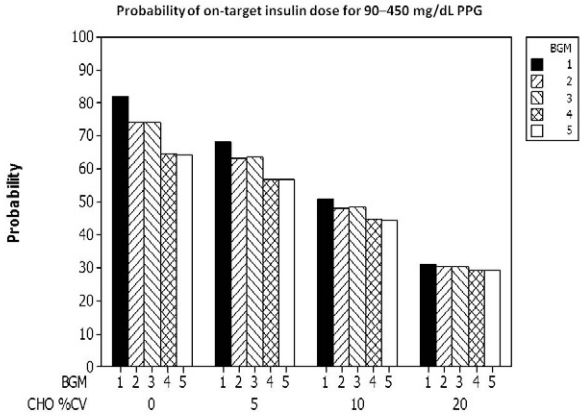
A Monte Carlo simulation study was performed to predict the impact on insulin-dosage accuracy of varying blood glucose meter (BGM) performance in the presence of increasing carbohydrate (CHO) estimation errors. The simulation predicted the likelihood of on-target insulin doses and clinically significant insulin dose errors in a patient, calculating insulin doses based on BGM results and CHO estimates. The study included: 5 BGMs (BGM1 [bias –1.35%, CV 4.84%, performance of LifeScan's OneTouch® Verio™ brand BGM, 10% total error; BGM2 [bias –2%, CV 6%, 15% total error]; BGM3 [bias 2%, CV 6%, 15% total error]; BGM4 [bias –4%, CV 7%, 20% total error]; BGM5 [bias 4%, CV 7%, 20% total error]); 4 levels of CHO estimation error; and 3 levels of pre-prandial glucose (PPG; 90-150 mg/dL, 150-270 mg/dL, and 270-450 mg/dL). When CHO %CV was 0%, the likelihood for on-target insulin dosages ranged from 50.1-98.5% for all BGMs. The likelihood was dependent on BGM accuracy and precision, and PPG range. Increasing CHO error led to fewer on-target insulin doses and more insulin dose errors, and reduced the impact of BGM performance on these outcomes. BGM1 had the most on-target insulin doses (range, 31.0-81.8%) compared with BGMs 2-5 (range, 29.2-74.1%; Figure). The likelihoods of insulin overdose and underdose errors for BGM1 at 0% CHO error were 0.4% (other BGMs 0.9-9.0%) and 0% (other BGMs 0-0.4%), respectively, which increased at 20% CHO error to 19.9% (other BGMs 17.4-28.9%) and 8.0% (5.8-10.7%), respectively. Both BGM and CHO estimation errors contribute to erroneous insulin doses. Compared with the 4 other BGMs, BGM1 was associated with the most frequent on-target insulin dosages.



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2339-PO

Evaluation of Reproducibility Using Strips for Blood Ketene Measurements in Routine Clinical Management

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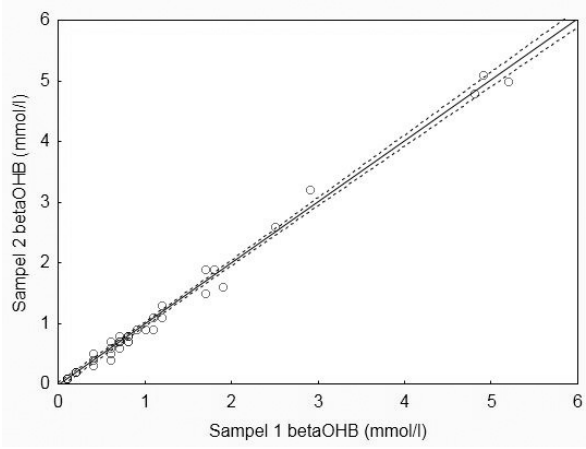
Measurement of β-Hydroxybutyrate (βOHB) by strips has been recommended in managing diabetic ketoacidosis. The method is validated in laboratory environment but it´s reproducibility has so far not been tested in routine clinical management. The aim of this study was to evaluate the reproducibility of this method in an emergency department setting. All patients entering the acute ambulatorium at a County Hospital with a blood glucose measurement more than 14 mmol/l were investigated by an emergency department nurse using Precision Xceed™ Blood Ketone Meter (Abbott). If the patient had detectable levels of βOHB another nurse took a new capillary blood test within three minutes and evaluated βOHB concentration using the same method. Forty-eight patients (31 males, age 61±19,7 (mean ±SD) years), investigated within a six months period, had a βOHB range between 0.1 and 5.2 mmol/l. The mean βOHB concentration was 1.11±1.27 in sample 1 and 1.10 ±1.29 in sample 2. The correlation between sample 1 and sample 2 was 0.996. Also in a routine clinical management the Precision Xceed™ Blood Ketone Meter instrument seems to have a good reproducibility in measuring βOHB, thereby being a useful tool in acute diabetes care.



Supported by: Abbott, Inc.

2340-PO

Accuracy of a New Blood Glucose Monitoring System in the Hands of Users

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This study assessed the performance of a blood glucose monitoring system (BGMS) in development that can communicate with an insulin pump. The system uses a flavin adenine dinucleotide-glucose dehydrogenase enzyme test strip with a new proprietary electron mediator. A total of 110 subjects aged 19 to 86 years with type 1 (n = 37), type 2 (n = 63), or type unknown (n = 10) diabetes participated. Untrained subjects learned to use the BGMS using the labeling materials provided and tested fingerstick and palm (alternative site testing) samples; health care professionals (HCPs) also tested subject fingerstick samples on the BGMS. All results were compared to YSI 2300 STAT Plus™ reference results. Subjects completed a questionnaire on the ease of use of the BGMS and clarity of user guide instructions. Overall, 100% of subject and HCP capillary results and 97.3% of subject palm results met current ISO 15197:2003 accuracy criteria (Table 1). Similar results were seen based on proposed more stringent criteria. Regression analysis showed strong correlation between BGMS results and reference results (adjusted R^2 >98% for all regressions). By Parkes Error Grid analysis, 100% of capillary results were in Zone A; 97.2% of palm results were in Zone A and the remainder in Zone B. Based on questionnaire results, the majority of subjects agreed or strongly agreed that the BGMS was easy to use (91.8%), user instructions easy to understand (86.4%), and meter display easy to read (95.5%) and see and understand the results (98.2%). In conclusion, this new BGMS that communicates with an insulin pump demonstrated accuracy in the hands of users and showed favorable ease of use.

Table 1. Results Within ISO 15197:2003 Minimum Acceptable Performance Criteria

Sample type	Glucose concentration	Data comparison	Number (%) of results within the specified error limits			
			±5 mg/dL	±10 mg/dL	±15 mg/dL	±20 mg/dL
Capillary	<75 mg/dL	Subject vs YSI (n = 8)	8 (100%)	8 (100%)	8 (100%)[a]	8 (100%)
		HCP vs YSI (n = 8)	8 (100%)	8 (100%)	8 (100%)[a]	8 (100%)
	≥75 mg/dL		±5%	±10%	±15%	±20%
		Subject vs YSI (n = 102)	82 (80.4%)	101 (99.0%)	101 (99.0%)	102 (100%)[a]
		HCP vs YSI (n = 101)	82 (81.2%)	99 (98.0%)	101 (100%)	101 (100%)[a]
Palm (AST)	<75 mg/dL		±5 mg/dL	±10 mg/dL	±15 mg/dL	±20 mg/dL
		Subject vs YSI (n = 7)	6 (85.7%)	7 (100%)	7 (100%)[a]	7 (100%)
	≥75 mg/dL		±5%	±10%	±15%	±20%
		Subject vs YSI (n = 102)	61 (59.8%)	90 (88.2%)	98 (96.1%)	99 (97.1%)[a]

ISO, International Organization for Standardization; HCP, health care professional; AST, alternative site testing.
[a]Current ISO 15197:2003 minimum acceptable performance criteria (ie, ≥95% of results shall fall within ±15 mg/dL or ±20% for samples with glucose concentrations <75 mg/dL and ≥75 mg/dL, respectively).

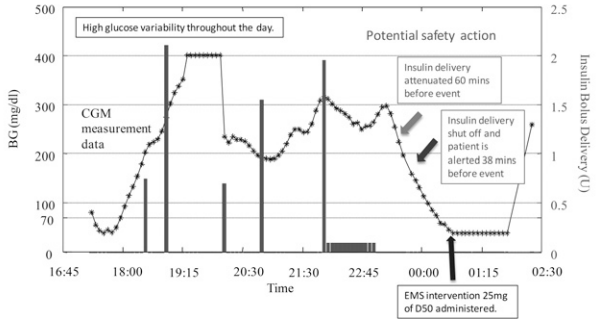
Supported by: Bayer HealthCare LLC, Diabetes Care

2341-PO

Documented Personal Experience With Severe Hypoglycemia Allowed for Retrospective Evaluation of the Effectiveness of a CGM-Based Safety System

MOLLY K. MCELWEE, COLLEEN HUGHES-KARVETSKI, BORIS P. KOVATCHEV, *Charlottesville, VA*

Prevention of hypoglycemia with tight glycemic control is central for patients with type 1 diabetes (T1DM). Insulin pumps (CSII), continuous glucose monitoring (CGM), and regular SMBG can serve as valuable tools alerting patients of hypoglycemic risk. Unfortunately, the most informed and compliant CSII users can experience severe hypoglycemia (SH) with insulin still being infused at the time of SH. This case report presents a SH event experienced by the author (MM), distinctively well documented by CSII, CGM, and SMBG data. The SH episode occurred at night, after high glucose variability. MM was wearing a CGM and a CSII at the time of the event; had hypoglycemic seizure and required EMS intervention. Using this data to test retroactively the action of a Safety Supervision System (SSS) designed to continuously monitor hypoglycemic risk and intervene as necessary. The SSS, currently implemented in a cell phone and in contrast to existing hypoglycemia alerts that are use CGM signal alone, is informed by glucose and insulin-on-board data processed by a model of glucose-insulin kinetics. Figure 1 shows the course of the event and how the SSS would have intervened: 60 minutes prior to SH the system would have attenuated and discontinued insulin delivery; 38 minutes before the event, the SSS would have alerted that without any additional insulin, hypoglycemia is imminent. This alert would have been presented to the patient and caregiver via the system's remote monitoring capability. Automatic safety measures provide opportunity to reduce the incidence of SH, particularly overnight.



2342-PO

Glucometric Reports Across a 4 Hospital System Demonstrate Objective Comparisons Between Medical Units and Hospitalist Groups

ATHENA PHILIS-TSIMIKAS, ROBIN MORRISEY, BRIEN ACKERLY, KEITH JOHNSON, KATHY BRENNER, GLORIA PEARCE, *La Jolla, CA*

Specific glucose targets within a hospital environment are currently advocated by national clinical guidelines. It is critical to develop standardized methods for compiling and analyzing inpatient glucose data. "Glucometrics" permit objective comparisons among patient care units, hospitals and staff

For author disclosure information, see page 797.

MDs. Scripps is a 4 hospital, 5 campus health system in San Diego, CA with approximately 20,000 patient visits per year with a diagnosis of DM. Glucose meters and the point of care (POC) glucose collection process are standardized across the system. A systemwide glucometrics report was created that captures and centralizes all POC glucose data from all 5 sites. Multiple data sources are integrated in an enterprise data warehouse to allow the comparison and benchmarking of glucose data across the system. Results of the reports across the system reveal significant variation between hospital units as well as between hospitalist group practices. Figures 1 and 2 These reports set the baselines that allow opportunities to implement QI projects and assess the success of changes over time. It may be valuable to replicate similar reporting practices more broadly so that comparisons and benchmarking can occur nationwide.

Figure 1.-Sample glucometric report from hospital med-surg units

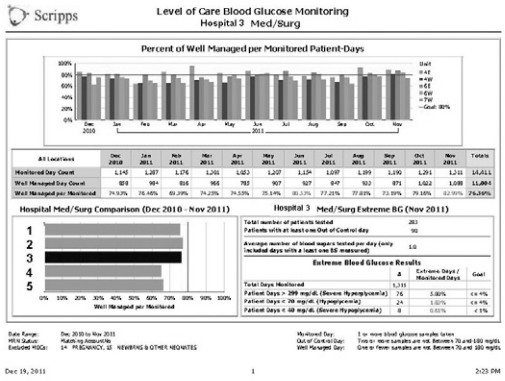
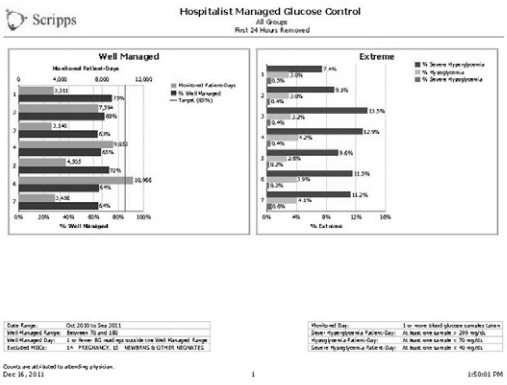


Figure 2.-Sample glucometric report for Hospitalist groups



Supported by: Woltman Family Foundation

2343-PO

Patterns of Glycemic Variability (GV) in Indian Type 2 Diabetes(T2DM) patients on Insulin and Oral Hypoglycemic Agents (OHAs) and Its Correlation With A1c and Hypoglycemia

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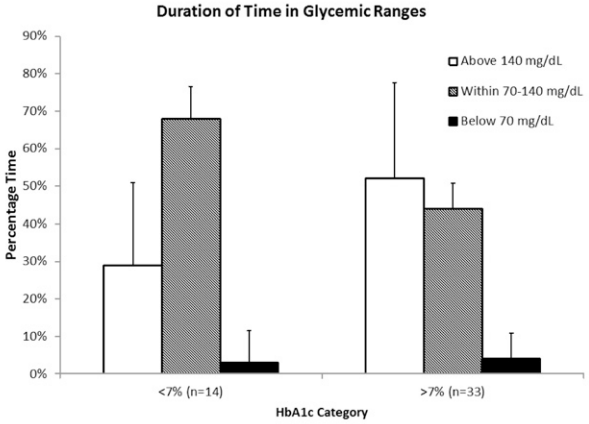
GV is a better predictor of diabetes complications not detected by A1c. We evaluated extent of GV in South Indian T2D patients on insulin & OHA with continuous glucose monitoring (CGM) system (iPro® 2), for 3-5 days. CGM of 47 patients with A1c <11% were analyzed (82% male, age 53 ± 11 yrs, A1c 7.9 ± 1.4, duration of T2D 13 ± 8 yrs, BMI 26 ± 3.5). Standard Deviation (SD), Mean Absolute Difference (MAD), & descriptive measures of glycemic patterns in CGM reports were compared among A1c categories using t-test and Mann-Whitney U Test & among treatment groups using ANOVA. Predictors of number of low excursions were identified using negative binomial regression models. Daily CGM values showed a mean highest value of 231 ± 60 mg/dl and mean lowest value of 84 ± 23 mg/dL. SD was 36.3 ± 15.9 and MAD% was 8.6 ± 3.8. Duration with glucose values above 140mg/dl was 45 ± 27% and duration with glucose values less than 70 mg/dl was 4 ± 7%. Multiple regression showed higher A1c statistically significantly associated with higher SD (b=4.1, t=2.2,p=0.02). Patients with A1c ≥7% had significantly higher duration of time more than 140 mg/dL but no significant difference in time below 70 mg/dL, when compared with patients with A1c <7% (Fig. 1). Patients had average 0.47±0.7 low excursions/day. Number of low excursions was statistically significantly associated with SD and T2D duration but not with A1c, gender, treatment groups, or BMI. This study contributes to normative data for GV & shows link of SD to higher A1c values, and suggesting possible utility of SD in predicting risk of hypoglycaemia.



2344-PO

WITHDRAWN

2345-PO

Evaluation of Blood Glucose Monitoring System Pattern Alert Messages in a Home Setting: Patient Reported Insights

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Blood glucose monitoring systems (BGMSs) that contain on-meter pattern recognition software are intended to advise users via timely on screen messages about recent high and low glucose patterns. This enables users to gain insights into these events and to consider making changes in diabetes management or lifestyle. However, there are minimal data on user perception of these messages or user awareness of why specific patterns were generated. A clinical study was conducted to evaluate user perceptions of patterns generated during 4 weeks home use of the OneTouch® Verio®Pro BGMS by 101 individuals with Type 1 or Type 2 diabetes who self-adjust insulin. Participants provided feedback (using pre-defined reason codes or free text; Table) in home diaries about the patterns they received during routine testing. In total, 987 coded reasons and 199 free text reasons were recorded. This study provides insights on how BGMS users interpret on-meter pattern alert messages and identify opportunities for improving glycemic control. The users' observations may also facilitate conversations with HCP's.

Participant Responses to Specific Pattern Alerts		
Alert Type	**n**	**Coded Reasons**
Before meal high	557	Snacking (37%), Miscounting carbohydrates (15%), Insufficient mealtime insulin (14%)
Fasting high	209	Insufficient basal insulin (46%), Snacking at night (32%), Rebound hyperglycemia (21%)
Low	221	Activity (41%), Too much insulin (25%), Miscounting carbohydrates (16%)
		Free Text Reasons
Before meal high	105	Food or snacking (21%), Don't know (14%), Rebound hypoglycemia (13%)
Fasting high	70	Insufficient insulin or wrong ratio to carbohydrates (21%), Food or snack at bedtime (21%), Illness or infection (14%)
Low	24	Insufficient food (29%), Don't know (25%), Too much insulin / over- correcting high glucose (12%)

Clinical Diabetes/ Therapeutics
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2346-PO

Saliva Analysis as New Diagnostic Test in Diabetic and Non-Diabetic

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Normal range for amylase activity, Glucamylase: 1 unit of enzyme activity catalyzes the production of 1.0mg (1.0ml) of glucose in 1 hour (40 C pH = 4.6); Amylase: 1 unit of enzyme activity is the amount of enzyme that will dextrinize 1.0mg (1.0ml) of soluble starch in 1 hour (60 C pH = 6.0). To study saliva activity in diabetic and non-diabetic subjects 750 fresh saliva samples were collected from 200 diabetic and 50 non-diabetic subjects. All subjects were fasting over night for 12 hours. Glucose oxidase testing was used to detect amylase activity (Glucose level) in the samples. Three identical 10 mls samples of fresh well-prepared saliva were accepted from each patient for the study. One sample from each subject was used as marker and tested for pH changes and sugar hourly for 24 hours. 1 ml of flour powder was added in each second sample (250 flour sample). 1 ml of sucrose was added in each third sample (250 sucrose samples). pH changes together with glucose readings were tested hourly in each study sample for 24 hours. Results showed that 750 (250 marker+250 flour+250 sucrose study sample) fresh saliva samples of non-diabetics and diabetic patients showed pH of 9 to 7 on immediate testing. 250 marker samples showed no significant change in pH and zero sugar reading for 24 hours. 235 flour, 223 sucrose study samples showed decrease in pH 5>, in association with glucose detection in samples. 2 flour and 2 sucrose samples showed decrease in pH from 9 to 7 in association with glucose yielding within 24 hours. 8 isolated flour, 11 isolated sucrose diabetic samples, 4 same patient flour and sucrose diabetes samples, 5 flour and 14 sucrose non diabetic samples showed decrease in pH 5> without glucose yielding in 24 hours. Zero non-diabetics (same subject) showed absent activity. Decreased in pH in study samples were noticed to be associated with increase in glucose yielding. Determination of saliva alpha amylase activity could predict early diabetes, or early saccharides related disease. Detection of glucose in a sample containing mixtures of saliva and disaccharides or saliva and polysaccharides, above normal ranges will indicate saliva amylase malfunction or inactivity.

Supported by: Saccharides Science and Technology

CLINICAL THERAPEUTICS/NEW TECHNOLOGY—INSULIN DELIVERY SYSTEMS

2347-PO

WITHDRAWN

2348-PO

A Nurse-Directed Computer Program, that Adjusts Subcutaneous Multiple Daily Injections (MDI) of Insulin, Achieves a 3.1% A1c Improvement With Out-Patients

PAUL C. DAVIDSON, BRUCE W. BODE, JOHN CLARKE, HARRY R. HEBBLEWHITE, *Atlanta, GA*

This study examines the performance of a computerized algorithm for adjusting subcutaneous MDI insulin regimens with out-patients. This algorithm determines a meal bolus by adjusting the dose given for the same interval of the previous day. Example: Breakfast Bolus = [Yesterday's Breakfast Bolus]*AF, where AF is an Adjustment Factor, that is governed by [Yesterday's pre-Lunch BG]. Each subsequent interval is handled in a similar manner. The Basal dose is governed by the pre-Breakfast BG from earlier the same day. Adjustment for insulin dosing was made possible by the patients' reporting of insulin doses and BG values to the dosing nurse daily. This regimen was studied in 19 patients. Of these, 16 patients had complete pairs of A1c's, (before and after). Mean A1c Before=9.7% and Mean A1c After=8.1%; P<0.002. The 10-week average term of treatment prevented an optimal lowering of the final A1c, due to red cell lifespan. Because of this, a set of calculated final A1c's (19 patients) was determined from the average of BG's from the final 3 days, using the ADA published correlation. The average pre-study A1c and its calculated equivalent BG (9.6% and 229mg/dl) decreased significantly to the final 3-day average BG and its calculated equivalent A1c (6.5% and 140mg/dl); P<0.0005. The percent of all BG's < 60 was 1.6%. The number of BG's < 40 was zero. We suggest that this algorithm may be a valuable tool for adjusting subcutaneous MDI regimens. A study of three months duration will yield more conclusive results by avoiding the need to calculate final A1c values by correlation. The algorithm is currently being incorporated into a server-based, enterprise platform for continuous, on-going dosing guidance.

2349-PO

Predictors of Success in Insulin Pump Therapy—Data Analysis from Register of Patients Treated With Insulin Pump

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The aim of the study was to find parameters suitable for prediction of successful or alternatively unsuccessful course of insulin pump treatment. We used Register of patients treated with insulin pump (CSII) in the Czech Republic as a source of data. A total of 1729 patients with complete data were included in the analysis. The patients were divided according to a change in glycemic control (ΔHbA_{1c}) after 2 years of CSII treatment into 3 groups: improved ($\Delta HbA_{1c} \leq$ -10%; 52%), deteriorated ($\Delta HbA_{1c} \geq$ +10%; 18%) or stable (ΔHbA_{1c} from -10% to +10%; 30%) glycemic control. Data are presented as median [Q1;Q3]. The group with deteriorated glycemic control showed a significantly lower age at onset of CSII treatment, shorter diabetes duration, lower initial insulin daily dose and more frequent indication "patient's request" compared to groups with improved or stable glycemic control. The group with improved control had a higher frequency of indication "bad control" and „neuropathy" (p<0.001) in comparison to group with stable or deteriorated glycemic control. The values of HbA_{1c} before the onset of CSII treatment (improved 8.6 [7.3;9.9], stable 7.2 [6.4;8.3] and deteriorated 6.1 [5.1;7.1] %, p<0.001) and after 2 years of CSII treatment (6.3 [5.4;7.2] vs. 7.2 [6.3;8.2] and 7.7 [6.5;8.9] %, p<0.001) differed significantly. The groups did not differ in initial BMI values. A significant increase in BMI during the treat-

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ment was found in all groups (p<0.001). Likewise, a significant reduction in insulin dose in course of CSII treatment occurred in all groups. Based on the analyzed data from the Register it is evident that CSII treatment is effective even in the long-term perspective and has its justified indications despite its higher cost. On the other hand, there exists a group of patients, where the CSII treatment has a limited or even negative contribution to the glycemic control. The treatment thus needs to be monitored and if not beneficial, its termination should be considered.

2350-PO

Patient Preference and Clinical Outcomes Associated With Initiation of Insulin Glargine Therapy for Type 2 Diabetes Using Disposable Pen versus Vial

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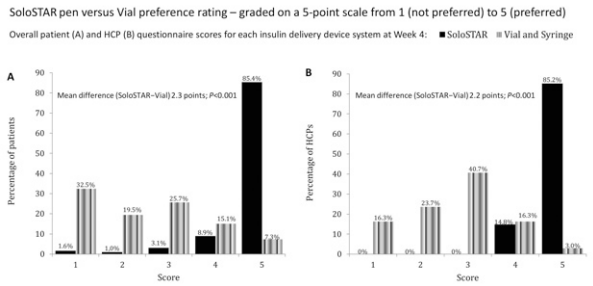
Recent data suggest that initiation of insulin glargine (GLA) treatment using SoloSTAR® (Pen), rather than vial and syringe (Vial), provides improved treatment persistence in patients with type 2 diabetes mellitus (T2DM). This ongoing open-label, randomized, multicenter U.S. study (NCT01226043) assesses patient and health care provider (HCP) preference, and change in clinical endpoints following GLA administration via Pen vs. Vial. The per-protocol preliminary results are presented here. There were 405 T2DM patients (median age 59 years, 54% men, mean body mass index 35 kg/m^2) who were randomized to receive GLA via SoloSTAR or Vial for 2 weeks, followed by a 2-week crossover to the alternate device. Then, 333 patients were re-randomized to receive Pen or Vial for an additional 36 weeks. The primary endpoint was patient preference for Pen or Vial measured on a 5-point scale (1=not preferred, 5=preferred) using the Insulin Injection Preference Questionnaire (IIPQ) at the end of Week 4. Secondary endpoints included HCP preference, change in fasting plasma glucose (FPG), and achieving target FPG <110mg/dL at 10 weeks. The Figure shows IIPQ and HCP preference scores. Patients and HCPs overwhelmingly preferred Pen use. The mean change in FPG from Week 4 to Week 10 was similar for both patient cohorts (least-square mean change –14.3 mg/dL for Pen and –14.9 mg/dL for Vial; *P*=0.875). A similar percentage of patients achieved the FPG goal of <110mg/dL (28.8% vs. 30.7%; *P*=0.935). Use of the SoloSTAR® pen was preferred by both patients and HCPs compared to GLA taken by vial and syringe.



Supported by: sanofi-aventis

2351-PO

Efficacy of Insulin Pump Treatment in Young Adult Patients With Type 1 Diabetes Mellitus

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It is generally accepted that in adult type 1 diabetes (T1DM) patients the continuous subcutaneous insulin infusion (CSII) model is more effective than the multiple daily injections (MDI) one. However, it is not clear whether all T1DM adult age groups equally benefit from CSII therapy. Especially, adherence to recommended CSII-related behaviors may be of concern in young adults with variable daily activities. We aimed to compare the glycemic control in young T1DM subjects on CSII (age range 18-26 years) with older patients and to identify potentially modifiable behaviors influencing the efficacy of the treatment. Overall 140 adults with T1DM were examined; they were divided into two subgroups: 77 patients younger than 26 years of age and 63 older subjects. Their last available insulin pump and blood glucose meter downloads as well as HbA1c level were reviewed. Younger individuals were characterized by significantly worse treatment outcomes as compared to the older ones: the mean HbA1c levels were 7.6±1.3% and 6.9±1.3%, respectively (p=0.000011), while the mean glucose levels based on glucose meter downloads were 161±33.6 mg/dL and 136±21.8 mg/dL (p=0.000003), respectively. The frequency of self-monitoring of blood glucose (SMBG) was lower in younger individuals (5.3±2.1 vs. 7.0±2.8 daily, p=0.0005, respectively), they were also less frequently using advanced pump functions, such as bolus calculator (48% vs. 67% users, p=0.0014, respectively). In conclusion, the efficacy of CSII treatment observed in young T1DM adults was worse as compared to older patients. The possible reasons include lower SMBG frequency and less frequent use of advanced insulin pump options.

CLINICAL THERAPEUTICS/NEW TECHNOLOGY—PHARMACOLOGIC TREATMENT OF DIABETES OR ITS COMPLICATIONS

2352-PO

Dosage and Duration of Glimepiride Therapy among Patients With Type 2 Diabetes

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Background and aims: Understanding the usage patterns of glimepiride and other antidiabetic agents is an important first step to improving glycemic control among type 2 diabetic patients. The objectives were to assess average time to change in daily dose of glimepiride and the mean change in HbA1c at time of dosage change among initiators of glimepiride monotherapy. Materials and methods: Using the General Practice Research Database, we identified a cohort of new initiators of glimepiride monotherapy between 1998 - 2010. New initiators were required to have at least 6 month of follow-up prior to initiation of glimepiride and 12 months of follow-up in the database after their first prescription of glimepiride. Change in glimepiride therapy was defined as change in dose, discontinuation of glimepiride or addition of another antidiabetic agent. HbA1c values (mmol/mol) within ± one month of glimepiride initiation and therapy change were captured. The average daily dose of glimepiride and the mean HbA1c were calculated at initiation and change of therapy. The average time (in weeks) until a change in daily dose of glimepiride occurred was calculated. Results: We identified 10,243 glimepiride initiators. The mean age was 63.35 years (sd ± 12.64) and 54.4% were males. The mean glimepiride dose at initiation was 1.94 mg (sd ± 1.32) and the median dose was 1 mg. HbA1c values were available for 52% of the cohort at initiation and their mean HbA1c was 73.94. Over a mean follow-up of 5.4 years, change in therapy occurred in 6795 glimepiride initiators representing 66.3% of the cohort. The average time to therapy change was 51 weeks (sd ± 68 weeks) and the median was 24 weeks. The average daily dose at time of therapy change was 2.91 (sd ± 1.46). The median dose was 2. The mean HbA1c at therapy change was 70.81. Conclusions: Given that HbA1c was highly elevated at the time of glimepiride initiation, and average time to therapy change was 51 weeks, earlier review and uptitration of glimepiride dose is indicated for many patients.

2353-PO

Dapagliflozin Improves Glycemic Control and Reduces Body Weight in Patients With T2DM across the Treatment Continuum

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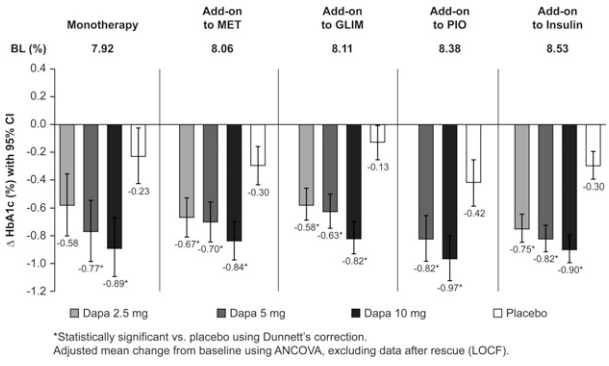
Dapagliflozin (DAPA), a selective SGLT2 inhibitor, reduces plasma glucose independently of insulin by increasing renal glucose excretion. The efficacy of DAPA in patients with T2DM across 5 clinical trials was assessed. Patients with T2DM received DAPA (2.5, 5, or 10 mg/d) or placebo for 24 wk as monotherapy (NCT00528372, N=274, main cohort) or add-on to metformin (MET, NCT00528879, N=546), glimepiride (GLIM, NCT00680745, N=596), pioglitazone (PIO, NCT00683878, N=420) or insulin (INS, NCT00673231, N=807). The primary endpoint for all trials was mean change from baseline in HbA1c at wk 24. Secondary endpoints included change from baseline in fasting plasma glucose (FPG), postprandial glucose (PPG, tested in add-on to GLIM and add-on to PIO studies), and body weight. The primary endpoint was analyzed by ANCOVA, excluding data after rescue (LOCF). Secondary endpoints were analyzed by hierarchical testing. Mean baseline HbA1c ranged from 7.9% to 8.5%. Placebo-corrected adjusted mean changes from baseline in HbA1c for DAPA 10 mg/d ranged from -0.5% to -0.7% (*P*<0.001 in all studies) (Figure). DAPA also reduced FPG in all studies, and PPG in the 2 trials where it was tested. Body weight was reduced by 1.5 to 2 kg with DAPA 10 mg/d, compared with placebo in the add-on to MET, add-on to GLIM, add-on to PIO, and add-on to insulin trials (*P*<0.0001 in all 4 studies), but was not significantly reduced in the monotherapy trial. DAPA produced significant improvements in glycemic control and body weight in patients with T2DM across the treatment continuum, consistent with its insulin-independent mechanism of action.

For author disclosure information, see page 797.



Supported by: Bristol-Myers Squibb/AstraZeneca

Clinical Diabetes/ Therapeutics
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2354-PO

Elucidating Mechanism of Action of DPP4 Inhibitor, Alogliptin, on Japanese Meal—From the Aspect of Proinsulin, Insulin and Glucagon

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To investigate the effect and mechanism of alogliptin, DPP4 inhibitor by tolerance tests with meal reflecting patients' daily dietary life.35 consecutive diabetes patients (men 28, age 63±10, and BMI 26±11) of Japanese type 2 diabetes who consented to use of alogliptin (ALO) were enrolled. Before and 1 month after the start of prescription of 25mg ALO, meal tolerance tests (511 kcal containing 56% carbohydrates and 24% fats) were performed, in which plasma glucose (PG mg/dL), immunoreactive insulin (IRI pmol/L), glucagon (IRG pmol/L) and intact proinsulin (PRO pmol/L) were examined at fasting, 15, 30, 60, 120 minutes after load. 9 cases were drug naive and 26 cases were combination therapy. HbA1c ameliorated after ALO treatment (basal / post treatment) (7.4±1.0 / 6.9±0.5, P<0.001). Fasting PG (143±36 / 126±38, P<0.05) and Free Fatty Acid (0.74±0.31 / 0.60±0.24, P<0.05) (mEq/L) decreased. HOMA-beta improved (31±25 / 47±35, P<0.001) with increase in fasting IRI. Post challenge PG (PPG mg/dL) decreased (15min: 155±42 / 138±30, 60min: 252±55 / 207±43, 120min: 233±62 / 189±58, P<0.05). Improvement in PPG was significantly larger than that in FPG. IRI/IRG ratio of fasting and 30min elevated significantly (1.6 / 2.0, 4.1 / 5.0, respectively). The values of post-treatment PRO/IRI ratio (P/I) was significantly lower at every time point (fasting: 0.27±0.02 / 0.20 ±0.09, 15min: 0.17±0.02 / 0.13±0.02, 30min: 0.13±0.02 / 0.09±0.05, 60min: 0.12±0.01 / 0.09±0.04, 120min: 0.16±0.01 / 0.13±0.05). Both in the basal and post treatment, P/I continued to decrease until 60min and then increased at 120min. Each value of P/I time course showed a significant difference from the precedent. ALO treatment ameliorated proinsulin handling and insulin secretory capacity in beta-cell along with mild inhibition of abnormal glucagon secretion from alfa-cell, and thus affected glucose and fatty acid metabolism under daily Japanese dietary life.

2355-PO

Comparison between Premix Insulin and Basal Bolus In Type I DM

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This is one year follow up 57 type I DM patients (34 Female, 23 Male), Age 21±2.8 and duration of DM 7.6±3.9 year. The numbers of visits to the clinic for this one year follow up average 5 visits for all patients per year. Home blood sugar monitoring had been adopted in all patients with phone calls to adjust the correct dose. Group 1: 30 patients on Premix (70/30) given twice per day Group 2: 27 patients on Basal insulin dose given before bed time and Bolus insulin dose given 3 times prior each meal. There was high significant difference in both groups before and after one year follow up but there was no difference between these two groups in all blood sugar findings. Group 1 : Before HBA1c 10.6±2.3 , After HBA1c 8.7± 1.3 Before FBS 11±5.8, After 10.4±4.5 Before PPBS 14.8± 8.4, After 10.2±3.7 Group 2 : Before HBA1c 11.2±2.6 , After HBA1c 9.5± 1.7 Before FBS 14.7±8.4, After 10.7±6.4 Before PPBS 18.1± 7.3, After 12.7±7.1 However there was significant clinical findings between two groups: The occurrence of hypoglycemia in group 1 weather sever hypoglycemia occurred in one patient required hospitalization as well as frequent mild to moderate hypoglycemia. Furthermore Group 2 not only did not experience hypoglycemia they could fast 30 days Ramadan in the majority of cases. While Group 1 could fast few days in spite of adjusting their doses. Conclusion: basal bolus is the drug of choice in type I DM especially in the Muslim world.

2356-PO

Efficacy and Safety of Gemigliptin in Patients With Type 2 Diabetes

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This study was designed to assess the efficacy and safety of a DPP IV inhibitor, gemigliptin (LC15-0444) 50mg versus placebo in patients with type 2 diabetes. We conducted a 24-week, randomized, double-blind, placebo-controlled phase III trial in 182 patients (74 from Korea and 108 from India) with type 2 diabetes. After initial 2 weeks of exercise/diet program followed by another 2 weeks of single-blind placebo run-in period, eligible patients were randomized to gemigliptin 50mg or placebo group and received the assigned treatment for 24 weeks. HbA1c and fasting plasma glucose (FPG) were measured periodically, and oral glucose tolerance tests were performed at baseline, week 12 and week 24. At week 24, gemigliptin treatment led to significant reductions in HbA1c compared with placebo in HbA1c (-0.71%). A significantly greater proportion of patients achieved an HbA1c <7% with gemigliptin than with placebo. The placebo-subtracted FPG change from baseline at week 24 was -19.80 mg/dL. The overall incidence rate of adverse events in the gemigliptin and in the placebo was similar between the two groups. In conclusion, this study demonstrated the efficacy and safety of gemigliptin 50mg administered once daily as a monotherapy in type 2 diabetes patients.

2357-PO

WITHDRAWN

For author disclosure information, see page 797.

ADA-Funded Research

2358-PO

Pramlintide Dose Escalation Efficacy vs. Conventional Therapy in Type 2 Diabetes Mellitus (DEFCon2)

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Patients with type 2 diabetes mellitus (DM2) have defects in both insulin sensitivity and insulin secretion. Metabolic control can be difficult in patients who are insulin resistant and higher doses of insulin are often required. Pramlintide is an adjunct to insulin treatment in patients with DM2, decreasing A1c, weight and insulin dose. Since patients who are insulin resistant may also be amylin resistant, it is possible that those patients who do not have a glycemic response to the indicated dose of pramlintide (120 mcg ac) may need higher doses. Pramlintide in doses of up to 360 mcg BID has been safely and successfully used in weight loss trials. In this 6 month pilot study comparing efficacy and safety of pramlintide 120 mcg ac to high dose (360 mcg ac), 39 insulin using DM2 patients were randomized into 4 groups: pramlintide naïve patients received either 120 mcg TID or 360 mcg TID and patients who were already on pramlintide either continued 120 mcg TID or increased to 360 mcg TID. Outcomes included change in A1c, weight and adverse events. Data on insulin use were also collected.

	Δ A1c (%)	Δ Weight (kg)	Δ Total daily insulin (%)
Naïve 120 mcg	-0.33	-5.0*	-6.5
Naïve 360 mcg	-0.25	-1.9	-7.3
Treated 120 mcg	+0.34	-1.5	+3.8
Treated 360 mcg	+0.23	-2.0#	-9.3

*p=0.006, #p=0.052; Data are mean

This pilot study using 360 mcg pramlintide compared to 120 mcg demonstrated that the drug was well tolerated with no significant safety signals. The overall rate of hypoglycemia did not increase with higher doses. One episode of severe hypoglycemia occurred. Although a trend towards better glucose control was noted in the naive groups, the study was not powered to detect a difference. Further studies are needed to determine whether high dose pramlintide is an effective treatment for DM2 and which patients are likely to achieve the greatest benefit.

Supported by: Amylin Pharmaceuticals

2359-PO

Continuing Basal Insulin Titration after Reaching the Fasting Glucose Target

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Previous clinical trials of basal insulin in T2DM have shown that even though the target fasting morning self-monitored plasma glucose, FPG, was reached, its maintenance required continued upward titration of insulin dosage. A 12 w study of 20 subjects with T2DM on non-insulin treatment and an A1c >7.0% were initiated with once nightly insulin detemir. The dosage was increased 3 U if the preceding average 3 d FPG was > 110 mg/dl but decreased 3 U for mean FPG < 80 mg/dl or for any confirmed (< 70 mg/dl plus symptoms) hypoglycemia . After the goal was obtained, the titration continued for the remainder of the 12 w. Self-titration was reinforced during weekly phone calls and every 4 w clinic visits. During these clinic contacts, hypoglycemia was recorded. Weight and A1c were measured at baseline and each 4 w period. The mean A1c was reduced from 8.5 (0.9) to 6.9 (0.7) %, $p < 0.001$, and the weight increased from 106 (26) to 107 (26) kg, $p = 0.179$. The mean dosage when the glucose goal was first achieved was 60 (34) U and 74 (33) U at the end of 12 w. The FPG goal was reached in 35 (24) d. The mean FPG at the first glucose goal was 99 (12) mg/dl and at 12 w, 106 (25) mg/dl ($p = 0.192$). The rate of dosage increase after attaining goal was significantly ($p < 0.02$) correlated to the FPG variation (SD) during the same period ($p < 0.02$) and to the SD of the FPG during the first days of initiation of basal insulin treatment ($p < 0.025$) but not to three consecutive FPGs taken over a ~ 5 min period at baseline ($p > 0.5$). The rate of dosage increase tended, but not significantly, to be associated to the frequency of hypoglycemia ($p < 0.25$ but > 0.2) and to weight gain ($p < 0.1$ but > 0.05). FPG variability at the beginning of insulin treatment and after the initial glucose goal is reached is associated with the need for further dose escalation. The consequences of continued dosage titration could be weight gain and hypoglycemia.

Supported by: Novo Nordisk, Inc.

2360-PO

An Analysis of Deterioration after Initial Improvement by Sitagliptin—Is there the Case of "Secondary Failure" With Sitagliptin?

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The aim of the present study is to assess the long-term efficacy of sitagliptin (SITA) after initial improvement. Subjects consisted of 191 Japanese patients with T2DM who receive SITA for more than 24 consecutive weeks. After 24 weeks, administration of SITA led to significant reductions of the average HbA1c level (7.4±1.0 %) relative to baseline (8.5±1.3 %) ($p<0.001$). The subjects were divided into three groups according to the responsiveness to treatment with SITA. A "non-responder group" with 31 subjects was defined as patients whose HbA1c levels were not improved more than 0.5% in 24 weeks despite administration of SITA. Average HbA1c levels were 8.2±0.8, 8.2±0.8 and 8.3±1.0 % at 0, 12 and 24 weeks, respectively. A "responder group" with 149 subjects was defined as patients whose HbA1c levels were improved more than 0.5% after administration of SITA and this effect lasts more than 24 weeks. Average HbA1c levels were 8.6±1.4, 7.6±1.0, 7.2±0.9 % at 0, 12 and 24 weeks, respectively. A "rebound group" with 11 subjects was defined as patients whose HbA1c levels were once improved more than 0.5% in first 12 weeks and then deteriorated more than 0.5% in last 12 weeks. Average HbA1c levels were 8.6±1.1%, 7.5±0.9 and 8.4±1.0 % at 0, 12 and 24 weeks, respectively. At the initiation of administration and after first 12 weeks, statistically significant differences in HbA1c levels were not observed among three groups. Tendency of alterations in dietary therapy or changes of concomitant medications were not observed among three groups. Moreover, statistically significant differences at clinical features including age, sex and types of concomitant medications were not observed among three groups. It is important to observe the clinical course carefully because not all of glucose lowering effect of SITA last for long-term. The mechanism of deterioration after first improvement needs to be clarified.

2361-PO

Vildagliptin more Effectively Achieves a Composite Endpoint of Reaching HbA1c Target Without Hypoglycemia or Weight Gain Compared With SUs: A Pooled Analysis of Clinical Trials

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Previous studies have shown that vildagliptin as add-on therapy to metformin in patients with type 2 diabetes mellitus (T2DM) has similar efficacy on HbA1c as sulphonylureas (SUs). In this pooled analysis, we aimed to measure the overall clinical benefit of vildagliptin compared with SUs by assessing the number of patients reaching a composite endpoint of HbA1c <7%, no hypos (symptoms and plasma glucose <3.1 mmol/L), and no weight gain (<3%). We also investigated whether there were differences in reaching the composite endpoint in relationship to age of patients or duration of diabetes. To this end, two add-on to metformin studies (n = 3033) comparing vildagliptin (n = 1541) to SUs (glimepiride and gliclazide: n = 1492) were pooled and the relative success rate (SR) was calculated by taking the ratio of the number of patients achieving composite endpoint in vildagliptin and SU groups. The baseline HbA1c was 7.9% for both vildagliptin and SUs. After 52 weeks, a higher proportion of patients reached the composite endpoint with vildagliptin (32.3%) than with SUs (21.9%). The overall SR of vildagliptin compared with SUs, along with the relative SR with respect to age of patients or duration of diabetes is presented in the table. This pooled analysis demonstrated that vildagliptin as add-on therapy to metformin showed a better clinical benefit - as defined by the composite endpoint of reaching HbA1c <7%, with no hypos and no weight gain - than SUs added to metformin after 52 weeks of treatment regardless of age of patients or duration of diabetes.

Success rate (SR) (HbA1c <7% , no hypos, no weight gain)			
	Vildagliptin	SU	Vildagliptin vs. SU
	n/total (%)		Relative SR (95% CI)
Overall	497/1541 (32.3)	327/1492 (21.9)	1.47 (1.31 - 1.66)
Age (years)			
<50	77/299 (25.8)	43/297 (14.5)	1.78 (1.27 - 2.49)
≥50 - <60	158/528 (29.9)	113/491 (23.0)	1.30 (1.06 - 1.60)
≥60 - <70	206/556 (37.1)	136/541 (25.1)	1.47 (1.23 - 1.77)
≥70 - <80	56/158 (35.4)	35/163 (21.5)	1.65 (1.15 - 2.37)
Duration of diabetes (years)			
<2	94/287 (32.8)	66/267 (24.7)	1.32 (1.01 - 1.73)
2 - 5	168/510 (32.9)	96/455 (21.1)	1.56 (1.26 - 1.94)
>5	235/744 (31.6)	165/770 (21.4)	1.47 (1.24 - 1.75)

Supported by: Novartis Pharmaceuticals Corporation

Clinical Diabetes/ Therapeutics PUBLISHED ONLY

2362-PO

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2363-PO

Evaluation of the Anti-hyperglycemic Action of Insulin Sensitizers and the Mitochondrial Target of Thiazolidinediones (mTOT) in Drosophila Melanogaster

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We have recently reported the discovery of mTOT, a previously unrecognized mitochondrial target of the insulin sensitizing TZDs. Because mTOT is well conserved phylogenetically, we evaluated whether the fly ortholog could bind and respond to insulin sensitizers including PPARγ independent TZDs MSDC-0160 and MSDC-0602. Indeed, mitochondrial fractions from wild-type flies contained a protein of about 18-19 kDA that specifically interacted with a TZD probe. Database homology searches indicated that the mTOT fly ortholog ia a member of a small protein family. Using the unparalleled set of genetic tools available for *Drosophila* studies, we rapidly generated flies with RNAi knockdowns for the mTOT ortholog and another family member. Unexpectedly, binding of the TZD probe was lost on knockdown of either of the 2 genes, suggesting a functional complex. Antibodies to either protein were able to immunoprecipitate the other, supporting the possibility of a complex. We used a previously described *Drosophila melanogaster* model of diet-induced insulin resistance that bears similarity to the pathophysiology of T2D. Wild-type flies raised on a high sugar diet have elevated hemolymph glucose and reduced longevity compared to those reared on the regular diet. Treatment of these flies with MSDC-0160 or MSDC-0602 both lowered glucose and extended life span, while a modified analog that did not bind the complex was ineffective. Interestingly, preliminary studies indicate that the RNAi knockdown of either of these genes also reduces hemolymph glucose levels and extends life span. The fact that gene target suppression by RNAi and drug treatment have similar metabolic effects suggests that the TZDs may be attenuating the activity of this mitochondrial complex. The *Drosophila* diabetes model is now being used to further explore the function of this newly identified protein complex and the mechanism of action of insulin sensitizers.

2364-PO

Assessing Bone Fracture Risk for Pioglitazone Relative to Insulin

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A retrospective cohort study using i3 InVision Data Mart was conducted to assess the risk of bone fracture in type 2 diabetes mellitus patients treated with pioglitazone (PIO) or insulin mainly as third-line therapies. The key outcome was incident cases of bone fracture requiring hospitalization; a secondary endpoint was cases of bone fracture not requiring hospitalization. Kaplan-Meier curves were generated for these outcomes in the PIO and insulin groups based on adjustment with inverse probability weights derived from propensity scores. Hazard ratios (HR) for PIO versus insulin and 95% confidence intervals (CIs) were estimated using Cox proportional hazards models. A total of 56,536 patients (PIO group: 38,588; insulin group: 17,948) aged ≥45 years were identified from May 1, 2000 to June 30, 2010 (mean follow-up: 2.2 years for PIO and 1.9 years for insulin). A small non-statistically significant difference in the incidence rate of bone fracture requiring hospitalization was observed between the treatment groups in favor of PIO; the HR for PIO versus insulin was 0.86 (95% CI [0.74, 1.01], p=0.058). The incidence rates of bone fracture requiring hospitalization were largely similar between the two groups throughout the follow-up period. Analysis by gender showed HRs for PIO versus insulin of 0.80 for males (95% CI [0.64, 1.02], p=0.068) and 0.90 for females (95% CI [0.73, 1.10], p=0.304). Incidence of bone fracture not requiring hospitalization as a secondary endpoint was also lower for PIO versus insulin (HR 0.91, 95% CI [0.84, 0.98], p=0.012). The results suggest pioglitazone is not associated with an increased risk of bone fracture relative to insulin.

2365-PO

Vildagliptin Added to Metformin on β-Cell Function After an Euglycemic Hyperinsulinemic and Hyperglycemic Clamp in Type 2 Diabetic Patients

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The aim of this study was to evaluate the effect of vildagliptin + metformin on glycemic control and β-cell function in type 2 diabetic patients. One hundred and seventy one Caucasian type 2 diabetic patients, naïve and with poor glycemic control, were instructed to take metformin for 8±2 months until a mean dosage of 2500±500 mg/day, then they were randomly assigned to take vildaglipin 50 mg twice a day or placebo in addition to previously taken metformin, for 12 months. We evaluated at 3, 6, 9, and 12 months: body mass index (BMI), glycemic control, fasting plasma insulin (FPI), homeostasis model assessment insulin resistance index (HOMA-IR), homeostasis model assessment β-cell function index (HOMA-β), fasting plasma proinsulin (FPPr), proinsulin/fasting plasma insulin ratio (Pr/FPI ratio), C-peptide, glucagon, adiponectin (ADN), and high sensitivity-C reactive protein (Hs-CRP). Before, and after 12 months since the addition of vildagliptin, patients underwent a combined euglycemic hyperinsulinemic and hyperglycemic clamp, with subsequent arginine stimulation, to assess insulin sensitivity and insulin secretion. After 12 months of treatment, vildagliptin + metformin gave a better decrease of body weight, glycemic control, HOMA-IR, and glucagon, and a better increase of HOMA-β compared to placebo + metformin ($p<0.05$ for all). Vildagliptin + metformin were more effective than placebo + metformin in increasing M value [+0.90±0.99 μmol min^{-1} kg^{-1} ($p<0.05$ vs placebo + metformin)], first and second phase C-peptide response to glucose and C-peptide response to arginine [+0.61±0.48 nmol/L ($p<0.05$ vs placebo + metformin), and +4.80±1.76 nmol/L ($p<0.05$ vs placebo + metformin)]. Also the disposition index was higher with vildagliptin + metformin ($p<0.05$). In conclusion, the addition of vildagliptin to metformin gave a better improvement of glycemic control, insulin resistance, and β-cell function compared to metformin alone.

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For author disclosure information, see page 797.

2367-PO

Site-Specific PEGylation of Exenatide Analogues Improved their Glucoregulatory Activity

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Exenatide is a 39-amino-acid peptide widely used to manage type 2 diabetes mellitus. However, it has a short plasma half-life, thus requires a twice daily injection regime. Therefore, effects of site-specific PEGylation of exenatide on therapeutic effects were examined. The exenatide analogue suitable for subsequent PEGylation was designed first. Analogue PB-105 showed the same glucoregulatory activity as exenatide. Site-specific PEGylation of PB-105 was performed to produce PB-110 (PEG5kDa), PB-106 (PEG20kDa), PB-119 (PEG 23KDa), PB-107 (PEG30kDa) and PB-108 (PEG40kDa). Their effects on intracellular cAMP, acute glucoregulatory activity and pharmacokinetic, pharmacodynamic, and safety profile were studied in mice, rats and monkey. The results demonstrated that PEGylation shifted the concentration-response curve of PB-105 to the right in a parallel, PEG MW-dependent manner but with an inflexion point of at least 20 kDa. The activities of PB-107 and PB-108 were reduced by 90% and 99% respectively. PEGylation affected in vivo glucoregulatory activity in the same 'Inflexion-Shift' fashion at least at 20 kDa, but linearly increased plasma duration and systemic exposure without inflexion. Therefore, PB-119 was nominated as the candidate. PB-119 had a plasma t1/2 approximately 32-fold that of PB-105, and systemic exposure was increased approximately 25-fold. In addition, the mass of beta cells in pancreas was increased as a result of PB-119 administration. Furthermore, some side effects such as nausea/vomiting associated with exenatide was alleviated. In conclusion, site-specific PEGylation of exenatide with a permanent amide linkage affects its activity in an 'Inflexion-Shift'fashion. PB-119 exhibited superior glucoregulatory activity compared with exenatide, and is a putative new analogue for treating diabetes; it possesses no loss of in vitro activity, prolonged plasma duration,superior in vivo glucoregulatory activity, and less side effects compared with exenatide.

2368-PO

Classification of Subjects With Preserved C-peptide as "Clinical Non-Responders" Occurs Frequently With Published Responder Definitions and May Attenuate Biologic Significance

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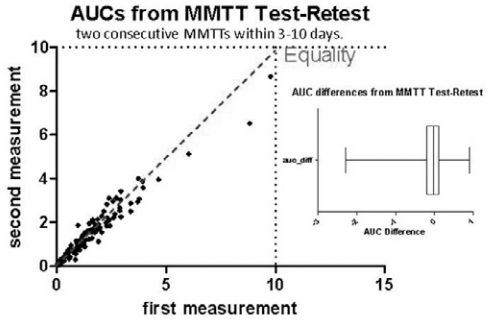
Figure 1 displays C-peptide AUC data from 132 subjects with T1D who had 2 MMTT within 3-10 days. Given the short time interval between measurements, we assume that this data represents intra-test variability for subjects who preserve C-peptide and conclude that change in C-peptide over time is variable even when preserved. Recently, 2 definitions of "clinical responder" based on change in C-peptide AUC over time have appeared: The "Coefficient of Variation (CV)" definition was used in a T-cell study and the "Percent" was used in a study of monoclonal antibody therapy in T1D. Under the CV definition, a "responder" can still have a decrease provided their CV does not exceed the median CV found in the data presented in Fig. 1. The percent definition classifies a responder as anyone who maintains at least 92.5% of baseline. We investigated the rate at which each of these two definitions classify subjects who preserve C-peptide as "non-responders" by simulating the random sampling of 100 subjects from the "C-peptide Preserved" population in Fig. 1 and recording the percent classified as a "non-responder". We found that 20%-22% subjects with preserved C-peptide were classified incorrectly as non-responders with the CV definition and 45%-53% with the Percent definition. It is well known that response misclassification can reduce power by understating biologic effect. Further attention to defining responder is thus critical in the evaluation of response to clinical trials and in mechanistic studies.



8-35 years of age with diabetes for 1 month to 3 years diagnosed by ADA criteria with no eligibility limit for C-peptide

Supported by: TrialNet, NIDDK, NIAD, NICHHD, NCRR, JDRF

2369-PO

A New Option for Type 1 Diabetes: GLP-1 Analogues

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Insulin replacement is currently the mainstay of treatment for type 1 diabetes, but its shortcomings are clear. Addition of Glucagon-like peptide 1 (GLP-1) analogues could potentially improve residual native beta-cell insulin production, reduce inappropriate glucagon secretion, suppress appetite and promote weight loss ultimately leading to improved glycemia, lower glucose variability, and lower insulin doses. We performed a retrospective chart review of patients with type 1 diabetes who were initiated on a GLP-1 analogue between March and October 2011. We identified 11 patients (9 females and 2 males) who were initiated on liraglutide and had a follow-up visit within 3 months (age 32.8±11.2 years; duration of diabetes 18.2±9.2 years; all on insulin pump therapy). Additionally, 7 of these patients had a second follow-up visit at approximately 5 months. At 3 months there was a significant decrease in weight (3.4% of total body weight) and total daily dose (TDD) of insulin (19.0% of which 13.6% was basal and 23.9% was bolus). Both HbA1c and daily glucose variability were significantly decreased as well (see table). These effects were sustained at 5 months.

Baseline vs <3 months and 5 months of GLP-1 Therapy

	Baseline (n=11)	<3 months	p-value	Baseline (n=7)	5 months	p-value
Weight (kg)	70.6 (9.7)	68.2 (10.0)	0.01	69.8 (10.7)	66.4 (9.9)	0.04
TDD (units)	39.9 (12.0)	32.3 (11.4)	0.0007	42.7 (11.2)	36.6 (14.0)	0.02
Basal (units)	19.0 (6.5)	16.4 (6.6)	0.01	20.4 (6.3)	18.3 (7.2)	0.1
Bolus (units)	20.9 (9.1)	15.9 (7.9)	0.002	22.2 (10.4)	18.3 (10.1)	0.05
Glucose (mg/dl)	169.5 (37.5)	152.3 (34.5)	0.08	177.1 (43.6)	161.9 (34.5)	0.12
Glucose SD (mg/dl)	65.9 (14.8)	58.1 (15.0)	0.03	67.6 (16.3)	67.4 (17.7)	0.9
HbA1c (%)	7.4 (0.7)	7.0 (0.7)	0.02	7.5 (0.8)	6.6 (0.7)	0.004

Liraglutide could be a useful adjunct to insulin therapy in type 1 diabetes. There was a significant decrease in weight, TDD of insulin (bolus > basal), and HbA1c that was seen within 3 months and sustained at 5 months. The lower exogenous insulin dose is beneficial and possibly reduces inflammation and vascular dysfunction. The weight loss likely helps maintain this lower insulin dose and both contribute to the overall improvement in glycemic control measured by HbA1c.

2370-PO

WITHDRAWN

For author disclosure information, see page 797.

2371-PO

WITHDRAWN

2372-PO

Safety and Tolerability of Exenatide Once Weekly in Patients With Type 2 Diabetes: An Integrated Analysis of 4328 Patients

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Exenatide once weekly (EQW) is an extended-release GLP-1 receptor agonist (RA) for the treatment of T2DM. The objective of this retrospective analysis was to characterize the safety and tolerability of EQW compared with other GLP-1RAs and other frequently-used therapies. Individual patient data were analyzed from the ITT population of 4328 T2DM patients from 8 randomized Phase 3 trials (26-52 weeks in duration). Incidence, exposure-adjusted incidence (EAI), and risk difference and its 95% CI were calculated for pooled EQW, exenatide twice daily (EBID), and non-GLP-1RA comparator (metformin, pioglitazone, sitagliptin, insulin); comparisons between EQW and liraglutide were analyzed separately from a single head-to-head trial. Incidence of discontinuations due to AEs was low in all groups. The most frequent AEs with EQW, gastrointestinal (GI)- and injection (inj)-site–related AEs, were generally mild and incidences decreased over time. Incidences of GI-related AEs were highest across therapies in the GLP-1RA class and lower with EQW compared to EBID or liraglutide; inj-site–related AEs were highest with EQW compared to all other groups. Hypoglycemia occurred infrequently without SFU use, with a higher incidence in pooled non-GLP-1RAs regardless of concomitant SFU use. EAIs for pancreatitis, pancreas cancer, thyroid cancer, and renal-related AEs were generally similar between groups. This integrated analysis found that the overall safety profile of EQW was similar to that of EBID and liraglutide, with improved GI tolerability, and to that of the pooled non-GLP-1RA comparator.

	Randomized EQW Trials			EQW vs Liraglutide Head-to-head Trial	
Event (incidence, %)	EQW N=1934	EBID N=606	Non-GLP-1RA Comparator N=1338	EQW N=461	Liraglutide N=450
All GI-related AEs	35.0	46.27*	23.7**	26.0	41.8†
Injection site-related AEs	7.1	2.6*	0.7**	5.2	1.1†
Hypoglycemia, with SFU	12.4	12.6	33.3**	15.5	12.2
Hypoglycemia, no SFU	2.0	0.8	3.9**	2.4	2.6
Serious AEs	3.2	3.0	5.2**	2.8	2.4

EQW = exenatide once weekly; EBID = exenatide twice weekly; RA = receptor agonist; GI = gastrointestinal; AE = adverse event, SFU = sulfonylurea. Significant differences ($P<0.05$) between groups are noted with * for comparison of pooled EQW vs pooled EBID, ** for pooled EQW vs pooled non-GLP-1 RA comparator, and † for EQW vs liraglutide in a single head-to-head trial. Injection site-related AEs include injection site rash, pruritus, erythema, and urticaria. Hypoglycemia includes minor and major events.

2373-PO

The Effectiveness and Safety of Starting Biphasic Insulin Aspart 30 (Premix) in Older versus Younger Adults With Type 2 Diabetes (T2DM): Results from the A_1chieve Study

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A_1chieve was a 24-week, non-interventional study in 28 countries across four continents, designed to evaluate the safety and clinical effectiveness of insulin analogs in 66 726 people with T2DM in clinical practice. The current subgroup analysis was to investigate the effectiveness of premix analog in older (>65 yr; n=3796) or younger (≤65 yr; n=23 276) insulin-naïve adults of the A_1chieve study. At baseline, adults aged >65 years had a mean age of 71.1 (SD 4.9) years and diabetes duration of 9.3 (7.4) years; adults aged ≤65 years had a mean age of 50.0 (9.4) years and diabetes duration of 5.7 (4.5) years; A1C was 9.5 (1.9) and 9.5 (1.7) %, respectively. The addition of premix resulted in significant improvement in glycemic control, after 24 weeks of treatment, in both subgroups ($p\leq0.001$) (Table). The incidence of overall hypoglycemic events increased in both subgroups, but the incidence of major events decreased significantly ($p<0.001$) (Table). Over 80% of people completed the study on twice-daily premix and the final dose was 0.47 U/kg in both subgroups. Quality of life (QoL), as assessed by EQ-5D 100-point visual analog scale, reported significant improvement at 24 weeks in both groups ($p<0.001$) (Table). In the A_1chieve study, treatment with premix was associated with improvements in glycemic control in insulin-naïve people with T2DM. Treatment was well tolerated and improved QoL in both older and younger adults.

Clinical outcomes after 24 weeks of treatment with premix

		>65 years	≤65 years
A1c (%)	Baseline	9.5 (1.9)	9.5 (1.7)
	Change	-2.2 (1.8)*	-2.2 (1.6)*
FPG (pre-breakfast) (mg/dl)	Baseline	192.6 (63.3)	200.9 (60.7)
	Change	-66.2 (64.7)*	-73.1 (58.6)*
PPPG (post-breakfast) (mg/dl)	Baseline	274.8 (81.2)	281.9 (74.4)
	Change	-94.0 (88.3)*	-105.5 (77.3)*
Hypoglycemia (overall) (event/person-year [% with event])	Baseline	0.99 (3.8)	0.94 (4.0)
	Final visit	1.49 (6.1)*	0.98 (4.0)‡
Hypoglycemia (major) (event/person-year [% with event])	Baseline	0.15 (0.8)	0.08 (0.4)
	Final visit	0.00 (0.0)*	0.00 (0.3)*
Body weight (kg)	Baseline	67.5 (12.3)	70.6 (12.6)
	Change	1.0 (3.9)*	0.2 (3.4)*
Insulin dose (U/kg)	Day 1	0.42 (0.19)	0.42 (0.17)
	Final visit	0.47 (0.20)	0.47 (0.21)
Quality of life (VAS 0-100)	Baseline	63.7 (16.6)	62.6 (17.0)
	Change	13.1 (16.6)*	15.4 (17.0)*

Mean (SD) or %; *$p\leq0.001$, ‡$p=0.961$; FPG, fasting plasma glucose; PPPG, post-prandial plasma glucose; SD, standard deviation; VAS, visual analog scale.

2374-PO

WITHDRAWN

2375-PO

Dawn Revisited: Does NPH Insulin Treatment Reduce Glycemia More Than Lantus?

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Whether the early morning rise in glucose levels (dawn phenomenon) is better controlled with a peaking insulin (NPH) compared with non-peaking glargine insulin (Lantus) is unknown. Fifteen individuals (53% females, age 46.5±2.5 y, BMI 25.8±3.3 kg/m^2, A1c 7.7±0.7%) with type 1 diabetes (fasting C-peptide <0.1, duration 28.6±9.7 y) completed both arms of the crossover

For author disclosure information, see page 797.

study. At study entry, subjects were treated with glargine (n=10) or NPH (n=5) insulin as part of a multiple daily injection regimen. For the 4 weeks prior to overnight sampling on the CRC, insulin regimens were adjusted to achieve intensive glucose control. Basal insulin (glargine or NPH) was given at 22:00, with pre-meal rapid acting insulin doses adjusted based on carbohydrate counting and SMBG results. After completion of the sampling, subjects were switched to the alternative insulin for 3-4 weeks prior to retesting. A continuous glucose monitoring system (CGMS) was worn for ~3 days prior to and during overnight sampling for data collection only. Mean hourly blood glucose levels were ~ 40 mg/dl lower with NPH than glargine between 04:00 - 06:00 (the dawn period), with area under the curve (AUC), the primary outcome, significantly lower during this time (p=0.049). AUC trended lower with NPH from 22:00 to 8:00 (p=0.057). Insulin levels were significantly higher at 5:00 - 7:00 with NPH compared with glargine; levels at other times were not significantly different. CGMS data analyzed with a spline method, confirmed a difference in the BG patterns (p= 0.004). NPH was associated with lower BG levels than glargine, with two time periods (10:05 -10:25 and 15:00 -19:00) with statistically significant differences. There were no significant differences between NPH and glargine in mean serum cortisol and glucagon levels. The analyses of the AUC glucose data support the hypothesis that NPH insulin results in higher insulin levels during the dawn period with more effective suppression of the dawn phenomenon than the non-peaking glargine insulin.

2376-PO

Assessment of the Relationship Between the Use of a Telemedicine System and Blood Glucose Control in Patients With Type 1 Diabetes

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The telemedicine system DIABEO, based on a smart-phone that computes insulin doses according to blood glucose levels and food intakes and transmits these data to a remote care provider thanks to a secure website, has been shown to reduce HbA1c by 0.9% in patients with poorly controlled type 1 diabetes (HbA1c ≥ 8%) in TELEDIAB 1 study. In this sub-study analysis, we aimed at assessing how the effective use of the system had been a determinant factor *per se* in the improvement of glucose control. Patients using DIABEO in TELEDIAB 1 study were classified according to their actual use of DIABEO (n=113). Adherent users were defined as having a proportion of informed meals above 67% (median of the population). Adherent users were older and were more often involved in managerial activities. They had a longer duration of diabetes and were more familiar with functional insulin therapy (FIT). HbA1c at baseline was lower in adherent users than in the others (8.9±0.9% vs. 9.4±1.2%, p=0.02). At 6 months, adherent users had a significantly lower HbA1c (8.4±0.9% vs. 8.7±1.2%, p=0.005). However, the non-adherent users showed a greater reduction in HbA1c. Among them, the proportion of patients who had an HbA1c reduction over 1% was 43% vs. only 16% among the adherent users (p=0.002). According to these identified features, adherent users appear as patients with a moderately impaired glucose control who benefitted from assistance in insulin dose computing while non-adherent users look as patients with a poorer glucose control for whom repeated motivational support through frequent consultations led to an improvement in glucose control. Further multiparameter analyses should help in a better identification of the patients who benefit the most from DIABEO *per se* and, hence, in whom a telemedicine system is the most cost-effective.

Supported by: sanofi-aventis, Voluntis and Orange

2377-PO

WITHDRAWN

2378-PO

Impact of Diabetes Duration on Efficacy and Safety of a Basal-Plus Regimen of Insulin Glargine Plus Once Daily Insulin Glulisine: A Pooled Analysis From 4 Clinical Trials

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The "basal-plus" regimen is an increasingly common initial step in insulin therapy intensification. This pooled analysis evaluated the efficacy and safety of adding a single bolus dose of insulin glulisine to basal insulin glargine in persons with type 2 diabetes of known different durations (≤ 6, 6 to 12, and > 12 years). Pooled data were analyzed from 4 randomized, multicenter studies that included subjects with poor glycemic control who were initiated on glargine (basal) to which glulisine (plus) was added once daily for up to 6 months. Glargine dose was titrated to protocol-defined blood glucose targets in 2/4 studies. Glulisine was titrated in all studies to protocol-defined fasting (FBG) or postprandial (PPG) glucose targets. PPG was measured 2 h after glulisine injection. Measurements were taken at baseline and endpoint as specified in each trial. A total of 681 patients were included. Glycemic control was similar across groups at baseline. The basal-plus regimen resulted in significant decreases in A1C and PPG in all groups at endpoint (Table). There was no significant change in FBG or body weight in any group; glulisine dose increased in all groups. Percentage of patients with A1C < 7% at endpoint was similar in each group ($P = 0.4$), as was the prevalence of severe hypoglycemia (as defined in each trial; $P = 0.3$). Basal-plus insulin treatment using glargine plus a single dose of glulisine significantly reduces A1C and PPG across a range of diabetes duration with similar rates of severe hypoglycemia and without significant weight gain.

	Duration of diabetes, years		
	≤ 6 (n = 187)	6 to 12 (n = 268)	> 12 (n = 226)
A1C, %			
baseline	7.4 (0.9)	7.6 (0. 8)	7.7 (0.9)
endpoint	7.2 (1.0)[a]	7.1 (0.8)[a]	7.2 (0.9)[a]
< 7% at endpoint	43.3	48.5	43.8
FPG, mg/dL			
baseline	122 (39)	118 (33)	118 (42)
endpoint	130 (45)	121 (34)	119 (35)
PPG, mg/dL			
baseline	184 (40)	196 (43)	198 (47)
endpoint	136 (34)[a]	139 (38)[a]	142 (44)[a]
Glargine dose, U			
baseline	38.5 (34.1)	37.7 (23.1)	32.4 (20.0)
endpoint	45.8 (44.6)	41.7 (27.9)	37.6 (26.5)[b]
Glulisine dose, U			
baseline	5.0 (2.3)	5.1 (2.4)	4.6 (1.8)
endpoint	14.3 (13.1)[a]	13.7 (11.9)[a]	11.8 (8.5)[a]
Severe hypoglycemia, n (%)			
Weight, kg	1 (0.5)	5 (1.9)	6 (2.7)
baseline	93.7 (22.8)	90.7 (19.3)	85.2 (17.3)
endpoint	94.8 (23.5)	91.4 (19.9)	86.4 (18.2)

[a]$P < 0.001$ vs baseline; [b]$P = 0.019$ vs baseline; Values are mean (SD), unless otherwise noted.

Supported by: sanofi-aventis

2379-PO

Effect of the Administration of Exenatide in Different Meals Schedules on Glucose Concentrations throughout 24 h in Type 2 Diabetes Patients With Failure to Metformin Monotherapy

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Exenatide is a glucagon-like peptide-1 agonist that improves blood glucose in patients with type 2 diabetes by many different mechanisms, predominantly lowering postprandial glucose, and additionally reduces body weight. Exenatide is prescribed prior to morning and evening meals or before the two main meals of the day, however, there is controversy in populations with different dietary patterns on the best time of application. The aim of this study was to evaluate the effect of the administration of exenatide in different meals schedules on glucose concentrations throughout 24 h in type 2 diabetes patients with failure to metformin monotherapy. A randomized, single blind, clinical trial was performed in 18 adult patients with type 2 diabetes, overweight or obesity, fasting glucose <210 mg/dl, A1C between 7 to 9% and failure to metformin monotherapy. All patients received exenatide 5 µg bid, SC during 30 days. Different meals schedules were assigned at

random: a) before breakfast and lunch; b) before lunch and dinner, and c) before breakfast and dinner. At the beginning and 30 days latter a metabolic profile and glucose concentrations throughout 24 h were measured. Areas under the curves (AUC) of glucose were calculated. Statistical analyses were done with Kruskal-Wallis, Mann-Whitney U, Wilcoxon and x^2 tests. All groups were similar in basal characteristics. There were significant decreasing of fasting glucose (8.7±1.7 vs. 7.2±1.1 mmol/l, p=0.046), A1C (7.9±0.7 vs. 7.0±0.7 mmol/l, p=0.028) levels and AUC of glucose concentrations throughout 24 h (225±61 vs. 167±36 mmol/l*h, p=0.028) with the administration of exenatide prior breakfast and lunch. In conclusion, exenatide administrated before breakfast and lunch showed a better control of glucose concentrations throughout 24 h in type 2 diabetes patients with failure to metformin monotherapy.

2380-PO

The Combination Therapy With Metformin and Vildagliptin Decreases Lymphocytes Count in patients With Type 2 Diabetes Mellitus

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There is concern about the effect of DPP-4 inhibitors on immune system as a consequence of the lack of DPP-4 selectivity. The aim was to investigate the effect of Vildagliptin (V) on White Blood Cells (WBC) in patients with type 2 diabetes (T2DM). Sixty-four patients with recently diagnosed T2DM were randomly assigned to Metformin (M) 1700 mg/day (median age 57 years, range 19-70) or to Metformin+Vildagliptin (M+V) (M 1700mg/day + V 100 mg/day, median age 53 years, range 32-70). Anthropometric parameters (body weight BW, body mass index BMI, systolic blood pressure SBP, diastolic blood pressure DBP), White Blood Cells count (Neutrophils N, Lymhocytes L), glycemic control (glycated hemoglobin HbA1c), lipid profile, liver enzymes, serum Creatinine (Cr) and urine Albumin/ Creatinine ratio (A/C) were assessed at a baseline and after 6 months. Side effects with emphasis on infections were also recorded. Lymphocytes decreased significantly in patients with M+V after 6 months (L 1670 ± 837.1 vs 1350 ± 611.7, p= 0.04) while WBC and N did not change (p=NS). There were no difference between the two groups in anthropometric parameters (p=NS), glycemic control (p=NS), lipid profile (p=NS), liver enzymes (p=NS), SCr (p=NS) and A/C ratio (p=NS) throughout the study. There were one urinary tract infection in M group and two upper respiratory tract infections in M+V group. Both therapies improved glycemic control effectively and were well tolerated in patients with recently diagnosed T2DM. The combination therapy with M + V decreased significantly lymphocytes count but this effect had no impact on infections frequency. However, the effect of combination therapy with M + V on WBC and infections should be determined in large long-term studies.

2381-PO

An Integrated, Multistudy Analysis of Alogliptin Safety

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Alogliptin (Alo) is a selective inhibitor of dipeptidyl peptidase-4 for the treatment of type 2 diabetes mellitus. We performed an integrated analysis of controlled phase 2 and 3 studies to evaluate the safety of Alo. Subjects who received at least one dose of study drug were included in the analysis of 11 pooled studies and were categorized by treatment assignment as Alo (n=4162) or comparator (including placebo) (Com; n=1855). Demographics were similar between groups. The majority of subjects were aged <65 years (Alo, 78%; Com, 72%), female (both 51%), and white (Alo, 73%; Com, 71%), with BMI ≥30 kg/m^2 (Alo, 55%; Com, 53%), and had mild renal impairment (MDRD: eGFR ≥ 60 - < 90 mL/min/1.73 m^2 criteria) (both 68%); mean baseline A1c was 8.3% (both). A lower proportion of Alo vs Com subjects required hyperglycemic rescue (11% vs 21%). Similar proportions of subjects in both groups experienced ≥1 adverse event (AE) (Alo, 65%; Com, 64%). The only AEs occurring at ≥5% in either group were urinary tract infection (Alo, 4.9%; Com 5.2%) and headache (both 5.0%). Serious AEs were reported by 4% of subjects in each group and deaths attributed to AEs occurred at 0.1% for both groups. A lower proportion of Alo vs Com subjects experienced a major adverse cardiovascular event (MACE: 0.3% Alo vs 0.5% Com); the hazard ratio for MACE for Alo vs Com was 0.65 (upper bound of 1-sided 97.5% CI = 1.41). Incidence of hepatic enzyme elevation (Alo, 0.4%; Com, 0.3%) was low in both groups. Rare events of rash and pruritus were reported with Alo. Three subjects in the Alo group (0.1%) reported acute pancreatitis as compared to none in the Com group. This analysis suggests that Alo is safe and well tolerated with a safety profile similar to that of other DPP-4 inhibitors.

2382-PO

Quality of Life (EQ-5D) among Type 2 Diabetes Mellitus Patients Treated With Dapagliflozin for 24 Weeks

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Dapagliflozin is a first in class, oral sodium-glucose co-transporter 2 (SGLT2) inhibitor, in clinical development for the treatment of type 2 diabetes mellitus (T2DM). Dapagliflozin lowers blood glucose by increasing urinary glucose excretion and is associated with improvements in HbA1c and reductions in body weight. This study evaluated the health status and quality of life (QOL) among T2DM patients treated with dapagliflozin in a randomized clinical trial. Subjects with T2DM (BMI >= 25 kg/m^2; men 56%, women 44%; mean age, 61 years) who had inadequate glycemic control on metformin (MET) alone were enrolled in a 24-week, international, double-blind, randomized, placebo-controlled study to evaluate the effect of dapagliflozin in combination with MET on total body weight (NCT00855166). Subjects completed the EQ-5D questionnaire at baseline and at week 24. Subjects treated with dapagliflozin 10 mg + MET (n = 87) were compared with subjects treated with placebo + MET (n = 89), based on ANCOVA model with treatment group and gender as effects and baseline value as a covariate. EQ-5D index baseline means (SD) were 0.85 (0.16) and 0.82 (0.15) for dapagliflozin and placebo, respectively. Corresponding 24-week values were 0.88 (0.17) and 0.87 (0.16), respectively. The ANCOVA model indicated no difference (-0.01; CI [-0.05, 0.03]; p-value 0.49). EQ-5D visual analog scale (VAS) baseline means (SD) were 72.8 (19.39) and 73.7 (15.49) for dapagliflozin and placebo, respectively. Corresponding 24-week values were 77.4 (15.21) and 78.3 (10.65), respectively. The ANCOVA model indicated no difference (-0.6; CI [-3.9, 2.8]; p-value 0.74). Results indicated that the patients maintained high QOL scores from baseline to week 24 in both treatment groups as measured by EQ-5D index and VAS. Health status and QOL were maintained at a high level during treatment with dapagliflozin, a novel, selective SGLT2 inhibitor.

Supported by: Bristol-Myers Squibb/AstraZeneca

2383-PO

WITHDRAWN

2384-PO

Efficacy of Alogliptin is Not Affected by Hispanic Ethnicity or Race

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Alogliptin (A) is a highly selective dipeptidyl peptidase-4 inhibitor. This ad hoc analysis of 6 phase 3 studies was used to determine whether A was efficacious irrespective of Hispanic ethnicity and race. All studies were randomized, double-blind, placebo-controlled, with A given at doses of 12.5 mg QD and 25 mg QD. Additional arms from 1 study not containing placebo (PBO) or A alone were not included in this analysis. Models were stratified by study and adjusted for baseline (BL) A1c. Compared to PBO, statistically significant (P<0.001) decreases from BL in the mean A1c levels at week 26 were observed in both Hispanic and non-Hispanic subjects treated with either dose of A. Relative to PBO, non-Hispanic subjects had a slightly greater reduction from BL in their A1c levels (Table); however, the interaction between Hispanic ethnicity and treatment was not statistically significant. A statistically significant and similar percentage of subjects in both ethnic groups achieved the A1c goal of ≤7.0% compared to PBO. The effect of race (White, Black, and Other) on the efficacy of A was also evaluated. A was effective in all races with statistically significant (P<0.001) decreases from BL in the mean A1c levels at week 26 for both doses of A compared to PBO (Table). Greater PBO-corrected reductions in A1c values were observed for the Black and Other race groups than for Whites (P=0.030 for interaction); however, both groups had higher BL A1c values compared to Whites. The percentage of subjects achieving the A1c goal of ≤7.0% was similar across all race groups These data indicate that efficacy of A is not affected by ethnicity or race.

For author disclosure information, see page 797.

LS Mean (SE) Change from Baseline in A1c by Ethnicity and Race						
	PBO (N=622)	n	A 12.5 mg (N=1005)	n	A 25 mg (N=993)	n
Ethnicity						
Hispanic or Latino	-0.24 (0.06)	200	-0.62 (0.05)*	339	-0.74 (0.05)*	339
Not Hispanic or Latino	-0.01 (0.04)	410	-0.56 (0.03)*	651	-0.65 (0.03)*	633
Race						
Whte	-0.08 (0.04)	439	-0.56 (0.03)*	706	-0.60 (0.03)*	685
Black	-0.02 (0.12)	49	-0.62 (0.10)*	69	-0.79 (0.10)*	68
Other	-0.12 (0.07)	122	-0.61 (0.06)*	215	-0.89 (0.06)*	219

*P<0.001 vs PBO

2385-PO

Gradual Intensification of Premixed Insulin Lispro Therapy vs. Basal +/- Mealtime Insulin in Patients With Type 2 Diabetes Eating Light Breakfasts

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Insulin therapy in type 2 diabetes mellitus (T2DM) should be tailored to individual patients' (pts) needs. We tested if, in those eating light breakfasts, premixed insulin analogues may be an option to substitute basal/mealtime insulin. The randomized, open-label, 48-week, parallel study compared algorithms of initiation/intensification of insulin therapy. One, 2 or 3 injections of insulin lispro mix 75/25 and/or 50/50 (LM) or glargine +/- 1, 2 or 3 injections of insulin lispro (BM) were used in T2DM pts not controlled with oral antihyperglycemic medications, consuming <15% daily calories at breakfast. The objective was to test the hypothesis that LM was non-inferior to BM for glycemic control, measured by A1c after 48 weeks; assessed using ANOVA adjusted for baseline A1c and a non-inferiority margin of 0.4%. Patients (n=344: 176 [51%] females, mean [SD] age 54.3 [8.8] years, BMI 29.4 [4.6] kg/m^2, baseline HbA1c 9.02 [0.97] %) were randomized to LM (n=171) or BM (n=173). In the per-protocol analysis "LS means" (95%CI) endpoint HbA1c were 7.40 (7.15 - 7.65) and 7.55 (7.27 - 7.82) in LM and BM arms, respectively. The between-treatment difference was -0.14% (-0.42, 0.13); non-inferiority was met and was confirmed by analyses on the full analysis set (n=321). Mean HbA1c changes at week 48 were -1.68 (1.35) % (LM) and -1.66 (1.31) % (BM); p=0.967. HbA1c targets of <7.0% and ≤6.5% were achieved by 48.2% and 24.8% (LM) vs. 36.2% and 18.5% (BM) of pts. SMBG profiles, body weight changes of +2.31 (3.3) kg and +2.32 (3.7) kg and total insulin doses of 46.20 (28.4) IU/day and 46.45 (31.4) IU/day at 48 weeks were similar in LM and BM, respectively. Overall (65% vs. 60%) and severe hypoglycemia rate (2% vs. 4%) were similar in LM and BM groups (p=0.75); however, more LM pts had nocturnal episodes (34% vs. 24%; p=0.04). The proposed algorithms using insulin lispro mixes could be an alternative to basal +/- meal-time insulin strategy in T2DM patients eating light breakfasts.

Supported by: Eli Lilly and Company

2386-PO

The Effects of Nateglinide versus Acarbose on Lipid Profiles in Drug Naïve Type 2 Diabetic Patients

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Dyslipidemia in type 2 diabetic patients is related to the absence of early-phase insulin secretion. Nateglinide has been shown to be effective in restoring early-phase insulin secretion. This effect may be beneficial to the lipid profiles. This study aimed to compare the effects of Nateglinide and Acarbose on fasting and postprandial lipid profiles in drug naïve type 2 diabetic patients. A total of 38 drug naïve type 2 diabetic patients (20 females) aged 35 to 75 years old were enrolled. All subjects were randomized to receive Nateglinide, 120 mg three times daily (Na group, n=19) or Acarbose, 50 mg three times daily (Ac group, n=19) for 12 weeks. A 70 g instant noodle ration served as a standard meal test was performed at baseline, 4 weeks and 12 weeks. Blood samples were collected fasting and 2 hours after the standard meal test. The fasting and postprandial lipid profiles and blood glucose were measured. The efficiencies of nateglinide (120mg, tid) and acarbose (50mg, tid) for lowering postprandial hyperglycemia were similar. The postprandial low-density lipoprotein cholesterol level decreased significantly after 4 weeks and the fasting total cholesterol level decreased significantly after 12 weeks of treatment with nateglinideand. Acarbose did not affect fasting or postprandial lipid profiles after 4 or 12 weeks of treatment. The effect of nateglinide in restoration of early-phase insulin secretion may be associated with improvement in dyslipidemia in type 2 diabetic patients.

2387-PO

WITHDRAWN

2388-PO

The Effects of Initial Insulin Detemir Prior to Gliclazide-MR versus Sole Gliclazide-MR Treatments on Endothelial Functions in Addition to Life-Style Modification and Metformin Therapy in Patients With Type 2 Diabetes

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Background: In type 2 diabetes mellitus (T2DM), there is a lack of the comparison of different treatment alternatives especially in terms of pleomorphic effects, among which the effects on endothelial functions are the most important. Objectives: The main aim of this study was to compare the effects of initial insulin detemir (iD) prior to gliclazide-MR (GMR) versus sole GMR treatments on endothelial functions in addition to life-style modification and metformin therapy as a second step in T2DM patients. Methods: Thirty nine patients with T2DM were randomized into two treatment arms: 15 patients in the iD arm and 24 in the GMR arm (Figure 1). To determine the NO-mediated endothelial functions, flow-mediated dilatation (FMD) was performed on the day of reaching euglycemic status. Results: Both treatment arms were indifferent in terms of age, basal body-mass index and body-fat mass as well as HbA1C levels. Both treatment protocols were equally effective in controlling blood glucose levels. Both groups equally improved the NO-mediated endothelial functions of the patients, as determined by the FMD results. Although there was no significant difference between GMR and iD treatment arms in improving endothelial functions, a better amelioration in FMD results was observed during insulin detemir treatment. Conclusion: The addition of iD prior to GMR treatment was not superior in improving NO-mediated endothelial vasomotor functions compared with the addition of sole GMR as a second step T2DM treatment.

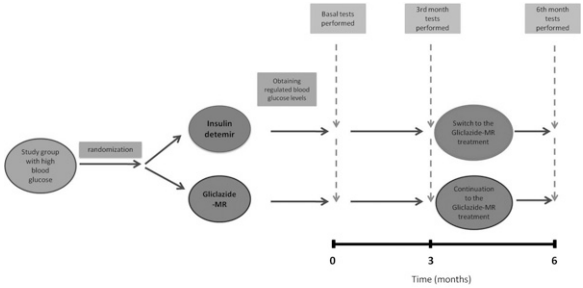

Figure 1: The summary of the work plan of the study

Supported by: The Scientific and Technological Research Council of Turkey (110S119)

2389-PO

Real Time Imaging of Heterogeneous Amylin Fibril Growth Mechanisms

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Fibrillar amylin plaques have been found in the interstitial spaces between pancreatic β-cells of most type 2 diabetes patients. These amyloid plaques cause distinct changes in membrane morphology and result in β-cell death. Research is still in progress to identify the toxic species involved and the mechanisms by which fibrils or oligomers associate with β-cell membranes resulting in toxicity. Here, we imaged fibrillization of amylin using real time total internal reflection fluorescence microcopy (TIRFM). TIRFM of amylin aggregation shows three types of aggregation processes, seed growth, fibril elongation, and thickening. Fibril elongation appears to be unidirectional if we consider that multiple fibrils grow in opposite directions with different rates starting from a common seed. The dimensions of the seeds and their ability to bind the dye ThT, together with EM data suggests that they are not

the types of oligomers thought to provide the primary nucleation sites for fibrillization reactions but rather dense clusters or plaques of short fibrils, that act as secondary nucleation sites. After fibrils are formed, some of the fibrils show an increase in fluorescence intensity that we attribute to the growth of new fibrils alongside those previously formed. All three aggregation processes observed by TIRF are suggestive of secondary (heterogeneous) nucleation, a mechanisms in which nucleation occurs on preformed fibrils. Consistently, electron micrographs show changes in fibril morphology well after fibrils are first formed, and the growth processes observed by fluorescence microscopy occur after the corresponding solution reactions have reached an initial apparent plateau. Taken together, the results highlight the importance of secondary nucleation in the fibrillization of amylin, as this could provide a pathway to continue fibril growth once an initial population of fibrils is established.

2390-PO

Insulin Regimen in Adults With Type-1 Diabetes in the Middle East: Results From the International Diabetes Management Practices Survey (IDMPS)

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IDMPS is an ongoing 5-y multinational observational study documenting the current quality of care provided to people with type 1 or type 2 diabetes. Feasibility analyses were previously performed to validate the chances of pooling the data collected during 3 y in the Middle East. The aim was to identify patient profiles associated with insulin regimen in type 1 diabetes mellitus (T1DM) patients in the Middle East. Patient profiles of 1316 patients were determined using logistic regression analysis. The most common insulin regimen was basal-prandial therapy (51.1%), followed by premix (29.9%), basal therapy alone (10.4%), and other regimens (8.7%). The mean duration of the basal-prandial therapy treatment was 10.9 ± 8.5 y. In patients treated with the basal-prandial regimen, 54.9% used vials and syringes and 51.6% used insulin pens. The number of insulin injections/day was 3.9 ± 0.7, and 95.4% received 3 to 6 injections/d. Basal and prandial daily doses were 0.47 ± 0.23 and 0.37 ± 0.27 IU/kg respectively. Of the patients on the basal-prandial regimen 40.2% were treated with insulin analog and 59.8% with regular insulin. Mean A1C levels were 8.1 ± 1.8 and 26.2% had A1C levels < 7%. Patients treated with premix insulin received a daily dose of 0.76 ± 0.28 IU/kg. The number of premix insulin injections/d was 2.1 ± 0.3, and 88.3% received 2 insulin injections/d. Their mean A1C levels were 8.7 ± 2.1% and 17.3% had A1C levels < 7%. Basal-prandial insulin therapy was significantly associated with glucometer use (OR = 2.1, $P = 0.007$), self-management (OR = 1.8, $P = 0.006$), total daily dose (OR = 1.1 for changes of 0.1 UI/kg, $P = 0.003$), and patient recruited by specialists (OR = 2.3, $P < 0.001$). In the Middle East, the use of the basal-prandial regimen in T1DM patients was associated with self-management and better glycemic control. Since the basal-prandial regimen is recommended by international guidelines, further education on this regimen would be beneficial.

Supported by: sanofi-aventis

2391-PO

Three-Year Treatment Pathways after Initiation of Exenatide With Oral or Insulin Therapy in US

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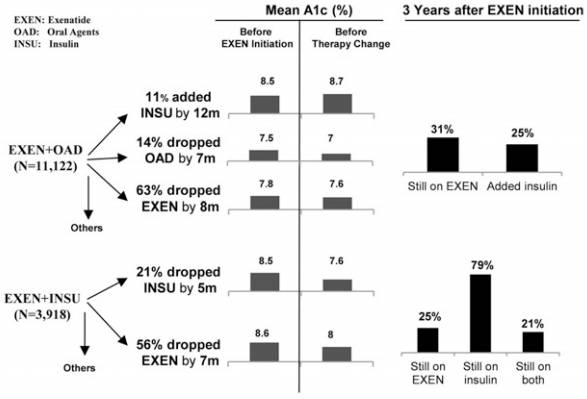
There is limited data concerning long-term treatment flow for patients initiating GLP-1 therapy. Patients initiating exenatide (EXEN) from Apr 2005 to Jun 2007 with oral agents (OADs) or insulin were identified from IMPACT™ Database and followed for 3 years to examine therapeutic transitions. About 15% of patients had A1C values available. Mean age was 53 years for OAD group (n=11,122) and 55 years for insulin group (n=3,919). After adding EXEN to OADs, 31% patients stayed on EXEN and 25% added insulin 3 years after EXEN initiation. After adding EXEN to insulin, 25% stayed on EXEN, 79% on insulin and 21% on both at 3 years. Majority of patients had their first medication change within 1 year of EXEN initiation after adding EXEN to OADs or insulin. Greater A1C improvements were observed after adding EXEN to insulin instead of OADs (see Figure 1). Of those who discontinued EXEN, 31% restarted EXEN in OAD group and 22% restarted EXEN in insulin group after 7 months. In summary, the data shows increased insulin use over 3 years in patients who initiate EXEN with oral therapy. A greater A1C reduction is achieved after initiation of EXEN in combination therapy with insulin relative to OADs. Furthermore, a greater A1C benefit of EXEN in combination therapy with insulin instead of OADs is observed even in patients who later discontinue EXEN, suggesting the possibility of multiple treatment objectives in patients initiating GLP-1 therapy.



Supported by: sanofi-aventis

2392-PO

A Simple Brief Predictive Test of the Basal Insulin Dose—A Pilot Study

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The recommended initial dose of basal insulin in T2DM is 10 U or 0.1-0.2 U/kg. Since the dose, D, at targeted fasting plasma glucose, PG, is usually ≥ 0.4 U/kg, titration may be lengthy and not pursued. Increasing the initial dose beyond these recommendations may lead to hypoglycemia. We proposed that one can estimate the D from a simple brief assessment of insulin sensitivity (IS) prior to beginning insulin. 20 fasting T2DM subjects who had an A1c > 7.0% and not taking insulin, were injected with 0.1 U/kg of insulin aspart. The decline in PG was measured from baseline to the 2nd and 4th h. $IS = (PG_{baseline} - PG_{2nd\ or\ 4th\ h})$/ U of insulin aspart injected. The estimated final dose, ED, was calculated from 400 or 500/IS. After an initial dose, once-nightly insulin detemir, was increased 3 U/3d if the mean FPG was > 110 mg/dl or decreased 3 U if < 80 mg/dl or for any confirmed hypoglycemia, i.e., PG < 70 mg/dl and symptoms. Self-titration was done by the subject and reinforced by 1 w phone calls and 4 w clinic visits. Hypoglycemia was assessed during each phone contact and visit. The mean (SD) age was 54 (11) years, BMI was 36 (6) kg/m2, and diabetes duration was 9 (5) years. Target glucose and the D were reached prior to 12 w but titration was continued until the end of the study. The D was 60 (34) U or 0.58 (38) U/kg. A1c at baseline decreased from 8.5 (0.9) to 6.9 (0.7) % (p = <0.001) at 12 w. 13 episodes of confirmed hypoglycemia occurred (2.8 episodes/subject/year). The baseline weight correlated poorly with the D (r = 0.179). Excluding those whose calculated dose was ≥ 90 U (n=6), the ED using the 400 or 500 as the numerator correlated well with the D ($r > 0.6$, $p < 0.02$). Using a formula numerator of 500 or 400 and comparing to D, yielded a mean overdose of 15 U or an under dose of 0.6 U, respectively. A 2 h simple rapid insulin tolerance test at the beginning of basal insulin therapy may provide a close estimate of the D and therefore aid in titration.

Supported by: Novo Nordisk, Inc.

2393-PO

Tolerability and Biomarker Response of PF-04620110, a Novel Diacylglycerol Acyltransferase 1 (DGAT-1) Inhibitor, in Healthy Overweight or Obese Adult Subjects After Administration as a Modified-Release Formulation

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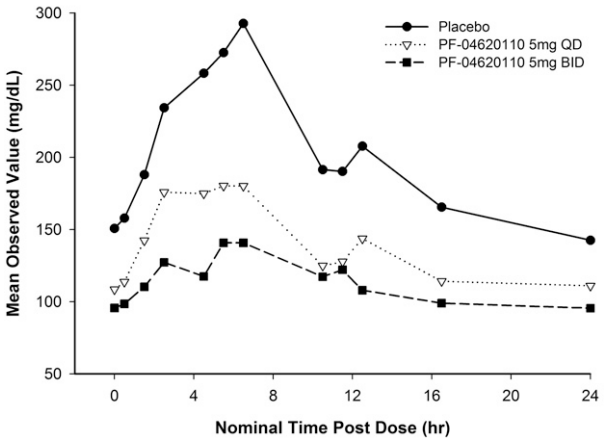
PF-04620110, a DGAT1 inhibitor has been shown to decrease triglyceride (TG) and insulin with improved GLP-1 secretion in healthy subjects; however tolerability has been limited due to GI AEs. To determine if modified release (MR) could improve GI tolerability, a randomized, double-blind, placebo-controlled study examined the safety, tolerability and biomarker response of PF-04620110 in 26 healthy overweight and obese (HOVs) subjects after 14 days administration of placebo (PBO) or PF-04620110 given as MR formulation at 5 mg QD or 5 mg BID. On Days 0 (baseline) and 14, the same breakfast (MMTT), lunch and dinner were offered with intensive sampling to assess 24 hour profiles of glucose, insulin, TG and total GLP-1. The reduction

For author disclosure information, see page 797.

in 24-hour weighted mean (WM) insulin was dose responsive and up to 29% greater than PBO (Test/PBO ratio: 0.71, 80% CI: 0.58-0.87). Similarly WM TG decreased in a dose related manner up to 38% vs PBO (Test/PBO ratio: 0.62, 80% CI: 0.52-0.75). A clear increase in WM GLP-1 was only observed in the 5 mg BID group: 82% vs PBO (Test/PBO ratio: 1.82, 80% CI: 1.42-2.33). As expected in HOVs, minimal glycemic effects were observed. While these results appear promising, GI tolerability remained the limiting factor for the MR formulation. PF-04620110 was safe and well tolerated at the low dose of 5 mg QD while the 5 mg BID was identified as the maximum tolerated dose (MTD) with an increase in GI-related AEs and diarrhea severity.

Mean Observed Values for Triglycerides on Day 14



2394-PO

Metabolism of Insulin Glargine at Steady-State after S.C. Injection of Therapeutic and High Dose of Glargine in Subjects With Type 2 Diabetes Mellitus

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Previous studies showed that after subcutaneous (s.c.) injection of insulin glargine (GLA), GLA undergoes cleavage of the di-arginine in 30-B position with formation of metabolite 1 (M1) and subsequent loss of threonine (30-B) (metabolite 2, M2). Aim of the present cross-over study was to establish metabolism of GLA after s.c. injection of therapeutic and also high doses of GLA in T2DM subjects on long-term use of GLA. Ten subjects were studied during 24 h of fasting after s.c. injection of 0.4 and 0.8 U/kg GLA in the morning (at 10.00 h, 2 separate occasions, euglycemic clamp). Blood samples were taken to measure plasma concentrations of GLA, M1 and M2 over 24 h period by a specific liquid chromatography tandem mass spectrometry (LC/LC-MS method). Results of 6 subjects (age 66±7 yrs, diabetes duration 17±11 yrs, BMI 28.1±4.3 kg/m^2, A1C 7.3±0.9%) are presented as area under curve (AUC) and C_{max} of GLA, M1 and M2.

	AUC*		Cmax*
	pmol·h·L^{-1}	%*§	pmol·L^{-1}
Glargine (0.4 U/Kg)	97 (0;408)	4.8 (0;16.3)	20 (0;48)
Glargine (0.8 U/Kg)	286 (102;679)	10 (2.5;15.7)	43 (22;61)
M1 (0.4 U/Kg)	1893 (1727;2283)	95.2 (83.7;100)	105 (95;130)
M1 (0.8 U/Kg)	3470 (2400;4070)	90 (84.2;97.5)	176 (129;218)
M2 (0.4 U/Kg)	0 (0;0)	0 (0;0)	0 (0;0)
M2 (0.8 U/Kg)	0 (0;7)	0 (0;0.1)	0 (0;14)

*median (*25*%; 75% percentiles); § percentages of total insulin AUC (sum of Glargine, M1 and M2) The results confirmed that also on long-term use of GLA, even after high doses (0.8 U/kg) of GLA, GLA and M2 are barely present in plasma, and that GLA is nearly totally metabolized to the active metabolite M1. M1 represents 95 and 90% and GLA only 5 and 10% of the s.c. injected GLA (0.4 U/kg and 0.8 U/kg, respectively) in T2DM.

2395-PO

Insulin Degludec Results in Consistently Lower Rates of Nocturnal Hypoglycemia Despite Lower FPG Levels Compared to Insulin Glargine in Seven Trials With T1DM or T2DM

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Basal insulin analogs have a reduced risk of hypoglycemia compared to NPH insulin but hypoglycemia remains a major impediment to achieving recommended FPG targets. Insulin degludec (IDeg), a new basal insulin that forms soluble multi-hexamers after sc injection has an ultra-long and stable glucose-lowering effect, with low day-to-day variability. These properties may lead to less nocturnal hypoglycemia. We investigated the relationship between FPG and nocturnal confirmed hypoglycemia from all phase 3a, randomized, treat-to-target (FPG <90 mg/dL; <5 mmol) clinical trials in which once-daily IDeg and insulin glargine (IGlar) were compared. Trials (T1DM: 2 trials [n=957]; T2DM: 5 trials [n=3360]) were open-labeled and 26 or 52 weeks in length. Confirmed hypoglycemia was defined as PG <56 mg/dL (3.1 mmol/L) or severe episodes requiring assistance, and nocturnal hypoglycemia occurring between 00:01 and 05:59. For all trials (7 out of 7), mean end-of-trial FPG levels were consistently lower for IDeg than IGlar, reaching statistical significance in 3 trials (Table). Similarly, IDeg was associated with a 23-40% lower rate of nocturnal confirmed hypoglycemia relative to IGlar, which was statistically significant in 4 out of 7 trials, regardless of type of diabetes or background therapy. In conclusion, while once-daily IDeg treatment achieves consistently lower FPG levels compared to IGlar it is also associated with reduced rates of nocturnal confirmed hypoglycemia in individuals with T1DM and T2DM.

Trial ID	Patients	Number Randomized (n)		Mean EOT FPG (mg/dL)		Nocturnal Hypoglycemia	
		IDeg	IGlar	IDeg	IGlar	Rate Ratio (IDeg/IGlar)	95% CI
3579	T2DM (BOT)	773	257	106.2	114.7*	0.64*	[0.42; 0.98]
3672	T2DM (BOT)	228	229	105.7	113.1*	0.64	[0.30; 1.37]
3586	T2DM (BOT)	289	146	99.9	101.8	0.62	[0.38; 1.04]
3668	T2DM (BOT)	229†	230	105.3	112.1*	0.77	[0.44; 1.35]
3582	T2DM (BB)	744	248	121.7	127.3	0.75*	[0.58; 0.99]
3583	T1DM (BB)	472	157	141.1	149.0	0.75*	[0.59; 0.96]
3770	T1DM (BB)	164†	164	149.4	151.3	0.60*	[0.44; 0.82]

†Given once-daily in a compulsory, rotating morning and evening dosing schedule, creating 8-40 h intervals between doses; *Significant (95% CI excluding 1); BOT, basal oral therapy; BB, basal bolus therapy; EOT, end-of-trial.

Supported by: Novo Nordisk A/S

2396-PO

WITHDRAWN

2397-PO

Dapagliflozin Is More Effective than Glipizide in Achieving the Composite Outcome of Glycemic Control, Weight Reduction, and Lack of Hypoglycemia

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Management of diabetes often results in trade-offs between glycemic control and untoward effects of weight gain and hypoglycemic events. Dapagliflozin (DAPA), a selective SGLT2 inhibitor, reduces hyperglycemia and body weight with a low risk of hypoglycemia by increasing urinary glucose excretion in an insulin-independent manner. Key results of a randomized, double-blind trial (NCT00660907) of DAPA (up to 10 mg/d, n=400) vs glipizide (GLIP, up to 20 mg/d, n=401) as add-on therapies to metformin (MET, median 2000 mg/d) in subjects with T2DM inadequately controlled on MET (mean baseline HbA1c 7.72%), have been published elsewhere. This post-hoc analysis assessed proportion of subjects achieving the clinically relevant composite endpoint HbA1c <7%, no major or minor hypoglycemic (hypo) events and weight loss ≥ 3%. Proportion with HbA1c <7% at 52 weeks (LOCF) was evaluated; subjects with HbA1c <7% at baseline were excluded (21% in DAPA + MET [84/400] arm and 19% in GLIP + MET [78/401] arm). Major/minor hypo events included those with onset on/after first date of double blind treatment and on/prior last day of ST treatment + 4 days. Proportion of patients with total body weight reduction of ≥ 3% from baseline to week 52 LOCF was calculated. Confidence intervals (CI) for the difference between study arms were calculated using the exact method. At 52 weeks, the composite endpoint was achieved by 20.6% of subjects in the DAPA + MET arm (65/316) versus 1.9% in the GLIP+MET (6/323) arm. The difference of DAPA +MET versus GLIP+MET was 18.7% (95% CI: 14.3%, 23.8%). In summary, more subjects treated with DAPA + MET achieved the composite endpoint of HbA1c <7%, ≥3% weight loss, and lack of hypoglycemia at 1 year compared with subjects receiving GLIP + MET. These results demonstrate that DAPA, with its non insulin-dependent mechanism of action as well as glucosuric effect, can positively impact key treatment parameters while avoiding hypoglycemia.

Supported by: Bristol-Myers Squibb/AstraZeneca

2398-PO

Topical Administration of Allogeneic Mesenchymal Stem Cells Seeded in a Collagen Scaffold Augments Wound Healing and Increases Angiogenesis in the Diabetic Ulcer

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Non-healing diabetic foot ulceration is the most frequent reason for hospitalization in people with diabetes. Topically applied mesenchymal stem cells (MSCs) are an attractive novel treatment to augment diabetic wound healing. We hypothesized that topically applied allogeneic MSCs increase wound healing and support angiogenesis. Allogeneic non-diabetic bone-marrow derived MSCs were seeded in a type 1 collagen scaffold. The cells were applied topically to a full thickness cutaneous wound in the alloxan-induced diabetic rabbit ear ulcer model using a dose escalation strategy. The experiments were performed under license with ethics committee approval. The groups included: untreated wounds, collagen scaffold alone, collagen seeded with 50,000, 100,000 or 1,000,000 MSCs. Percentage wound closure after 1 week was assessed using wound tracings. Diabetic wound neovasculature was analyzed using stereology. 1,000,000 MSCs demonstrated significantly increased percentage wound closure when compared to untreated wounds. Collagen and MSC seeded collagen scaffolds demonstrated increased blood vessel density and decreased radial diffusion distance when compared to controls. Blood vessels were longer and more convoluted in wounds treated with collagen seeded with 1,000,000 MSCs. Allogeneic non-diabetic MSCs seeded in a collagen scaffold demonstrate augmented cutaneous wound healing in a pre-clinical model. Collagen and collagen seeded with MSC treatments result in increased angiogenesis when compared to untreated wounds but augmented wound healing was observed only at higher cell doses. This biomaterial mediated MSC therapy leads to augmented wound healing with increased angiogenesis, which is a central patho-physiological deficit in the non-healing diabetic foot ulcer.

Supported by: Molecular Medicine Ireland

2399-PO

Improved Glycemic Control With Stepwise Introduction of Insulin Analog Mixture in Type 2 Diabetic Patients

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This multicenter, open-label post-marketing clinical study assessed the efficacy and safety of the stepwise introduction of insulin lispro mixture-50/50 (LM50/50) in type 2 diabetes mellitus (T2DM) patients suboptimally controlled with oral antidiabetic drugs. All patient started 16 weeks of treatment QD, the frequency of injection was increased to BID if the patient could not achieve HbA1c <6.9%, and then to TID if the patient could not achieve HbA1c <6.9% after 16 weeks of treatment BID. Following that, 91 patients still had not achieved HbA1c <6.9% after 16 weeks of treatment BID. Study was completed by 116 patients, 19 patients discontinued. The most common reason for discontinuation was physician decision (36.8%), followed by patient decision (26.3%). Final insulin regimen was QD in 9 patients, BID in 21 patients and TID in 91 patients. At endpoint (48 weeks), 25 patients (18.5%) achieved HbA1c <6.9%, and 71 patients (52.6%) HbA1c <7.4%. HbA1c significantly decreased from baseline to endpoint by 1.27±0.98% (p<0.0001, t-test). In 7-point self-monitoring of blood glucose levels, decreases from baseline at all points were observed. These decreases were especially marked after breakfast and after dinner. Body weight increased from baseline to endpoint by 1.28±3.14 kg (p<0.0001, t-test). At endpoint, patients on QD, BID, and TID received 7.14±3.17, 12.45±6.30 and 22.41±14.29 units/day of insulin, respectively. The most frequent treatment-emergent adverse event was nasopharyngitis (32.6%, 44/135 subjects), followed by upper respiratory tract inflammation (8.9%, 12/135 subjects). The incidence of hypoglycemia episodes was 65.9% (89 subjects, 535 episodes), most of which occurred during daytime. Five severe hypoglycemia episodes (3 patients) were reported during the study. In conclusion, over 48 weeks, stepwise introduction of LM50/50 may be one treatment option, because it is simple with favorable safety for good glycemic control in T2DM patients.

2400-PO

Evaluating Overall Glycemic Management of People With Type I Diabetes in the U.S.

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Glycemic management of people with T1DM in the US was evaluated using the Ingenix Impact National Managed Care Database that includes medical and pharmacy history of > 60 million US people. People were identified who had new onset or chronic diabetes plus continuous medical and prescription benefit coverage during the 12 months before (baseline) and 12 months after (follow-up) the first date of diagnosis recorded in the study period (1/1/2007 to 6/30/2009). People with T1DM were identified by a diagnosis of diabetic ketoacidosis (ICD-9 code 250.1x) or by having ≥ 1 inpatient primary or secondary diagnoses or ≥ 2 outpatient primary or secondary diagnoses of T1DM (ICD-9 code 250.x1 or 250.x3) without any T2DM diagnoses. People with insulin resistance diagnoses were excluded to ensure inclusion of only T1DM. T1DM patients were further required to have A1C results from the database. Study measurements included demographic and clinical variables, insulin usage patterns, co-medications, laboratory test results, hypoglycemia, and hospital and emergency room (ER) visits. A total of 2558 people were identified (47.9% female, mean [SD] age of 40.1 [17.5] y). Comorbidities included hyperlipidemia (45.4%) and hypertension (39.9%). Co-medications included multiple classes of antihypertensives (10.7-52.8%) and statins (18.8%). At diagnosis, basal, prandial and premix insulin were taken by 51.5, 64.0 and 11.1% of people, respectively. Mean (SD) follow-up A1C was 8.3 (1.9) %. Other data is shown in table. Our analysis of subjects with T1DM in the US showed that mean A1C levels one year after diagnosis are well above the recommended target goal of < 7%.

For author disclosure information, see page 797.

	Follow-up: % of Patients
Insulin type	69.3
Basal	80.8
Prandial Premix	12.4
Hypoglycemia	18.1
ER-treated, % of hypoglycemia	31.4
Hospital inpatient, % of hypoglycemia	9.1
Hospitalizations, any cause	28.4
Diabetes-related, % of any cause	89.3
Diabetes as primary cause, % of any cause	51.9
ER visits	38.0
Diabetes-related, % ER visits	69.2
Diabetes as primary cause, % ER visits	37.9

ER, emergency room

Supported by: sanofi-aventis

2401-PO

Postprandial Proinsulin / Insulin Ratio in Non-Diabetic Controls and in Type 2 Diabetic Patients According to Different Pharmacolgical Interventions

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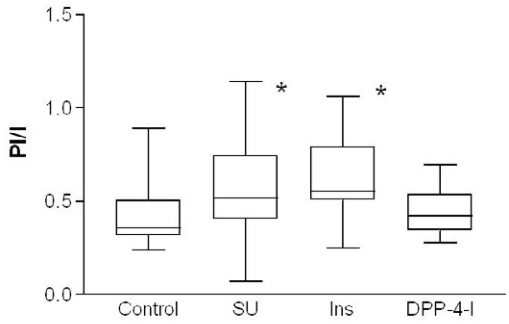
Type 2 diabetes mellitus is characterized by insulin resistance and a decline in beta-cell function. This exploratory study recruited 65 patients with T2DM and 17 non-diabetic controls subjects (Con). Eligible T2DM patients had been treated for ≥ 6 mo with insulin glargine (Ins), sulfonylureas (SU), or DPP-4 inhibitors (DPP-4-I) in addition to maximal tolerated metformin. All study subjects underwent a standardized test meal with a 5 hour postprandial monitoring of BG, Insulin and proinsulin levels. For statistical analysis the area under the curve (AUC_{0-5}) was calculated.The Con were 64.9 ± 6.3 years in age, and presented with a BMI of 27.1 ± 3.7 kg/m² (mean ± SD), while the T2DM patients were 64.5 ± 7.4 years old with a BMI of 30.9 ± 2.9 kg/m². As shown in table 1, postprandial blood glucose excursions were comparable in between the diabetic groups and were significantly higher compared with controls. Insulin and proinsulin levels were highest in the SU group compared with all other groups. Compared to controls, the Proinsulin/ Insulin ratio was increased in the Ins and the SU group but not in the DPP-4-I group (figure 1). Treatment with DPP-4-I revealed most physiological pp beta cell function.

Postprandial AUC for BG, insulin and Proinsulin (mean / SD; * = p<0.05 vs. control))

	Ins	SU	DPP-4-I	Controls
AUC BG (mmol/l)	1799 / 280 *	1807 / 282 *	1736 / 394 *	1079 / 133
AUC Ins (pmol/l)	72026 / 68983	109916 / 60079 *	72920 / 33688 *	47201 / 20668
AUC Proinsulin (pmol/l)	4933 / 2070 *	9003 / 4348 *	4428 / 2115	2466 / 698



2402-PO

WITHDRAWN

2403-PO

Efficacy and Safety of Liraglutide in 195 Patients With Type 2 Diabetes in India: A Retrospective Analysis

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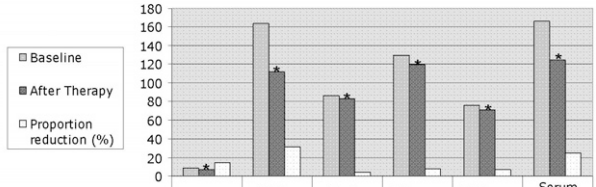
We evaluated efficacy and safety of liraglutide in Indian patients with type 2 diabetes mellitus (T2DM) at a Diabetes Research Center in South India in real-life situation. We retrospectively analyzed case records of 195, T2DM patients (male: 108; female: 87) receiving liraglutide therapy for at least 6 months. Patients were followed up weekly via Diabetes Tele Management System (DTMS®) by a multidisciplinary team of doctors, dietitians, nurses etc. The mean age, weight and mean duration of T2DM were 45.87 years, 86.41 kg and 6.48 years respectively. Liraglutide was administered as 1.8mg OD in addition to prior oral antidiabetic drugs/insulin or both along with other medications for coexisting disorders. With 6 months of liraglutide therapy, significant reduction in glycemic and non-glycemic parameters were noted (Figure 1). Total 49.23% and 37.95% patients achieved HbA1c

For author disclosure information, see page 797.

reduction <7% and <6.5% respectively. Weight loss ≥ 10 kg was noted in 7.18% patients. Twenty two (11.28%) patients reported adverse events (AE), most common (>1%) being vomiting (3.08%); tiredness (2.05%); loose motion (1.54%); nausea, flatulence, headache, giddiness (all 1.03%). All were mild to moderate & none were hospitalized. 3.08% patients withdrew due to AE. Liraglutide is relatively new addition to existing antidiabetic therapy with a multitude of benefits. In selective Indian T2DM patients it provides significant improvement in glycemic control, reduction in body weight, blood pressure, cholesterol and is well tolerated.

Figure 1: Improvement in glycemic and non-glycemic parameters with Liraglutide therapy



	HbA1c, %	FPG, mg/dL	Body weight, kg	SBP, mm of Hg	DBP, mm of Hg	Serum Cholesterol, mg/dL
Baseline	8.14	163.81	86.41	129.31	76.18	166.68
After Therapy	6.96	111.6	82.37	119.59	70.88	124.86
Proportion reduction (%)	14.50	31.87	4.68	7.52	6.96	25.09

FPG: Fasting plasma glucose; SBP: systolic blood pressure; DBP: Diastolic blood pressure; * p significant compared to baseline value

2404-PO

Vildagliptin is Effective in Subjects With Diabetes Recurrence after Gastrointestinal (GI) Bypass Surgery

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New studies have been developed in mildly obese diabetic subjects in order to evaluate safety and efficacy of metabolic surgery for glycemic control. One of the first procedures performed was the duodenal exclusion (DE). We have studied 33 TDM2 subjects with less than 10 y of DM history and fasting C peptide over 1.0 ng/dl (inclusion protocol criteria) submitted to DE that did not achieve glycemic control 3 months after surgery. Preoperatively, Group 1 was taking oral antidiabetic drugs (18 subjects) and group 2 was under oral drugs and insulin (15 subjects). The goal of this study was to compare the efficacy of the association of vildagliptin and metformin in subjects with presumedly the worst (group 2) or the best (group 1) β cell function. Initially, an optimized metformin doses (1.0 g BID) was employed in group 1 and the association 100 mg of vildagliptin and an optimized metformin doses was used in group 2. HbA1c was evaluated at baseline and at 3, 6, 9 and 12 months of treatment. As a result, the pharmacogical intervention in group 1 presented the same efficacy in the decrease of A1c when compared (ANOVA) to group 2 after 12 months of treatment (8.3% SD 2,0 X 7.2% SD 2,1; p=0,761). Anova repeated measures showed that there is no difference of vildagliptin efficacy in all follow up time points. Patients are responders since the DPP IV inhibitor introduction. The use of metformin and vildagliptin can be an effective tool to treat subjects submitted to DE that fail to achieve early glycemic control, once even the patients with a presumed worst β cell function had a decrease in A1c after 1 year of treatment with this association, probably due to a synergistic effect on improving the GLP1 secretion that happens after any GI rerouting surgical intervention.

2405-PO

WITHDRAWN

2406-PO

Metformin Represents a Promising Treatment Modality for Diabetic Encephalopathy

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Diabetic patients commonly develop cognitive impairment, defined as diabetic encephalopathy, which is involved in increased neuronal apoptosis and impaired adult neurogenesis in the hippocampal regions, followed by hippocampal atrophy. Recently, metformin has been shown to protect against neuronal apoptosis and to normalize impaired adult neurogenesis in the hippocampal regions. Therefore, *in vivo* and *in vitro*, the neuroprotective effect of metformin against diabetic encephalopathy was investigated. We compared hippocampal atrophy between 400 type 2 diabetic patients and 400 control subjects, and determined the important factors affecting hippocampal atrophy using VSRAD. *In vitro*, rat pheochromocytoma cells used commonly as neuronal cell models were exposed to 25mM glucose and/or 1mM MG with/without biguanides (100 μM metformin, 200 μM phenformin), or, 2 mM AICAR (an AMP kinase activator). Additionally, by using immunohistochemistry method, we investigated whether the number of progenitor cells or young neurons in the hippocampal regions was influenced by treatment with metformin. Diabetic patients with poor glycemic control, and marked glycemic fluctuation were associated with hippocampal atrophy, while the use of metformin was negatively associated with hippocampal atrophy. *In vitro*, oxidative stress triggered PTP opening, cytochrome *c* release, BcL-2 downregulation, caspase-9 and -3 activation, and cell apoptosis. Biguanides or AICAR protected against oxidative stress-induced apoptosis through inhibiting PTP opening, cytochrome *c* release and caspase-9 and -3 activation. We also found an increase in progenitor cells or young neurons in the hippocampal regions after metformin treatment. In conclusion, metformin treatment may prevent hippocampal atrophy through protecting neuronal apoptosis and increasing neural stem/progenitor cell proliferation in the hippocampal regions, and thus represent a promising treatment modality for diabetic encephalopathy.

2407-PO

Anthropometric and Metabolic Effects of Long-Acting Insulin Analogues in Young Children: Randomized Cross-Over Study

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We evaluated the effects of long-acting insulin analogues, glargine and detemir, on body weight and metabolic control in young children with type 1 diabetes. A 24-week, randomized, open label, two-period, cross-over study comparison between bedtime glargine and twice-daily detemir was performed. Sixteen children with type 1 diabetes on MDI treatment (Male: 8; age: 8.6±1.6 years; BMI 18.4±2.0 kg/m2; A1C 6.98±0.49%; duration of diabetes: 4.21±1.5 years; mean±SD) were randomized to first receive either insulin glargine (once a day) or detemir (twice a day) for 12 weeks. A run-in period for 8 weeks was performed with the purpose to achieve an A1c below 7.5%. On both occasion meal boluses with insulin glulisine were delivered according to CHO counting. Data were analyzed using repeated-measures ANOVA via generalized hierarchical linear models. A greater weight gain was observed during detemir treatment (31.79→33.37Kg, mean values) than with glargine (32.06→32.24Kg, mean values) p=0,0076; BMI was similar in both groups.

For author disclosure information, see page 797.

Fasting blood glucose (BG) was lower in glargine group (146,8±7,3mg/dL; mean±SE) than in detemir (167,4±7,3mg/dL; mean±SE), p=0,0104. Glucose variability (SD of BG levels) and A1c did not differ between the two treatment groups. Total daily insulin dose increased during detemir treatment from the beginning to the end of the study (0.35±0.1 vs 0.47±0.2U/Kg/die, mean±SD; p <0,0001). In conclusion, long-acting insulin analogues were both effective for maintaining a good glucose control. Fasting plasma glucose was better with insulin glargine and furthermore insulin glargine has the advantage that can be given once a day. In our study the treatment with detemir was associated with a weight gain without changing of BMI, suggesting a high growth rate of these young children. Further studies are needed to elucidate the effects of long-acting insulin analogues on growth.

2408-PO

Luseogliflozin (TS-071) a Novel, Potent and Selective SGLT2 Inhibitor, Did not Affect the PK of Several Oral Diabetic Agents in Clinical

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The combination therapy is an important factor for oral diabetic agents, therefore, drug-drug interaction is critical for drug development in this area. The objective of this study was to evaluate the potential pharmacokinetic interactions between Luseogliflozin (LUSEO) and several oral hypoglycemic agents alone and in combination in healthy volunteers. As typical oral hypoglycemic agents or expected combination drugs, glimepiride, metformin, pioglitazone, voglibose and sitagliptin were selected. The trial design for glimepiride, metformin and sitagliptin were open-label, 3-way crossover. The design for pioglitazone and voglibose were open-label, add-on effect of repeat dosing. Plasma concentration of unchanged compounds (LUSEO, glimepiride, metformin, pioglitazone, sitagliptin) and active metabolites of pioglitazone were determined using LC/MS/MS. Lack of interaction was defined as the ratio of geometric mean (GMR) and 90% CI for combination:monotherapy being within the range of 0.80-1.25. Although co-administration of LUSEO and pioglitazone had a small effect on the pharmacokinetics thus 16% increase in LUSEO Cmax (GMR 1.16, 90% CI 1.04-1.30) with 6% decrease in LUSEO AUC (GMR 0.94, 90% CI 0.90-0.98), 12% decrease in pioglitazone Cmax(GMR 0.88, 90% CI 0.75-1.05) with 10% decrease in pioglitazone AUC(GMR 0.90, 90% CI 0.77-1.04), the changes were within the range. Thus the clinical drug interaction trials suggest that LUSEO could be coadministered with several oral hypoglycemic agents without any dose adjustment for either agent.

Coadministered drug	LUSEO exposure		Coadministered drug exposure	
	GMR (Coadmin/Mono)	95% CI	GMR (Coadmin/Mono)	95% CI
glimepiride	1.00	0.98-1.03	1.07	1.04-1.10
metformin	0.99	0.96-1.01	1.04	0.95-1.14
pioglitazone	0.91	0.87-0.95	0.90	0.77-1.04
voglibose	1.00	0.96-1.04	NA	NA
sitagliptin	0.99	0.95-1.03	1.03	1.01-1.05

2409-PO

Effects of Rifampin and Mefenamic Acid on the Pharmacokinetics and Pharmacodynamics of Dapagliflozin

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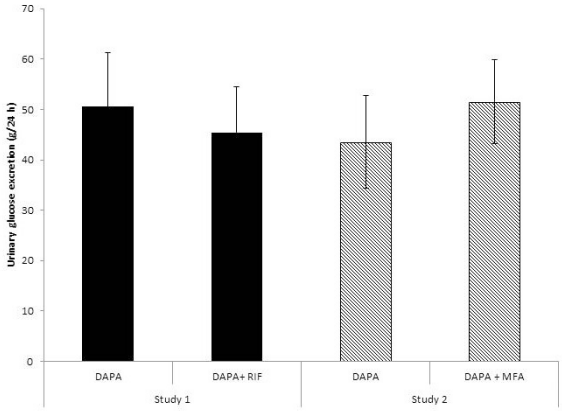
Dapagliflozin (DAPA) is a selective SGLT2 inhibitor that decreases serum glucose by promoting urinary glucose excretion (UGE). DAPA is primarily metabolized via the uridine diphosphate-glucuronosyltransferase (UGT)1A9 pathway to its major inactive metabolite, dapagliflozin 3-O-glucuronide. Here, the results of 2 open-label, nonrandomized, single-sequence studies are reported in which the effect of 2 potential UGT1A9 modulators, rifampin (RIF - a pleiotropic drug-metabolizing enzyme inducer; study 1) and mefenamic acid (MFA - a strong UGT1A9 inhibitor; study 2), on the PK and PD (assessed by UGE) of DAPA in healthy subjects were evaluated. In study 1, 14 subjects received DAPA 10 mg alone and in the presence of RIF 600 mg QD (6 days). In study 2, 16 subjects received DAPA 10 mg alone and in the presence of MFA 250 mg q6h (5 days). RIF reduced total exposure ($AUC_{0\text{-}inf}$) of DAPA by 22% and MFA increased DAPA $AUC_{0\text{-}inf}$ by 51% (Table). No clinically meaningful effect of RIF or MFA on the peak exposure (C_{max}) or T½ of DAPA or on DAPA-mediated UGE (Figure) was observed. In conclusion, modest changes in DAPA exposure were seen with RIF and MFA with minor changes in UGE; none were considered clinically meaningful.

	Study 1			Study 2		
DAPA PK parameters	DAPA	DAPA + RIF	Ratio of geometric means (90% CI)	DAPA	DAPA + MFA	Ratio of geometric means (90% CI)
Geometric mean C_{max} ng/mL	147	136	0.931 (0.799, 1.112)	148	167	1.13 (1.03, 1.24)
Geometric mean $AUC_{0\text{-}inf}$ ng·h/mL	554	432	0.780 (0.731, 0.832)	539	813	1.51 (1.44, 1.58)
Mean T½ h (SD)	12.8 (4.9)	11.4 (5.9)		12.7 (5.2)	13.7 (5.6)	



Supported by: AstraZeneca/Bristol-Myers Squibb

2410-PO

The Efficiency and Safety of Sitagliptin in Diabetes: A Systematic Review

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Sitagliptin, a dipeptidyl peptidase-4 inhibitor, is now widely used in diabetes patients. We aimed explore its efficiency and safety in the method of systematic review. We systematically searched CCTR (3rd issue, 2011) and MEDLINE (1950-2011), and collected all randomized controlled trials of sitagliptin in diabetes patients, with follow-up duration longer than 12 weeks. Twelve trials were finally included. Compared with placebo, sitagliptin can reduce HbA1c (overall MD, -0.70%; 95%CI, -0.80~-0.60%; P<0.00001) and fasting plasma glucose (overall MD, -20.32mg/dL; 95%CI, -23.82~-16.82mg/dL; P<0.00001). But compared with other oral hypoglycemic agents (OHAs, including metformin, glipizide, voglibose, liraglutide, saxagliptin, pioglitazone, and rosiglitazone), sitagliptin had similar effect on HbA1c (overall MD, 0.04%; 95%CI, -0.18~0.26%) and fasting plasma glucose (overall MD, 3.68mg/dL; 95%CI, -8.16~15.52mg/dL). Sitagliptin could significantly lower the triglyceride level compared with placebo (overall MD, -18.89mg/dL; 95%CI, -28.84~-8.94mg/dL) but not other OHAs (overall MD, -3.42mg/dL; 95%CI, -8.73~1.88mg/dL). However, no obvious effects on total cholesterol, HDL-c, and LDL-c were found compared with either placebo or other OHAs. Compared with placebo, sitagliptin had higher incidence of all adverse events (overall RR, 1.08; 95%CI, 1.01~1.17) and hypoglycemic events (overall RR, 2.05; 95%CI, 1.30~3.21), while compared with other OHAs, it had lower risk of all adverse events (overall RR, 0.93; 95%CI, 0.88~0.97), hypoglycemic events (overall RR, 0.45; 95%CI, 0.22~0.93), upper respiratory infections (overall RR, 0.50; 95%CI, 0.28~0.89), and diarrhea (overall RR 0.63; 95%CI, 0.42~0.94). No significant differences were found in all cause mortality, myocardial infarction, pancreatitis, and other adverse events. In conclusion, sitagliptin is an effective and safe OHA in diabetes treatment with some triglyceride level lowering effect.

2411-PO

Comparison of Physician Practice Patterns for Older Adults compared to NHANES Medicare Cohort of T2DMs on Oral Therapy

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The results of a physician survey were contrasted to data from the National Health and Nutrition Examination Surveys (NHANES) to identify potential gaps in therapy for diabetes. Physician diabetes specialists at the Joslin Diabetes Center were surveyed on their treatment preferences/patterns. NHANES data (2001-08) were analyzed to identify diabetic patients and evaluate disease prevalence, comorbidities and glycemic control (HbA_{1c}<7.0 %).

The association (logistic regression) between sociodemographics, comorbidities, glycemic control, and use of combination vs monotherapy was examined. Comorbidities in NHANES are similar to those reported by physicians: hypertension, hyperlipidemia and dyslipidemia. Physician survey results were contrasted with NHANES for older adults (>45-<65yo) and elderly (≥65yo). Physicians (n=15) reported treating younger (18-45 yo) and older adult diabetic patients more aggressively than elderly patients, expecting younger cohorts to reach goal more effectively. The elderly are treated more conservatively than older adults, to avoid serious side effects. NHANES reported highest glycemic control in the elderly. In each age group (not younger adults), control increased from 2001-06 to 52.5% (243/511), but dropped in 2007-08 to 47.1% (349/761). Physician survey and NHANES report those with poor glycemic control more often placed on combination (vs mono) therapy; physicians see combination therapy as a tool to get patients to goal. Combination therapy in NHANES was significantly associated with education (OR 1.858, P 0.013), obesity (OR1.879, P<0.001), and long history of diabetes (OR 1.026, P 0.025). Surveyed physicians report treating younger, older and elderly adults with differing levels of conservative vs. aggressive approach. Glycemic control reported in NHANES has declined in recent years. Both NHANES and physician surveys highlight the need for safe options when escalating diabetes therapy.

Supported by: Takeda Pharmaceuticals

2412-PO

The Biological Behaviors of Rat Dermal Fibroblasts can be Inhibited by High Levels of mmp9

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Aims:Studies show that increased matrix metalloproteinase 9 (MMP9) in diabetic skin contributes to skin vulnerability and refractory foot ulcers. Changes of biological behaviors of skin fibroblasts were observed in this study to investigate the mechanisms of MMP9 in diabetic foot ulcers healing. Methods: Fibroblasts were seperated into three groups: the control, MMP9 group treated with a final concertration 22.0mmol/L glucose and 100μmol/L homocysteine, TIMP1 group which were treated with 22.0mmol/L glucose, 100μmol/L homocysteine and 100μg/L TIMP1. Realtime PCR, ELISA and Gelatin zymography were used to detect the expression of mRNA, protein and the activity of MMP9. Flow cytometry and CCK-8 were used to detect cell proliferation and viability. ELISA assay was used to detect collagen secretion. Scratch test and transwell were used to evaluate horizontal and vertical migration of cells. Results: The levels of MMP9 mRNA and protein in high MMP9 group and TIMP1 group had no statistically difference, but both of them higher than that in control group (P<0.01). The activity of MMP9 protein in high MMP9 group was much higher than those in control group and TIMP1 group (P<0.01). Compared with control group, cells in high MMP9 group had decreased proportion of S phase cells (6.54% vs 9.31%), proliferation index (11.3% vs 13.8%), cell viability (1.35 vs 1.76), collagen secretion (352.8 pg/ml vs 1126.4 pg/ml), horizontal migration rate (21.3% vs 38.7%) and vertical migration cells (71.2 vs 90.6, all P<0.01). After interfered by TIMP1, the proportion of S phase cells (7.75%), proliferation index (12.5%), cell viability (1.64), collagen secretion (828.6 pg/ml), horizontal migration rate (31.5%) and vertical migration cells (85.3) were increased compared with high MMP9 group (P<0.05 or P<0.01). Conclusions:The biological behaviors of skin fibroblasts with high expression of MMP9 were inhibited, and the inhibited effect can be decreased by TIMP1.

2413-PO

Using Computerized Provider Order Entry to Safely Initiate Inpatient Subcutaneous Insulin Therapy

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Background: Although insulin is the preferred treatment for hyperglycemia in the hospital setting, timely initiation remains an ongoing challenge. The primary aim of this study is to evaluate a comprehensive yet simple to use computer-based provider order entry (CPOE) system that auto-calculates initial basal and bolus insulin doses for inpatients in non-critical care. Methods: Five subcutaneous insulin order sets were launched in November, 2010 that provided starting doses based on patient weight and expected sensitivity to insulin during acute illness. Data was obtained from point of care blood glucose (BG) tests to calculate population, patient-day and patient-stay means. Descriptive statistics were used to compare mean rates of hypo and hyperglycemia on adult non-critical care inpatient units in a 1000 bed academic medical center. Results: There was a significant decrease in hypoglycemia in the population studied from 1.35% in 2010 to 1.12% in 2011. At the same time, BG tests in range decreased significantly from 74.19% in 2010 to 71.04% in 2011. BG tests above 200 mg/dl increased significantly from 24.47% in 2010 to 27.85% in 2011. Conclusions: Findings suggest that utilizing an electronic insulin order set is an effective strategy to initiate insulin therapy and lower rates of hypoglycemia in the hospital setting. The decline of results in the target range and increased rates of hyperglycemia may be due to overly conservative initial dose calculations and lack of electronic support to titrate doses as needed. Future research should include an automated titration system to facilitate timely dose adjustments.

Year by BG (Population)				
Year	BG 0-69 mg/dl	BG 70-199 mg/dl	BG > 200 mg/dl	Total Tests
Jan - Oct 2010	993 (1.35%)	54669 (74.19%)	18030 (24.47%)	73692
Jan - Oct 2011	781 (1.12%)	49723 (71.04%)	19490 (27.85%)	69994
p-value	0.0001	<0.0001	<0.0001	143686

2414-PO

Pharmacokinetic and Pharmacodynamic (PK-PD) Modeling of the Effect of an SGLT2-Selective Inhibitor, Tofogliflozin (TOFO), on Renal Glucose Excretion in Rats

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In order to understand the in vivo inhibitory mechanism and to design the most suitable pharmacokinetic profile of an SGLT inhibitor for diabetes treatment, a mechanism-based PK-PD model which considers the different functions of both SGLT1 and SGLT2 would be useful. Thus, we developed a mechanism-based PK-PD model for SGLT inhibitors as follows. First, using the relationship between renal glucose clearance and plasma glucose level in SD rats and data on glucose affinity obtained from in vitro rat brush border membrane vesicle experiments, a PD model analysis was performed based on a nonlinear parallel tube model to express the renal glucose transport mediated by SGLT1 and SGLT2. In the model, the heterogeneous localization of SGLT1 and SGLT2 in the proximal tubule was assumed. This model suitably expressed the relationship between plasma glucose level and renal glucose excretion in rats. As a result of analysis, in vivo glucose transport capacities mediated by SGLT1 and SGLT2 were estimated. Next, a PK-PD model was developed to analyze the inhibitory effect of TOFO and an SGLT1/2 inhibitor, phlorizin (PHZ), on renal glucose reabsorption. The PK-PD analyses were performed using the plasma concentration-time profiles of both compounds and glucose, and the cumulative urinary glucose after iv bolus administration of compounds. The model suitably expressed the concentration-dependent inhibitory effect of TOFO and PHZ on renal glucose reabsorption in rats, and the in vivo rat inhibition constants of TOFO were estimated to be 18 nM for SGLT2 and 30,400 nM for SGLT1, and those of PHZ were 252 nM for SGLT2 and 67 nM for SGLT1, suggesting that the estimated in vivo inhibition constants were comparable to in vitro activities. In conclusion, the present PK-PD model was useful for expressing renal glucose movement including the inhibitory effect of SGLT inhibitors, moreover, could be applicable to predicting in vivo efficacy from in vitro data.

2415-PO

Clinical Outcomes of Elderly Patients Initiating Exenatide Twice Daily Compared to Insulin Glargine

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The safety and efficacy of exenatide twice daily (EBID) and insulin glargine (glargine) have been studied in clinical trials that included few elderly patients. This study examined the clinical effectiveness of EBID compared to glargine in large patient population of 65 years and older with type 2 diabetes treated in ambulatory care settings. A retrospective analysis was conducted using the General Electric electronic medical record database. Patients aged 65 years and older with type 2 diabetes who initiated EBID (n=1023) or glargine (n=2238) were identified between 1 November 2006 and 30 April 2009 with 12 months of pre- and post-index continuous eligibility. Propensity score matching (1:1) was used to balance baseline differences between the cohorts. The effectiveness endpoints were changes in A1C (primary endpoint), weight, body mass index (BMI), and blood pressure (BP). Matched cohorts were compared using paired t-tests and nonparametric tests as appropriate. The matched EBID and glargine patients (n=804 each) were comparable in their baseline characteristics, including age (70 vs. 71 years), female sex (55 vs. 55%), and diabetes-related complications (27 vs. 28%). In the 12-month follow-up period, EBID patients experienced significantly greater mean reductions than glargine patients in A1C (-0.49 vs. -0.22%, P<0.01), weight (-2.78 vs. -0.21 kg, P<0.01), BMI (-0.99 vs. 0.06 kg/m^2, P<0.01), and systolic BP (-2.22 vs. 1.03 mmHg, P=0.011). More EBID than glargine patients reached the A1C goal of <7% (54 vs. 43%, P<0. 01).

For author disclosure information, see page 797.

There were no significant differences in diastolic BP between the cohorts. The elderly patients initiating EBID experienced significant improvements in A1C, weight, BMI, and systolic BP compared to glargine-treated patients. This study suggested the differences in clinical effectiveness of EBID and glargine for treatment of type 2 diabetes in an elderly patient population treated in ambulatory care settings.

2416-PO

Levels of FPG and HbA1c Control and the Relationship to BMI in T2D Patients Treated With Basal Insulin and OAD Therapy

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The introduction of very long-acting basal human insulin analogues has led to an increased use of once-daily basal insulin injections alongside OAD therapy. This study investigates both HbA1c and FPG levels in T2D patients to assess any relationship between achieving HbA1c (<7%) and FPG (<140mg/dl) goals. BMI was calculated for each patient to see if there was any association with these levels of control. Data were drawn from the 2011 Adelphi Disease Specific Programme in T2D in the US and 5 EU countries. In all 350 Diabetologists / Endocrinologists and 500 Primary Care Physicians provided data for 6210 patients. As well as indicating therapies used, physicians were asked to provide demographic information including height / weight plus latest lab values for HbA1c, FPG etc. Chi-square was used to test for differences. 147 patients in the US and 334 in the EU received basal insulin +OAD, no GLP-1 or other insulin and had valid measures for HbA1c, FPG and BMI. Only 19% were well controlled on both measures, whilst 39% were not controlled on either measure. However, the largest group (40%) were controlled on FPG but not HbA1c. No differences were observed between the US and the EU. For BMI, the US and EU samples were analysed separately as mean BMI in the US was higher (32.8 v 28.4, p<0.0001). In the US, 67% of patients not controlled on either measure and 67% controlled on FPG but not HbA1c had a BMI >30 compared with 53% of those well controlled on both measures. In the EU, the proportions for each of these 3 groups were 32%, 30% and 25% respectively.A significant proportion (40%) of T2D patients treated with basal insulin and OAD therapy achieved FPG goal but not HbA1c. This implies that post-prandial glucose levels are poor, so it can be argued that in addition to basal insulin, these patients need agents that control post-prandial peaks in order to achieve their HbA1c goal. This imbalance is also associated with increasing BMI as is lack of control of both FPG and HbA1c, especially in the US.

2417-PO

Blood Glucose Lowering Effect of Tridax Procumbens in Individuals With Type 2 Diabetes

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Recent pre-clinical studies assessing the anti-hyperglycemic potential of *Tridax procumbens Linn* have shown significant glucose-lowering effects in animal models of diabetes. In this study we evaluated blood glucose lowering effects of *T. procumbens* in individuals with type 2 diabetes. An 'asava' (a hydro-alcoholic extract of *T. procumbens*), prepared according to Ayurveda guidelines, showed absence of microbial contamination, aflatoxins, and heavy metals. *T. procumbens* asava demonstrated significant inhibition of lipid peroxidation and strong antioxidant activity as indicated by higher trolox equivalent antioxidant capacity, ferric reducing antioxidant potential, DPPH free radical scavenging ability, hydrogen peroxide scavenging activity, and metal ion-chelating effect compared to butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), α-tocopherol, and curcumin. Following approval from the Kolhapur Independent Ethics Committee, India, 20 individuals diagnosed and treated for type 2 diabetes for 16 $\pm$ 8.0 years, were recruited from Kolhapur, India (10 men, 56 $\pm$ 7.8 years; 10 women, 61 $\pm$ 15.0 years). Patients were supplemented with 15 ml of *T. procumbens* asava, twice daily, for a period of 4-weeks, along with their anti-diabetic medication. Fasting blood glucose levels (Pre-treatment: 152.4 $\pm$ 34.09 mg/dl vs. Post-treatment: 128.5 $\pm$ 16.98) were significantly decreased following 4 weeks of asava supplementation. Further, 2-hour post-prandial blood glucose levels (Pre-treatment: 262.0 $\pm$ 75.16 vs. Post-treatment: 189.6 $\pm$ 41.98) were significantly decreased at the end of the 4-week study period. No side-effects or adverse events were reported. To our knowledge, this is the first clinical report of the anti-diabetic effect of *Tridax procumbens*. Our studies demonstrating strong antioxidant capacity and significant blood glucose lowering effect, suggest that *T. procumbens* asava can offer a complementary approach in the management of type 2 diabetes.

2418-PO

Sitagliptin-Treated Patients Are More Likely Than Sulfonylurea-Treated Patients to Meet the Goal of A1C < 7% Without Weight Gain or Symptomatic Hypoglycemia

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The utility of any antihyperglycemic agent is determined by the balance between its efficacy and safety. Sitagliptin (SITA) and sulfonylureas (SUs) both provide clinically meaningful reductions in glycemic parameters in patients (pts) with type 2 diabetes. SITA is generally weight neutral, and is associated with a low risk of hypoglycemia while SUs are associated with body weight gain (BWG) and an increased risk of symptomatic hypoglycemia (HYPO). BWG and HYPO may be more prominent in pts who achieve near-normalization of glucose control. In the present post hoc analysis, data were pooled from 3 randomized, double-blind studies in which pts with inadequate glycemic control (mean baseline A1C =7.6%) on diet alone or on metformin were treated with either SITA (n=972) or an SU (glipizide or glimepiride; n=982). At Week 25/30, the goal of A1C <7.0% was met by 565 (58.1%) and 622 (63.3%) of SITA- and SU-treated pts, respectively. Three safety parameters were assessed for pts meeting this goal: the proportion who had (1) no BWG, (2) no HYPO, and (3) neither BWG nor HYPO. For all 3 assessments the proportions of pts were significantly greater with SITA than with SU (all p<0.001; Table). Similar findings were observed when pts were subgrouped by age, <65 and ≥65 years. Patients who achieve the glycemic target of A1C <7% on SITA are more likely to do so without BWG or HYPO than pts who achieve this goal when treated with an SU.

Outcome	SITA % (n/N)	SU % (n/N)	Difference in % (95% CI)†	p-value†
No BWG	75.9 (423/557)	36.6 (225/614)	39.1 (33.8, 44.2)	<0.001
No HYPO	92.4 (522/565)	71.5 (445/622)	20.9 (16.7, 25.1)	<0.001
Neither BWG nor HYPO	69.7 (388/557)	26.9 (165/614)	42.7 (37.3, 47.7)	<0.001
<65 years	67.2 (295/439)	27.4 (133/486)	39.7 (33.6, 45.4)	<0.001
≥65 years	78.8 (93/118)	25.0 (32/128)	54.0 (42.6, 63.7)	<0.001

†Stratified by study.
The denominator for the "No HYPO" endpoint is the number of patients with A1C <7% at Week 25/30. The denominator for the "No BWG" and the "Neither BWG nor HYPO" endpoints is the number of patients with A1C <7% at Week 25/30 and with a body weight measurement at Week 25/30.

Supported by: Merck Sharp and Dohme Corp.

2419-PO

WITHDRAWN

2420-PO

Improvement in Glucose Outcomes after the Introduction of Inpatient Insulin Analogs in a Teaching Hospital

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We compared the glycemic outcomes in patients treated with analog insulins glargine and lispro (AI), to those on conventional insulins NPH and regular (CI). This was part of a multidisciplinary development of computerized insulin protocols, staff training and electronic monitoring of implementation. We studied 3345 patients treated from October 2010 and December 2011. The glucose(glc) values (83,550) were electronically obtained from the medical records and correlated with the type of insulin received by the patient at that time; units of analysis included patient-days(PD), patient-stays(PS), and sample. We excluded the units that contained both types of insulin regimens concurrently. The average glc, hypoglycemia rate (< 70 mg/dl), severe hypoglycemia rate (< 50 mg/dl), severe hyperglycemia (>300 mg/dl) and glc variability (maximal glc value -minimal glc value) per unit of analysis were evaluated (Table). We conclude that the use of insulin analogs in the inpatient setting is associated with equal or slightly better glucose control outcomes and significantly decreased glycemic variability compared with conventional insulins.

Table #1

Unit of analysis	Patient-day (PD)			Patient-stay(PS)			Sample		
Number of Units	15239*			3133*			83550		
	Analog	Conventional	P	Analog	Conventional	P	Analog	Conventional	P
n(%)	11235 (73.7%)	4004 (26.3%)		2377 (75.9%)	756 (24.1%)		55825 (66.8%)	27725 (33.1%)	
Mean Glucose (mg/dl)	177.9±62	175.8±61	0.07	189.5±57	186.4±56	0.185	177.1±77	177.5±78	0.49
Hypoglycemia rate (%)	10.9	11.4	0.32	26.5	28.8	0.21	3.9	3.8	0.84
Severe Hypoglycemia rate (%)	2.7	3	0.45	8.3	10.1	0.14	0.9	1.1	0.055
Severe Hyperglycemia rate (%)	17.2	16.5	0.29	43.1	43.9	0.69	7.4	7.3	0.55
Variability (mean ± SD)	98.7±64	101.6±67	0.02	185.9±97	197.9±100.4	0.003	NA	NA	

* 3117 PD and 212 PS excluded due to use of both types of insulin for the same unit of measurement or to only one glc value in that unit

2421-PO

WITHDRAWN

2422-PO

Long-Term Safety, Tolerability and Efficacy of Ipragliflozin in Japanese Patients With Type 2 Diabetes Mellitus: IGNITE

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Ipragliflozin (IPRA, ASP1941) is a novel selective sodium glucose co-transporter (SGLT) 2 inhibitor, currently in phase 3 clinical development for type 2 diabetes mellitus (T2DM) treatment. This open-label, uncontrolled monotherapy 52-week study assessed the safety and efficacy of 50 mg IPRA (increased to 100 mg at Week 20 when A1c target levels were not met) in Japanese T2DM patients. To assess food effects, 182 patients were randomized to receive IPRA before (A) or after breakfast (B). A 6-week wash out period was included for 106 patients. At Week 20, 70 patients received 100 mg and the rest of the patients continued on 50 mg. At week 20 and 52, the change from baseline in A1c (%) was comparable in both groups (table), as was the proportion of patients reaching A1c levels < 7.4 % (Week 52). Body weight decreased with -2.8kg (Week 20) and -3.4kg (Week 52). After Week 24 patients on 100mg lost more weight than those continuing on 50mg. Overall, systolic (-6.4 mmHg) and diastolic blood pressure (-3.3 mmHg) decreased at Week 52. Treatment-emergent adverse events (TEAEs) were observed in 90% of patients. Incidences of hypoglycemia, genital tract infection, and urinary tract infection were 1.6%, 2.2%, and 6.0%, respectively. Conclusion: IPRA (50-100mg) given for 52 weeks was well tolerated and showed a sustained efficacy with a safety profile as expected in T2DM patients in both groups. Administration of IPRA before or after breakfast resulted in comparable efficacy and safety. Body weight reduction continued after week 24 and reductions in blood pressure were also observed.

	Total n = 181	Group A n = 94	Group B n = 87	Total n = 181	Increased to 100 mg n = 70	Maintained at 50 mg n = 111
	A1c (%)* mean (SD)			Body Weight (kg) mean (SD)		
Baseline	7.93 (0.79)	7.99 (0.80)	7.86 (0.79)	67.49 (12.17)	66.87 (12.18)	67.88 (12.21)
Week 20†	7.39 (0.72)	7.42 (0.68)	7.37 (0.76)	64.70 (12.13)	64.09 (12.29)	65.08 (12.06)
Change from Baseline to Week 20†	-0.53 (0.67)	-0.58 (0.69)	-0.49 (0.65)	-2.79 (1.68)	-2.78 (1.73)	-2.80 (1.66)
EOT†	7.41 (0.81)	7.43 (0.79)	7.40 (0.83)	64.08 (12.06)	63.11 (12.18)	64.69 (12.00)
Change from Baseline to EOT†	-0.51 (0.80)	-0.56 (0.83)	-0.46 (0.77)	-3.41 (2.30)	-3.77 (2.68)	-3.19 (2.00)

*A1c levels measured as defined by the Japan Diabetes Society (JDS) and estimated as National Glycohemoglobin Standardization Program (NGSP) equivalent value (A1C (%) = A1C (JDS)% + 0.4%). † LOCF: Last Observation Carried Forward.

2423-PO

Use of Insulin Detemir Is Associated With Improved Glycemic Control Without Clinically Meaningful Weight Gain: Findings from the A_1chieve Study

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Weight gain is a common problem with insulin therapy and can present a major barrier for people with type 2 diabetes (T2DM) and their physicians when starting insulin. A_1chieve was a non-interventional study evaluating the safety and clinical effectiveness of insulin analogs in people with T2DM (n=66 726) in routine clinical care in 28 countries across four continents. This A_1chieve subgroup analysis investigated the effectiveness and the effect on body weight associated with starting basal insulin detemir (detemir) in 12 078 insulin-naïve people. In total, 11 337 (93.9 %) people also received oral glucose-lowering drugs. Overall A1C was poor at baseline (mean) 9.5 (SD 1.6) %, and improved significantly to 7.4 (1.1) % (p<0.001) by week 24. Fasting plasma glucose and postprandial plasma glucose showed significant reductions from baseline of -75 (58) and -98 (75) mg/dl respectively (p<0.001). Results from seven global regions supported the overall findings (Table). There was no significant increase in incidence of hypoglycemia. There was a significant reduction in body weight from a baseline of 76.5 (16.3) to 76.2 (15.4) kg (p<0.001). This was echoed across regions, except for East Asia, North Africa and Latin America, where small increases in body weight were seen. These results confirm the effectiveness and safety of detemir in this group and support findings from other studies of weight neutrality or weight loss among people receiving detemir.

For author disclosure information, see page 797.

Glycemic control and body weight following 24 weeks' treatment with insulin detemir by region

	All regions	China	South Asia	East Asia	North Africa	Middle East/ Gulf	Latin America	Russia
n	12 078	88	2608	3195	1250	3560	405	972
A1C (%)								
Baseline	9.5 (1.6)	8.5 (1.8)	9.4 (1.4)	9.6 (1.9)	9.5 (1.7)	9.6 (1.6)	9.9 (2.2)	9.4 (1.5)
Change	-2.1 (1.6)*	-1.6 (1.6)*	-2.1 (1.5)*	-1.8 (1.9)*	-1.7 (1.7)*	-2.3 (1.5)*	-2.3 (2.1)*	-2.1 (1.3)*
FPG (mg/dl)								
Baseline	201.3 (58.4)	170.3 (66.7)	200.4 (49.7)	207.8 (71.3)	207.7 (64.4)	199.9 (55.7)	218.8 (76.3)	187.5 (42.9)
Change	-75.0 (58.0)*	-56.1 (65.4)*	-69.6 (43.7)*	-78.8 (75.7)*	-70.8 (70.5)*	-78.7 (53.3)*	-89.5 (77.1)*	-72.5 (42.8)*
PPPG (breakfast) (mg/dl)								
Baseline	270.1 (74.8)	238.8 (50.9)	291.4 (60.6)	273.9 (90.0)	263.8 (80.1)	274.0 (75.3)	285.7 (101.8)	217.3 (50.7)
Change	-98.3 (75.4)*	-87.6 (57.0)*	-100.2 (65.4)*	-96.5 (99.0)*	-75.2 (94.9)*	-112.5 (71.7)*	-121.7 (92.9)*	-75.0 (48.8)*
Hypoglycemia (overall), (events/person-year [% of individuals with event])								
Baseline	1.14 (4.1)	0.3 (1.1)	1.02 (6.4)	1.14 (3.7)	1.73 (4.2)	0.83 (2.6)	0.80 (2.5)	2.05 (5.5)
Week 24	1.33 (4.4)†	0.23 (1.8)†	0.10 (0.6)*	0.97 (3.7)†	2.11 (6.3)	1.31 (4.6)*	0.64 (3.0)†	4.66 (13.4)*
					(p=0.0251)			
Body weight (kg)								
Overall								
Baseline	76.5 (16.3)	71.7 (11.1)	70.2 (10.9)	64.7 (12.3)	74.7 (13.2)	87.2 (15.0)	77.8 (16.7)	84.9 (15.7)
Change	-0.3 (4.0)*	-0.6 (4.1)†	-0.5 (3.5)*	0.5 (3.8)*	0.9 (3.5)*	-1.1 (4.7)*	0.0 (4.2)†	-0.8 (3.3)*
People receiving OGLD pre-study								
Baseline	77.0 (16.3)	71.3 (9.7)	70.8 (10.9)	64.8 (12.3)	74.7 (13.2)	87.3 (15.0)	77.7 (16.8)	85.0 (15.7)
Change	-0.4 (3.9)*	-0.9 (4.8)†	-0.8 (2.9)*	0.4 (3.8)*	0.9 (3.5)*	-1.1 (4.7)*	0.0 (4.1)†	-0.8 (3.2)*
No OGLD pre-study								
Baseline	67.7 (13.6)	72.6 (14.0)	64.3 (8.9)	63.3 (11.8)	74.4 (13.5)	81.5 (13.7)	79.6 (15.2)	82.5 (18.2)
Change	1.4 (5.4)*	0.1 (2.2)†	3.0 (6.3)*	1.1 (3.8)	0.7 (5.9)†	-1.9 (5.2)	0.7 (6.1)†	-0.9 (5.8)†
						(p=0.014)		

Mean (SD) or as stated; *p<0.001; †p=NS; Overall hypoglycemia includes major and minor events; FPG, fasting plasma glucose; NS, not significant; OGLD, oral glucose-lowering drug; PPPG, postprandial plasma glucose.

2424-PO

GLP-1 Receptor Agonists can cause Reflux Oesophagitis, Oesophageal Stricture, and Cough Athma, in Japanese Patients of Diabetes

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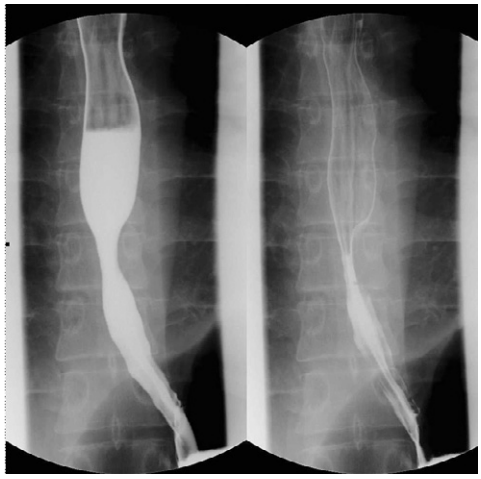
We encountered two patients who presented oesophageal stricture or cough athma during long-term therapy with a GLP-1 receptor agonist. This serious adverse event has not been reported before in Japan. 1st case. 39-year-old Japanese man presented with HbA1c of 10% and obesity. After nine months of liraglutide (0.9 mg/day) treatment, the patient complained of a choking sensation when swallowing food. Fluoroscopy revealed oesophagus stricture (Fig.1). After treatment with rabeprazole and/or teprenone, his symptoms improved. 2nd case. 43-year-old Japanese man. After exenatide therapy, HbA1c dropped from 10% to 7%. However, nausea and cough athma appeared due to reflux oesophasitis. He needed rabeprazole. Although these two patients seemed symbolic who showed GERD (Gastroesophageal Reflux Disease), at our HDC Atlas Clinic, among 96 diabetic patients who received liraglutide or exenatide, 57 patients needed rabeprazole and/or teprenone. Hence, 59% needed medication. In conclusion, nausea, vomiting, or GERD is common in Asians by GLP1-agonist treatment. Therefore, we propose that, Asians, especially Japanese, should be more careful about the occurrence of GERD, and future risk of esophageal cancer, than Caucasians. If possible, prophylaxy use of anti-emetic or proton pump inhibitor medication should be considered in Japanese. Fig.1 Esophageal stricture after 9 month of liraglutide treatment in a type 2 diabetes patient.



2425-PO

WITHDRAWN

2426-PO

WITHDRAWN

2427-PO

Variability of Postprandial Hyperglycemia (PPHG) When A1C Remains ≥7.0% After Treatment of Type 2 Diabetes Mellitus (T2DM) With Oral Agents and Insulin: Implications for Prandial Treatment

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When adding basal insulin to oral therapy doesn't maintain A1C <7.0%, treatment of PPHG is needed. Individual patterns of hyperglycemia may determine treatment effectiveness. To define these we studied self-monitored blood glucose (SMBG) profiles from 6 studies in which insulin glargine or a comparator insulin/oral therapy was added to prior therapy and titrated for 24 weeks (N=1699). We selected patients with A1C ≥7.0% and complete profile data at Week 24 (n=496): mean (SD) age 60 (10) years, duration of T2DM 9.6 (6.3) years; Week 24 body mass index (BMI) 30.7 (4.5) kg/m^2, insulin dose 0.45 (0.26) U/kg, A1C 7.8 (0.8) %, fasting plasma glucose 126 (33) mg/dL. SMBG values before breakfast (B), lunch (L), and dinner (D) averaged 122 (34), 140 (49), and 149 (52) mg/dL, respectively and 179 (55), 174 (50), and 190 (59) mg/dL 2 hours after B, L, or D. Increments of glucose after B, L, and D averaged 57 (51), 34 (48), and 41 (53) mg/dL, respectively. Characteristics of patients with highest postprandial glucose (PPG) and largest increment from pre- to postprandial at each meal were identified (Table). Highest PPG was most frequent after D (44%), but largest increment most often after B (46%). For both definitions of the most problematic meal, subgroups were similar in clinical characteristics (Table). In conclusion, individual postprandial patterns differ widely; similarity of clinical characteristics suggests differing eating behaviors underlie such patterns. SMBG testing of individuals may allow appropriate targeting of meals.

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Characteristic	Highest glucose post-breakfast n/N (%) 145/496 (29.2)	Highest glucose post-lunch n/N (%) 135/496 (27.2)	Highest glucose post-dinner n/N (%) 216/496 (43.5)	Highest increment post-breakfast n/N (%) 229/496 (46.2)	Highest increment post-lunch n/N (%) 129/496 (26.0)	Highest increment post-dinner n/N (%) 138/496 (27.8)
Mean (SD) age, years	59.6 (9.7)	60.1 (9.4)	60.4 (9.7)	61.0 (10.3)	60.5 (8.6)	58.2 (9.2)
Women, n (%)	60 (41.4)	56 (41.5)	109 (50.5)	113 (49.3)	48 (37.2)	64 (46.4)
Mean (SD) T2DM duration, years	9.3 (6.1)	10.3 (6.7)	9.3 (6.2)	9.9 (6.4)	9.8 (6.4)	8.8 (6.0)
Mean (SD) Week 24 BMI, kg/m^2	30.7 (4.0)	30.3 (5.0)	30.9 (4.5)	30.3 (4.5)	30.8 (4.9)	31.1 (4.0)
Mean (SD) Week 24 insulin glargine dose, U/kg/day	0.48 (0.29)	0.43 (0.26)	0.45 (0.22)	0.46 (0.27)	0.42 (0.25)	0.46 (0.23)
Mean (SD) Week 24 A1C, %	7.7 (0.7)	7.8 (0.8)	7.8 (0.8)	7.9 (0.8)	7.7 (0.6)	7.7 (0.8)

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2428-PO

Insulin Regimen in Adults With Type 1 Diabetes in Latin America: Results From the International Diabetes Management Practices Survey (IDMPS)

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IDMPS is an ongoing 5-year multinational observational study documenting the current quality of care provided to people with type 1 or type 2 diabetes. Feasibility analyses were previously performed to validate the chances of pooling the data collected during 2005 and 2009 in Latin America. The aim was to identify patient profiles associated with insulin regimen in type 1 diabetes mellitus (T1DM) patients in Latin America. Patient profiles of 2693 patients were determined using logistic regression analysis. The most common insulin regimen was basal-prandial therapy (65.4%), followed by basal therapy alone (23.7%), and other regimens (10.9%). The use of basal-prandial therapy increased steadily from the first to the fourth survey (59.5% to 73.9%) with a mean duration of treatment of 13.8 ± 10.9 years. The majority of the patients used insulin pens (56.0%) and 47.6% used vials and syringes. The number of insulin injections/day was 4.2 ± 1.0, and 92.9% of these patients received 3 to 6 injections/day. Basal and prandial daily doses were 0.51 ± 0.23 and 0.23 ± 0.17 IU/kg, respectively. Of the patients on basal-prandial insulin therapy 52.4% were treated with insulin analog and 47.6% with regular insulin. Basal-prandial insulin therapy was significantly associated with age (< 40 vs > 65 years; OR = 2.3, $P = 0.003$), time since diagnosis (OR = 0.7 for 5-year changes, $P < 0.001$), time on insulin treatment (OR = 1.5 for 5-year changes, $P < 0.001$), glucometer use (OR = 1.8, $P = 0.012$), self-management (self-monitoring blood glucose and insulin self-adjustment); (OR = 3.5, $P < 0.001$), total daily dose (OR = 1.3 for changes of 0.1 UI/kg, $P < 0.001$) and patient recruited by specialists (OR = 1.6, $P = 0.009$). The increase in use of the basal-prandial insulin regimen in T1DM patients was strongly associated with self-management performance in Latin America during 2005 and 2009. Therefore the promotion of self-care would improve compliance with this insulin regimen.

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2429-PO

Study of Once-Daily Levemir (SOLVE™): Weight Changes Associated With the Initiation of Once-Daily Insulin Detemir in Chinese Patients With Type 2 Diabetes

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Concern over weight gain is a barrier to the initiation of insulin therapy in patients with type 2 diabetes (T2DM). SOLVE™ is an observational study of insulin detemir initiation in patients with T2DM treated with one or more oral antidiabetic drugs (OADs) across 10 countries. The aim of this sub-analysis is to describe the weight changes associated with once-daily insulin detemir initiation in China. A total of 3272 patients were enrolled in China. Of these, 2988 patients completed the 24-week study (58% male, age 56.2±10.8 years, BMI 25.3±3.3 kg/m^2, body weight 69.8±12.1 kg, duration of diabetes 7.1±5.2 years, OAD therapy 6.3±5.1 years, and baseline HbA_{1c} 8.3±1.7%). Insulin dose at the end of the study was 16.6±7.7 U (0.24±0.11 U/kg). Neither serious adverse drug reactions (SADR) nor major hypoglycemic event was reported during the study period. After 24 weeks of treatment, HbA_{1c} decreased to 7.2% (a change of -1.17%, p<0.001), and weight decreased to 69.7 kg (a change of -0.15 kg, p<0.05). The observed weight sparing effect was more pronounced in patients with the higher BMI (see Table). The percentage of patients with weight loss >1 kg was higher with increasing baseline BMI (from 20% to 45%). In conclusion, patients with poorly controlled T2DM achieved significant reductions in HbA_{1c} at initiation of once-daily insulin detemir therapy without weight gain. Insulin detemir may be a better choice for patients with higher BMI compared to other insulin preparations.

Weight change in different BMI categories				
BMI (kg/m^2)	< 25	25-30	30-35	≥ 35
Weight change (kg)				
Baseline	61.9±8.0	74.7±8.6	88.7±10.1	100.2±15.2
Change	0.3±2.7	-0.4±3.7	-1.3±3.6	-1.8±4.1
p value	p < 0.001	p < 0.001	p < 0.001	p = 0.062

2430-PO

In Japanese Patients With Type 2 Diabetes, Clinical Predictors for Effectiveness of Liraglutide Treatment are Different between Obese and Non-Obese Patients

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It is known that Japanese patients with type 2 diabetes are less obese than diabetic patients in the U.S. and Europe, and the cause of diabetes in Japanese patients is mainly associated with β-cell dysfunction. We compared the clinical characteristics of Japanese patients with type 2 diabetes who were either responders or non-responders to liraglutide (LIRA). In total, 171 patients who were treated with LIRA were involved in the study, with 61% classified as responders (>0.3% decrease in HbA1c) and 26% classified as non-responders (>0.3% increase in HbA1c). The average duration of follow-up was 126.8 days. Both groups lost 2.0 kg of body weight on average with the treatment. The responders had significantly higher HbA1c levels, and 73% of non-responders had already received metformin prior to the treatment. The efficacy of LIRA in combination with oral antidiabetic agents was 72%, and the efficacy upon switching from insulin to LIRA alone was 51%. Moreover, the efficacy of switching from basal-supported oral therapy to LIRA was 64%, whereas switching from multiple daily injection and biphasic insulin was approximately 40% effective. The efficacy was also not different between a group of non-obese patients (BMI<25) and a group of obese patients (BMI≥25). In the non-obese patients, the fasting C-peptide was significantly lower in the non-responders than in the responders (1.2 vs. 1.8 ng/ml; P<0.05). In the obese patients, the C-peptide in the urine was significantly higher in the non-responders than in the responders (153.3 vs. 103.8 μg/day; P<0.05). Based on multivariate analysis, the efficacy of LIRA was independently correlated with the HbA1c level (Odds ratio [OR] 1.58), the BMI (OR 0.89) and the fasting C-peptide/glucose level (OR 2.94). These data indicate that a reduction of the endogenous insulin secretion in non-obese patients and a resistance to insulin in obese patients are associated with a resistance to LIRA treatment.

2431-PO

The Safety and Effectiveness of Adding Once-Daily Insulin Detemir to Oral Hypoglycaemic Agents in Patients With Type 2 Diabetes in a Clinical Practice Setting

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Insulin initiation is often delayed despite years of poor glycemic control in patients with type 2 diabetes mellitus (T2DM) treated with oral hypoglycemic agents (OHAs). This international observational study was conducted in 10 countries. Adverse event data (including hypoglycemia) and glycemic control were recorded before and 24 weeks following insulin initiation. Patients continued routine clinical management under the care of 3219 health care providers.17374 participants (53% male) were included in the analysis. Mean baseline values (± SD) were: age 62 ± 12 years; BMI 29.3 ± 5.4 kg/m^2; HbA1c 8.9 ± 1.6%; and duration of diabetes and OHA use was 10 ± 7 and 8 ± 7 years, respectively. After 24 weeks, HbA1c decreased to 7.5 ± 1.2% and mean weight change was -0.6 kg (95% confidence interval [CI] -0.7, -0.5 kg, p<0.001). There were 23 serious adverse drug reactions (SADRs) affecting 18 (0.1%) participants during the study; 14 SADRs were severe hypoglycemic events. The incidence of severe hypoglycemic events decreased from 4 to <1 per 100 person-years (p<0.001), whereas the incidence of any minor hypoglycemia event increased from 1.58 to 1.83 events per person-year (p<0.001). Insulin dose increased from 13 ± 6 IU (0.16 ± 0.09 IU/kg) at the start of the study to 22 ± 16 IU (0.27 ± 0.17 IU/kg) by 24 weeks. An evaluation of demo-

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graphic and treatment factors demonstrated that independent predictors of end of study HbA1c included baseline HbA1c, duration of diabetes, number of OHAs, concomitant use of sulphonylurea at the time of insulin initiation, insulin dose, and change in OHA regimen. The addition of once-daily insulin detemir to patients with T2DM on OHA therapy in routine clinical practice resulted in reductions in HbA1c and weight, with low rates of hypoglycemia. Concerns about hypoglycemia or weight gain should not deter the initiation of basal insulin analogues in patients receiving OHAs with poor glycemic control.

Supported by: Novo Nordisk A/S

2432-PO

Decreased Renal Function Inducing C-peptide Level Increase in Serum and Decrease in Urinary in Type 2 Diabetes Mellitus

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The purpose of this study is to observe the effect of decreased renal function on serum and urine C-peptide levels in type 2 diabetes mellitus. The selected 635 type 2 diabetic patients with normal liver function who did not receive sulfonylureas or repaglinid/nateglinide were divided into 4 groups according to the estimated creatinine clearance rate (Ccr) using Cockcroft-Gault formula, including >90, 60-90, 30-60 and <30 ml/(min· 1.73m2) respectively. Area under curve (AUC)of insulin and C-peptide were also accounted. Along with the gradual decrease of renal function, serum C-peptide was gradually increased and urinary C-peptide was gradually decreased. The decreased renal clearance of serum C-peptide in patients with insufficient renal function might cause the increased serum C-peptide. It was suggested that clinicians should pay more attention to the islet β cell function in type 2 diabetic patients with decreased Ccr.

Insulin and C-peptide levels According to Ccr: x±s-1

Ccr	n	Fasting INS	Fasting C-P	HOMA-IR
ml/(min·1.73m^2)		mIU/L	pmol/L	
>90	322	8.1±3.4	610±111	1.01±0.65
60-90	205	9.9±5.3	630±146	1.16±0.57
30-60	66	9.6±5.0	837±269[ab]	1.18±.0.43
<30	42	10.1±6.1[a]	1019±209[ab]	1.28±.0.43[a]

Insulin and C-peptide levels According to Ccr: x±s-2

Ccr	HOMA-IS	INS AUC	C-P AUC	Ccr	urine C-P mete (8h)
ml/(min·1.73m^2)		h··mIU/L	h··pmol/L	ml/(min·1.73m^2)	nmol
>90	3.80±0.76	111.9±24.1	5211±932	103.2±13.3	7.6±2.8
60-90	3.92±0.85	126.2±26.7	6580±1023[a]	75.4±9.2[a]	6.4±1.9[a]
30-60	3.94±0.82	138.4±28.6[a]	8718±1782[ab]	45.8±8.9[ab]	4.7±1.6[ab]
<30	4.07±0.92[a]	139.1±30.8[a]	10328±2345[ab]	23.8±4.1[abc]	3.0±1.0[abc]

a P<0.05, compared with >90 group. b P<0.05, compared with 60-90 group c P<0.05, compared with 30-60 group

2433-PO

Adding Daily Basal Long Acting Insulin by Subcutaneous Injection to Continuous Subcutaneous Insulin Infusion Significantly Decreases the Incidence of Diabetic Ketoacidosis in Type 1 Diabetics

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Type 1 Diabetics who use Continuous Subcutaneous Insulin Infusion (CSII) may be at an increased risk for developing Diabetic Ketoacidosis (DKA) due to occasional pump malfunctions. This includes occasional incidences such as bent or occluded catheters, noncompliance, poor insertion technique, and user errors. Therefore, we studied the incidence of DKA in type 1 Diabetics who have used CSII only versus those who used CSII with a daily long acting basal subcutaneous insulin injection. Hospital records and office charts from 2006 to 2011 were reviewed for the occurrences of DKA. There were 52 patients who have used CSII only and 23 patients who have used CSII with a daily long acting basal subcutaneous insulin injection. Our population included children, adolescents, and adults, Caucasians and non-Caucasians, different body mass indexes, multiple educational backgrounds, and different glucose control levels. There were no significant statistical differences in the demographic characteristics between the two groups. Our results show that adding a daily basal insulin injection along with the CSII significantly reduced the occurrences of DKA (P< 0.001, OR=6.49, CI 95 %= 3.38 to 12.5). Of the 16 patients who used both treatment modalities, their incidence of developing DKA while on CSII with a daily long acting basal subcutaneous insulin injection was significantly less than using CSII only (P=0.012, OR=7.27, CI 95%=1.44 to 36.22). Those who used CSII with a daily long acting basal subcutaneous insulin injection were 6.49 times less likely to experience DKA than using CSII only. For those who have frequent DKA's while on CSII, we recommend a trial of adding a daily basal insulin by subcutaneous injection before discontinuing the CSII altogether.

2434-PO

Comparison of GLP-1R Expression in C-Cells Isolated from Rat and Human Thyroid Gland

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In rodent thyroid gland, some GLP-1R agonists have been shown to induce C-cell proliferation. Rodents appear to be particularly sensitive and it remains unclear whether this is a drug class effect. The mechanism underlying this rodent-sensitive effect is not fully understood, but may involve a GLP-1R-mediated pathway. To evaluate if there is rodent-specific GLP-1R expression, we investigated GLP-1R expression levels in C-cells isolated from untreated human and rat thyroids. Rat and human C-cells were excised by laser capture microdissection from paraffin-embedded thyroid glands and total RNA was isolated. Quantitative Real-Time PCR was performed to analyze GLP-1R gene expression levels; GLP-1R expression levels were normalized to β-Actin levels. GLP-1R expression in rat C-cell fractions (n=15) was reflected in a cycle time (CT) mean value of 27.4 ± 1.5 and a value of 4 when normalized to β-Actin (Table). In a study with human C-cell fraction (n=2), only marginal GLP-1R expression levels were observed, reflected by a CT mean value of 33.6 ± 0.6, close to the sensitivity limit of the test system (CT=35) and 10.4 when normalized to β-Actin. In a second study with human tissue (n=7), no relevant GLP-1R expression was demonstrated in C-cell fractions. Thus, GLP-1R expression analysis in human and rat thyroid gland tissue revealed higher GLP-1R expression in rat C-cells compared to human C-cells, with a CT difference of at least 6 CTs, corresponding to a 64-fold higher RNA content in rats. The higher GLP-1R expression in rats may underlie the particular sensitivity of rodents for GLP-1R agonist-induced proliferation of thyroid C-cells.

Expression of the GLP-1R in rat and human thyroid C-cell fractions

Target	Expression level, mean CT value ± SD [range]		
	Study 1 : Rat C-cells (n=15–18)	Study 2 : Human C-cells (n=2)	Study 3 : Human C-cells (n=7)
β-Actin*	23.5 ± 1.1 [21.7–24.9]	23.2 ± 0.4 [23.0–23.5]	24.6 ± 3.8 [19.3–30.6]
Calcitonin†	18.1 ± 1.3 [16.4–21.8]	20.7 ± 1.0 [20.0–21.4]	26.6 ± 2.8 [22.8–30.4]
GLP-1R	27.4 ± 1.5 [24.1–29.5]	33.6 ± 0.6 [33.2–34.0]	Undetectable (all values >35, except one [34.9])
ΔCT GLP-1R‡	4.0 ± 1.35	10.4 ± 0.23	Not applicable

CT=cycle time (N.B. higher CT value=lower gene expression)
*Expression of the housekeeping gene β-Actin was used for quality control; †Calcitonin gene expression was used as a marker for the presence of C-cells
‡GLP1-R value normalized to β-Actin

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2435-PO

Lack of Interaction Between the Sodium Glucose Cotransporter-2 Inhibitor Empagliflozin and Warfarin in Healthy Subjects

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Empagliflozin (EMPA) is a potent, highly selective sodium glucose cotransporter-2 inhibitor in development for treatment of type 2 diabetes mellitus. This open-label crossover study investigated potential drug-drug interaction between EMPA and the anticoagulant warfarin. Eighteen healthy male subjects (mean [range] age 34.8 [21-46] years) received EMPA 25 mg qd alone for 5 days (treatment A), followed by EMPA 25 mg qd for 7 days (days 6-12) co-administered with a single 25 mg dose of warfarin (racemic mixture of *R*- and *S*-enantiomers) on day 6 (treatment B), and a single 25 mg dose of warfarin alone (treatment C). Dosing schedule was AB then C or C then AB, with a washout period of ≥14 days between AB and C or C and AB. Based on standard criteria, co-administration of EMPA and warfarin had no effect on the pharmacokinetics of either drug (Table). No clinically relevant effects on the anticoagulant action of warfarin, measured using prothrombin time or the international normalized ratio (INR), were observed. Geometric mean ratio (GMR) (95% CI) for peak INR was 0.87 (0.73-1.04) and for area under INR-time curve from dosing to 168 h was 0.88 (0.79-0.98). Nine subjects experienced an adverse event (AE); all mild/moderate in intensity, the most frequent was headache. No AEs with EMPA or combined administration were reported as drug-related. Tolerability was 'good' for all treatments. In conclusion, no

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drug-drug interaction was observed between EMPA and warfarin, and the combination was well tolerated, indicating no dose adjustments of either drug are necessary for co-administration of EMPA and warfarin.

Analyte	Parameter	GMR % (90% CI) Empagliflozin + warfarin/empagliflozin	Geometric coefficient of variation (gCV) %
Empagliflozin	$AUC_{\tau,ss}$	100.89 (96.86, 105.10)	7.0
	$C_{max,ss}$	100.64 (89.79, 112.80)	19.9
		GMR % (90% CI) Empagliflozin + warfarin/warfarin	gCV %
R-warfarin	$AUC_{0-\infty}$	98.49 (95.29, 101.80)	5.7
	C_{max}	97.89 (91.12, 105.15)	12.4
S-warfarin	$AUC_{0-\infty}$	95.88 (93.40, 98.43)	4.5
	C_{max}	98.88 (91.84, 106.47)	12.7

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2436-PO

WITHDRAWN

2437-PO

The Relationship between BMI and Glycemic Control after Mono-therapy With Metformin XR Tablets in Newly Diagnosed Chinese T2DM Patients

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Recent global studies report the safety and efficacy of mono-therapy with metformin XR (Glucophage XR) in normal-weight patients with Type 2 Diabetes Mellitus (T2DM); however, this has not been investigated in Chinese T2DM patients. This open-label, 3-arm, multicenter trial in newly diagnosed Chinese T2DM patients was conducted in 20 sites in China. A total of 371 patients were enrolled into 3 groups according to their baseline BMI (normal weight, 24kg/m^2 >BMI≥ 18.5kg/m^2, n=125; overweight, 28 kg/m^2 >BMI≥ 24 kg/m^2 , n=122; obese, BMI≥ 28 kg/m^2 , n=124) as defined in the 2008 Chinese Diabetes Society guidelines. The primary efficacy endpoint of this study was the change from baseline in HbA_{1c} after a 16-week oral administration of metformin XR. Secondary endpoints were the change from baseline in fasting plasma glucose (FPG), the relative changes from baseline in fasting lipids (TC, LDL-C, HDL-C, and TG), and changes from baseline in CRP, PAI-I, and adiponectin. Patients were treated with an oral dose of metformin XR for 16 wks. The initial dose was 500 mg/d; up-titrated by increments of 500 mg/wk to 1500mg/d, unless intolerance or hypoglycemia occurred. A maximum dose of 2000 mg/d metformin XR was permitted from Weeks 4-16. Metformin XR is safe and efficacious in the treatment of normal weight as well as overweight and obese Chinese patients with newly diagnosed T2DM, achieving a mean reduction HbA_{1c} of 1.80%. Differences between the normal weight and obese groups suggest that the effect of BMI on the response to metformin is clinically relevant. Improvement in FPG was also demonstrated, with a mean reduction of 2.097 mmol/L in FPG from baseline to final study visit. Fasting lipid levels improved in all groups (↓TC of 0.195 mmol/L; ↓LDL-C of 0.211; mmol/L, ↑HDL-C of 0.037 mmol/L; ↑ adiponectin of 4.865 ng/mL). In conclusion, body weight had no impact on the efficacy of Metformin XR in newly diagnosed Chinese patients with T2DM.

Supported by: Bristol-Myers Squibb

2438-PO

Enhancing Effects of DPP-IV Inhibitor on Glycemic Control Depends on Combined SU: A Pilot Cross-over Study

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DPP-IV inhibitors often cause the critical hypoglycemia when used in combination with certain types of SU. Recently, it is reported that the cAMP sensor Epac2 is a direct target of some type of SUs, and this unique effect depends on molecular architecture of each SU. We hypothesized that enhancing glucose lowering effects of DPP-IV inhibitor depend on combined SU, and compared the glucose lowering effect of Gliclazide (GLC) with Glimepiride (GLM) in both condition of use and nonuse of Sitagliptin (STG). We targeted at the type 2 diabetic outpatients with A1C over 7.9 %, and fasting C-peptide over 1.0 ng/ml. Preliminary, we determined GLC 80mg/ b.i.d. to be equivalent in order to obtain the same A1C level as GLM 3mg/ once daily by comparing multiple combination of dosages of each drug for 3 months period. Subsequently, we compared the glucose lowering effects of both SUs with and without the treatment of STG 50mg/once daily at the determined dose of both SUs (GLM 3mg/once daily vs. GLC 80mg/b.i.d.). This was a prospective and randomized cross-over study. We switched from the first drug to the second drug 3 months after the administration of the first drug. The patients were estimated A1C level 3 months after the administration of the first or second drug. STG was started 0-3 month(s) before the beginning of administration of the first drug. N=13 patients without STG (5/13; administrated GLM as the first drug) obtained the same A1C level with both SUs (GLM vs. GLC; 8.74 vs. 8.7%, respectively, P=0.850). On the other hand, N=13 patients (8/13; administrated GLM as the first drug) under the STG 50mg/day treatment with GLM 3 mg/day obtained more powerful glucose lowering effect than with GLC 80mg/day (GLM vs. GLC; 7.82 vs. 8.33%, respectively, P=0.0014). Among the patients with the combination therapy, 2/13 complained of mild hypoglycemia when treated with GLM. These results clinically suggest some types of SUs have the new target of the antidiabetic effect.

2439-PO

Experience With Sitagliptin as Add-on to Insulin in Type 2 Diabetic Patients

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Type 2 diabetes mellitus (DM2) is a progressive disease. Metabolic control worsens with time and treatment adjustments are needed. The last step is insulin, usually in combination with metformin. Over 60% of DM2 on insulin are not under control. There is room for improvement, with better and safer drugs or treatment strategies. Guidelines endorsed by medical societies are followed. However, as they have some delay in the introduction of new drugs, the latter are being used following the label. The indication of sitagliptin was extended to be used as add-on to insulin, with o without metformin, by EMA at the end of 2009. We present 29 non-controlled (HbA1c 8,6 ± 1,2%) DM2 patients (20 male) treated with insulin and metformin. Mean age 62,5 ± 10,1 years, duration of DM2 17,7 ± 8,1 years and treated with insulin for 6,7 ± 5,8 years with 1 to 5 doses (mean 2,4 ± 1,2). HbA1c improved 0,74% ± 1,24. There were no changes in weight, BMI, or dose of insulin. The improvement was not related to sex, age, BMI, duration of DM2, time on insulin treatment, number of insulin doses, or total IU of insulin per kg Hypoglycemia was a complaint in 10 out of 29 patients, in 3 of them was fairly frequent. After adding sitagliptin, it decreased to 5 out of 28 patients and in none was frequent. As expected, there was also a significant difference (p 0,04) in the reduction of HbA1c between the highest (-1,6%) and the lowest (-0,4%) quartile of HbA1c. Ten out of 29 patients reached HbA1c goal ≤7%. Sitagliptin as add-on to insulin and metformin in DM2 improves HbA1c safely. Its effect is independent of the age of the patient, the duration of the disease, the number of doses and the total daily dose.

N=29	Total Insulin IU/day	Basal insulin IU/day	Prandial insuliin IU/day	Weight (kg)	BMI	HbA1c
Pre	70,6 ± 47,7	53,5 ± 32,4	17,2 ± 21,2	90,0 ± 16,7	32,8 ± 5,9	8,6± 1,2
Post	73,3 ± 45,3	58,0 ± 35,7	15,3 ± 20,2	90,1 ± 17,8	32,9± 6,3	7,9± 1,4
p	0.601	0,255	0,284	0,853	0,683	0.003

2440-PO

Lack of Interaction Between the Sodium Glucose Cotransporter-2 Inhibitor Empagliflozin and Hydrochlorothiazide or Torasemide in Patients With T2DM

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Empagliflozin (EMPA) is a potent, selective sodium glucose cotransporter-2 inhibitor in development for treatment of T2DM. This open-label crossover study investigated interactions between EMPA and diuretic agents hydrochlorothiazide (HCT) or torasemide (TOR). Patients with T2DM (n=22 treated,

For author disclosure information, see page 797.

mean [range] age 54 [40-65]) were randomized to receive EMPA 25 mg qd for 5 days (Treatment A) and one of the following treatments: Treatment B, HCT 25 mg qd for 4 days followed by HCT 25 mg qd with EMPA 25 mg qd for 5 days; or Treatment C, TOR 5 mg qd for 4 days followed by TOR 5 mg qd with EMPA 25 mg qd for 5 days. Subjects received either dosing schedule AB, BA, AC or CA, with a washout period of ≥7 days between A and B or C. Based on standard criteria, co-administration of EMPA with HCT or TOR had no effect on exposure ($AUC_{\tau,ss}$) or $C_{max,ss}$ of EMPA, HCT or TOR (Table). There were no major changes in the EMPA terminal elimination half-life (15.3 h with EMPA alone, 14.8 h with HCT, and 16.1 h with TOR co-administration) or renal clearance (36.7 ml/min with EMPA alone, 30.2 ml/min with HCT, and 32.5 ml/min with TOR co-administration) when co-administered with HCT or TOR. Similar findings were observed for HCT and TOR. EMPA was well tolerated, no serious adverse events were reported. In conclusion, no drug-drug interaction was observed between EMPA and HCT or TOR. Pharmacokinetic assessments indicate that no dose adjustments of EMPA, HCT or TOR are necessary for co-administration of EMPA with HCT or TOR.

Table

	Geometric mean ratio % (90% CI) of combination vs monotherapy			
Analyte	EMPA		HCT	TOR
Parameter	EMPA + HCT / EMPA	EMPA + TOR / EMPA	HCT + EMPA / HCT	TOR + EMPA / TOR
$AUC_{\tau,ss}$	107.08 (97.11, 118.07)	107.83 (100.14, 116.11)	96.27 (89.08, 104.05)	101.44 (99.06, 103.88)
$C_{max,ss}$	102.78 (88.55, 119.29)	107.50 (97.90, 118.04)	101.77 (88.63, 116.85)	104.43 (93.81, 116.25)

Supported by: Boehringer Ingelheim

2441-PO

Metformin-Associated Lactic Acidosis (MALA): Myth or Reality?

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More than 50 years after its introducing in 1957 (1996 in USA), metformin is used today in more than 90 countries. It is the most efficient, safe and costless anti-hyperglycemic agent in the treatment of type 2 diabetes Mellitus. Its principal risk remains Metformin-Associated lactic Acidosis (MALA), subject of controversies. We present a personal series of all cases of MALA diagnosed by the same Diabetologist in an 8 year-period in an Emergency department admitting 16000 patients yearly. 4 cases of MALA are diagnosed in this 8 year-period. The incidence is 3 for 100000 patients admitted in Emergency. The indication of the metformin was not relevant in 1 case (mitochondrial disease) and subject of discussion in 2 others (with chronic alcoholism in on case and chronic use of Anti-Inflammatory Drugs in the other). Patient 4, with a mild asthma, was treated with 3000 mg of Metformin. The clinical presentation is misleading in the 4 cases. The evolution was favorable in 50% of the cases, fatal in 2 cases (severe impaired renal function, hepatic insufficiency). Serum lactic acid over than 5 mmol/L at admission (normal value < 2 mmol/L) in a context of metabolic acidosis is the key of the diagnosis. Co-morbidities often make MALA diagnosis difficult. Checking serum lactic acid systematically for metformin treated patients admitted for an acute problem is the main "take home message" of this report. Diagnosed and treated without delay, the evolution of MALA can be quickly favorable. In UKPDS, Metformin given not more than 2550 mg daily has shown to reduce total mortality but no clinical evidence for the superiority of higher doses in studies. We suggest, in addition to the strict respect of contraindications, the integration of the benefit-risk balance when prescribing higher doses. Finally, the expertise of diabetologists in Emergency rooms could improve the quality of care for diabetic patients. Helpful in the management and prevention of complications, it is enhancing educational messages of safety for patients and physicians.

2442-PO

Insulin-Degrading Enzyme as a Therapeutic Target in Diabetes

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Insulin-degrading enzyme (IDE) is an atypical zinc-metallopeptidase that plays an essential role in terminating the insulin response and is also linked to the pathogenesis of type-2 diabetes mellitus. Despite widespread interest in IDE spanning more than a half century, the role of IDE in regulating insulin and glucose homeostasis in vivo remains poorly understood and inhibitors of this important peptidase have remained elusive until only recently. Here, we present the phenotypic analysis of conventional and conditional IDE knockout mice, as well as our recent progress in developing and characterizing IDE inhibitors. Genetic deletion of IDE results in marked fasting hyperinsulinemia throughout life, with insulin and glocose tolerance changing markedly as a function of age. At 2 months of age, IDE knockout mice exhibit significantly improved glucose and insulin tolerance, lower body mass and reduced fasting blood glucose levels, but convert to an opposite phenotype by 6 months of age. Characterization of conditional IDE knockout mice is underway and our progress will be presented. We also describe the development of a number of novel IDE inhibitors derived from a rational design approach as well as multiple high-throughput compound screening campaigns, including highly potent (Ki ~2 nM) and selective peptide hydroxamate IDE inhibitors. We report on our progress developing more drug-like variants of the former together with the discovery and initial characterization of several novel scaffolds, including sulfonamide hydroxamates, thiocarbamates, and novel cysteine-modifying compounds, all which conform to Lipinski's Rule of Five and which exhibit Ki values in the range of 90 to 800 nM. Preliminary in vivo testing reveals that IDE inhibitors significantly potentiate the hypoglycemic action of insulin, a result which is in good agreement with the phenotype observed in young IDE knockout mice and which augurs well for the therapeutic utility of IDE inhibitors as a tractable approach to treating and managing diabetes.

2443-PO

Changes in Basal and Bolus Insulin Requirements During Pramlintide Initiation and Dose Escalation in Young Adults With Type 1 Diabetes

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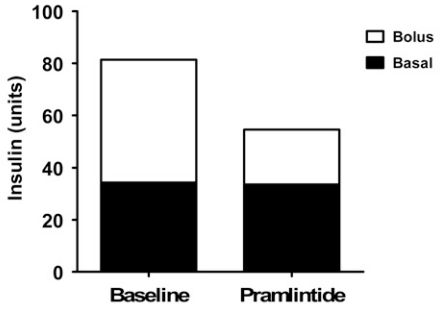
Pramlintide has been increasingly used as an adjunct to insulin in older adults with type 1 diabetes to reduce prandial glucose excursions, but its use in young adults is limited. As part of a study evaluating the effect of short-duration pramlintide therapy on closed-loop insulin delivery, we initiated and advanced pramlintide doses in drug-naïve subjects during open-loop insulin pump therapy and evaluated changes in basal and bolus insulin requirements, blood and sensor glucose levels in 4 patients with T1D (age 19-23 y, duration 7-16 y, A1c 6.3-8.0%). Over 3 weeks, pre-meal pramlintide doses were increased by 15 mcg each week to 45 mcg after telephone contact with study nurse practitioner and review of BG and CGM uploads. Mean total daily dose of insulin decreased from 81 units at baseline to 55 units after 3 weeks of pramlintide, primarily due to lower bolus insulin requirements (Figure). Despite the 32% reduction in insulin doses, average sensor glucose levels decreased from 145 to 115 mg/dL . None of the subjects experienced severe hypoglycemia or gastrointestinal distress, but all reported some loss of appetite. Pramlintide use was associated with a 56% reduction in bolus insulin requirement and concomitant reduction in average sensor glucose levels. Use of CGM with frequent upload and review by clinicians can facilitate the safe and efficient initiation of pramlintide in naïve subjects.



Supported by: JDRF (22-2009-799), NIH (R01 DK085618, UL1 RR024139, P30 DK045735)

2444-PO

Partners for Better Health in Adolescents With Type 2 Diabetes ("Buddy Study")—An Update

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We report on a non-pharmacologic intervention for adolescents with type 2 diabetes mellitus (T2DM). Patients are randomized to a) conventional follow-up every 3 months or to b) assignment to a 'Buddy' (a young, healthy, motivated lay volunteer, age 18-25 yrs). Buddies contact patients weekly (e.g., via phone/texting) and meet in person at the patient's home or a site determined by the patient on a monthly basis. The goal of this partnership is to establish a supportive relationship and includes reminders of clinic visits and motivation to adhere to prescribed medications. Inclusion criteria for patients are age 12-20 yrs and hemoglobin A1c (A1c) > 7%. Study duration

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is 6 months (3 visits in both study arms) and data are collected with systematic questionnaires and a secure database. Pill counts and prescription refill frequency are assessed in both arms. Primary outcome is change in A1c and secondary outcomes include changes in body weight, home glucose monitoring, treatment compliance, attendance at scheduled visits, and quality of life. After almost 2 years, only 10 patients have been randomized (recruitment goal: 30 patients per study arm) and loss to follow-up has been high (see table). We conclude that in contrast to similar studies in adults with T2DM involving frequent patient contact, we experience remarkable difficulties with recruitment and retention. Patients often actively avoid contact with our young study volunteers (Buddies). Despite the early stage of this study, we predict that this intervention is unlikely to effectively improve motivation of youths with T2DM to achieve better blood glucose control.

Buddy Study Patient Data

Patient ID	Race	Age [yr]	Study Arm	Enrollment	Baseline A1c [%]	3-mo F/U A1c [%]	6-mo F/U A1c [%]
1	AA	15	Conventional	3/2010	16.2	no-show	>14
3	AA	21	Conventional	4/2010	7.2	7.5	7.5
5	AA	17	Conventional	12/2010	12.9	11.9	no-show
6	Asian	17	Conventional	2/2011	11.1	9.6	13.0
9	AA	13	Conventional	9/2011	8.1	no-show	scheduled
2	White	21	Buddy	3/2010	10.3	11.4	11.7
4	White	16	Buddy	6/2010	8.0	9.5	no-show
7	AA	15	Buddy	8/2011	8.9	8.8	scheduled
8	AA	17	Buddy	9/2011	13.5	no-show	scheduled
10	Hispanic	17	Buddy	9/2011	11.3	no-show	scheduled

Supported by: NIDDK

2445-PO

Clinical Characteristics of Patients With Uncontrolled Type 2 Diabetes (T2DM) on One or Two Oral Agents According to Intensification of Therapy With Insulin, Glucagon-Like Peptide 1 Agonists (GLP-1), or Additional Oral Anti-Diabetes Agents (OAD)

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As T2DM prevalence increases, it is important to identify treatment strategies that achieve desired A1C over extended periods to reduce risk of complications. Recommendations for intensification of T2DM therapy in patients with A1C≥7% on 1-2 OAD are inconsistent. Electronic medical records (EMR) are able to identify ample numbers of T2DM patients who are candidates for additional therapy based on A1C criteria. We queried an EMR to identify clinical characteristics of patients with A1C≥7% on 1 or 2 OAD from January 2007 to December 2010 according to intensification of therapy with insulin (Group1 n=412); GLP-1(Group2 n=54); OAD(Group3 n=1997); or no additional therapy(Group4 n=4134). Patients taking insulin or GLP-1 therapy at time of A1C≥7.0% were excluded. Baseline clinical characteristics of these patients are summarized in the table:

Variable	Group 1 N=412	Group 2 N=54	Group 3 n=1997	Group 4 N=4134	Group 1-3 p-value*	Intensified vs. No Intensified p-value**
Female, %	52%	57%	46%	51%	0.045	0.005
Race, %						
White	72%	80%	76%	75%		
Black	15%	11%	13%	15%	0.585	0.036
Other	1%	0%	1%	1%		
Unknown	13%	9%	10%	9%		
Age, years med (IQR)	60.0 (52.7, 70.5)	57.2 (45.1, 63.6)	61.8 (53.8, 72.2)	63.4 (54.1, 74.0)	<0.001	<0.001
BMI, m/kg^2 med (IQR)	33.2 (29.1, 38.4)	37.3 (31.5, 41.8)	32.5 (28.5, 37.6)	32.3 (28.3, 37.3)	<0.001	0.017
HbA1c, % med (IQR)	8.5 (7.7, 10.3)	7.8 (7.4, 8.8)	7.9 (7.3, 8.8)	7.5 (7.2, 8.4)	<0.001	<0.001

*Chi-square or Kruskal-Wallis four-way non-parametric test; **Chi-square of Wilcoxon rank-sum pairwise non-parametric test IQR: Inter Quartile Range

The majority of T2DM patients with an A1C≥7.0% did not receive intensification of therapy. This group was older and had lower A1C than those who received additional therapy. Among patients undergoing intensification, those who received insulin had higher A1C, while those who received GLP-1 were younger and more obese. Through EMR we identified and assessed medication utilization in uncontrolled T2DM patients, allowing insights into factors involved in choosing between insulin and GLP-1 and related clinical decision making.

Supported by: sanofi-aventis

2446-PO

Study of Once-Daily Levemir (SOLVE™): Safety and Efficacy of Once-Daily Insulin Detemir in Routine Clinical Practice in Chinese Patients With Type 2 Diabetes

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Complementary data from large scale studies in real-life settings is essential to monitor safety of insulin treatment. SOLVE™ is an observational study of insulin detemir initiation in patients with type 2 diabetes (T2DM) treated with one or more oral antidiabetic drugs (OADs) across 10 countries. This abstract reports the sub-analysis of data from China, and the aim is to provide insights on the impact of initiating once-daily insulin detemir in routine clinical practice. Safety (serious adverse drug reactions (SADR), hypoglycemic events and body weight) and efficacy (HbA_{1c}) data were collected and analyzed. A total of 3272 patients were enrolled in China. Of these, 2988 patients (91.3%) completed the 24-week study. The main reason for patient's discontinuing was lost to follow-up. Baseline characteristics were as follows: 58% male, age 56.2±10.8 years, BMI 25.3±3.3 kg/m^2, duration of diabetes 7.1±5.2 years, OAD therapy 6.3±5.1 years. Insulin dose at the end of the study was 16.6±7.7 U (0.24±0.11 U/kg). During the study period, neither SADR nor major hypoglycemic event was reported. Incidences of minor and nocturnal hypoglycemic events were 2.20 events per patient year (ppy) and 0.36 events ppy, respectively. Weight decreased from 69.8 kg at baseline to 69.7 kg at 24 weeks (a change of -0.15 kg, $p<0.05$). After 24 weeks of treatment, HbA_{1c} decreased from 8.3% to 7.2% (a change of -1.17%, $p<0.001$). The proportion of patients reaching an HbA_{1c} target of 7.0% was 49.1% at the end of study compared to 19.1% at baseline. In conclusion, this study confirmed that insulin detemir administered once daily as add-on to OADs, is a safe and effective option for Chinese patients with T2DM not effectively controlled by OAD therapy.

2447-PO

Addition of Sitagliptin or Vildagliptin to Uncontrolled Type II DM With Oral Hypoglycemic Medications

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This is 3 months follow up Group 1: 126 type II DM patients (70 male , 56 female) , Age 50.98 ±12.2. These patient received Sulphonylurea as well as Metformin 1000mg bid yet their HBA1c prior addition of Sitagliptin was 8.7± 0.18 and after 3 months of addition of Sitagliptin was 7.8±0.16 . Group 2: of 76 type II DM patients (40 male , 36 female) , Age 47.8 ±13.2. These patient received Sulphonylurea as well as Metformin 1000 bid yet their HBA1c prior addition of Vildagliptin was 8.5± 0.22 and after 3 months of addition of Vildagliptin was 7.4±0.18 . Student T test was applied and was highly significant between these groups (Before and After treatment). This indicate that adding Sitagliptin or Vildagliptin made the uncontrolled DM significantly improved -0.88 with confidence interval was - 1.19 to - 0.57 and p value is < 0.001. However no significance if we compare both groups together. Conclusion: Addition of Sitagliptin or Vildagliptin improve DM control in previously uncontrolled DM.

2448-PO

Effect of the Dipeptidyl Peptidase-4 Inhibitor Sitagliptin on Insulin Secretion during the Meal Tolerance Test in Type 2 Diabetic Patients

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Background and AIM: Poorly functioningβ-cells in type2 diabetic patients secrete greater amounts of proinsulin relative to insulin and a decline in this ratio has been suggested to be a marker of improved β-cell function. Dipeptidyl peptidase-4 inhibitor (DPP-4 inhibitor) has been reported to reduce the proinsulin to insulin ratio in the fasting state. The aim of this study was to assess the effect of DPP-4 inhibitor on change of the proinsulin to insulin ratio during meal tolerance test in type 2 diabetic patients. METHOD: The subjects of this study were eight drug naive type 2 diabetic patients (5 males and 3 females). A meal tolerance test was performed with and without DPP-4 inhibitor sitagliptin (50mg). Blood samples were obtained before meals and every 30min after meals over a 180min period to determine the levels of plasma glucose, insulin and proinsulin. A meal tolerance test was conducted for two consecutive days to exclude the effect of an improvement of glycemic control. RESULTS: The plasma glucose level at 180min after a meal

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tolerance test was significantly decreased with sitagliptin treatment (from 215.6±68.1 mg/dl to 192.1±65.1 mg/dl, p<0.05), while plasma insulin level at 120min increased with the treatment of sitagliptin (from 41.8±51.8 μU/ml to 54.3±35.5 μU/ml, p<0.05). The proinsulin to insulin ratio at 120min with sitagliptin (0.25±0.16) showed a significant decrease (p<0.05) compared to those without sitagliptin (0.31±0.23). The difference in the plasma proinsulin to insulin ratio, with and without sitagliptin treatment significantly correlated with 24-h urinary c-peptide excretion and body mass index (r=0.564, r=0.736, p<0.05, respectively). CONCLUSION: Our findings suggest that the DPP-4 inhibitor sitagliptin induced a recovery of pancreaticβ-cell function, as evidenced by the decrease in the proinsulin to insulin ratio in type 2 diabetic patients. This improvement was independent of a correction of hyperglycemia.

2449-PO

Effectiveness of Diabetes Control With Vildagliptin vs. other OADs: Baseline Characteristics of Patients Enrolled in the EDGE Study

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Effectiveness of Diabetes control with vildaGliptin and vildagliptin/mEtformin (EDGE) is a prospective, multinational cohort study in adult type 2 diabetes mellitus (T2DM) patients. The purpose of the EDGE study is to compare the effectiveness and safety of vildagliptin with other OADs in T2DM patients inadequately controlled on monotherapy. Patients only became eligible after the treatment decision was final. They were assigned into one of two cohorts depending on which add-on OAD was selected: (i) vildagliptin or (ii) other OADs (including any sulfonylurea, thiazolidinedione, glinide, α-glucosidase inhibitor or metformin but excluding any DPP-4 inhibitor or GLP-1 mimetics/analogues). Overall 45868 patients in 27 countries across the world were enrolled. Due to inconsistency in the data, 2077 patients were excluded from the analysis. The table shows the main baseline characteristics of the patients. The overall average patient was 57.8 years old, had 5.5 years of diabetes duration, had a BMI of 29 kg/m^2 and an HbA1c of 8.2%. HbA1c was better controlled in Southeast Asia/Europe (7.7 - 7.9%) than in India, Lat Am and Middle East (8.6%, 8.5% and 8.5%, respectively). Patients in Southeast Asia/India had lowest BMI (25.2 - 26.6 kg/m^2) with a shorter duration of diabetes (4.3 - 5.7 years) compared with high BMI (30.3 kg/m^2) and longer duration of diabetes (6.3 years) in Europe.

	N (ITT)	Age (y) Mean (SD)	T2DM duration (y) Mean (SD)	BMI (kg/m^2) Mean (SD)	HbA1c (%) Mean (SD)
Southeast Asia	2401	57.2 (11.4)	5.7 (5.4)	25.2 (3.4)	7.7 (1.3)
Europe	22073	62.3 (10.9)	6.3 (5.6)	30.3 (5.2)	7.9 (1.3)
India	10692	51.8 (9.9)	4.3 (4.1)	26.6 (4.0)	8.6 (1.1)
Lat Am	3846	55.9 (12.4)	5.7 (6.1)	29.5 (5.3)	8.5 (1.7)
Middle East	4779	52.1 (10.2)	4.2 (3.9)	29.4 (4.7)	8.5 (1.3)
Overall	43791	57.8 (11.8)	5.5 (5.2)	29.0 (5.1)	8.2 (1.3)

Baseline characteristics of the patients enrolled in this large epidemiological study show that the point at which physicians intensify treatment varies remarkably among EDGE patients from different regions.

Supported by: Novartis Pharmaceuticals Corporation

2450-PO

Effect of Olmesartan 40 mg/Amlodipine 10 mg on Adipocytokines and Insulin Resistance in Hypertensive Patients With Diabetes Mellitus Type 2

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The aim of this study was to investigate the efficacy of olmesartan 40 mg/amlodipine 10 mg in blood pressure control, adipocitokynes (adiponectin and leptin) and insulin resistance in subjects with hypertension and diabetes mellitus. A total of 29 patients with diabetes mellitus type 2 and hypertension, who have inadequate blood pressure control (systolic pressure >130 mmHg and/or diastolic pressure >85 mmHg) without receiving antihypertensive therapy, were enrolled. After recruitment, patients were asked to remain in the same pre-study regimen of diet. Antihypertensive therapy was olmesartan 40mg/amlodipine 10 mg (mid). At the beginning of the study and after 3 months of treatment total-cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, body mass index (BMI), blood pressure, insulin resistance (HOMA), adiponectin and leptin blood levels were evaluated. Average age was 51.7±12.9 years, an average weight of 96.2±22.1 kg and an average body mass index of 34.8±5.7 kg. Sex distribution was (13 females and 16 males). Blood pressure improved; diastolic pressure decreased (92.6±9.4 mmHg vs 84.7±9.8 mmHg;p<0.05) and systolic pressure decreased (158.5±16.3 mmHg vs 144.1±18.6 mmHg;p<0.05), too. Glucose (121.9±68.7 mg/dl vs 118.6±45.4 mg/dl;ns), insulin (13.5±6.9 mUI/l vs 14.7±7.8 mUI/l;ns), HOMA (4.2±3.0 mg/dl vs 4.4±3.2 mg/dl;ns), adiponectin (7.5±3.3 ng/ml vs 7.8±3.5 ng/ml:ns), leptin (11.9±5.9 ng/ml vs 11.6±5.4 ng/ml;ns), total-cholesterol (237.8±53.2 mg/dl vs 217.1±57.1 mg/dl), LDL-cholesterol (157.6±46.3 mg/dl vs 136.8±53.1 mg/dl), HDL-cholesterol (52.2±11.1 mg/dl vs 53.2±11.2 mg/dl), triglycerides (153.8±65.5 mg/dl vs 138.3±63.1 mg/dl) did not change in a significant way. Olmesartan 40 mg/amlodipine 10 mg improved blood pressure without metabolic effects in patients with suboptimal control of hypertension and diabetes mellitus.

2451-PO

Incretins for Perioperative Care—A Pilot Study in Orthopedic Surgery

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There is substantial evidence linking hyperglycemia in surgical patients with worse outcome. Since NICE-SUGAR study appeared, it became more important to avoid hypoglycemia. Data about the therapeutic applications of incretin analogues in inpatients settings are scarce. In the present study, we tested the usefulness of liraglutide (L) as a perioperative non-insulin agent in stable type 2 diabetes undergoing orthopedic surgery (hip2, knee9, spine7, others4). The outcomes were unacceptable hyperglycemia, hypoglycemia, complications (surgical site infections), and length of hospital stay and doses of insulin if required. Twenty-two subjects with informed consents (the mean age and HbA1c:66.2 and 7.8%) were recruited and L was introduced after cessations of OADs and was continued through the entire period of hospital stay including the operation day (day0). Meal was resumed on day1. The mean glucose levels on day -1,0,1,3,7 were 131.7,148,170.6.155.2 and 147.1mg/dl, respectively. Additional insulin was not necessary. By comparison with the medical records of similar surgical procedures, there were no increased poor clinical outcomes. Moreover, there was an additional benefit of body weight loss enabling efficient rehabilitation. Insulin needs frequent glucose measurement and adjustment of dose by well trained medical providers, especially in post-operative period. The present results demonstrated a possible application of L in selected stable patients who are expected to consume meals at regular intervals without adjustment of dose or hypoglycemia. Limitations of the present study are retrospective non- randomized manner, and the small number of the subjects. If L is not tolerated due to side effects or is ineffective, it is impossible to eliminate insulin protocol. In conclusion, L is effective for stable diabetic subjects as an perioperative non-insulin agent without hypoglycemia. Much research is necessary before widespread application is instituted.

2452-PO

Safe Use of Erythropoiesis-Stimulating Agents (ESAs) Among Diabetic Patients Undergoing Dialysis

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Approximately half of all dialysis patients also have diabetes. One area for survival improvement is proper management of anemia since diabetic patients have a higher prevalence compared to non-diabetics. Erythropoiesis-stimulating agents (ESAs) were approved to treat anemia twenty years ago, but uncertainty remains regarding an optimal hematocrit (HCT) treatment target and appropriate dosing. Currently, the use of a single HCT target range and dosing protocol for all dialysis patients *ignores the presence of diabetes*. Preliminary research findings indicate a hazard ratio of 1.32 vs. 1.06 for all-cause mortality among diabetics and nondiabetics, respectively, for patients exposed to the highest vs. medium ESA doses. We use an innovative causal inference statistical method to adjust for time-dependent confounding to determine the effect of different anemia management strategies using 2007 - 2008 data for all Medicare-certified dialysis patients whose underlying cause of renal failure is diabetes. We are testing two different anemia management strategies: 1) We hypothesize that HCT target of 30-33%—lower than the National Kidney Foundation-recommended HCT target (33-36%)—is associated with improved patient outcomes among dialysis patients *with diabetes. Preliminary findings suggest that the lower target is associated with better outcomes such as improved mortality and fewer adverse cardiovascular outcomes; and* 2) We hypothesize that among *diabetic patients* who do not achieve the target HCT range even after use of high ESA doses (nonresponders), subsequent low dose therapy (<5,000 U/admin) is associated with better outcomes. *Preliminary findings suggest that escalating dose for hyporesponsive diabetic patients does not improve survival and may*

lead to increased hospitalization for adverse cardiovascular events. In conclusion, early results suggest a need for differential anemia treatment strategies for renal failure patients based on the presence of diabetes.

2453-PO

Pramlintide-Induced Shift Towards Euglycemia Based on Self-Monitored Blood Glucose Profiles in T1DM

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To further understand the effect of pramlintide (PRAM) on glycemia, this post-hoc analysis of 2 clinical trials in patients with T1DM evaluated the proportion of pre- and postprandial readings from self-monitored 7-point glucose profiles that fell above, below, or within glycemic targets based on AACE and ADA guidelines. Four time periods were analyzed: baseline, Wk 1-4, Wk 5-15, and Wk 16 to study end. Trial 1, open-label clinical practice trial: Patients (N=218, age 43±11 y, weight 81.9±17.6 kg, BMI 28.7±5.2 kg/m^2, A1C 8.0±1.0%, T1DM duration 21±11 y) received PRAM for 6 mo, PRAM was titrated from 15 to 60 mcg over 4 wks while reducing mealtime insulin. Trial 2, placebo (PBO)-controlled trial: Patients were randomized to PRAM (n=115, age 42±14 y, weight 82.1±17.8 kg, BMI 28.0±4.8 kg/m^2, A1C 8.1±0.8%, T1DM duration 20±12 y) or PBO (n=133, age 41±12 y, weight 80.6±17.2 kg, BMI 27.7±4.7 kg/m^2, A1C 8.1±0.8%, T1DM duration 21±12 y) for 29 wks, titrating PRAM as above. A shift to more favorable glycemia (more readings in the euglycemic range and less hyperglycemia) was seen with PRAM starting during Wk 1-4 and was sustained throughout the studies. Percentage of readings in the hypoglycemic range (<70 mg/dL) remained relatively stable.

Mean Percentage of Blood Glucose Readings in the Euglycemic Range in Patients with T1DM Based on AACE and ADA Guidelines at Baseline and Week 16 - Study End

		Trial 1		Trial 2			
		Baseline: Insulin	End: PRAM + Insulin	Baseline: Insulin	End: PRAM + Insulin	Baseline: Insulin	End: PBO + Insulin
Euglycemia (% of measurements)	AACE	27.7±1.4	32.7±1.8*	22.6±1.2	27.8±0.8*	24.1±1.2	25.0±0.8
	ADA	44.3±1.7	52.5±2.2**	37.3±1.3	43.9±1.1*	38.2±1.5	40.9±1.0

Euglycemia: preprandial 70-130 mg/dL, postprandial 70-180 mg/dL (ADA); preprandial 70-<110 mg/dL, postprandial 70-<140 mg/dL (AACE). *P<0.05, ** P<0.001 vs baseline in Trial 1 and vs PBO in Trial 2. Values are mean±SE.

In these studies PRAM also exerted a small improvement in A1C with a reduction in daily insulin dose and body weight. The safety profile was consistent with the Prescribing Information. In this post-hoc analysis adjunctive use of PRAM + insulin in T1DM allowed more effective glycemic control than insulin alone, shifting overall glycemia towards the euglycemic range.

2454-PO

WITHDRAWN

2455-PO

Real World Outcomes of Adding Rapid Acting Insulin vs Switching to Analog Premix Insulin among Patients With Type 2 Diabetes Treated With Insulin Glargine

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ADA guidelines recommend treatment intensification for type 2 diabetes (T2DM) patients if basal insulin fails to achieve glycemic control. However, real-world data are limited. Using IMPACT®, a national managed care database, real world outcomes among T2DM patients previously treated with insulin glargine (GLA) were compared, those who added rapid acting insulin (RAI) to GLA (GLA+RAI) vs those switching to analog premix (PMX). Cohorts were matched at baseline by 1:1 propensity score matching, resulting in 746 matched patients (373 in each cohort; 42.2% women; mean baseline age 56.4 years; A1C 9.5%; # oral anti-diabetes drugs 1.7; GLA daily unit 40 U/day). Analysis was conducted using intent-to-treatment approach. During 1-year follow up, GLA+RAI patients were more persistent (52.0 vs 43.2%; P=0.0156; persistence days: 274 vs 249; P=0.002) than PMX patients, in terms of continuing on GLA versus switching to and continuing on PMX, but similar in A1C reduction from baseline (-0.79 vs -0.71; P=0.6455), percentage of patients achieving A1C < 7.0% (15.5 vs 13.7%; P=0.5956), hypoglycemia-related event rate (11.3 vs 11.8%; P=0.8186), and total health care cost ($20,553 vs $21,683; P=0.5964). However, in the PMX group almost half (48.8%, n=182) used GLA or RAI during the follow up, among whom 40% switched back to GLA, 44.5% used GLA and PMX alternatively or concomitantly, 10% used RAI and PMX concomitantly, and 5.5% used RAI only. Only 5% in the GLA+RAI group used PMX during the follow up. This real-world study showed that T2DM patients who switched from GLA to PMX still used or switched back to GLA or RAI relatively often. Further study needs to be conducted to better understand this issue and help clinicians optimize outcomes for T2DM patients.

Supported by: sanofi-aventis

2456-PO

Insulin Regimen Changes and Quality of Life among Japanese Patients With Type 2 Diabetes: The INSIGHTs Observational Study

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To assess the changes in Quality of life (QOL) associated with changes in insulin regimen in patients with type 2 diabetes mellitus (T2DM), we conducted a multicenter, observational study (INSIGHTs; INSulin-changing study Intending to Gain patients' insights into insulin treatment with patient-reported Health outcomes in actual clinical TreatmentS). Patients with T2DM who planned to change insulin regimen (type of insulin, injection device, and/or number of injections) were entered this study. Primary outcome measure was change from baseline to endpoint (12 weeks) in QOL assessed by the Insulin Therapy-Related Quality of Life (ITR-QOL) questionnaire. Secondary outcome measures included changes from baseline to endpoint (12 weeks) in HbA1c, daily dose of insulin, and adherence of insulin injections. A total of 625 patients were evaluated. Most (83.4%) patients changed the type of insulin, 29.3% changed the number of injections, and 20.2% changed the injection device. In terms of number of injections, 13.3% of patients injected once a day, 38.6% twice a day, 31.8% three times a day and 16.3% four times a day at baseline. For the patients who changed number of injections, 72.7% increased number of injection and 27.3% decreased, and most (83.1%) patients increased/decreased the number of injection in a stepwise fashion. QOL assessed by the ITR-QOL did not worsen during the study in any type of changes. Glycemic control improved, as evidenced by decreased HbA1c (baseline: 8.21 ± 1.47%; endpoint: 7.85 ± 1.31%; P<0.001). Daily doses of insulin were stable during the study (baseline 30.7 ± 21.8IU, endpoint 31.5 ± 20.1IU). There was no significant change in adherence of insulin injections at both baseline and endpoint. In conclusion, individual modification of insulin regimen improved glycemic control in patients with T2DM without worsening QOL.

2457-PO

New Mechanism and Protective Effect of GLP-1 on Endothelial Cell

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Objective: The major complication of diabetes mellitus is cardiovascular problem. But the aspects of vascular complication are some different in macrovascular and microvascular features. so this study was conducted to investigate the different response and mechanism of human microvacular endothelial cell (HMVEC) and human aortic endothelial cell (HAEC) in high glucose and in pretreatment with GLP-1. Research design and Methods: Expression of the Notch-1, 4, GLP-1 receptor, GIP receptor was examined in HMVEC, HAEC by RT-PCR, Western blot analysis. Angiogenesis of HMVEC, HAEC was evaluated based on wound healing assay and angiogenesis assay. Results: GLP-1, GIP receptor and notch 1,4 were expressed in HMVEC and HAEC. Although, there was no angiogenesis and wound healing effect in high glucose stressed HAEC and/ or pretreatment with VEGF or Ex-4, but in HMVEC, angiogenesis and wound healing effect were shown. Also. Notch-1,4 signaling was changed in HMVEC. Conclusions: Our findings suggested that regulation of Notch-1,4 signaling in Ex-4 treated HMVEC induce angiogenesis and wound healing effect. Modulation of Notch 1,4 signaling may hold promise as a novel therapeutic strategy for the treatment of diabetic microvascular complications.

For author disclosure information, see page 797.

2458-PO

Usefulness of Exenatide Therapy in Patients With Type 2 Diabetes Under Undesirable Glycemic Control

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The purpose of this study is to evaluate the utility of exenatide in patients with type 2 diabetes mellitus who have not achieved desirable glycemic control with the previous conventional therapy. Subjects of this study were 63 out-patients (man 26/women 37, age 64.8±11.1 years old, BMI 27.5±6.0,on insulin 32)with HbA1c more than 6.9%, or with repeating hypoglycemia even lower than 6.9%. We prescribed exenatide to these subjects for 6 months; 5 mcg at first, and 10 mcg after 1 month, twice a day in morning and evening together with the previous treatment after reducing the dose of sulfonia urea. Insulin-treated patients were switched to exenatide after confirming endogenous insulin secretional capacity by measuring CPR after intravenous glucagon test. We examined glucose and HbA1c levels, lipid profiles, and body weight before and after the exenatide therapy. We also measured serum CPR before and two hours after meal load and evaluated insulin secretional capacity using fasting CPR and ΔCPR. Three patients discontinued the use of exenatide within 3 months because of nausea. All of them felt nausea also after glucagon test. Other 23 cases experienced mild nausea but it relieved within 2 weeks. HbA1c,fasting plasma glucose, and 2-hour-postprandial plasma glucose significantly decreased from 7.2±1.2 to 6.2±0.7%(p=0.0036), 139±31 to 104±16 mg/dl (p=0.0025), 207±50 to 147±28mg/dl (p=0.00090). Fasting CPR and Δ CPR after meal load significantly increased from 2.2±0.98 to 2.4±1.1 ng/ml (p=0.0032),2.4±1.2 to 5.1±1.5ng/ml (p=0.00067). Plasma triglyceride significantly decreased from 180±126 to 144±86 mg/dl (p=0.027), and body mass index also significantly decreased from 27.5±6.0 to 23.8±9.1 (p=0.012). No significant change was seen in blood pressure, LDL and HDL-cholesterol levels. These date show that exenatide therapy increased the insulin secreting capacity. It is useful in the control of body weight, glucose and lipid control in type 2 diabetes.

2459-PO

Contributing Factors for Initiation of GLP-1 Agonist, DPP-4 Inhibitor or Insulin after Metformin or Sulfonylurea in US

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Therapeutic options for Type 2 diabetes after metformin (MET) or sulfonylurea (SU) include GLP-1 agonist (GLP-1), DPP-4 inhibitor (DPP-4) or Insulin. Contributing factors to the choice of therapy are not well understood. Patient cohorts stable on MET or SU (≥6 months) in 2008 and 2009, as baseline (BL), were identified from the IMPACT™ claims database and evaluated for the initiation of GLP-1, DPP-4 or insulin in the subsequent year of 2009 and 2010, respectively. Stable MET or SU users were identified in 2008 (n=153,582) and 2009 (n=148,704). Rate of GLP-1 use was 1.3% to 1.8% and DPP-4 use was 5.4% to 6.1% from 2009 to 2010. Yearly insulin initiation rate remained stable at 3.5%. Mean A1c at BL was 8.1% in those who initiated insulin in 2009 and 8.4% in 2010. Mean A1c at BL was 7.5% for GLP-1 and 7.6% for DPP-4 initiators. At BL, insulin initiators were 85% on MET, 75% on SU and 3 out of 4 on ≥2 oral agents while GLP-1 and DPP-4 were initiated with 90% BL MET use, less with SU (60%) and two thirds on ≥2 oral agents. Insulin and DPP-4 initiators had a similar mean age of 57 years, while GLP-1 initiators were about 5 years younger, with more female (51% versus 40% and 43% for DPP-4 and Insulin, respectively) and nearly twice as many medical claims for obesity (21% vs 11% and 13%, respectively). In comparison with DPP-4, insulin initiators had more BL comorbidities, e.g. twice as many renal disease (8% for insulin vs 4% for DPP-4), 30% higher cardiovascular disorders (20% vs 15%) and over 70% more hospital admissions (16% vs 9%). GLP-1 initiators had the least BL comorbidity burden with 3% renal disease, 10% cardiovascular disorder and 8% hospital admissions. In summary, the data shows an increased use of GLP-1 and DPP-4 therapy from 2009 to 2010. Insulin is more likely used in patients with A1c above 8%. GLP-1 is more likely to be initiated in patients with younger age, female gender, lower comorbidity and more obesity.

Supported by: sanofi-aventis

2460-PO

Effect of Aliskiren Addition to Losartan on Fibrinolysis in Diabetic Hypertensive Patients: A Three-Way Crossover Study

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The aim of this study was to assess the effect of aliskiren and losartan on plasma PAI-1 antigen and tPA activity in hypertensive patients with type 2 diabetes. After a 2 week placebo period 105 outpatients with grade 1-2 hypertension and well controlled type 2 diabetes (HbA_{1c} <7%) were randomized to losartan 100 mg od or to aliskiren 300 mg od or to their combination for 12 weeks in three crossover periods. At the end of placebo period and of each treatment period blood pressure, plasma PAI-1 antigen and plasma tPA activity were assessed. Both monotherapies similarly reduced systolic blood pressure (SBP; p<0.001) and diastolic blood pressure (DBP; p<0.001), but the reduction was greater with aliskiren/losartan combination (SBP -21.6 mmHg, p<0.01 vs both monotherapies; DBP -18.1 mmHg, p<0.01 vs both monotherapies). Plasma PAI-1 antigen was unaffected by aliskiren alone, while it was significantly increased by losartan (+4.2 ng/ml, p<0.05 vs placebo); the aliskiren/losartan combination produced a more marked increase in plasma PAI-1 antigen (+9.4 mg/ml, p<0.01 vs baseline, p<0.05 vs losartan). The tPA activity showed no significant change with aliskiren, a decrease with losartan (-0.04 IU/ml, p<0.05 vs baseline) and a greater decrease with the combination (-0.08 IU/ml, p<0.01 vs baseline). In conclusion, the renin inhibitor aliskiren amplified the fibrinolysis impairment induced by losartan in diabetic hypertensive patients. It might be due to reduced formation of the protective Ang II breakdown products. The clinical relevance of this effect remains to be clarified.

2461-PO

The Comparative Study of Dipeptidyl Peptidase-IV Inhibitor and Sulfonylurea on the Effect of Improving Glucose Variability and Oxidative Stress in Type 2 Diabetic Patients With Inadequate Glycemic Control on Metformin

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Aims: Our study tries to compare the effect of sitagliptin on 24-hour blood glucose variability and oxidative stress marker to that of sulfonylurea such as glimepiride. Methods: A 4-week, randomized, double blind-labeled prospective design was used. We recruited total 26 patients who were treated with metformin for at least 2 months(more than 1000mg) and glycemic changes obtained by CGM and these data are averaged over all subjects. Results: The comparison of HbA_{1c} between baseline and follow-up showed that HbA_{1c} was significantly reduced from 7.1 ± 0.4 % to 6.8 ± 0.3 % in sitagliptin group (p=0.002) and from 7.3 ± 0.4 % to 6.9 ± 0.4% in glimepiride group (p<0.001). Fasting glucose level showed a tendency to decrease between baseline and 4-weeks in sitagliptin group (from baseline 137.5 ± 18.5 to 125.0 ± 19.4 mg/dL, p=0.622) and significantly decreased in glimepiride group (from baseline 139.6 ± 26.6 to 118.9 ± 20.0 mg/dL, p<0.001). The sitagliptin group and the glimepiride group led to similar HbA1c levels (p=0.709) and fasting glucose level (p=0.526) after 4 weeks and there was no significant differences between two groups. The MAGE were significantly decreased in sitagliptin group (from baseline 96.6 ± 8.0 mg/dL to 72.1 ± 13.1 mg/dL, p=0.002), but no significant difference in in glimepiride group (from baseline 103.0 ± 27.2 mg/dL to 89.2 ± 26.1 mg/dL, p=0.175). Conclusions: We proved that sulfonylurea can be converted into sitagliptin without problems. In addition, when sitagliptin is used in combination with metformin, the patients showed much more efficient blood glucose controlling effects.

2462-PO

Saxagliptin Monotherapy or Combination Therapy: Outcomes by Duration of Type 2 Diabetes

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To determine whether duration of type 2 diabetes (T2D) affects response to saxagliptin 5 mg/d, data stratified by disease duration (≤3 y, >3 to <5 y, ≥5 y) were analyzed from 5 pooled placebo-controlled studies of saxagliptin monotherapy or saxagliptin added to metformin, glyburide, or thiazolidinedione (n=1681 in saxagliptin 5 mg and placebo arms). At week 24, improvements in glycemic control were greater with saxagliptin 5 mg/d than with placebo in all groups of disease duration (Table). The incidences of adverse events were similar across disease duration groups (70.5%-72.7% with saxagliptin, 65.8%-76.9% with placebo). This analysis shows that saxagliptin 5 mg/d is effective and well tolerated in T2D patients regardless of disease duration.

	Adjusted Mean Change From Baseline (SE) at Week 24*	≤3 y n=735	Difference (95% CI)	>3 and <5 y n=262	Difference (95% CI)	≥5 y n=684	Difference (95% CI)
SAXA 5 mg vs PBO (5 pooled studies)	HbA_{1c}, %	–0.7 (0.1) vs –0.2 (0.1)	–0.5 (–0.7, –0.4)	–0.6 (0.1) vs 0.1 (0.1)	–0.7 (–0.9, –0.5)	–0.7 (0.1) vs 0.2 (0.1)	–0.8 (–1.0, –0.7)
	FPG, mg/dL	–12.2 (2.1) vs –1.1 (2.2)	–11.1 (–17.0, –5.1)	–15.6 (3.4) vs –0.1 (3.4)	–15.5 (–24.8, –6.2)	–14.8 (2.2) vs 3.9 (2.3)	–18.7 (–24.6, –12.8)
	PPG, mg/dL	–55.1 (4.0) vs –21.0 (4.4)	–34.1 (–45.7, –22.5)	–54.7 (6.5) vs –11.6 (6.7)	–43.0 (–61.1, –25.0)	–44.6 (4.2) vs 1.0 (4.4)	–45.6 (–56.9, –34.3)
	Proportion of patients achieving HbA_{1c} <7%	165/387 (42.6%) vs 87/323 (26.9%)	15.1%† (7.5%, 22.6%)	43/128 (33.6%) vs 21/126 (16.7%)	15.8%† (5.1%, 26.5%)	104/347 (30.0%) vs 37/330 (11.2%)	17.8%† (11.6%, 24.0%)

*Last observations carried forward. †Differences are based on proportions weighted by Mantel-Haenszel approach. n values listed in each disease duration category are for SAXA 5 mg and placebo groups combined. FPG=fasting plasma glucose; HbA_{1c}=glycated hemoglobin; MET=metformin; PBO=placebo; PPG=120-minute postprandial glucose; SAXA=saxagliptin.

Supported by: Bristol-Myers Squibb/AstraZeneca

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2463-PO

WITHDRAWN

2464-PO

Meta-analysis of Efficacy and Safety Outcomes Associated With the Basal-Plus Regimen of Insulin Glargine and Insulin Glulisine among Type 2 Diabetes Patients With HbA_{1c} ≥8%

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To assess the efficacy and safety of the basal-plus insulin regimen (once-daily insulin glargine and insulin glulisine) among patients with type 2 diabetes inadequately controlled by basal insulin and oral anti-diabetic drugs (OADs), a meta-analysis was conducted using data from four randomized clinical trials of over 24 weeks. In order to reflect the clinical practice guidelines in France, the study population consisted of the patients with baseline HbA_{1c} ≥8% from the four trial populations without a control arm. Efficacy was measured by changes in HbA_{1c}, fasting (FBG) and post-prandial (PPG) blood glucose levels. Safety was measured through the episodes of severe hypoglycemia (as defined in each of the original clinical trials), as well as changes in weight and body mass index (BMI) during treatment. The 210 patients with HbA_{1c} ≥8% included in the meta-analysis had a mean age of 60.3 ± 8.8 years, duration of diabetes of 12.4 ± 7.7 years, baseline HbA_{1c} levels of 8.63% ± 0.62, and OAD use for 6.30 ± 5.57 years. At the end of study, glycemic control was improved with a mean decrease in HbA_{1c} levels of -0.84% (95% confidence interval (CI): -1.17, -0.51) and a significant decrease in PPG of -70.64 mg/dL (95% CI: -86.9, -54.4). There was no significant decrease in FBG with a mean difference of -1.07 mg/dL (95% CI: -13.75, 11.60). At the study endpoint, 18% of the patients achieved HbA_{1c} levels of <7%. 1.4% of patients experienced severe hypoglycemia. The meta-analysis showed that during treatment the average weight change is 0.81 kg (p=0.46), BMI change is 0.26 kg/m^2 (p=0.59). This meta-analysis without a control arm suggests that the basal-plus insulin regimen may improve glycemic control with a low level of severe hypoglycemia. Further study is necessary to evaluate the efficacy and safety of the basal-plus regimen in comparison to current treatment practices and with a longer follow-up period.

Supported by: sanofi-aventis

2465-PO

WITHDRAWN

2466-PO

Effect of Insulin Switching on A1C in Inadequately Controlled Asia Pacific Diabetes Patients

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Effects of switching from 1 insulin regimen to another in real-world patients with inadequately controlled type 1 (T1D) or type 2 diabetes (T2D) were examined prospectively in a non-interventional, open-label registry in 10 Asia Pacific countries. Inclusion required diabetes duration ≥ 5 y, A1C ≥ 8%, and prescribed switch in insulin regimen. Change in A1C and FBG over 6 months was measured. Of 1765 patients (mean weight = 67.2 kg), 115 had T1D (6.5%; mean age = 32.6 y) and 1650 had T2D (93.5%; 57.1 y). At study entry, 435 (24.6%: T1D, n = 76; T2D, n = 359) were using insulin only and 1330 (75.4%: T1D, n = 39; T2D, n = 1291) insulin + OAD. In total, 787 (44.6%) were using premixed insulin, 730 (41.4%) basal insulin, and 116 (6.6%) prandial + basal insulin. At baseline, 70.0% (1236/1765) switched between insulin classes, with 73.2% (576/787) switching from premixed insulin to glargine (T1D: 33.9%, 39/115; T2D: 32.5%, 537/1650). Mean baseline daily dose of all switched insulin was 27.7 ± 18.8 U. A1C and FBG declined significantly over 6 months in both diabetes types (Table). At Month 6, 17.5% (17/97) of T1D and 27.6% (402/1456) of T2D patients reached A1C < 7%. The most common reason for not achieving A1C < 7% was insufficient up-titration of insulin dose (377/958, 39.4%). This study's real-world nature precluded outcome optimization. 74 adverse drug reactions (all hypoglycemia_85.1% of mild severity) were reported by 2.8% (49/1765). Most hypoglycemic events at Months 3 (87.7%, 50/57) and 6 (94.1%, 16/17) were nonserious. Insulin switching in this non-interventional, open-label registry was safe and effectively lowered A1C in T1D and T2D patients.

	T1D	T2D
Patients, n	115	1650
Baseline A1C, % (SD)	9.8 (1.6)	9.8 (1.6)
Endpoint A1C, % (SD) *P* Value (ANCOVA) vs baseline	8.3 (1.8) <0.001	8.2 (1.7) <0.001
Baseline FBG, mg/dL (SD)	192.6 (85.7)	193.7 (78)
Endpoint FBG, mg/dL (SD) *P* Value (ANCOVA) vs baseline	131.6 (53.6) <0.001	140.6 (59.0) <0.001

Supported by: sanofi-aventis

For author disclosure information, see page 797.

ADA-Funded Research

2467-PO

Effect of Olmesartan 40mg/Amlodipine 10 mg on Visfatin and Insulin Resistance in Hypertensive Patients With Obesity

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The aim of this study was to investigate the efficacy of olmesartan 40 mg/amlodipine 10 mg in blood pressure control, visfatin levels and insulin resistance in subjects with hypertension and obesity. A total of 30 patients with obesity and hypertension, who have inadequate blood pressure control (systolic pressure >140 mmHg and/or diastolic pressure >90 mmHg) without receiving antihypertensive therapy, were enrolled. After recruitment, patients were asked to remain in the same pre-study regimen of diet. Antihypertensive therapy was olmesartan 40mg/amlodipine 10 mg (mid). At the beginning of the study and after 3 months of treatment total-cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, body mass index (BMI), blood pressure, insulin resistance (HOMA) and visfatin levels were evaluated. Average age was 52.43±16.4 years, an average weight of 96.4±14.6 kg and an average body mass index of 35.1±5.9 kg. Sex distribution was (14 females and 16 males). Blood pressure improved, diastolic pressure decreased (91.9±9.8 mmHg vs 84.4±9.8 mmHg;p<0.05) and systolic pressure decreased (157.6±17.3 mmHg vs 143.6±18.4 mmHg;p<0.05). Glucose (120.6±67.7 mg/dl vs 117.6±44.8 mg/dl;ns), insulin (13.3±6.7 mUI/l vs 14.7±7.5 mUI/l;ns), HOMA (4.1±2.9 mg/dl vs 4.4±3.1 mg/dl;ns), total-cholesterol (227.8±52.3 mg/dl vs 217.4±56.1 mg/dl:ns), LDL-cholesterol (147.6±45.1 mg/dl vs 136.5±62.7 mg/dl:ns), HDL-cholesterol (52.3±10.9 mg/dl vs 53.1±11.6 mg/dl:ns), triglycerides (152.5±64.3 mg/dl vs 137.3±63.7 mg/dl:ns) did not change in a significant way. Visfatin levels increased in a significant manner (7.2±1.8 mg/dl vs 7.9±1.7 mg/dl;p<0.05) Olmesartan 40 mg/amlodipine 10 mg improved blood pressure with a significant increase of visfatin levels in patients with suboptimal control of hypertension and obesity.

2468-PO

Starting Insulin Aspart is Associated With Improved Quality of Life Regardless of Age: Findings from the A_1chieve Study

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Type 2 diabetes (T2DM) can have a negative impact on health-related quality of life (HRQoL). However, measured HRQoL improves with better glycemic control. A_1chieve was a non-interventional study evaluating the safety and clinical efficacy of insulin analogs in people with T2DM (n=66 726) in routine clinical care in 28 countries across four continents. This subgroup analysis investigated the effectiveness of mealtime(s)-only insulin aspart (aspart), and its impact on HRQoL in insulin-naïve younger (≤65) and older (>65) adults. Participants were of mean age 49.1 (SD 10.6) and 71.3 (5.1) years respectively. Baseline A1C was poor (9.6 [1.8] and 9.5 [1.9] %), improving significantly after 24 weeks to 7.3 (0.9) and 7.4 (1.1) % (p<0.001). Significant improvements were seen in fasting plasma glucose and postprandial plasma glucose (p<0.001) at 24 weeks (Table). Advanced age and insulin use are recognized risk factors for hypoglycemia and an expected, non-significant increase in overall incidence of hypoglycemia was seen in older participants, but rates were still low. Reported rates in the younger group decreased (p<0.001). In both groups, insulin dosing decreased during the study. HRQoL was measured by EQ-5D 100-point visual analog scale. Significant improvements were seen at 24 weeks in both groups (p<0.001); there was no significant weight change. These results demonstrate combined HRQoL and glycemic benefits seen with the initiation of aspart in people with T2DM.

Glycemic control, body weight and HRQoL following 24 weeks' treatment with insulin aspart

	≤65 years	>65 years
n	2249	420
Insulin dose (U/kg/day)		
Week 0	0.42 (0.19)	0.42 (0.19)
Week 24	0.41 (0.19)	0.45 (0.23)
Injection frequency (OD/BID/TID/>TID [% of individuals])		
Baseline	4.6/34.5/54.9/6.0	4.0/22.9/65.7/7.4
Week 24	5.9/62.6/25.9/5.6	4.6/53.3/36.8/5.4
A1C (%)		
Baseline	9.6 (1.8)	9.5 (1.9)
Change	-2.4 (1.9)*	-2.0 (1.8)*
FPG (mg/dl)		
Baseline	209 (71)	190 (73)
Change	-72 (60)*	-53 (58)*
PPPG (mg/dl)		
Baseline	301 (87)	273 (94)
Change	-108 (76)*	-87 (78)*
Hypoglycemia (events/person-year [% of individuals with event])		
All events		
Baseline	1.54 (6.0)	1.95 (5.5)
Week 24	0.65 (2.5)*	2.11 (5.7)
Major		
Baseline	0.12 (0.8)	0.22 (1.2)
Week 24	0.0 (0.0)*	0.0 (0.0)†
Minor		
Baseline	1.42 (5.8)	1.73 (4.8)
Week 24	0.65 (2.5)*	2.11 (5.7)†
Body weight (kg)		
Baseline	68.6 (11.9)	65.7 (11.4)
Change	0.2 (2.7)	0.3 (3.1)
	(p=0.018)	
Health-related quality of life (VAS 0-100)		
Baseline	62.3 (17.7)	64.2 (16.6)
Change	16.7 (17.7)*	12.1 (16.7)*

Mean (SD) or as stated; *p<0.001; †p=NS; BID, twice a day; FPG, fasting plasma glucose; OD, once daily; PPPG, postprandial plasma glucose; SD, standard deviation; TID, three times a day; VAS, visual analog scale.

2469-PO

Thyroid Stimulating Hormone Suppression Associated With Metformin

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A 70 year old woman with atrial fibrillation, hypertension, high cholesterol, thyroid nodules, subclinical hyperthyroidism, and type 2 diabetes was evaluated. There were no symptoms referable to hyperthyroidism. Blood pressure was 114/80, pulse 78, there was no proptosis or lid lag, thyroid was bilaterallyenlarged and firm with a left lobe nodule measuring 5 cm and right lobe nodule measuring 2 cm. Over several years TSH levels varied from 0.02 to 0.39 uIU/mL, with normal free T4 and total T3 levels. Thyroid uptake/scan revealed heterogeneous distribution of iodine with minimal uptake on the left and increased uptake on the right. Metformin was discontinued and subsequent TSH levels normalized, and have remained normal for one year (most recent TSH was 0.74 uIU/mL). Many drugs can affect thyroid function. Metformin is the most widely used drug for type 2 diabetes. Recently it has been reported that metformin might interfere with thyroid function. Possible mechanisms include a subtle increase in the gastrointestinal absorption of levothyroxine, enhancement of inhibitory feedback of thyroid hormones on TSH secretion, or a deficiency in hypothalamic dopamine. Metformin administration improves endogenous hypothalamic dopaminergic tone while decreasing insulin resistance. Here we describe a patient with diabetes and subclinical hyperthyroidism which improved after discontinuation of metformin. Future studies are needed to elucidate the mechanisms of the TSH-lowering effect of metformin. In a patient on metformin with abnormal

For author disclosure information, see page 797.

thyroid function tests, metformin should be considered as a contributing factor to the underlying thyroid dysfunction.

2470-PO

BIAsp 30 Once Daily is Well Tolerated and Non-Inferior to Insulin Glargine Once Daily Both in Combination With Metformin and Glimepiride in Chinese and Japanese Subjects With Type 2 Diabetes

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Biphasic insulin aspart 30 (BIAsp 30) once daily (OD) as initiating insulin therapy can improve glycaemic control effectively and safely, but data in Asian populations is lacking. This open-labeled, randomized 24-week trial investigated the efficacy and safety of BIAsp 30 OD compared to insulin glargine (IGlar) OD in subjects with type 2 diabetes in China and Japan. Eligible insulin naïve subjects entered a 3-week run-in period to optimize treatment of metformin and glimepiride, and were then randomized (1:1) to BIAsp 30 or IGlar group. A total of 521 subjects (mean ±SD age: 56.3±9.6 yrs, BMI: 25.7±3.4kg/m^2, duration of diabetes: 9.4±6.9 yrs, baseline HbA_{1c}: 8.2±0.9%) were randomised. After 24 weeks of treatment, the estimated reductions in HbA_{1c} from baseline were 0.68% and 0.56% with BIAsp 30 and IGlar, respectively. BIAsp 30 was non-inferior to IGlar (estimated mean treatment difference [FAS]: -0.12 % [-0.25; 0.02] $_{95\%CI}$). The percentage of subjects achieving HbA_{1c}<7% were comparable between the two groups (~30%). Mean 9-point self measured plasma glucose values generally decreased in both groups. Subjects treated with BIAsp 30 showed significantly lower mean plasma glucose (PG) levels at 2 hours after dinner, at bedtime and at 02:00 to 04:00 am in the following day. Subjects treated with IGlar had lower mean PG level before dinner. No safety concerns were raised in this trial. A total of 7 serious AEs (2 with BIAsp 30 and 5 with IGlar) were reported and only 1 was probably related to trial product (IGlar). The rates of hypoglycemic episodes and minor hypoglycemic episodes (PG value < 3.1 mmol/l) were generally low and comparable in both groups, and only 1 severe hypoglycemic episode was reported with IGlar. In conclusion, BIAsp 30 OD in combination with metformin and glimepiride was well tolerated and as effective as IGlar OD as measured by HbA_{1c} reduction.

2471-PO

Clinical Effect of Aerosol Inhalation of Amphotericin B in Lower Respiratory Tract Fungal Infections in Elderly Diabetics

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Due to an aging population, widespread use of antibiotics, immunosuppressive agents, fungal infections is increasing. Diabetes, especially among older people, due to old age, tissues and organs degradation, high blood sugar and metabolic disorders, resulting in significantly lower immune function, making it a fungal infection in high-risk populations.To investigate the Clinical effect and safety of aerosol inhalation of amphotericin B in lower respiratory tract fungal infections in elderly diabetics. Amphotericin B (Amphotericin B, AMB) has become the treatment of choice for severe fungal infections medicine drug with broad-spectrum anti-fungal activity, but intravenous drug adverse reactions and more limited their use. Amphotericin B inhalation method is simple and effective, and few adverse reaction. 42 elderly diabetics with lower respiratory tract fungal infections were randomly divided into observation group and control group. The observation group use of amphotericin B 25mg sterile water for injection 20ml, each taking 10-12.5mg aerosol inhalation, oxygen flow rate 8-10L/min, continuous 15-20min, 2 times / day, 10-14 days of treatment. Amphotericin B alone control group, intravenous infusion of 25mg, 1 times / day , 10-14 days of treatment. The Clinical effective rate in trial group and control group were 66.6% and73.6%(P> 0.05),adverse reaction rates were23.8 % and 80.9%(P<0.05) respectively. The aerosol inhalation of Amphotericin B is effective and safe in lower respiratory tract fungal infections in elderly diabetics.

2472-PO

The Efficacy and Safety of the Combination Usage of Mitiglinide and Dipeptidyl-Peptidase-4 Inhibitor Sitagliptin

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Background: This study was aimed to examine the efficacy and the safety of the combination usage of mitiglinide and sitagliptin. Method: 14 type 2 diabetes patients, those who had already taken 30 mg per day of mitiglinide for longer than 14 weeks and their HbA1c was stable between 6.5 % and 8.5 %, are given 50 mg per day of sitagliptin. At the beginning of sitagliptin and 12 weeks later, meal-tolerance tests were carried out. Test meal, comprised of 3 blocks of Calorie-mate bar (Otsuka pharmaceuticals, Japan) and 1 pack of Calorie-mate jelly (Otsuka pharmceuticals), was composed of 11.5 % of protein, 37.9 % of fat, 50.6 % of carbohydrate, 497.5 kcal in all. After 12 weeks, glimepiride was replaced mitiglinide if his HbA1c increased more than 7.0. Remaining patients were examined another 12 months. Results: 12 weeks later, HbA1c (%) decreased significantly from 7.48±0.61 to 6.59±0.68 (p<0.0001) and 1,5-anhydroglucitol (1,5AG) (mg/dl) significantly increased from 6.04±3.41 to 10.54±5.91 (p<0.0001). Fasting plasma glucose (mg/dl) and insulin (microU/ml) changed from 164.9±21.7 and 4.18±3.15 to 154.1±20.3 and 4.62±2.14, respectively. Hypoglycemic symptom was not observed. At meal tolerance test, plasma glucose concentration at 60 min and 120 min significantly decreased from 245.3±53.4 and 235.6±77.9 to 212.5±39.8 (p<0.05) and 200.3±63.8 (p<0.05), respectively. Plasma insulin at 120 min significantly increased from 17.83±8.41 to 26.36±13.16 (p<0.05). 12 weeks later, 3 patients were dropped and so were 4 patients during 12 weeks and 9 months. Therefore, remaining 7 patients were further analyzed. HbA1c decreased significantly from 7.06±0.43 at 0 week to 6.04±0.31 at 12 weeks (p<0.0005), 6.37±0.23 (p<0.05) at 9 months, and 6.36±0.47 (p<0.05) at 15 months, respectively. 1,5AG significantly increased from 8.10±3.50 at 0 week to 15.20±4.48 at 12 weeks (p<0.005), 12.40±2.94 (p<0.005) at 9months, and 14.94±4.43 (p<0.005) at 15 months, respectively.

2473-PO

Control of Postprandial Hyperglycemia With Intensive Insulin Treatment is Fundamental to Prevention of End Stage Renal Disease

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Diabetic nephropathy is the most common cause of chronic kidney disease (CKD), which progresses to end stage renal disease (ESRD) requiring dialysis in some patients. We ask if CKD progression is preventable by glycemic control with intensive insulin treatment. Data was obtained from 46 office treated patients (28 F, 18 M) with established diabetes. Mean age was 62.2 (range 39 - 86) years. They were followed for a mean period of 14.2 (1.5 to 115) months. Diabetes was diagnosed by 2-h postprandial (2hPP) glucose of > 11.1 mmol/L and treated with long acting insulin after breakfast and dinner and regular insulin based on finger-stick glucose 2-h post meal and bedtime. Hypertension was treated with therapy exclusive of renin-angiotensin inhibitor drugs. Glucose, urea nitrogen, serum creatinine (Scr), estimated glomerular filtration rate (eGFR), and glycosylated hemoglobin (HbA_1c), and blood pressure (BP) were recorded. Values were compared between first and last visits using a paired two-tailed t-test. $P < 0.05$ was significant. Patients were divided by 2hPP glucose of < or > 11.1 mmol/L. In the all patients group, fasting glucose was significantly lower at the last versus the first visit (8.4 $\pm$ 0.6 vs 10.3 $\pm$ 0.7mmol/L, p=0.0173), and was associated with a significantly reduced Scr (100.3 $\pm$ 5.2 vs 110.9 $\pm$ 7.8 µmol/L, p=0.0134). Little change in eGFR was found between visits. Mean eGFR was no worse than CKD stage 1 in all groups at the last visit. Less than 50% of 46 patients achieved glucose control of < 11.1 mmol/L with a highly significant reduction of HbA_1c (9.14 $\pm$ 0.52 vs. 7.60 $\pm$ 0.45 %, p=0.0148). Average BPs were normal in both visits in all groups, but diastolic BP was significantly lower in the all patients group at the last visit (77.0 $\pm$ 1.5 vs. 81.6 $\pm$ 1.9 mmHg, p=0.0297). Thus the paradigm of therapy in this study may not be affirmative in uniformly achieving tight glycemic control (< 11.1 mmol/L) but is effective in preventing progression of diabetes related CKD.

2474-PO

Self-Administered Insulin versus Supervised Insulin Administration: An Observational Study

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Introduction: This is a small study done on a group of 80 patients in rural India. They were monitored by a team of "Anganwadi" workers; these are rural multipurpose health workers. Usually they are from the same village that they work in, hence they are well acquainted with the people of the village better able to communicate& understand them. They are given a basic health education the job of going house to house to check the health status of the community at large. Method: A group of 80 patients was selected from a village in India and were divided into two groups of 40 each. All the persons selected for the study were type-II diabetics not responding to oral hypoglycemics. One group was taught self-administration of insulin, and also about the importance of rotation of sites of injection. The other group was monitored by a team of anganwadi workers. The anganwadi workers as well as the individual patients were taught the basics about care and management of a diabetic. Results: The group on self-administered Insulin showed more episodes of deranged glycemic states and increased morbidity when compared to the group which was being supervised. Even within the group on self-administered insulin we noted fewer incidences of deranged glycemia

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ADA-Funded Research

in patients who regularly rotated the site of injection when compared with those who kept on taking injections at the same site. Conclusion: From our study we have come to a conclusion that supervised administration of insulin even in the domestic setup is better than self administration of insulin.

CLINICAL THERAPEUTICS/NEW TECHNOLOGY—TREATMENT OF INSULIN RESISTANCE

2475-PO

Lactation Intensification Improves Insulin Sensitivity and Biomarker Profile post-partum in Women With Recent Gestational Diabetes Mellitus (GDM)

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Since lactation is known to favourably impact glucose disposition in women with recent GDM, an attempt was made to both intensify and prolong lactation behaviour in order to assess sustainability of its effect on insulin sensitivity and vascular risk biomarkers. This is of clinical and therapeutic relevance for these patients who are at high risk of subsequent development of type 2 diabetes and vascular disease. The study was observational, prospective, cohort longitudinal in type. Fifty- one women with recent GDM were recruited, half of whom were randomly selected for intensive education and encouragement by a Lactation Consultant to breastfeed exclusively to 6 months and intensively up to 12 months post-partum. A breastfeeding score was employed to compare the difference in metabolic and biomarker outcomes between the lowest (LQ) and highest (HQ) breastfeeding quintiles. The results for HQ vs. LQ included lower mean fasting glucose levels (mmol/L) at 6 months (4.5 sd 0.28 vs. 5.4 sd 0.41, p=0.02) and composite 6 and 12 months (4.6 sd 0.22 vs. 5.5 sd 0.34, p=0.0007); lower fasting insulin (mU/L) (3.7 sd 1.9 vs. 6.4 sd 2.4, p=0.07), c peptide (nmol/L) (0.5 sd 0.2 vs. 0.8 sd 0.2, p=0.046) and HOMA-IR (mmol.mU/L2) (0.78 sd 0.41 vs. 1.57 sd 0.65, p=0.046) for composite 6 and 12 months data. At 3 months, hsCRP (mg/L) was also lower for HQ group (2.5 sd 2.5 vs. 6.6 sd 5.1, p=0.035). Conversely, adiponectin levels (mg/L) at 6 months were higher for the HQ group (22 sd 0 vs. 8.1 sd 3.6, p=0.025). Although study numbers were small and some attrition in participation occurred by the end of the study, significant results were nevertheless obtained, showing sustained improvement in biomarkers and insulin sensitivity for up to 12 months with intensified lactation. This could impart a legacy benefit on such patients' future metabolic and vascular health and is worth pursuing as a health promotion intervention.

Supported by: Redcliffe Hospital Foundation; Merck Sharp and Dohme Ltd.

2476-PO

Psychological Insulin Resistance in Patients With Type 2 Diabetes: A First Indian Study

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Psychological insulin resistance (PIR) is defined as patient reluctance to initiate insulin therapy. This is the first Indian study to determine factors associated with insulin acceptance in patients with type 2 diabetes. A total of 150 patients participated in this observational study. Data were obtained by face-to-face interview using 5 validated diabetes questionnaires- Diabetes Attitude Scale (DAS), Diabetes Knowledge Test (DKT), Diabetes Self-Efficacy Scale (DSES), Interpersonal Processes of Care Survey-18 (IPC-18), and Barriers to Insulin Treatment (BIT) scale. Patients with type 2 diabetes, age ≥18 years, and treatment with oral hypoglycemic agents were the inclusion criteria; type 1 diabetes, severe psychiatric disease, dementia, and on current/previous insulin treatment were exclusion criteria of the study. Statistical analyses were performed using ANOVA and t-test with $P<0.05$ considered as significant. A multiple, linear regression model was constructed to find relationship between DAS, DKT, DSES, IPC-18 and BIT. Females had significantly higher psychological barriers than males. They had higher fear of pain during insulin injection and regular blood-sugar checks and also considered pills to work better than insulin. Patients who were more educated believed that insulin is a better treatment in comparison to oral hypoglycemic agents. In addition, patients with higher income group reported more fear of injection and had higher feeling of insulin dependence. The regression model showed that patients who had strong self-efficacy and better interpersonal processes with their healthcare providers were less reluctant to use insulin treatment ($R^2 = 0.095$; $p < 0.05$). In conclusion, diabetes self-efficacy and better interaction with clinicians plays a vital role in reducing the patient reluctance to use insulin.

2477-PO

WITHDRAWN

2478-PO

Screening for Insulin Resistance by Non Invasive Assessment of Sudomotor Function

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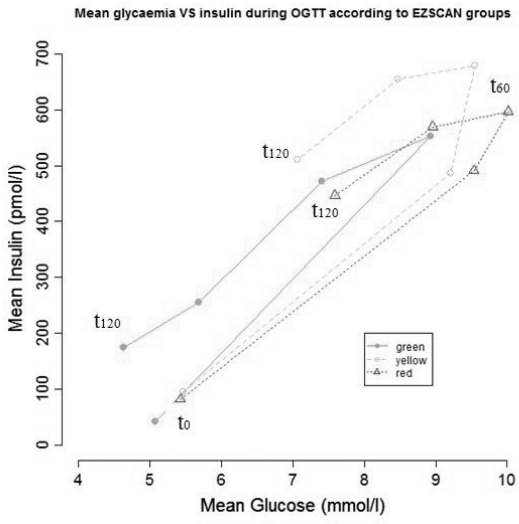
There is a lack of simple, fast, reproducible and cheap methods for screening people at risk of insulin resistance (IR). Sudomotor dysfunction due to small C-fiber neuropathy is observed in patients with IR or diabetes. EZSCAN was recently developed to assess sweat gland function through measurement of electro skin conductance (ESC). Subjects are asked to put palms of the hands and soles of the feet in contact with stainless-steel plates during 2 minutes. A small tension is applied (<4V) and ESC is measured depending on the level of sweat chlorides attracted and reacting with the plates. The aim of the study was to evaluate the ability of EZSCAN to predict IR in subjects at high risk. 98 subjects with a family history of diabetes, obesity or dyslipoproteinaemia from the city of Dresden (46% male, mean age 62.9±11.1 yrs, mean BMI 28.0±4.2 kg/m2) were involved in the study and had an oral glucose tolerance test (OGTT) with measurement of plasma glucose and insulin at 0, 30, 60, 90 and 120 minutes. EZSCAN results are given in colour codes for diabetes risk based on hands and feet ESC: Green - No risk; Yellow - Low risk (subjects with potential IR); Red - High risk. Based on EZSCAN measurements 6 subjects were classified as green, 46 as yellow and 46 as red. No significant difference was observed in BMI between the 3 groups. Matsuda index was 7.3±3.2, 3.5±1.7 and 4.0±2.2, $p<0.001$ (ANOVA) after adjustment on age and BMI for subjects of green, yellow and red groups respectively. Mean insulin level as a function of mean glucose level at each time of OGTT are given in the figure. EZSCAN is a new simple, quick and non invasive method for identifying subjects at high risk for IR.



2479-PO

WITHDRAWN

Clinical Diabetes/ Therapeutics
PUBLISHED ONLY

2480-PO

Adiponectin and Tumor Necrosis Factor-∞ at 8-14 weeks Gestation and Response to the Glucose Challenge Test: The Parity Inflammation and Diabetes (PID) Study

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There is growing interest in the use of inflammatory biomarkers, such as adiponectin and tumor necrosis factor-alpha (TNFR2), to predict third trimester maternal glucose tolerance. Evidence, however, is largely limited to cross-sectional analyses of cytokines in the latter half of pregnancy and lack of adjustment for BMI and gestational weight gain. Our objective was to determine whether first trimester adiponectin and TNFR2 levels were independently associated and predictive of maternal glucose tolerance, as measured by the 1-hour glucose challenge test (GCT), after adjustment for important potential confounders. Prospective study of a racially/ethnically diverse group of healthy pregnant women (N=211) enrolled in the Parity, Inflammation and Diabetes Study. Non-fasting serum levels of adiponectin and TNFR2 were measured at 8-14 weeks gestation. Results of the 1-hour GCT were abstracted from medical records. Multiple linear regression models were developed to determine the association of adiponectin with the GCT, adjusting for demographics, diet, pre-pregnancy BMI and gestational weight gain. Adiponectin levels were inversely related to pre-pregnancy BMI (17ug/ml (BMI <25) to 11ug/ml (BMI ≥30).TNFR2 increased across BMI. Before adjustment, adiponectin was statistically significantly associated with response to the GCT (Regression coefficient (RC) -0.68; 95% CI: -1.29, -0.06]). Adjustment for pregravid diet and physical activity attenuated the association (RC -0.74; 95% CI: -1.43, -0.05). After adjustment for BMI, the association was no longer statistically significant (RC -0.6; 95% CI: -1.30, 0.10). Gestational weight gain further diminished the association. TNFR2 was not associated with the GCT. First trimester adiponectin is not an independent predictor of maternal response to the 1-hour GCT, butappears to be a mediator of the effect of pre-pregnancy BMI on maternal glycemia.

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases

2481-PO

WITHDRAWN

2482-PO

Exenatide Improves Insulin Resistance in High-Fat Fed-Mice by Multiple Mechanisms

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It has been demonstrated that an increase in circulating branched chain aminoacids (BCAAs) may predict the development of type 2 diabetes, and may also have implications in the insulin resistance, since these aminoacids activate mTOR, impairing insulin signaling. Exenatide, which is an agonist of glucagon-like peptide (GLP)-1 receptor, lowers postprandial glucose excursions by multiple effects, such as inhibition of glucagon secretion and delayed gastric emptying, and improves beta-cell function, besides promoting satiety and weight loss. However, the effect of exenatide on peripheral insulin sensitivity and signaling was not investigated yet. In the present study, we examined the effects of exenatide treatment on circulating levels of BCAAs, insulin signaling and sensitivity, glucose tolerance and beta-cell mass in mice fed with a high fat diet (HFD). Administration of exenatide (twice daily, during 5 days) led to improvement in glucose tolerance, insulin sensitivity, observed by increased glucose uptake during euglycemic hyperinsulinemic clamp, and in insulin signaling in liver, muscle, hypothalamus and adipose tissue (increased insulin receptor, IRS-2 and AKT phosphorylation levels), with a reduction in circulating BCAAs and in mTOR phosphorylation in adipose tissue. In parallel, the beta-cell compensatory response was improved, as evidenced by a reduction in beta-cell mass. Moreover, we observed a decrease in the activation of inflammatory pathways, such as JNK and IKK, and in the activation of endoplasmic reticulum (ER) stress in adipose tissue and liver of exenatide-treated mice. In conclusion, these results demonstrated that exenatide improves insulin resistance by multiple mechanisms, such as reduction of circulating levels of BCAAs, with a decrease in mTOR activation in adipose tissue, and reduction of the activation of JNK, IKK and ER stress, improving the insulin signaling in liver, muscle, adipose tissue and hypothalamus; it also leads to a reduction in beta-cell mass.

Supported by: FAPESP, CNPq, INCT

2483-PO

Effects of a 12-Week Course of Thiazolidinedione Treatment on Body Composition and Bone Mineral Density

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We are conducting a mechanistic study of the genetic determinants of non-response to thiazolidinedione (TZD) therapy, an important problem that affects as many as 1/3 of patients. At completion, 75 non-diabetic participants will have been treated with pioglitazone (titrated to 45 mg/d) for 12 weeks. This short duration of treatment is thought safe despite the known association of TZDs with weight gain and fracture risk. However, to verify this assumption, we performed an analysis of data from the first 24 participants as well as 9 participants in a similar study of rosiglitazone (titrated to 8 mg/d). The results of this analysis will be of interest not only to us but also to those who propose to use TZDs in a pulsatile fashion (e.g., 3 months on/3 months off) for the prevention of diabetes. Whole body DXA scans for bone mineral density (BMD) and percentage body fat were performed at study entry and after 12 wk of TZD treatment. Anthropometric measurements were obtained at these time points and after a subsequent 12 wk weight management (WM) program. Subjects were 17 females and 16 males (mean ± SD age 48.8 ± 7.9 yrs). At entry and at the end of 12 wk TZD treatment, BMD was 1.24 ± 0.13 and 1.23 ± 0.13 g/cm3, respectively. This difference is numerically < 1% and was not statistically significant (p = 0.31). Body fat percentage increased from 33.4 ± 7.2 to 35.6 ± 7.0 (p = 0.006). This increase in body fatness was accompanied by an increasing trend in body weight from 89.8 ± 13.0 to 91.6 ± 14.5 (p = 0.07) and waist circumference from 101.8 ± 19.3

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ADA-Funded Research

to 105.1 ± 9.1 cm (p = 0.50). However, these trends were obliterated after the subsequent 12 wk WM program (final values 89.0 ± 12.8 kg and 102.3 ± 10.4 cm), suggesting that normalization of weight gain occurs quickly in the presence of a WM program. This analysis corroborates our assessment that 12 wk administration of a TZD followed by a WM program is not associated with bone loss or permanent weight gain.

Supported by: NIH

2484-PO

Insulin Sensitizers Regulate Pyruvate Oxidation through a Mitochondrial Target (mTOT)

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Thiazolidinediones (TZDs), such as pioglitazone and rosiglitazone, promote insulin sensitization in human skeletal muscle and increase its capacity to oxidize fatty acids. As PPAR-γ agonists, however, these TZDs cause marked side effects that can be clinically prohibitive (including plasma volume expansion, increased adiposity, congestive heart failure, and cardiovascular risk). A target of insulin sensitizers located in the mitochondrial inner membrane, mTOT was recently identified by photoaffinity crosslinking and proteomics. It was suggested that the insulin-sensitizing pharmacology of TZDs involves this target, perhaps through regulation of a mitochondrial signal. We find MSDC-0160, a prototype compound with higher affinity binding to mitochondria versus PPARγ, acutely and selectively inhibits pyruvate oxidation at clinically relevant concentrations in permeabilized human and rodent myocytes. MSDC-0160 at 10μM reduces uncoupler-stimulated respiration rates by roughly 50% in cells oxidizing pyruvate, but has no effect on the rate of oxidation of glutamate, succinate, or palmitoyl carnitine. In contrast, MSDC-1473, a close analog that is not insulin sensitizing and does not bind to mTOT, has no effect on pyruvate-driven respiration. Virally mediated overexpression of mTOT necessitates an increased concentration of MSDC-0160 in order to achieve inhibition of pyruvate oxidation. Prolonged treatment with active compound stimulates a marked increase in the expression of ETF dehydrogenase of β-oxidation. This increase is entirely absent upon mTOT knockdown. Our data indicate mTOT is a previously uncharacterized component of the regulation of mammalian pyruvate oxidation. Moreover, we suggest that insulin sensitizing agents act acutely via mTOT, regulating the utilization of pyruvate and thereby promoting a beneficial shift towards fatty acid oxidation in skeletal muscle myocytes.

Supported by: NIH R42 DK081298

2485-PO

Short-Term Intensive Therapy Significantly Improves Hepatic Insulin Resistance in Newly Diagnosed Type 2 Diabetic Patients

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Some studies have demonstrated short-term intensive therapy (IT) might improve β-cell function (assessed by HOMA-B and AIRins) and insulin sensitivity. Since both insulin secretion and hepatic insulin extraction contribute to AIRins, whether AIRins improvement after IT is due to the improved hepatic insulin sensitivity is unclear. Our study will discuss further on the effect of IT on hepatic insulin sensitivity in newly diagnosed type 2 diabetic (T2D) patients. 52 newly diagnosed T2D patients were randomly assigned to IT (with insulin or oral hypoglycemic agents) for 2 weeks. Intravenous glucose tolerance tests (IVGTT) were conducted and blood glucose, insulin and C-peptide were determined before and after IT. Since the comparison between acute insulin response of insulin (AIRins) and of C peptide (AIRcp) during IVGTT may estimate hepatic insulin extraction, AIRcp/AIRins was used to assess hepatic insulin sensitivity. After IT, HOMA-IR significantly decreased in patients with either FPG < 11.0mmol/L (n=24) (P <0.01) or FPG≥11.0 (n=28) (P <0.01), whereas HOMA-B (P <0.01) and AIRins (P <0.01) dramatically increased. But in subjects with FPG <11.0mmol/L, AIRcp and AIRcp/AIRins showed no significant difference before and after IT. As for subjects with FPG≥11.0, AIRcp (3.5 ± 1.5 vs. 5.0 ± 1.9, P <0.01) markedly increased and AIRcp/AIRins (21.6±13.0 vs. 12.7±4.0, P <0.01) significantly decreased after IT. In the subgroups of patients with both BMI<25 (n=20) and BMI ≥ 25 (n=32), AIRins markedly increased (P <0.01) , but AIRcp showed no significant difference after IT. AIRcp/ AIRins (11.9 ± 4.5 vs. 5.0 ± 1.9, P <0.1) significantly decreased in patients with BMI≥25. We found IT markedly improved AIRins in newly diagnosed T2D patients and AIRcp/AIRins in subjects with obesity or glucotoxicity notably decreased. But AIRcp didn't obviously change. So AIRins improvement after IT, due to the reduced hepatic insulin extraction, may indicate improved hepatic sensitivity.

2486-PO

Five Cases of Extreme Insulin Resistance Due to Mutations of Insulin Receptor-Phenotype/Genotype Correlations and Response to Therapy

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Insulin receptor (INSR) gene mutations cause severe insulin resistance syndromes known as Donohue syndrome (DS), Rabson-Mendenhall syndrome (RMS) and type A insulin resistance. We investigated the INSR gene in five patients: four infants, two clinically classified as DS and two as RMS and 1 adolescent with type A. All patients were diabetic and hyperinsulinemic; insulin (mUI/L) levels were: DS1= 3935; DS2= 3500; RMS1= 2000; RMS2= 3234, type A=389. All patients with DS or RMS had hypoglycemic episodes. Patients with DS carried mutations that are predict to disrupt INSR function: homozygous mutation R974X (numbering including signal peptide) (DS1), and mutations IVS20+1G>T/A119V (DS2) (A119V was reported to have an insulin binding that is 1% of wild type). RMS patients bore mutations E238K/E1074Q (RMS1) and R41W/IVS5+2T>C (RMS2). Patient with type A carried the heterozygous mutation R1201Q. Patients with DS -never treated with insulin- died at 3 months of age because of severe DKA or sepsis. Patient RMS1 (now 22 months old), initially treated with insulin i.v. (17 U/kg/d) + metformin (300 mg/d) with poor results (HbA1c >10%), was switched to IGF1 therapy (Mecasermin, 0.6 mg/Kg/d) with improvement of metabolic control: Hba1c=7.7%. In addition, less glycemic excursions at continuous glucose monitoring (CGM) were observed during IGF1 tretment, that was stopped after 11 months. Patient RMS1 was recently readmitted to the hospital for pneumonia; however neither dramatic worsening of metabolic control or ketosis was observed. Patient RMS2 (10 months old) was switched from high-dose insulin to metformin (75 mg t.i.d.) at 1 month of age, reaching acceptable glycemic control; metformin was stopped after 7 months, without any modification of glucose levels at CGM. Our data suggest that mutant INSR W41, K238 and Q1074 found in RMS patients may have some residual function. However, the effect of therapy is not predictable from molecular genetic data.

2487-PO

Effects of Jian Pi Zi Shen Decoction on Inflammatory Factors in Serum and Liver of Diabetic Rat

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Jian Pi Zi Shen decoction, a traditional herbal drug of Chinese medicine, has been used to treat diabetes mellitus *in clinic*. However, the effects of Jian Pi Zi Shen decoction on glucose metabolism are not known. The objective of our study is to determine the effects of Jian Pi Zi Shen decoction on inflammatory factors such as TNF-α, IL-6 and CRP in both serum and liver of diabetic rat. 30 diabetic rats were induced by intraperitoneal injection of streptozocin.and randomly divided to T2DM group, Jian Pi Zi Shen decoction group (1 ml/100g·d) and Rosiglitazone group(6 mg/kg·d,as a positive control). In addition, 10 normal Wistar rats performed as a control group. All rats were fed with high-fat diet. After 4 weeks, the fasting glucose, triglyceride, TNF-α, IL-6 and CRP levels were assayed, respectively. The mRNA levels of both TNF-α and IL-6 in liver were tested using RT-PCR. In the present study, compared to the control group, the fasting blood glucose, TNF-α, IL-6 and CRP levels were increased in other 3 groups ,respectively (*p<0.01*). However, compared to T2DM group, the fasting blood glucose, TNF-α,IL-6,CRP and triglyceride were significantly decreased in both Jian Pi Zi Shen decoction group (*p<0.01*) and Rosiglitazone group (*p<0.01*). As expect, the fasting blood glucose, TNF-α, IL-6, CRP ,as well as triglyceride,levels were similar in Jian Pi Zi Shen decoction group and Rosiglitazone group (*p>0.05*). Similarly, compared to the control group, the mRNA expressions of TNF-α and IL-6 were increased in the other 3 groups, respectively (*p<0.01*). But compared to the T2DM group, the TNF-α and IL-6 mRNA levels were decreased in both Jian Pi Zi Shen decoction group and Rosiglitazone group (*p <0.01*). Interestingly, the decrease of IL-6 mRNA level induced by Jian Pi Zi Shen decoction was much more significant than Rosiglitazone (*p<0.05*)**.** In conclusion, the effects of Jian Pi Zi Shen decoction on glucose metabolism may, due to decrease the inflammatory factors such as TNF-α, IL-6 and CRP in serum and liver of diabetic rats.

Supported by: China Government

2488-PO

How to Manage Glycemic Control With Early Insulinization in Iran?

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Prevalence of diabetes in Iran has been increased in adult population with a high proportion of poorly controlled. Information evaluating the efficacy of insulin glargine for patients with type 2 diabetes were sub-optimally controlled on their previous oral antidiabetic regimen is limited in Iran. Therefore we conducted a national, multicenter non-randomized study to evaluate the effect of glargine on control of diabetes in T2DM who were previously receiving OADs. 300 patients with diagnosed type 2 diabetes less than of 5 years duration and HgA1c greater than 7 who had treated at least with two oral anti-diabetes drugs (OADs) including Metformin and Glibenclamide enrolled. Insulin glargine were prescribed as single subcutaneous daily injection for the eligible patients. Titration and dose adjustments and decisions were at the discretion of the physician. HgbA1C was measured at enrollment, week-12 and week 24. Glycaemic control improved significantly in patients with significant improvements in FBG and HbA1c.After 24 weeks the mean decrease in FBG was 92.3 ± 78.8 mg/dl and in 2-h PPBG was 111.9 ± 106.2 mg/dl .The mean decrease in HbA1c was 1.7% (± 1.4). It should be noticed that 54.9% of patients had HbA1c >9 at the beginning of study but at the end of study 22.4% of the subjects reached to HbA1C target of less than 7% and 65% had HbA1C≤7.5% . The mean daily basal insulin dose at initiation was 12.1 (SD=8.2) IU/day and increased to 20.2 (SD=9.1) IU/day at week 24. The reported rate of all hypoglycemia episodes was less than five percent. No major and or nocturnal hypoglycemia were reported during the entire period of the study. The mean body weight change during the study was not statistically significant. These results indicate that in type 2 diabetes, insulin glargine at early stages was associated with significant improvements in glycaemic control.

Supported by: sanofi-aventis

2489-PO

The Role of Hypothalamic PP2A in Central and Peripheral Insulin Signaling

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The molecular mechanism in the negative regulation of insulin action is attributed to agents that enhance serine/threonine phosphorylation of the receptor itself or its downstream effectors such as insulin receptor substrate-1 (IRS-1). Therefore, changes in the activity of serine threonine protein phosphatases, may lead to a alterations in insulin signaling, the exact mechanism of how such serine threonine protein phosphatases act, is not completely understood. Brain insulin resistant state is characterized by disturbances in transducing the signal from IR/IRS/AKT, changing feeding behaviour and body weight. Thus, the objective of this study was to evaluate the role of hypothalamic PP2A in the regulation of food intake, insulin actions and signaling in rats through selective decreases in PP2A expression in discrete hypothalamic nuclei. The antisense oligonucleotide (PP2A-ASO) was designed to blunt the PP2A expression in hypothalamic areas surrounding the third ventricle in control and obese rats. The exposure of rats to high fat diet resulted in a significant increase in the expression of hypothalamic PP2A. Central and peripheral insulin signaling was increased by PP2A ASO, as evidenced by increased phosphorylation of AKT in insulin-stimulated PP2A ASO-treated animals. PP2A ASO treated rats showed: decrease food intake, reduce body weight and reduced adiposity. Thus, these results provide new insights into the mechanisms by which reduction hypothalamic PP2A restores insulin sensitivity.

Supported by: FAPESP

2490-PO

Effects of Pioglitazone and Metformin Combination Therapy on High-Molecular-Weight Adiponectin Compared With Metformin Monotherapy in Type 2 Diabetes Mellitus Patients

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OBJECTIVE: Adiponectins comprise anti-atherogenic hormones and adipose tissue derivatives, known as adipokines, which mediate insulin resistance. This study aimed to evaluate the effects of pioglitazone (PIO) and metformin (MET) combination therapy on the serum level of high-molecular-weight adiponectin compared with MET monotherapy in type 2 diabetes mellitus (T2D) patients. METHODS: Eighteen T2D patients who had diet and MET therapies, but without adequate glycemic control (HbA1c > 6.9%), were randomly assigned to two therapy groups: MET + PIO group [(n = 10); MET (250-750 mg) plus PIO (7.5-30 mg)] and MET group [(n = 8); with increased MET dose (max. 1000 mg)]. Body mass index, blood pressure, waist circumference (WC), plasma glucose level, HbA1c level, insulin resistance indexes (HOMA-R and fasting insulin), lipid level, liver function parameters, renal function indices and serum adiponectin level were measured before and after 6 months of therapy. RESULTS: The serum adiponectin level was significantly higher after 6 months of therapy (10.8 ± 5.7 μg/ml) than before therapy (4.1 ± 2.2 μg/ml, $P < 0.01$) in the MET + PIO group, but The serum adiponectin level between after 6 months of therapy (3.9 ± 2.9 μg/ml) and therapy (4.0 ± 2.9 μg/ml) in the MET group The HbA1c were significantly lower after 6 months of therapy (MET+PIO: 7.4 ± 0.4%, MET: 7.8 ± 0.8%) than before therapy in both groups (MET+PIO: 8.2 ± 0.4%, MET: 8.5 ± 0.6%, $P < 0.05$). The glycated albumin level was significantly lower after 6 months of therapy than before therapy in MET group ($P < 0.05$) and tended to decrease in MET+PIO group. The HDL cholesterol levels were significantly lower after 6 months of therapy in the MET + PIO group than in the MET group. WC tended to increase in the MET + PIO group. CONCLUSION: MET + PIO therapy induces a significant increase in the serum level of adiponectin, which mediates glucose and insulin resistance, compared with MET in T2D patients.

2491-PO

Study Design and Baseline Characteristics of Beijing Pre-diabetes Reversion Program (BPRP)

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Background: Prediabetics are high risk population of both diabetes and cardiovascular disease. Studies had shown that intervention on prediabetes could reduce the risk of developing diabetes. No study have explore whether intervention could revert prediabetes to normal glycemic status. The purpose of this study is to examine whether lifestyle modification and/or pioglitazone could revert prediabetic state to normal and improve the risk factors of cardiovascular disease as well. Design: The study is a prospective, multi-centre, randomized, medication double blinded and placebo controlled clinical trial using 2x2 factorial design. The participants were randomized into four groups (conventional/intensive lifestyle intervention and 30mg pioglitazone/placebo) with a 3 years follow-up. Primary endpoint is conversion rate to normal glucose tolerance of different intervention. Secondary endpoints are as follow: 1) incidence rate for type 2 diabetes, 2) change of CV risk factors, 3) aggregate occurrence of CV event and death, 4) aggregate occurrence of hypertension, dyslipidemia and metabolic syndrome, 5) change of biological indices related to diabetes and its related conditions, 6) quality of life. Baseline Results: 4397 were assessed for eligibility with OGTT, and 1903 prediabetics were finally enrolled. 952 were in conventional group and 951 were in intensive group. Mean age of all participants are 52 years old and BMI is 25.8 kg/m^2. Mean fasting and 2-hour plasma glucose is 5.9mmol/L and 8.8mmol/L respectively. Mean HbA1c is 5.8%. There is no statistic difference between two lifestyle intervention groups for age, BMI, glucose level, β cell function, lipid level and urine albumin/creatinine ratio. Conclusion: BPRP is the first study to determine if lifestyle modification and/or pioglitazone could revert prediabetic state to normal in Chinese population, and to define the mechanism through which different intervention exerts its effect on glucose metabolism and CV risk factors.

Supported by: Beijing Municipal Science and Technology Commission, ID: D0905003040131

2492-PO

Intensive Insulin as Initial Treatment for Newly Diagnosed Type 2 Diabetes: A Novel Approach to Lasting Effects

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Type 2 Diabetes Mellitus (T2DM) is a chronic progressive disease which is often diagnosed after considerable pancreatic B-cell failure. Hyperglycemia management requires numerous medications, in addition to lifestyle modification, and still only appears to address disease elements. Intensive insulin as initial therapy, a novel approach, may limit the progressive damage of B-cell function and promises to achieve lasting glucose control - "the legacy effect". The natural disease progression of T2DM demands increased insulin production and secretion by the B-cells. The purpose of initiating a pulse of intensive insulin early in the disease is to rest the B-cells and possibly preserve the retardation of cell function overtime, improve cell mass, and promote lasting glucose control without oral medications or exogenous insulin. In this case series, a pulse of basal-bolus analogue insulin supplemented with correction scale insulin was initiated with a weight based algorithm. Ten newly diagnosed T2DM patients, including nine men and one woman

For author disclosure information, see page 797.

were treated with the insulin first protocol. The mean age was 54.4 years and weight was 216 lbs. Patients also received a complete diabetes educationprogram. The insulin protocol was offered for a mean of 18 weeks, including forced up titration, followed by target glucose dosing based on self blood glucose monitoring, and forced down titrations. The baseline HbA1c mean at diagnosis was 11.1% was reduced to 6.1% within 12 weeks and was maintained at 6.1% at one year. Mean weight improved to 210 lbs post therapy (12-27 weeks after initiation of insulin). Only one patient reported severe hypoglycemia during intensive therapy. To date, three of the ten patients continue to maintain a HbA1c less than 6.5% for as long as 43 months without oral medications or exogenous insulin post therapy. Early studies support the use of intensive insulin as initial treatment in newly diagnosed type 2 diabetes.

2493-PO

Pioglitazone Improves the Insulin Sensitivity of Meal Tolerance Test in Mildly Obese Japanese Patients With Type 2 Diabetes

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The aim of this study is to investigate the effect of pioglitazone on insulin sensitivity and anti-inflammatory action during a meal tolerance test in type 2 diabetes in Japanese population. Nineteen patients of type2 diabetes (mean: age 62.9, HbA1c 7.5, BMI 25.1) were enrolled and were added 15mg pioglitazone in addition to previous treatment. Before and six months after the administration of pioglitazone, we performed a meal tolerance test (test meal 460kcal) and we measured blood glucose, insulin after meal load until 180 minutes every 30minutes, and HbA1c, lipid profile, high sensitive CRP (hs-CRP), and adiponectin were also measured. After the administration of pioglitazone, HbA1c, HDL, adiponectin levels and the insulin sensitivity index (ISI; matsuda's index) were significantly improved ($p<0.05$). The hs-CRP tended to be decreased (table). In the body weight-related stratified analysis, the glycemic control improvement effect were stronger in the obese patients with BMI>25, but even in the patients with BMI<25, the adiponectin levels and ISI were improved. These results suggest that pioglitazone improves glycemic control by improving insulin sensitivity and has anti-inflammatory action. These actions are effective to the obese patients, but are also effective to the thin patients in Japanese population. Our results indicate that pioglitazone is effective for Japanese and other Asian populations, even in not so obese population.

Data are expressed as means ± SD.

	before administration	after administration	p value
Age	62.9±10.0		
Gender (M/F)	10/9		
BMI (kg/cm2)	25.1±2.7	25.5±2.8	P<0.01
HbA1c (%)	7.5±0.7	7.0±0.7	P<0.01
adiponectin (μg/ml)	4.10±1.68	7.96±4.80	P<0.01
hs-CRP (mg/dl)	0.076±0.089	0.063±0.102	N.S.
matsuda's index	6.50±3.40	8.57±3.41	P<0.01

2494-PO

Multiparametric Biomarkers as Determinants of Insulin Resistance

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The metabolic syndrome (MS) effects an impairment of various inflammatory and hormonal control systems. Insulin resistance (IR) causes early micro- and macroangiopathies through inflammatory processes, endothelial dysfunction and hormonal imbalances. The incidence of primary IR is about 20% including also the young. Thus, timely counter-measures on different therapeutic levels are important. In a 2-month clinical trial in 11 patients with MS treated with *Ginkgo biloba* (EGb 761, 2 × 120 mg/d), a spectrum of more than 20 cytokinic, inflammatory, lipidic, and oxidative stress biomarkers (BMs), all interconnected with each other, served for a detailed diagnosis and therapy monitoring. Fasting morning glucose was reduced from 94.4 to 90.2 mg/dL (< 0.03), insulin from 12.7 to 11.5 mU/L (< 0.04), and HOMA-IR from 3.07 to 2.64 mU/L × mg/dL (< 0.02). The beneficial effects on hepatic parameters (before/after treatment) were: GGT [U/L] 29.4 /25.7 (< 0.01), ALT [U/L] 25.5/22.2 (< 0.03), AST [U/L] 17.0/21.0 (< 0.002), ALP [U/L] 159.5/136.5 (< 0.002), CREA [μmol/L] 79.8/68.4 (< 0.001), URAC [μmol/L] 315.7/285.2 (< 0.005). Through the ginkgo therapy, the balance between the BMs was newly adjusted, and the correlation between the parameters became visible. The correlations (r, p) between HOMA-IR and various BMs are: IL-6 (0.71, <0.07), hs-CRP (0.68, <0.13), TNFα (-0.67, <0.04), TGFβ_1 (-0.89, <0.01), oxLDL/LDL (0.77, <0.07), Lp(a) (0.8, <0.05), GGT (0.85, <0.001), ALT (0.6, <0.05), AST (0.68, <0.03), ALP (0.72, <0.04), CREA (0.62, <0.04), URAC (0.73, <0.03). Many BMs are up- or down-regulated in the subthreshold range, but so much the more have an important early diagnostic, preventive and prognostic significance. The picture is the more complicated in that some inflammatory BMs (e.g., TNFα, TGFβ_1) in the sense of a cytokine balance behave inversely. Since ginkgo had beneficial effects on the whole BM spectrum and was tolerated without any side-effects, it may be used as complementary drug in the treatment of MS and diabetic patients.

Supported by: Schwabe Pharmaceuticals, Germany

HEALTH CARE DELIVERY—ECONOMICS

2495-PO

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2496-PO

WITHDRAWN

2497-PO

A Joint Transition Diabetes Care Pathway from Pediatrics to the Adult Diabetes Clinic: The Experience from a Single Centre in the UK

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The aim of our study was to assess the effectiveness of a staged transition process from pediatrics to adult diabetes care, based on a joint transition care pathway. Joint Transition Clinic (JTC) -3-4 appointments/patient over a year -Adult diabetologist and Diabetes specialist nurse (DSN) sit in -Pediatric team lead first two clinics; adult team lead subsequent clinics and transfer to YAC Young Adult Clinic (YAC) -Same adult team -Longer duration of appointments, open access to service, named DSN -Telephone reminder service to improve attendance rates at appointments -Seen 1-4 times/year for up to 3 years based on clinical needs, then transfer to adult clinic HbA1c at last pediatric clinic & mean HbA1c during JTC or YAC analysed.

Clinic Parameters		
N=65	Joint Transition Clinic (JTC)	Young Adult Clinic (YAC)
Mean age at entry	17.1 years (15.6 - 19.0)	18.5 years (16.7 - 20.5)
Number of appointments/patient	2.9 (1-8)	2.7 (1-7)
Attendance rates	72%	67%
No. of patients with failure to attend at least 1 appointment	52% (20 - once, 10 - twice, 2 - thrice, 2 - four)	49% (17 - once, 7 - twice, 7 - thrice, 1 - four)
Failure to attend any appointment	12% (1-4 appointments)	6% (2-3 appointments)
Mean change in HbA1c	+0.1% (-4.7 to +9.9%)	+0.2% (-4.4 to +4.3%)
Proportion of patients with HbA1c worsening by >1%	25%	19%
Mean duration of follow up	453 days (49-1323)	326 days (0-763) n=25

Clinical Outcomes - HbA1c					
Pediatric to JTC					
	JTC HbA1c	<7.0%	7.1 - 9.0%	9.1 - 11.0%	>11.0%
Pediatric HbA1c	N=				
<7.0%	6	1	3	0	2
7.1 - 9.0%	17	1	9	7	0
9.1 - 11.0%	26	0	7	17	2
>11.0%	16	0	3	2	11
Total	65	2	22	26	15
JTC to YAC					
	YAC HbA1c	<7.0%	7.1 - 9.0%	9.1 - 11.0%	>11.0%
JTC HbA1c	N=				
<7.0%	2	0	2	0	0
7.1 - 9.0%	22	1	13	7	1
9.1 - 11.0%	26	0	3	20	3
>11.0%	15	0	1	3	11
Total	65	1	19	30	15

39 on-going care in YAC; 25 transferred to other services [1 for insulin pump; 2 to pregnancy clinic; 15 to adult care; 7 to primary care (4 for repeated non-attendance)]; 1 died (Non-diabetic complication)

The attendance rates through this staged transition process were high, with improvement/maintenance of glycemic control that was sustained. Our care pathway provides an effective, patient-centred, coordinated, multi-professional team based staged approach to deliver transitional care.

2498-PO

The Relationship among Hyperglycemia when Emergency Admission With Medical Cost and Disease Prognosis in Hospitalized Patients

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Objective: To analyze the relationship among different blood glucose levels with medical cost, hospital stay and disease prognosis in emergency admitted patients. Methods: 4868 patients were checked for their blood glucose as soon as possible (not over 24 hours) when admitted into hospital and then divided into 2 groups, group 1 without and Group 2 with hyperglycemia which included the patients with diabetes or with stress hyperglycemia (patients with hyperglycemia, without diabetes history and/or with normal HbA1c level, normal glucose level during follow-up in hospital). The hospital stay in days, medical cost and diseases prognosis were compared between the patients with or without hyperglycemia. The patients were divided into younger group (n=2532,age < 60yrs) and older group (n=2336, age ≥ 60 yrs) for further analysis. There was no difference of age between the patients with or without hyperglycemia in the patients with coronary heart disease, and then, these patients were compared for their hospital stay, medical cost and disease prognosis. Results: There were 29.5% of these patients with hyperglycemia, including 11.4% with stress hyperglycemia. Patients with hyperglycemia had significant longer hospital stay (15 days vs. 10 days, *P*<0.01), more medical cost (mean, 14064.7 vs. 8980.9 Yuan RMB, *P*<0.01) and higher mortality in hospital (2.92% vs. 0.61%, *P*<0.01). Whatever younger group or older group, or in the groups with coronary heart disease, patients with hyperglycemia had significant longer hospital stay, more medical cost and higher mortality. Conclusion: The patients with hyperglycemia when admission had significant higher medical cost and poor disease prognosis.

Supported by: LifeScan

2499-PO

Persistent Hyperglycemia in Hospitalized Patients With Diabetes Despite Considerable Operating Expense

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Despite the ongoing controversy on different aspects of glucose control in hospitalized patients, it is beyond doubt that the prevention of hyperglycemia exceeding 10 mmol/L is essential. The aim of the study was to assess the glycemic outcome and indicators of a physician guided glucose management process at two general wards. 50 patients (age 71±12 years, BMI 28.3±6.1, 22 m/28 f, 47 DM2, 3 DM1, HbA1c 7.8±1.5%, 98% insulin, 26% oral agents) admitted for various reasons to the general wards of the departments of cardiology and endocrinology were analyzed regarding glucose control (mean blood glucose (bg), mean bg/day > 10 mmol/L) and indicators of the glucose management process (bg measurements/day, insulin injections/day, insulin dose/day). The data were analyzed per population and per time period of stay (admission [first half of stay] vs. discharge period [second half of stay]). For the length of hospital stay (14.3±8.1 days) the mean bg/patient-day was 9.7±2.8 mmol/L. No significant improvement was observed when comparing the admission to the discharge period, mean bg 9.8±2.7 mmol/L vs. 9.5±3.0 mmol/L, p=0.28, respectively. 34% of patients (17 of 50) had persistent hyperglycemic levels (mean bg/day > 10 mmol/L) during the discharge period and despite an average bg sampling frequency of 2.9 ± 0.8 measurements/day, no insulin dosing was performed in 9% of bg/days > 10 mmol/L. Both, the mean daily insulin dose (admission period 27.2±16.9 IU vs. discharge period 29.8±17.6 IU, p=0.21) and the mean number of insulin injections/day (1.8±0.4 vs.1.9±0.5, p=0.40) did not increase in these patients. The recommended target range of < 10 mmol/L could not be established in every third patient during the hospital stay. Analysis of the glucose management process demonstrates considerable operating expenses as indicated by a high bg sampling frequency, but a lack of translation to adequate therapy. Implementation of corrective measures (e.g. structured treatment protocol) is inevitable.

Supported by: European Commission, Project REACTION (FP7 248590)

2500-PO

Individualized Diabetes Care Provided by a Diabetologist-Directed Clinic at the Los Angeles County Medical Center Achieves Glycemic Control With Less Medication Burden

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The diabetes clinic at the Los Angeles County(LAC) Medical Center is a diabetologist-staffed specialty clinic managing underserved patients who have failed management by primary care physicians(PCP) and staged disease management(SDM) programs. n=96, Responders(Resp) defined by HBA1C ≤8%. HBA1C: initial(11.6+/-1.8), D/C (8.35+/-2.06), changes(-3.2%). 52% responded. Resp: n=50, HBA1C: initial(11.2+/-1.71), D/C(6.986+/-0.62), (P<0.05), change (-4.21%) [figure 1]. Nonresp, n=46, HBA1C: initial (11.07+/-1.96), D/C (10.15+/-1.90), (P<0.05), change 0.92% A subanalysis of 21 consecutive Resp: 10 patient were on insulin at entry. Average admission insulin at entry (84.5+/-56.52U), on discharge (11.05+/-26.64), (P<0.05), [Figure 2], 60% of patients previously on insulin had D/C their insulin. A diabetologist-staffed specialty clinic can provide further glycemic control in the majority of the underserved, LAC patients, despite previously failing PCP and SDM programs. Patients achieved glycemic targets with less medication burden, suggesting the benefits of this clinic is due to the individualization of care and not due to the rapid up-titration of meds.

For author disclosure information, see page 797.

Figure 1:
Responders HBA1C ≤8%

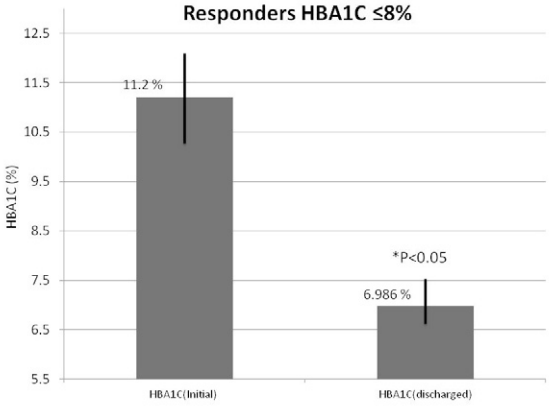
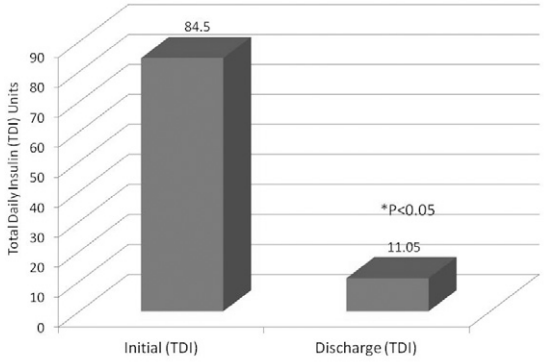


Figure 2:
Responders with insulin on entry



2501-PO

The Cost and Productivity Consequences of Non-Severe Hypoglycemic Episodes (NSHE) in Patients Receiving Sulfonylurea or DPP4 Dual Combination Oral Therapy

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Hypoglycemia is a major consideration in the management of blood glucose in people with type 2 diabetes. NSHE occur more frequently than severe episodes and account for the majority of hypoglycemic burden. Recent data has quantified the per-event cost of NSHE in terms of productivity loss and out-of-pocket expenses. The aim of this study was to model the cost implications for NSHE in relation to sulfonylurea or DPP-4 based dual combination blood glucose lowering regimens Published patient source data was used to obtain workplace productivity costs, out-of-pocket (OOP) expenses and estimates of the frequency of NSHE. The IMS CORE Diabetes Model (CDM) a validated and widely used simulation model was initiated with dual therapy patient profiles derived from NHANES and efficacy profiles for metformin + sulfonylurea (M+S) versus metformin + DPP-4 (M+D) obtained via a mixed treatment comparison. Costs (2010) and benefits are in USD and discounted at 3%. In the published patient source data mean weighted productivity cost of each NSHE was $34.87 with monthly OOP of $35.56; at a frequency of 1 NSHE per week M+D is associated with an incremental annual cost of $212 compared to M+S after including the expected annual $2,240 cost offset associated with productivity and OOP expenses. Over a lifetime, the discounted cost per quality adjusted life year gained for M+D versus M+S was $2,419 Sulfonylurea based dual combination therapy is potentially associated with greater economic consequences for employers and patients compared with DPP-4 based dual therapy regimens. Therefore greater consideration should be given to the productivity related consequences of hypoglycemia with respect to dual therapy escalation, particularly in people with type 2 diabetes of a working age.

2502-PO

Patient Perspective of Quality of Care: Formative Analysis of the PACIC

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The Patient Assessment of Chronic Illness Care (PACIC); a 20-item measure of patients' perception of their care, is based on the Chronic Care Model (CCM). Conflicting results have been reported on the factorial validity of its 5 subscales (patient activation, decision support, goal setting, problem solving, follow-up). To assess the measure from the patient's perspective, we conducted a postal survey of randomly selected patients with diabetes; stratified according to providers in 34 primary care clinics in 3 mid-western states. In Fall 2009, 4,796 patients were mailed a survey that included the PACIC and questions on health status, diabetes control, self-care, and demography. Non-responders were sent a second survey 4 weeks later. A total of 2,055 patients responded (42.8%). Confirmatory factor analysis (CFA) was conducted to evaluate the 5-factor structure model and exploratory factor analysis (EFA) determined domains based on patient reported data. Our CFA does not confirm the 5-factor model. EFA reveals a factor structure of 4 domains with a distinctive patient's perspective: 1) Things my provider and healthcare team do for me, 2) Assistance in setting personal goals and developing action plans, 3) Inclusion and collaboration with my healthcare team, and 4) Providing ideas for seeking help and support in my self-management (e.g. help from my social network). The PACIC was developed by healthcare experts based on the CCM and reflects the provider-healthcare system's perspective. Based on our formative analysis we find that patients do not necessarily share expert's knowledge and conceptions. In summary, we find that the EFA based on patient's response to PACIC is a good source for eliciting how patients perceive quality of diabetes care delivery. The 4 factors found in our study underscore the importance of patient interaction and involvement with the health care team. We conclude that insights gained from the study will help improve measurement of health care delivery as well as patient education and self-care.

2503-PO

Attendance Rates in Adolescent Diabetes Clinic: A Robust Transition Process Enhances Adherence

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The transition from pediatric to adult diabetes care is a potential challenge during emerging adulthood. Attendance rates and loss to follow up are reasonable care indicators to assess patient's confidence and comfort with the transition service. Transition pathway: The pediatric team identify patients ready for transition. These patients are then seen in the Joint Transition Clinic (JTC), run by the pediatric team (Consultant & Diabetes Specialist Nurse-DSN), and the adult team sit it. The clinic runs in the pediatric department once a month. Typically, patients are seen 3-4 times over a year. The pediatric team lead the clinic on first 2 occasions; adult team lead subsequent appointments. The patient is then transferred to the Young Adult Clinic (YAC) under the same adult team, done at the same site. These patients get frequent appointments and longer consultation time with open access to the service and clinical support from the named DSN. In general, patients are seen 1-4 times over 1-3 years before formal transfer to adult care or family practitioner. A telephone reminder is provided by a non-clinical staff 3 days prior to the appointment to improve attendance rates. YAC also caters to new referrals for patients diagnosed with diabetes during adolescence (17-30 years).

Clinic Statistics	JTC	YAC
No. of clinics	31	35
No. of patients	90	143
No. of appointments	266	254
Appointments/patient	1-8	1-5
New appointments	90	89
Attendance rates	72.2%	75.2%
Patients with >1 appointment and failed to attend all	6	5
Discharged to family practitioner due to multiple non-attendance	2	4

Our staged transition pathway has been demonstrated to be an effective patient-centred and individualized process with good adherence to appointments, in comparison to previous adolescent diabetes clinic attendance rates of 45% prior to the introduction of this pathway. This has directly reflected on patient engagement, involvement and participation.

For author disclosure information, see page 797.

2504-PO

Improvement of Quality of Diabetes Care With Regional Electric Health Records

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The increase in diabetic patients and its complications requires regional disease management of diabetes mellitus (DM). In US and Europe, electric health records (EHR) has been reported to improve the quality of medical care with reasonable clinical outcomes and medical economics. We have constructed and operated a regional EHR since 2011 in Japan. Data were reported for 5,564 patients have been registered to our EHR. This EHR system consists of two mapping systems for disease management. First is a personal mapping system named "Case management MAP", which is a tool for case management of individuals to achieve optimized therapy using a data set for diabetes (BP, BW, HbA1c, eGFR, urinary albumin/protein, LDL-C, HDL-C, TG, max IMT of carotid artery, eye examination). Second is a regional disease management mapping system named "Regional disease management MAP", which is a tool to triage diabetic patients having a high priority for treatment and intervention from whole diabetic patients in the area based on abnormal values of a data set (HbA1c, eGFR, urinary albumin/protein, max IMT). The measurement of urinary albumin/protein at regional EHR use and paper-based site were 87.7% and 44.1%, respectively. The examination of max IMT at regional EHR use and paper-based site were 95.0% and 40.8%, respectively. On the other hand, "Case management MAP" has limitations in the overall optimization for providing various interventions to prevent disease progression of DM. The analysis of nutritional intervention using "Regional disease management MAP" revealed that 76.0% of the patients who need intensive dietary management have not received counseling by dietitian during past one year. Finally overall optimization of diet counseling was done. These findings support that the regional EHR greatly contributed to achievement of optimized therapy for the patients who require more intensive treatment and interventions to prevent the progression of diabetic complications such as diabetic nephropathy and macroangiopathy.

2505-PO

Internet-Based Telecommunication Method for Diabetic Patients With Self-Monitoring of Blood Glucose: First Experiences With the Dcont.hu System

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The current healthcare delivery system with short and infrequent clinical encounters does not meet the needs of a certain parts of diabetic patients. Web-based technologies provide a new approach to disease management. The Dcont.hu internet-based telecommunication system was developed for improving the care of patients with self-monitoring of blood glucose. The aim of the study was to evaluate the first experiences with the Dcont.hu system. Using Dcont.hu patients could upload glucose measurements to a shared electronic medical record using an interface on their home computer. Different statistics, graphics as well as tendencies over time became immediately available for the patients. The database from the first 6 months in the Dcont.hu system was analyzed. Totally, 217,558 blood glucose values were uploaded by 1.413 patients (859 men, 554 women) during the first 6 months after implementation of the system. More blood glucose values were uploaded by women (141,953) than men (75,605). The age of patients varied from 1 to 88 years (men: 43.8±18.8, women 38.1±18.5 years). The percentage of uploading was the highest (22.0%) in the 50.0 to 59.9 years age-group. A relatively high percentage of patients (17.6%) with age <20.0 years also used the system and uploaded nearly one-third (n=71,157 [32.7%]) of blood glucose values. In the total cohort, low (25.5 mmol/l) blood glucose values were rarely found (2.10% and 0.29%, respectively). The median value of blood glucose was 7.5 (IQR 5.5 - 10.3) mmol/l; women 7.3 (IQR 5.4 - 10.1) mmol/l, men: 7.9 (IQR 5.6 - 10.8) mmol/l; $p<0.05$. The internet-based telecommunication method proved to be useful and popular among diabetic patients with self-monitoring of blood glucose. Teleconsultation (synchronous or asynchronous) and extension of Web-based system to mobile phones could be the next step in supporting diabetic patients with self-monitoring of blood glucose.

2506-PO

WITHDRAWN

2507-PO

Diabetes Local Enhanced Service in Birmingham East and North Primary Care Trust

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Birmingham East and North Primary Care Trust (BENPCT), in the United Kingdom, invested in a diabetes Local Enhanced Service (LES). Participating GP Practices provided all essential and additional services for diabetic patients- including management of patients with Type 2 diabetes on diet and/or tablets, patients with Type 1 diabetes, and more complex Type 2 patients. 1) explore the difference between LES and Non-LES practices for Quality and Outcomes Framework (QOF) indicator outcomes for DM12 (percentage with diabetes in whom the last blood pressure is 145/85 or less), DM17 (percentage whose last measured total cholesterol within the previous 15 months is 5mmol/l or less) and DM23 (percentage with diabetes in whom the last HbA1c is 7 or less).2) To explore whether there is a significant difference between LES and Non-LES practices for hospital first and follow-up appointments. DM12 and DM17: The difference in achievement of these targets by LES and Non-LES practices was not statistically significant.DM23: probability of achieving DM23 targets by a LES and Non-LES practice is 53% and 43% respectively and this is statistically significant.LES practices referred less patients (0.10 compared with 0.20 for Non-LES practices) for a first hospital appointment and had less patients attending hospital for a follow-up than Non-LES practices (0.16 and 0.39 respectively). Both results are statistically significant. LES practices perform better in achievement of DM23 targets and also refer less patients to hospital, for both first and follow-up appointments. However, there may be confounding factors that need to be explored further.

Supported by: National Institute for Health Research (NIHR) through CLAHRC

2508-PO

WITHDRAWN

For author disclosure information, see page 797.

2509-PO

Optimizing Program Operations: Creating a Web-Based Application to Assign and Monitor Patient Outcomes, Educator Productivity and Service Reimbursement

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Financial survival of Diabetes Education Programs has demanded service providers efficiently monitor and optimize patient attendance, associated education outcomes and educator productivity to collectively enhance service reimbursement. Typically, Diabetes Education Programs have required multiple data collection systems to track each of these inter-related areas of program delivery, without availability of an integrated tracking tool. Existing electronic data systems were deemed insufficient in terms of software cost, information technology support, efficiency of data entry and available reports. The Diabetes Research Institute (DRI) in Miami designed and developed a PHP/MySQL Web-Based Data Management System (WBDMS) internally to optimize operation of its Diabetes Education Program. The data entry points established within the WBDMS exceeds the reporting requirements for ADA and AADE Education Recognized Programs, providing additional Service value. Software functionalities include patient demographics, diabetes type, referral source, patient learning challenges, visit information, patient clinical and behavioral outcomes that are reflective of the AADE7TM Self-Care Behaviors and reimbursement data for Diabetes Self-Management Education (DSME) and Medical Nutrition Therapy (MNT) Services provided. Internal evaluation of the WBDMS demonstrated increased fiscal value to the DRI's Diabetes Education Program, including prompt reports for ADA Education Recognition, key referrer and patient demographics providing for Service expansion, enhancement of individual and program clinical and behavioral outcomes, improved Service productivity and data required for grant applications and research. This new tool tracks billings and collections outcomes for all patients, significantly improves reimbursement and enables productivity assessment for individual service providers.

2510-PO

20 Years of Electronic Medical Records at Our Centre in India

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We report the EMR system at our Centre. It was first installed in 1992 when all patient data was stored as a soft copy. The FoxPro database was preceded initially by a free text paper system followed by an item-based paper record system, which were then logically transcribed into electronic format. We transported the data next to Paradox database and finally to MS Access which is presently being used. Essentially the fulcrum for identification is a unique EDC number, automatically generated when a new record is added. The record consists of different independent files linked by the EDC number (viz, Identifier, age, name, address, telephone number), the biographical, clinical and laboratory data, and a file containing follow up data. All three are seamlessly displayed on a single screen. We automated calculated fields, eg age at onset, BMI, automated diagnostic codes (eg hypertension, IHD, dyslipidemia), automated advise (eg foot care, smoking, recheck blood pressure if hgh). Recently we improved work flow by established a local area network system in which the biographical and laboratory data are entered even before the patient visits the physicians chamber, so that follow up data are also captured and the clinical encounter is made more productive. Currently we have a live EMR database of more than 40,000 subjects with diabetes mellitus. The key aspect for successful implementation was to establish a system, and a support group of software professionals. Also helping was the organic growth in terms of the physical and temporal order of entry weighing the time and depth of information that can be recorded. The workflow was evaluated and studied so that it merged with a usual clinical encounter. Practical considerations include support with hardware and software, daily backup and uninterrupted power supply. We have developed a prototype extension module where patients are provided SMS message, option is available for virtual data storage and possibility of integrating genomic data should they become available.

2511-PO

Refinement and Evaluation of a Comprehensive Disease Management Program for Diabetes and Cardiovascular Risk Reduction

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Emerging models of care, such as Accountable Care Organizations (ACOs), are linked with accountability, value and cost savings in primary care. Technology-driven diabetes healthcare can help interdisciplinary teams provide evidence-based medicine and effective diabetes education while facilitating team communication, population-based outcomes tracking, and meeting ACO requirements. We describe the Comprehensive Diabetes Management Program (CDMP), an interactive software application linked to an electronic medical record for diabetes and cardiovascular risk management based on national guidelines. CDMP provides clinical and behavioral self-management alerts that guide treatment decisions and structure medical care and diabetes education, and includes diabetes retinopathy screening. CDMP aggregates clinical, laboratory, pharmacy, provider, and patient data and incorporates it into treatment algorithms and clinical alerts to identify cardiovascular, renal, glucose control, foot, and retinal problems. Bilingual educational assessments and materials are integrated into CDMP along with behavioral assessments to create behavioral alerts to guide self-management education. Encounter forms create summary reports using drop down menus and free text, and are used to prioritize patient care needs. Notes and dashboard navigation guide CDMP team and provider treatment decisions including referrals and medication changes. A pilot of CDMP at a community health center improved key diabetes outcomes, and a refined version is now being evaluated in a large RCT. CDMP is an open source, license-free, scalable program that is well suited for emerging models of primary care.

Supported by: NIH (5R01DK084325-03)

2512-PO

A Novel Multi-Center Diabetic Eye Screening Program

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This multicenter study, by the INSIGHT researchers, is assessing the feasibility of digital photo eye screening in community-based public clinic and pharmacy settings to detect diabetic retinopathy in individuals with diabetes. This study focuses on barriers and enablers to the delivery of digital photo eye screening that prevent vision loss and promote eye health. Participants with diabetes in Baltimore, MD; Birmingham, AL; Miami, FL; and Philadelphia, PA are screened using a non-invasive, non-mydriatic fundus camera. Three photos per eye, per subject are taken. Visual acuity is tested using the Titmus V2 vision screener. Retinal images and visual acuity information are uploaded via the internet to the Wills Eye database. Following expert evaluation, results are reported to subjects and their primary care physicians. Prescreening and post-screening questions related to eye care utilization and patient satisfaction are asked by trained staff. Rates of patients who screen positive for diabetic retinopathy or diabetic macular edema and the severity of their conditions are determined. The rates of those who screen positive and receive follow-up care will also be determined. All screening-associated costs are being monitored. Screening began in December 2011. As of January 5, 2012, 25 of 2000 subjects have been screened, with an average age of 39 years. The average self-reported A1C level is 9.2% and 17 subjects self-identify as having medical insurance. The targeted completion date for 2000 subjects is June 1, 2012. This research project could provide an empirical basis for cost-effective screening and detecting diabetic retinopathy among persons with diabetes and reduce disparity in eyecare among socioeconomically disadvantaged groups.

Supported by: CDC

2513-PO

Relationship Between Social Capital and Type 2 Diabetes in Lorestan, Iran

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The aim of this exploratory study is to examine the relationship between social capital and the important public health variables of type 2 diabetes in the adult population in Lorestan province, Iran. We employed Multivariate Linear Model for co-relational analysis was conducted . Predictor variables included social capital, social trust & relationship, social support and individuals trust. HbA1c was considered as outcome variable. Social capital a, social trust & relationship and social support had significant linear relationships with control of diabetes; multivariate linear regression showed social

For author disclosure information, see page 797.

capital to be one of the important predictor of control of type 2 diabetes in rural and urban areas. Social capital was related inversely to HbA1c, indicating a protective effect. These exploratory study findings suggest that greater levels of social capital are protective against diabetes.

Supported by: Tehran University of Medical Sciences

PEDIATRICS—OBESITY

2514-PO

Parental Attitudes toward Regular and Diet Soft Drink Consumption

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Consumption of sugar-sweetened beverages is associated with weight gain and the development of obesity among children and adolescents. Artificially sweetened beverages (ASB) are increasingly used as an alternative, yet little is known about their health effects in children. This study evaluated parental attitudes toward sugar-sweetened and artificially-sweetened beverages, and assessed parental beliefs about their safety for child consumption. We utilized a convenience sample of parents attending a subspecialty pediatric clinic with their child. 102 parents of children between the age of 2 and 18 years completed a 35-item questionnaire. For each question, parents responded on a 5-point Likert scale, ranging from "Strongly disagree" to "Strongly agree." Frequency of parental agreement with each item was evaluated and parents reported the number of sugar-sweetened and artificially-sweetened beverages that their child regularly consumed. Nearly all parents (91%) reported that their child consumed sugar-sweetened beverages, while only one-third (37%) indicated that their child consumed artificially sweetened (diet) beverages. Approximately one quarter of parents (25.2%) indicated that diet beverages could be a good substitute for sugar-sweetened beverages, while 40.8% believed that diet drinks were unsafe. Distrust of diet drinks was associated with higher parental education (p=.03), higher parental age (p=.03), and younger child age (p=.03). Our findings suggest that in the Southeastern US, many parents believe that artificially sweetened (diet) beverages are unsafe for consumption among their children. Further well-designed interventional studies are needed to determine diet and health outcomes of artificial sweetener use among children in order to correctly advise parents.

2515-PO

Subclinical Atherosclerosis: Is it Possible to be Identified by Biological Markers in Youth?

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Atherosclerosis begins early in life and the first event of this atherogenic process is endothelial dysfunction (ED) that, if present, identify individuals at risk for cardiovascular disease (CVD). We aimed to evaluate the association between ED markers (soluble vascular cell adhesion molecule-1 [sVCAM], soluble intercellular adhesion molecule-1[sICAM], monocyte chemotactic protein-1[MCP], plasminogen activator inhibitor-1[PAI-1]) and risk factors for CVD (abdominal obesity [AO], adiposopathy and IR) in 128 Brazilian youth (1.88±0.83 BMIzs; 49.2% girls, 14.6±2.7y). Measurements: body mass index (BMI), waist circumference (WC), Homeostasis model assessment of IR (HOMA-IR), glucose, insulin, leptin, interleukin-6 (IL-6), C-reactive protein (CRP), tumoral necrosis factor-α (TNF-α), sVCAM-1, sICAM-1, PAI-1, MCP-1, high molecular weight adiponectin (HMW_Adn). AO was defined using WC, adiposopathy by the presence of three or more of adipocitokines (IL-6, TNF-α, HMW_Adn, Leptin, CRP) and IR by HOMA-IR. By anthropometry 66 (51.6%) and 51 (39.8%) had excessive and normal weight respectively and by International Diabetes Federation criteria 7.0% had MS. It was found associations between AO and sVCAM-1 (p=0.005) and adiposopathy and sICAM-1 (p<0.001) and also correlations between BMI-zs and leptin (p= 0.021;r=0.269) and CRP (p=0.037;r=0.240); WC and leptin (p=0.014;r=0,287) and CRP (p=0.001;r=0.365), insulin and number of components of adiposopathy (p<0.001;r=0,423); TNF-α and HOMA-IR (p=0.032;r=0.303) and leptin (p=0.007;r=0.387) and leptin and CRP (p=0.028;r=0.251). These observations suggest that AO in youth, which leads to adiposopathy, is associated with subclinical atherosclerosis supporting the hypothesis that the primary prevention of CVD should be performed very precociously. However the high variability found in terms of ED markers suggests other studies to determine the most sensible and precocious marker to identify groups at risk for CVD.

2516-PO

Lessons from EarlyBird—A 10y Longitudinal Study of Insulin Resistance

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Lessons from EarlyBird - a 10y Longitudinal Study of Insulin Resistance in Contemporary Children The prevention of diabetes depends on understanding the factors that lead to insulin resistance (IR), but only longitudinal studies can establish the relevant trends and their interactions. EarlyBird is a community-based cohort study of 300 contemporary children from 5y. By 15y of age, 55 of these apparently healthy youngsters have already shown impaired fasting glucose (IFG). Some unexpected findings are challenging established beliefs: · Most excess weight from birth through puberty was gained (ie centiles crossed) before 5y. · Patterns of weight gain differed according to age group. Before puberty, the mean BMI was skewed by a subgroup involving those whose same-sex parents were obese. Thus, by 8y, daughters (sons) of obese mothers (fathers) were ten (six) times more likely to be obese than those of normal weight mothers (fathers). With puberty, the BMI showed widening variance, suggesting the childhood population as a whole was becoming susceptible to weight gain. · The 'pubertal' rise in IR began well before puberty, independently of BMI. · Neither BMI nor IR distinguished the 55 children who developed IFG, but their HOMA β (a measure of beta cell function) was lower throughout. · Active children were demonstrably healthier, irrespective of BMI. · The activity level of children appeared, however, to be determined by a biological set-point, not the environment. · Time-lagged correlation further suggested that low physical activity was the result of overweight, rather than the cause. The trajectory leading to excess weight gain is set early in life. Obesity in the early years appears to be related to parental behaviours, whereas wider influences impact during puberty. However, neither the gain in weight nor IR is sufficient for IFG, which appears to require a primary defect of the beta cell. Physical activity is associated with better metabolic health, but the obese child tolerates less of it.

2517-PO

Relationship Between Pediatrician Advice and Parental Recognition of Child Overweight/Obesity

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Stemming the childhood obesity epidemic requires a change in the behavior of parents who are responsible for making dietary and lifestyle decisions for their children. The purpose of this study was to assess the relationship between pediatrician advice about weight/diet and parent recognition of child overweight/obesity. We administered a questionnaire to a convenience sample of parents of 5-15 year-old children presenting for well visits to an urban pediatric practice (n=116). Children's BMI was obtained from medical charts. Enrolled children had a mean age of 10.1 ± 3.2 years. Of all parents surveyed, 36% had a child classified as overweight (13%) or obese (23%). Only 31% of parents of overweight/obese children reported being advised by the pediatrician that their child was overweight. Thirty-one percent of all parents and 48% of parents of overweight/obese children reported receiving diet advice. Of parents of overweight/obese children, only 48% correctly identified their child as overweight/obese. Among parents who failed to identify their child as overweight/obese, none recalled receiving weight/diet counseling. Parents who correctly identified their child as overweight/obese had higher odds of being very concerned (vs. fairly concerned or less) about their child's weight (OR=16.9, 95% ci 1.7-165.9, p=0.015, adjusted for age and sex). In conclusion, the majority of parents of overweight/obese children do not report pediatrician counseling regarding weight, and parents who recalled pediatrician advice regarding weight/diet were more likely to express concern about their child's weight. Although this is not necessarily a causal relationship, the results suggest that pediatricians play a key role in promoting healthy weight and diet. This study underscores the importance of pediatricians being clear and direct with parents when communicating children's weight status and associated diet advice.

2518-PO

WITHDRAWN

For author disclosure information, see page 797.

2519-PO

WITHDRAWN

PEDIATRICS—TYPE 1 DIABETES

2520-PO

Mannose Binding Lectin (MBL) Levels in Children and Adolescents With Type 1 Diabetes

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MBL is one of the complement activation pathways not dependent of bacterial contact. Some complement system alterations seem to be related to levels of glycated hemoglobin (HbA1c) and infections in diabetic patients. To compare MBL blood levels between type 1 diabetic patients and age-matched controls and correlate them to metabolic control, time of diabetes, infection and microvascular complication. A hundred type 1 diabetic patients, 5-15 years, were included and devised by HbA1c into 2 groups: Group-1, well-controlled (HbA1c<7,5%, n=50) and Group-2, poorly-controlled (HbA1c>7,6; n=50). A hundred sex- and age-matched non diabetic subjects were included as controls. Serum HbA1c (HPLC) and MBL (ELISA) and microalbuminuria (3 dosages by turbidimetria) were determined in all patients. Serum glucose and MBL were measured in controls. Pubertal stage (Tanner) and body mass index (BMI) were calculated and presence of infection in the last year were reviewed. BMI ranges from 11.4-32.5 (18.7±4.3) and no infection were noted among diabetic patients. Group 1; time of diabetes: 3.7±0.4years, HbA1c: 7.2±0.2, microalbuminuria: 0-19mg/24hs (8mg/24hs), MBL levels: 150-8224 ng/mL (3096±2085). Group 2; time of diabetes: 4.2±0.4years, HbA1c: 10.4±0.2, microalbuminuria: 0-18mg/24hs (8.6mg/24hs), MBL levels: 95-9526 ng/mL (3067±2719). Controls: glycaemia<100mg/dl in all subjects, MBL levels: 81-9892 (3067±2844). There were no differences regarding BMI, pubertal stage and MBL levels between the 3 groups and no correlations of MBL levels and age, sex, HbA1c or microalbuminuria. However, MBL levels were lower among patients with less than 4 years diagnosis in Group 2. Although MBL activation of complement system has been related to the genesis of diabetes and microalbuminuria in adults, we did not find any correlation in this first study of MBL levels in children/adolescents. Considering poorly-controlled patients MBL levels is lower among those more recently diagnosed.

Supported by: FAMERP-BAP, FAPESP

2521-PO

The Effect of a Structured Transition Process from Pediatric Department to an Adolescence Clinic on Hba1c and Adherence in Young Type 1 Diabetes Patients

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As young patients with diabetes often get lost in the transition process we evaluated the effect of a structured transition process on adherence and HbA1c during the years 2006-2011. Data was collected and a questionnaire was sent to 95 young type 1 diabetes patients regarding their experiences during transfer from the paediatric department to the adolescence clinic . The patients were informed about the transition 1 year before the transition was effectuated. The paediatrician and the adult physician assessed if the patient could be transferred at 16 years of age or later. At the last visit in the paediatric clinic the young patient was introduced to the future doctor from the adolescence clinic. The same doctor will follow the patient after referral to adolescence clinic. In the adolescence clinic focus is on the patients needs and gradually to give the patients the responsibility for their own diabetes. The parents will gradually be less present at consultations. Age at transfer was 17.7± 1 years and diabetes duration was 10.3±4.8 years (mean ±sd). HbA1c during the first year of transfer was 8.8±1.5 % (percent) and at follow up 8.7± 1.4 % (mean±sd). All the patients was screened for late complications during the first year at the adolescence clinic: urinary albumin excretion measurement, fundus screening and biothesiometry were performed. No one had late complications and none of the 95 patients were lost at follow up. Half of the patients returned the questionnaires being satisfied with the transfer and emphasised the importance of being informed about the transition a year in advance. Ten would have liked to be transferred earlier. It is concluded that a tight structured process from the paediatric department clinic to the adolescence clinic is very important as the patients are not lost during the transition nor in follow up and that no rise in HbA1c was seen.

2522-PO

The "Honeymoon Phase" in Children With Type 1 Diabetes Mellitus (T1DM): Frequency, Duration and Predictive Factors at Onset

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Aim of the study was: to analyze the epidemiological features of paediatric T1DM at onset and their relation to remission frequency and duration in the first year of disease, to assess clinical efficacy of Glucose Evaluation Trial REMission (GETREM) protocol in terms of induction and maintenance of the "honeymoon phase" and to evaluate Insulin Dose-Adjusted A1C values at onset [IDAA1C = HbA1c% + (Insulin U/Kg/die x 4)] as a predictor of remission. 181 patients less than 15 years of age were admitted at our Department for T1DM onset and were treated according to GETREM protocol in the years 2008-2011. The following data were recorded at onset: age, sex, modality of onset according to ISPAD criteria, HbA1c, IDAA1C, fasting C-peptide and insulin requirement at the time of discharge. We considered as result variables both the percent of patients who achieved remission according to ISPAD criteria anytime during the first year of follow-up and remission duration in months for each patient. Clinical and lab parameters at onset were analyzed as predictors of remission in both forms by software R, R Development Core Team 2011. 46% of patients achieved partial or total remission during first year of follow up; in these patients mean remission duration was 7.22 months (SD 2.81 m). Variables at onset that were significantly related to remission were: - Age higher than 3 years: (% remission 53.2% vs 0%, p = 7.17 x 10-7) - Modality of onset: chetosis vs chetoacidosis (% remission 53.8% vs 34.7%, p = 0.01; mean duration of remission, if achieved, 7.7 vs 6.19 m, p = 0.03) - IDAA1C: a significant correlation was found between IDAA1C at onset and months of remission (p = 1.83 x 10-6, R2 = 0.12). We conclude that age under 3 years and severe metabolic impairment at onset are associated with lower rate and duration of remission in the first year of disease. Therefore we suggest considering early diagnosis and intensive treatment at onset as the potential goal to induce prolonged and/or complete remission phase.

2523-PO

Indices of Glycemic Variability in Pediatric Populations With T1D

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The Average Daily Risk Range (ADRR) and Mean Amplitude of Glycemic Excursions (MAGE) measure glycemic variability primarily in adult populations and provide a risk value for hypo- or hyperglycemia over a 30-day period.

The present study compared ADRR and MAGE indicators of glycemic variability in a pediatric sample. Blood glucose (BG) data were obtained from 107 youth with T1D ages 11-14 (M = 14.4, SD= 1.3), and analyzed for glycemic variability with ADRR and MAGE formulas. Results showed significant %s of the sample had BG values in the "high risk" category: 79% for ADRR values, and 91% for MAGE values. For comparison purposes, the % of BG values below (0-70 mg/dl), within (71-200 mg/dl), and above (201+ mg/dl) the ranges recommended by the American Diabetes Association (ADA) were calculated to determine independently the correspondence of each measure with ADA criteria. Pearson's r correlations determined the associations among the indices of glycemic variability with %s of BG levels below, within, and above range, as well as average BG level (M = 216, SD = 53.7) over the previous 30 days and with HbA1c (M = 8.8%, SD = 1.5). ADRR and MAGE had a moderate correlation with BG levels within range (-.70***; -.57***), a small correlation with BG levels above range (.41***; .29*), a moderate relation with average BG levels (r = .60***; r = .56***), and a small correlation with HbA1c (r = .42***; r = .40***). ADRR was more sensitive to hyperglycemic values than MAGE ($p < .05$) in this pediatric sample; however, BG %s below, within, and above range proved to be simpler to calculate and to more accurately portray BG patterns than a composite index from either glycemic variability measure. BG %s also are more readily interpreted by professionals and families. While ADRR and MAGE indicated that 80% or more of the population was high risk, almost half of all BG values in the sample were within the ADA recommended range. Nevertheless, over half of pediatric BG readings were out-of-range which suggests glycemic variability is a clinical issue in this population.

Supported by: NIDDK

2524-PO

Barriers to Successful Transition of Care in Emerging Adults With Type 1 Diabetes

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Emerging adults with T1D are at risk for poor outcomes in part due to reduced access to care during transition from a pediatric to an adult practice. The Naomi Berrie Diabetes Center cares for pediatric and adult patients with T1D in the same practice, thereby eliminating a potential barrier for successful transition. In order to analyze other barriers to transition, we conducted a retrospective chart review of 237 emerging adults (ages 18-26) with T1D seen at the Berrie Center between 2005-2010. The clinical characteristics of our emerging adult cohort are shown in Table 1. Forty-nine young adult patients with T1D (21%) transitioned from pediatric to adult care. Age at transition was 19.0 ± 2.1 years. A1C was significantly lower in patients who transitioned to adult care, 7.9 ±1.8% compared to those who were followed by a pediatrician, 8.9 ± 2.0% ($p<0.001$). There were no significant differences in other parameters such as T1D-related hospitalizations, history of psychiatric illness, or insulin pump use in the 2 groups. In our cohort of emerging adults with T1D, more than three-quarters of patients had not yet transitioned to an adult endocrinologist despite having access to care at the same facility where they received pediatric care. Our data do not demonstrate significant differences in clinical parameters other than A1C between those patients who transitioned and those who did not. The barriers to transition as perceived by pediatric patients, parents and clinicians need to be defined and addressed to improve transition of emerging adults with T1D to adult care.

Table 1.

	n=237
Age (years)	22 ± 2.5 (18-26)
% female	49%
Age at diagnosis (years)	9.4 ± 4.2 (1-20)
Duration of T1D (years)	12.7 ± 4.7 (2-24)
A1c (%)	8.7 ± 2.0 (4.6-14)
Insulin pump use	44%
A1C in patients on pump (%)	8.0
A1C in patients on MDI (%)	9.1 ($p<0.001$ compared to A1C on pump)
History college attendance	71%
History tobacco use	4%
History excessive alcohol use	4%
History psychiatric illness	7%
Dilated eye exam (past year)	51%
History of T1D hospitalization	7%

2525-PO

The Results of the National Insulin Pump Therapy Program for Children With Type 1 Diabetes

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Continuous subcutaneous insulin infusion(CSII) in prepubertal children type 1 diabetes(T1D) has been introduced in Polish Diabetic Centres since 2000. Due to the lack of education and treatment standards for CSII we have performed study, called National Pump Therapy Program, in 16 the Diabetic Centres in Poland. To assess impact of the national education for educator program in introducing CSII therapy in prebubertal children with T1D on glycemic control. The cross sectional, prospective study was conducted in two stages -the first one from 2003 to2005 - the education of educator - Health Care Providers (HCP), and the second one clinical data collection from 2005 to 2008 with the Central Laboratory assessment of HbA1c. We enrolled 1657 patients and assessed 1657 HbA1c, however demographic analysis was done in 920 patients where 79% get CSII therapy; data were recorded in the electronic net-database. The study group was divided in to 3 subgroups depending on the number of enrolled patients by the Diabetic Centre: small (S) < 100 patients(ps) ; medium (M) 100-200(ps) and large(L) >200(ps). The median age of analyzed patients was 8,5ys (range 1,2-14,0 ys), and 71,75% patients were in prepubertal age. In whole group the mean HbA1c was 7,46±1,1 %.(min-5%; max 12,1%); 60,1% patients get HbA1c below 7,5%. We noticed the significant differences in HbA1c between subgroups S vs M vs L (the mean HbA1c (%) :7,3±1,1 vs 7,4±1,0 vs 7,6±1,1 respectively, p=0,0001). We observed slightly higher HbA1c in children with longer duration of T1D (r=0,17, p<0,005). The national education of educator program offered for HCP before introducing CSII has impact on future optimal metabolic control in children switched on the pump therapy. The control of HbA1c was more optimal in small diabetic centre.

Supported by: WOSP

2526-PO

Comparison of the Effect of Insulin Glulisine to Insulin Aspart on Breakfast Postprandial Blood Glucose Levels in Prepubertal Children With Type 1 DM on MDI Therapy

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Postprandial blood glucose levels often reach ≥250 mg/dL in children on MDI or insulin pump therapy. Rapid-acting insulins including insulin aspart (NovoLog) and insulin lispro (Humalog) do not seem to effectively control postprandial glycemic excursion. In adults, insulin glulisine (Apidra) has been reported to have a faster onset and shorter duration of action than the other rapid-acting insulin analogs. However, there are no studies demonstrating this superior effect in children. Thirteen prepubertal children ages 4 to 11 years completed this study. Inclusion criteria included diagnosis of type 1 DM ≥ 6 months, HbA1C 6.9 to 10 %, on MDI with insulin glargine (Lantus) or insulin determir (Levemir) once daily and insulin aspart or insulin lispro premeal. Each subject received insulin glulisine alternating with insulin aspart pre-breakfast for 20 days. With a FBS of 70-180 mg/dL when no correction dose was needed, a prescribed breakfast with fixed amount of carbohydrates (45, 60 or 75 gms) was consumed following subcutaneous injection of the study insulin. Postprandial blood glucoses were obtained at 2 and 4 hours. Mean baseline blood glucose levels for insulin glulisine (133.4 ± 2.5 mg/dL) and insulin aspart (130.4 ± 2.5 mg /dL) were similar (p: 0.34). The increase in the 2-hour postprandial blood glucose was lower with insulin aspart (+ 94.7 ±15.8 mg/dL vs. + 110.9 ± 14.3 mg/dl, p: 0.01). Similarly, the 4-hour mean blood glucose was lower with insulin aspart (117.1 ± 6.7 mg/dL vs. 134.3 ± 5.3, p: 0.04). In conclusion, the effect of glulisine on breakfast postprandial blood glucose levels in prepubertal children with type 1 DM was inferior to insulin aspart, although the clinical significance of the difference is unclear.

Supported by: Novo Nordisk, Inc., sanofi-aventis, Spectrum Health "Healthy Kids-Healthy Lives"

2527-PO

Insulin Administration, Eating, and Physical Activity in Young Children With T1D: Timing Makes a Difference

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Management of type 1 diabetes (T1D) in young children can be challenging due to unpredictable eating behavior, unplanned physical activity, and difficulty communicating out-of-range blood glucose (BG) levels. Use of continuous glucose monitoring systems (CGM) may provide information about

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glycemic excursions and optimal timing of diabetes management behaviors. Baseline data from 4 children in a substudy of a larger ongoing RCT to promote management of young children's T1D are presented. Children ages 3, 5, 6, and 6 years (2 males, 2 females) wore a CGM for a 3 day blinded trial. All children were on a basal-bolus regimen and overall glycemic control was adequate (*M* A1c = 8.27; range 7.60-8.90). Case study data from CGM and daily phone interviews with parents (detailing insulin administration, food intake, physical activity) were examined. Across the 3 day trial, children spent an average of 38.25% of time between 100-200 mg/dl (conservative BG level targets for day and overnight hours). Children were hyperglycemic for almost half of the time (*M* = 47.5%; range 34-64%). Children were given an average of 4 insulin boluses per 24 hr period (range 2-10), and had an average of 5 food ingestions (range 3-8). For 2 of the 4 children, insulin was most often administered *after* food intake, and generally resulted in larger glycemic excursions than when administered prior to or at start of food intake. Reported physical activity was minimal, with children participating in the recommended 60 minutes of physical activity on only 28% of the monitored days. When physical activity did occur, a positive impact on glycemia was evidenced. Findings from these case reports add further evidence that management of T1D in young children can be particularly challenging for parents. Intervention efforts to provide parents with additional support may include strategies for supporting administering insulin *prior* to food intake, as well as ways to promote consistent engagement in physical activity.

Supported by: NIH (R01DK080102, K18DK095472)

PEDIATRICS—TYPE 2 DIABETES

2528-PO

Mean 24 hour Plasma GH Levels are Higher in Obese African-American Children With Type 2 Diabetes: A Pilot Study

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Obese children without type 2 diabetes (T2DM) have previously been shown to have lower mean 24 hour levels of insulin- counter regulatory hormones such as Growth Hormone (GH) and total cortisol (F) compared to lean children, potentially rendering them more insulin sensitive. We hypothesized that obese children with T2DM would have higher mean 24 hour levels of GH (GHm24h) and F (Fm24h) than obese patients without T2DM. Obese African-American (AA) children with and without T2DM participated in a preliminary 24 hour monitoring study of hormone levels. An indwelling venous catheter was placed and hormone samples drawn every half-hour for 24 hours. An aliquot was taken from each of the half-hourly samples to form a 24 hour pool for assessment of GHm24h, Fm24h, cortisone (Em24h), C-peptide (cP m24h) and free cortisol (fF24M). Differences of means between the groups were assessed statistically by t test. For fFm24h, Wilcoxon test was used due to non-normality of the data. Statistical significance was accepted at $p \leq 0.05$. GHm24h was higher while cPm24h was lower in obese AA children with T2DM compared to non-diabetic controls. There was a trend for higher Fm24h, fFm24h and Em24h in the T2DM group without reaching statistical significance due to small sample size. GHm24h was highly correlated with both Em24h (r=0.80, p=0.0049) and fFm24h (r=0.67, p=0.033) and inversely with cPm24h (r=-0.63, p=0.049). These preliminary findings suggest that higher GH levels and potentially higher cortisol levels are found in obese children with T2DM which may further increase insulin resistance and contribute to the diabetic diathesis.

Group	N	age	M/F	BMI-z	GHm24h	Em24h	Fm24h	fFm24h	cP m24h
Units		years			ng/mL	µg/dL	µg/dL	µg/dL	ng/ml
T2DM	6	14.52±3.03	2/4	2.19±0.42	1.48±0.41*	1.17±0.31	6.10±1.62	0.20±0.08	2.62±0.62*
Non DM	4	13.56±2.65	1/3	2.64±0.21	0.75±0.34	0.90±0.14	5.03±0.10	0.15±0.04	4.35±0.48
p-value		NS	NS	NS	0.0188	NS	NS	NS	0.0015

Supported by: CTRC of LSUHC and EFF Marilyn Fishman Grant for Diabetes Research

2529-PO

WITHDRAWN

2530-PO

Clinical Outcomes and Characteristics of Children With Type 2 Diabetes Phenotype and Positive GAD65 and/or IA2 Autoantibodies

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The TODAY trial is an NIH-sponsored multicenter study of T2D in youth aged 10-17 years who were screened for eligibility and randomization in 2004-9 and enrolled through the end of study in 2010. Eligibility requirements included a diagnosis of T2D for <2 years, a BMI of >85% and screening testing to confirm absence of islet cell autoimmunity and/or low fasting c-peptide. Surprisingly, 21 of the 93 (23%) children screened at UTHSCSA had positive autoantibodies (Ab+). These excluded patients had clinical features of T2D indistinguishable from the antibody negative participants. This study reviews the clinical outcomes that are available on these Ab+ children who received identical initial education to the T2D TODAY participating children. This review underscores that Ab+ diabetes may occur in the setting of obesity and phenotypic T2D. Further, it suggests that positive autoantibodies may result in more rapid diabetes progression, compared to autoantibody negative individuals. Of the original 21 children with positive autoantibodies, 14 (67%) have progressed to treatment with daily insulin regimens. Three were located during medical screenings on entry to adult correctional or juvenile detention facilities. Four of the 21 have been lost to follow-up. The percentage of individuals from this subpopulation returning to our system for medical care has increased over the past year. We attribute this to the fact that our academic practices are associated with two health care entities that are responsible for the majority of indigent care in San Antonio. These individuals continue to struggle with significant psychosocial barriers to medical care and as a group have poorly controlled diabetes with significant co-morbidities and more rapid progression to complications from diabetes.

PREGNANCY

2531-PO

Assessment of Metabolic Risk Using Glycated Hemoglobin in Women With Prior Gestational Diabetes Mellitus

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Due to their increased risk of type 2 diabetes, women with prior gestational diabetes mellitus (GDM) are recommended to undergo a 2-hour oral glucose tolerance test (OGTT) following their pregnancy. However, it appears that few women receive adequate follow-up and testing after their pregnancy. Our objective was to examine the adequacy of glycated hemoglobin (HbA1c) to assess the metabolic risk profile of women with prior GDM. The analysis included 185 women who had GDM between 2003 and 2009. HbA1c was measured and a 75g 2h-OGTT was performed to obtain fasting (FPG) and 2h- plasma glucose and insulin. HbA1c value of ≥5.7%, American Diabetes Association's cut-off for prediabetes, was used to categorize women at increased risk of diabetes. HOMA index for insulin sensitivity (HOMA-IS) was calculated and the presence of the metabolic syndrome, according to NCEP-ATP III criteria, was evaluated. Women were 36.2±4.8 years old and mean FPG and HbA1c were 5.9±0.7 mmol/L and 5.6±0.4%, respectively. Testing occurred 4.0±1.7 years following delivery. HbA1c was correlated with FPG (r=0.50; p<0.001), 2h-glucose (r=0.24; p=0.001) and HOMA-IS (r=-0.18; p=0.01). No association was observed with fasting and 2h- insulin concentrations. Compared to women with HbA1c level <5.7%, women who had a HbA1c ≥5.7% were more likely to have type 2 diabetes (OR 3.1, 95% CI [1.4-6.8]) and to be characterized with the metabolic syndrome (OR 2.2, 95% CI [1.1-4.5]). HbA1c levels ≥5.7% had 54.7% sensitivity and 82.4% specificity for elevated FPG (≥5.6 mmol/L). The same HbA1c level had 29.4% sensitivity and 92.1% specificity for elevated FPG and 2h-glucose (≥7.8 mmol/L) combined. These analyses suggest that women with HbA1c levels higher than 5.7% are at increased metabolic risk. However, the sensitivity of HbA1c is insufficient to detect glucose intolerance among women with prior GDM.

Supported by: CIHR and FRSQ

2532-PO

Gene Expression Analysis Demonstrates a Placental Dysfunction during Maternal Diabetes

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Nowadays, there is increasing evidence for a role of the perinatal environment in the metabolic programming of adult life. A disturbed intra uterine milieu due to maternal diabetes may favor the occurrence of chronic diseases

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in adulthood. The potential role of the placenta and particularly the implication of feto-placental genes on fetal programming remain to be investigated in animal models such as streptozotocin (STZ) induced diabetic rats. In our work, we: 1) evaluated the consequences of maternal hyperglycemia on pups metabolism; 2) used a systems biology approach to analyze differentially expressed placental genes to identify pathways involved in Intra Uterine Growth Retardation (IUGR) and in placental hypertrophy. We used 3 groups of animals: DS (n=5, receiving 65 mg/kg of STZ at G7), D30 (n=9, receiving sequentially STZ & 75 mg/kg of Nicotinamide at G7) and a control group (n=9). We have evaluated metabolic parameters in mothers during gestation and in pups at birth. Placental whole genome expression was performed to identify genes differentially expressed between experimental groups (Illumina and qPCR for confirmation). Diabetes, is more pronounced in DS than in D30. We observed an IUGR with placental hypertrophy in both treated groups. Histological observations showed a hypovascularization associated with an increase number of glycogen cells. These observations correlate with gene expression analyses showing significant change in expression of genes implicated in angiogenic and glycogen pathways. Especially, prolactin gene was highly upregulated (Fold change>4) in the DS group suggesting a role for antiangiogenic prolactin effect in observed hypovascularization In our model, maternal diabetes is responsible for IUGR with placental hypertrophy, associated with significant modification of placental gene expression putatively impairing angiogenesis. The observed IUGR may result from placental hypovascularization modifying the metabolic imprinting of the fetus.

Supported by: Eli Lilly and Company, DIAMENORD

2533-PO

Glycated Hemoglobin versus Oral Glucose Tolerance Test to Detect Glucose Abnormalities in Women With Previous Gestational Diabetes Mellitus

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In 2010 the American Diabetes Association (ADA) introduced the value of HbA1c at ≥ 6.5% for the diagnosis of diabetes. The impact of its implementation in women with previous gestational diabetes mellitus (GDM) is unknown. The aim of the study was to compare sensitivity and specificity of oral glucose tolerance test (OGTT) and HbA1c for the detection of glucose abnormalities in women with GDM at the postpartum. We studied 97 women with previous GDM at the postpartum (mean: 25 weeks), mean age (± SD): 36± 4 yr. After 75g OGTT women were classified in three groups: normal glucose tolerance (NGT), pre-diabetes (impaired glucose tolerance (IGT) and/or impaired fasting glucose (IFG)) and DM according to ADA diagnostic criteria. Clinical, biochemical variables and cardiovascular risk factors were analysed. HbA1c was determined by HPLC. Statistical analysis by mean of ANOVA, Pearson correlation test and ROC curve. We found a significative correlation between HbA1c and OGTT values (r:0.49, p<0.0001). 21% (20/97) showed pre-diabetes o DM with OGTT compared to 6% (6/97) with HbA1c ≥ 5.7% (p<0.01). Mean HbA1c (%) in NGT was 4.7± 0.4, compared to 4.9 ± 0.4 in pre-diabetes, and 5.7± 1.0 in DM (p<0.01). A cut-off value of > 5% HbA1c showed a sensitivity 100% and specificity 71% to detect DM in women with previous GDM. The use of HbA1c as a single criterion could delay diagnosis of abnormal glucose tolerance among women with histories of GDM, mainly in those with high risk of DM. We propose to mantain OGTT as the main criteria and HbA1c as an additional diagnostic test in postpartum women with GDM.

2534-PO

WITHDRAWN

2535-PO

WITHDRAWN

2536-PO

Physical Activity Behaviors and Blood Glucose Levels During First Trimester of Pregnancy in Urban Black Women

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Interventions based on diet and exercise/physical activity behaviors are effective for controlling weight gain as well as preventing type 2 diabetes. However, the impact of decreasing sedentary behaviors or increasing activity levels on gestational weight gain and glucose levels during pregnancy is unclear. Using baseline data from 55 women enrolled in a feasibility trial

For author disclosure information, see page 797.

of lifestyle intervention during pregnancy, we investigated associations between sedentary and activity behaviors and glucose levels during the first trimester of pregnancy. We measured self-report of time spent in activity and sedentary behaviors and glucose values from a 5-step, 2h oral glucose tolerance test (OGTT) in the first trimester (mean±SD gestational week: 14.4±2.8 weeks). Median (range) levels of total activity and sedentariness were 368.7(70.7,744.6) and 73.5(6.3,195.0) MET-h/week, respectively. Median(range) OGTT values at 0, 30, 60, 90 and 120 minutes were 83.4(57.4-128), 112.5(80-183), 108.5(70.4,205), 107.5(56.9,174) and 101.2(61.6,154)mg/dL, respectively. In multiple linear regression analyses, controlling for age, gravidity, socioeconomic factors, and family history of diabetes, we observed that an additional 7 MET-h per week in sedentary behavior (i.e. 1 extra hour per day watching television, reading magazines, or working at a computer) was significantly associated with 0.7 mg/dL higher fasting blood glucose, 1.1 mg/dL higher 30 min blood glucose, and 1.3 mg/dL higher 60 min glucose. We observed an association between higher sedentariness and blood glucose values among pregnant overweight and obese Black women in their first trimester. Interventions aimed at decreasing time spent in sedentary activities could have an impact on glucose levels during pregnancy.

2537-PO

Prevalence and Predictive Factors of Type 2 Diabetes (T2DM) in Women With Previous Gestational Diabetes: A Preliminary Result

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This cross-sectional study was conducted to examine the prevalence of abnormal glucose tolerance (AGT) in women with previous gestational diabetes mellitus (pGDM) and to determine the predictors of subsequent development of AGT in pGDM women. 212 pGDM women in the database of Department of OB-GYN, Siriraj Hospital were randomly invited to participate in the study. Among them, 88 women volunteered to participate. The mean age at the time of this study was 38+5 (26-49) years and duration after delivery of the index pregnancy (pregnancy in which GDM was first recognized) was 48+27 (6-120) months. Each subject underwent a complete history, gestational history, physical examination, and laboratory tests. 75-g OGTT were done in 84 subjects who have no known diabetes to determine glucose tolerance status. Four subjects had been diagnosed T2DM after delivery the index pregnancy. T2DM was diagnosed using definition of ADA. Of the 88 pGDM women, 71 (81%) had abnormal glucose tolerance (AGT-current) of any degree (IGT 38%, IFG with IGT 5% and DM 38%). Univariate analysis, women with AGT-current had significantly higher PG after 50-g glucose (50gG-GDM) and 1-hour PG level on the diagnostic 100-g OGTT obtained at the time of GDM (OGTT-GDM) than those of normal glucose (NGT). Moreover, women with AGT-current had >/= 3 abnormal PG values during OGTT-GDM more frequent than NGT (57% vs. 12%, p values =0.001). Multivariate analysis showed PG after 50gG-GDM >150 mg/dl and >/= 3 abnormal PG values during OGTT-GDM were the independent predictive factors for development of AGT later in their life (OR = 10.6 (CI 1.6-69.8) and 7.0 (CI 1.3-38.1)). In conclusion, the prevalence of AGT was high in women with pGDM during the first 7 years postpartum. GDM women who had PG after 50gG-GDM >150 mg/dl and >/= 3 abnormal PG values during OGTT-GDM should receive intensive postpartum care to prevent type 2 diabetes.

Supported by: Siriraj Grant for Research Development

2538-PO

Nicotinamide-Streptozotocin Treatment in Rat during Pregnancy: A Useful Animal Model to Study the Placental's Effects of Gestational Diabetes

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Gestational Diabetes Mellitus (GDM) is a complication that occurs between 24-28th weeks of pregnancy, characterized by an impaired glucose tolerance. GDM affects fetal growth and induces fetal programming of several chronic diseases including obesity, cardiovascular diseases, and diabetes. Several animal models have been developed to study the effects of an adverse intrauterine environment on the offspring development. A reliable animal model of GDM should present, throughout gestation, glycemic values close to what can be observed in GDM's women. Our work hypothesis was that the administration of streptozotocin (STZ, 65mg/kg, a specific β-cell poison) in combination with nicotinamide (NCT, 75 mg/kg, an antioxidant compound benefic on β-cell) to pregnant rats could stabilize the glycemia around mild values (2.34±0.51 g/L) and create a specific intrauterine environment able to induce placental gene modifications. We evaluated the phenotypic and metabolic parameters of NCT-STZ dams (n=13) and their offspring. In our NCT-STZ model, we evaluated by qRT-PCR, immunohistochemistry and western blot the expression of some placenta's genes and proteins already known to be modified in human GDM. We confirmed that the expression of some NCT-STZ placental genes showed the same expression trend as previously reported in human GDM's placenta. We then provided a new experimental animal model of GDM useful to study placental modifications and also phenotypic and metabolic alterations (malprogramming) occuring in offspring (mainly intrauterine growth retardation).

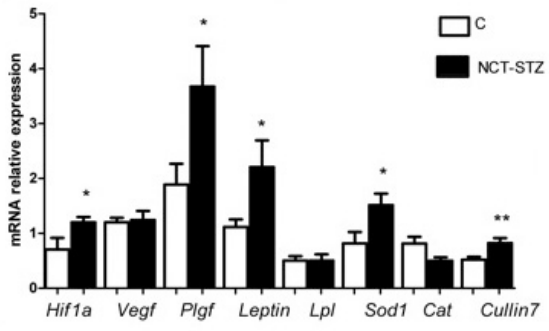

Fig: Genes expression evaluated in **NCT-STZ**'s placenta versus **C**ontrol

Supported by: Eli Lilly and Company, DIAENORD

2539-PO

Decreased total and High Molecular Weight Adiponectin are Associated With Gestational Diabetes in Chinese Americans

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Prevalence of GDM is higher in Chinese (7.3%) compared to Caucasians (1.6%) and a higher percentage of Chinese women fails the glucose challenge test (GCT) compared to Hispanic, African-American or White Non-Hispanic women. We examined the biomarkers of insulin sensitivity and inflammation and adipocytokines (Tables 1 & 2) in Chinese Americans at 24-28 weeks of gestation using ELISA assay. GDM subjects had higher circulating insulin but lower leptin and lower total & high molecular weight (HMW) adiponectin levels. Among the non-GDM subjects, those who failed GCT had higher insulin and resistin but lower total adiponectin levels. When the non-GDM subjects were divided into two groups (A1C<5.7% & >5.7%), subjects with A1C>5.7% had lower insulin and total adiponectin levels. In summary, insulin, leptin and resistin levels vary among the subgroups of borderline glucose intolerance in Chinese American women. However, GDM subjects consistently exhibit not only lower HMW adiponectin, confirming existing literature, but also lower total adiponectin levels across the spectrum of abnormal glucose tolerance. Lower levels of total adiponectin are important for contribution to the pathogenesis of GDM in Chinese Americans.

Table 1	Without Gestational Diabetes N=120	With Gestational Diabetes N=16
Age	30.86 ± 4.81	31.31 ± 4.27
BMI	24.54 ± 3.08	24.04 ± 2.84
Systolic BP	109.57 ± 9.42	107.31 ± 11.95
HgA1C	5.24 ± 0.38	5.29 ± 0.38
1H OGCT (mg/dL)	**112.50 ± 24.26**	**152.27 ± 12 (p<0.001)**
Insulin (mU/ml)	**63.56 ± 65.01**	**119.32 ± 92.10 (p<0.04)**
IGF-I (ng/ml)	**171.03 ± 58.53**	**203.42 ± 81.26**
IGFBP-I (ng/ml)	**169.00 ± 107.54**	**152.19 ± 93.29**
Leptin (ng/ml)	**20.12 ± 11.25**	**15.35 ± 7.70 (p<0.04)**
Total Adiponectin (mg/ml)	**8.93 ± 6.58**	**6.34 ± 4.11 (p<0.05)**
HMW Adiponectin (mg/ml)	**3.60 ±1.66**	**2.81±1.22 (p<0.04)**
CRP (mg/ml)	4.51 ± 4.37	3.18 ± 3.00
RBP4 (mg/L)	33.41 ± 8.73	32.33 ± 9.86
Resistin (ng/ml)	7.16 ± 2.89	7.18 ± 2.89
TNF-α (pg/ml)	12.03 ± 1.60	11.43 ± 1.13
IL-6 (pg/ml)	3.08 ± 1.15	2.68 ± 0.55
MCP-1 (pg/ml)	65.87 ± 10.54	65.36 ± 13.06
FGF-21 (pg/ml)	26.02 ± 11.97	26.37 ± 12.33

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Table 2

	Without Gestational Diabetes			
	1H OGCT<130 N=104	1H OGCT>130 N=22	HgA_{1C}<5.7 N=100	HgA_{1C}>5.7 N=16
Age	30.77 ± 4.9	31.67 ± 4.38	30.51 ± 4.95	32.25 ± 3.73
BMI (24 weeks AOG)	24.44 ± 2.94	25.04 ± 3.50	24.55 ± 3.19	24.42 ± 2.09
HgA_{1C} %	5.24 ± 0.40	5.26 ± 0.29	5.14 ± 0.31	5.87 ± 0.16 (p<0.001)
1H OGCT (mg/dL)	105.53 ± 16.94	157.59 ± 15.28 (p<0.001)	112.49 ± 24.33	112.94 ± 27.51
Insulin (µU/ml)	58.89 ± 63.90	95.11 ± 68.64 (p<0.03)	67.16 ± 70.53	48.59 ± 20.08 (p<0.04)
IGF-I (ng/ml)	174.95 ± 58.08	148.55 ± 60.26	170.00 ± 61.99	181.68 ± 41.73
IGFBP-I (ng/ml)	166.92 ± 107.31	168.45 ± 105.35	168.73 ± 109.59	167.92 ± 110.26
Leptin (ng/ml)	20.40 ±11.46	18.27 ± 9.37	20.03 ± 11.68	20.62 ± 7.90
Total Adiponectin (µg/ml)	9.41 ± 6.92	6.61 ± 2.60 (p<0.001)	9.06 ± 6.83	5.34 ± 2.97 (p<0.001)
HMW Adiponectin (µg/ml)	3.69 ± 1.70	3.09 ± 1.22	3.58 ± 1.71	3.39 ±1.37
CRP (µg/ml)	3.95 ± 2.55	2.64 ± 1.64 (p<0.01)	4.13 ± 3.44	6.66 ± 8.26
RBP_4 (ng/ml)	33.70 ± 8.60	31.71 ± 9.23	32.83 ± 8.23	34.18 ± 10.26
Resistin (ng/ml)	7.00 ± 2.91	8.49 ± 2.62 (p<0.03)	7.24 ± 2.93	6.36 ± 2.52
TNF-α (pg/ml)	12.01 ± 1.57	11.82 ± 0.78	11.95 ± 1.54	11.75 ± 1.25
IL-6 (pg/ml)	3.06 ±1.13	3.12 ± 1.10	3.12 ± 1.19	2.76 ± 1.02
MCP-1 (pg/ml)	65.66 ± 10.02	69.99 ± 12.65	65.75 ± 10.78	66.12 ± 10.02
FGF-21 (pg/ml)	25.94 ± 11.85	57.48 ± 49.35	25.84 ± 12.08	28.01 ± 12.69

2540-PO

A Scoring Algorithm Including Fasting Plasma Glucose Measurement and a Risk Estimation Model is an Accurate Strategy for Detecting GDM

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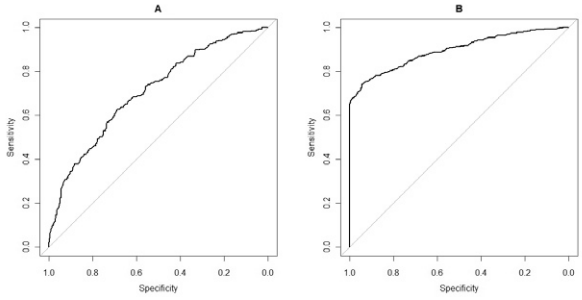
It is not finally clear how to construct a time and cost-effective screening strategy for gestational diabetes(GDM). Thus, we elaborated a screening algorithm combining i) fasting plasma glucose(FPG) measurement and ii) a risk prediction model focused on subjects with normal FPG levels to decide if an oral glucose tolerance test is indicated. 1336 women were prospectively screened for several risk factors for GDM within a multicenter study conducted in Austria. Of 714 women, who developed GDM, 461 were sufficiently screened with FPG. A risk prediction score was finally developed on the remaining 253 GDMs and 622 healthy females. The screening algorithm was validated on further 258 pregnant women. A risk estimation model including history of GDM, glucosuria, family history of diabetes, age, preconceptional dyslipidemia, and ethnic origin in addition to FPG was accurate for detecting GDM in subjects with normal FPG. Including a FPG pretest, the ROC-AUC was 0.90 (CI:0.88-0.91). A cut-off value of 0.25 was able to differentiate between low and intermediate risk with a high sensitivity (32.6% were correctly defined as healthy, while 3.9% of GDMs were misclassified). The validation cohort revealed comparable results. Moreover, we demonstrated a strong association between the risk estimation and macrosomia (OR:3.29,CI:1.87-5.87). This study demonstrated a new concept for accurate but cheap GDM screening. This approach should be further evaluated in different populations to ensure an optimized diagnostic algorithm. ROC-curves: normal FPG(A) and after including the FPG pretest(B).



Supported by: Austrian Diabetes Association

2541-PO

Streptozotocin-Treated Pregnant Rat: New Insights for an Old Model

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The fetal programming effect of the maternal intrauterine environment has been identified since the 90's by Barker *et al.* Retrospective studies on cohort have demonstrated the effect of maternal diabetes on the programming of obesity, diabetes and cardiovascular diseases in offspring. To date, various animal models have been used to study the pathophysiological mechanisms acting. Streptozotocin (STZ) is an antibiotic known since the 70's to specifically kill the rodent beta cells. Nowadays, STZ is still largely used, alone or in combination with other molecules, at different doses to generate animal models of type 1 and type 2 diabetes. To mimic gestational diabetes, pregnant Wistar rats received at day 7 of gestation (G7) an injection of STZ alone (65 mg/kg, n=5) or in combination with nicotinamide (NCT, 75mg/kg, n=9) (known to protect beta cells). The rats were sacrified at G20 and the pups were used for phenotypic and metabolic analysis. We observed, after injection, a maternal hyperglycemia, hyperketonemia and hypoinsulinemia reflecting the destruction of beta cells in dam's pancreases. The effect was less pronounced in dams receiving NCT. Considering pups' blood at G20, we observed also an hyperglycemia and an hypoinsulinemia. Analyzing the pups' pancreases by immunofluorescence, we observed a reduction of the number of the islets (stained by insulin and chromogranin A) and of the beta cells. Glucagon positive cells seemed not affected. The number of Pdx1 and Pax4 positive cells were also highly reduced in the treated pups. Of note, the pancreatic modifications were less pronounced in the group receiving NCT. Unless injection was done before the pancreatic development, it seems that STZ or one of its metabolites, at this dose, is able to cross the placental barrier and to kill the pups' beta cells. We demonstrated that this "old, well know model" is not suitable to study the transgenerational effect of chemically induced maternal diabetes.

Supported by: Eli Lilly and Company, DIAMENORD

2542-PO

Mild Immunosuppression during Pregnancy May Result in Decreased Insulin Requirements in a Subpopulation of Pregnancies Complicated by Type 1 Diabetes Mellitus

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Mild Immunosuppression during Pregnancy May Result in Decreased Insulin Requirements in a Subpopulation of Pregnancies Complicated by Type 1 Diabetes Mellitus We evaluated the change in GAD 65 to test our hypothesis that in T1DM pregnancy, as in normal pregnancy, there is a suppression of anti-β cell antibodies reflected by an increase in C-peptide levels and a concomitant reduction of insulin requirements. Between 2005 and 2009 we evaluated 28 T1DM women during the 3rd trimester of pregnancy and postpartum. The mean age was 31 ±4.6 years, with a mean duration of T1DM =16±9.1 years. Twenty patients had GAD measured by standardized relative index assay (GAD 65a). In 2009 the assay was internationally harmonized and 8 patients had GAD measured by NIDDK standardized assay (GAD 65b).

Type 1 Diabetes Mellitus	3rd Trimester	Post-Partum
GAD 65a ± SEM (n=20)	0.3 ±0.09	0.5±11*
GAD 65b± SEM (n=8)	158.6±119.5	208.2±147.7*
C-peptide±SD (ng/mL)	0.3±0.5	0.2±0.5
Basal Daily Insulin Use ±SD (Units)	39.1±27.1	19.6±14.5
Basal Insulin Units/kg/day	0.5±0.3	0.3±0.004
A1C (%)	6.0±0.7	6.4±0.9

* p=0.0012

A Wilcoxon signed rank test determined the median percentage change of GAD 65 from pregnancy to post-partum. The relation between GAD change and daily insulin change from pregnancy to post-partum was calculated with the Pearson correlation coefficient (correlation coefficient = 0.26296; p=0.2918) indicating there was no association between GAD decrease and basal daily insulin use. Among the patients studied, 2 women who had normal thyroid function had nearly non-detectable GAD levels with C-peptide levels >1.0. These data indicate the decrease in GAD 65 during pregnancy in most T1DM does not facilitate recruitment of residual β-cells in T1DM; however some patients may retain endogenous secretion of insulin such that insulin requirements are reduced.

For author disclosure information, see page 797.

2543-PO

WITHDRAWN

2544-PO

Assessment of Food Intake of Women With Pregestational Diabetes

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Objective: The objective of this study was to analyze the dietary intake of women with pregestational diabetes, estimating the prevalence of deficiency or excess of macronutrients and micronutrients in the diet. Method: Thirty-nine pregnant women with pregestational diabetes were evaluated in the first prenatal care assessment. Inclusion criteria were: pregnant women with pregestational diabetes, single pregnancy, gestational age less than or equal to 24 weeks. Pregnant women who present inability to understand or Record the nutritional guidance would be exclused. The women were interviewed with the application of a 24-hour recall (24 Hr) recording dietary intake information from three non-consecutive days, including one day of the weekend. We determined the nutritional status by body mass index before pregnancy, and then obtained the calculation of energy recommendations for further distribution of macronutrients in the diet of the pregnant women. The chemical composition of food was calculated providing data of the total energy (VET), macronutrients and micronutrients, wich were compared with dietary recommendations.Results: On the 39 pregnant women studied, there was an energy consumption lower than recommended, representing only 89% of the estimate. There was a greater distribution of daily energy intake from protein and lipid than expected and lower distribution of VET in relation to carbohydrates. There was inadequate intake of micronutrients with higher proportions of deficit of calcium, iron, copper, magnesium, selenium, potassium, vitamin B1, B5, C and folic acid. An excess of the following micronutrients was identified: phosphorus, sodium, iodine and vitamin B12. There was inadequacy of micronutrient with variable distribution between deficit and excess of manganese, zinc, vitamin A, vitamin D. Conclusions: There was a high frequency of inadequate diet in pregestational diabetic patients in terms of both total energy and the distribution of macronutrients and micronutrients.

2545-PO

Association of Gestational Diabetes Mellitus With Weight and Preventive Health Behaviors after Pregnancy: The CARDIA Study

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We compared pre- to post-pregnancy changes in weight, body mass index (BMI), waist circumference, diet and physical activity in women with and without gestational diabetes mellitus (GDM). Using the Coronary Artery Risk Development in Young Adults (CARDIA) study we identified women with at least one pregnancy during 20 years of follow-up (n=1,488 with 3,125 pregnancies). We used linear regression with generalized estimating equations to compare pre- to post-pregnancy changes in health behaviors and anthropometric measurements between 137 GDM pregnancies and 1,640 non-GDM pregnancies, adjusted for parity, age at the time of delivery, pre-pregnancy measure, race, education, mode of delivery, and interval between delivery and post-delivery examination. Compared with women without GDM pregnancies, women who developed GDM had higher pre-pregnancy mean weight (155.4 vs. 147.3 lb), BMI (26.3 vs. 24.7 kg/m2), but lower total daily caloric intake and similar levels of physical activity. Both GDM and non-GDM groups had higher average postpartum weight of 7-8 lbs and decreased physical activity, increased total caloric intake, but reduced fast food frequency about 1.4 years after pregnancy. Pre- to post- pregnancy changes in body weight, BMI, waist circumference, physical activity and diet did not differ between women with and without GDM in pregnancy, even after adjustment for age, race, education, parity, cesarean delivery, and the delivery to post-delivery exam interval. Regardless of GDM history, following pregnancy women similarly increased caloric intake, BMI and weight, decreased physical activity but reduced their frequency of eating fast food. Postpartum weight gain and adverse health behaviors are risk factors for the progression to type 2 diabetes, particularly among women with GDM, highlighting the imminent need for postpartum interventions aimed at risk reduction and long term surveillance.

Supported by: 5K23HL098476–02

2546-PO

Maternal BMI is Associated With Infant Umbilical Cord Insulin Levels

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To determine whether maternal obesity is associated with neonatal anthropometrics and metabolic parameters, we prospectively studied healthy pregnant women (n=31). Maternal BMI was assessed at the first prenatal visit (mean 15.0 ± 4.2 weeks) and at 36-40 weeks. Fasting lipids and glucose tolerance (75 g OGTT) were assessed at 30.3 ± 4 weeks and analyzed using ADA criteria; women with GDM were excluded from analysis. Neonatal anthropometrics and cord insulin were measured at birth. Early and late gestational maternal BMI were strongly associated (r=0.89, p<0.0001). Both maternal BMI were associated with maternal glycemia (2-hour OGTT) (r=0.59, r=0.62, both p<0.001) and LDL (r=0.42, r=0.35, p≤0.05). We next assessed relationships between maternal metabolism and fetal growth. Maternal glucose correlated with birth weight (r=0.34, p<0.03). Maternal insulin resistance (HOMA-IR) correlated with head circumference (r=0.55, p<0.01), but not birth weight (r=0.09, p=0.63) or length (r=0.18, p=0.34). Neither maternal BMI correlated with birth weight (r=0.09, r=0.01). However, there was a robust association between both gestation maternal BMI and cord insulin (early: r=0.55, p<0.001; final r=0.65, p<0.0001), which was accounted for in part by association between maternal glucose and cord insulin (r=0.36, p=0.02). There was no correlation between birth weight and cord insulin (r=0.008, p=0.96). Maternal weight gain during pregnancy tended to be inversely related to initial BMI (r=-0.23, p=0.18), as expected, but was not associated with final BMI (r=0.11, p=0.52) or offspring cord insulin (r=0.20, p=0.25). These results demonstrate a strong positive association between maternal BMI, maternal glycemia, and offspring cord insulin levels, even in mothers without GDM. Determining the mechanisms mediating the relationships between maternal obesity and offspring insulin levels will be an important research goal. Optimizing pre-pregnancy BMI and metabolism are key therapeutic goals in women of childbearing age.

Supported by: Fulbright/CAPES Program and CNPq

2547-PO

Glycemic Control and Weight Gain in Post-Pregnancy Follow-Up in Type 1 Diabetes Women

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Glycemic control during pregnancy complicated by type 1 diabetes mellitus (T1DM) is essential for clinical outcomes. Most pregnant T1DM women achieve normoglycemia but intensive insulin management is associated with weight gain. There is scarce data on glycemic control and weight change after delivery. We aim to examine post-pregnancy glycemic control and weight changes in T1DM women. We analysed 378 singleton pregnancies in T1DM women receiving medical care at the Department of Metabolic Diseases, Krakow, Poland. We identified 274 subjects that had participated in an intensive diabetes management program and had at least two follow-up visits after the delivery with HbA1c and weight measurements. Their mean age was 27.8±5.0 years, while diabetes duration 11.6 years±7.4. The mean initial HbA1c level during pregnancy was 7.0%±1.5, while pre-pregnancy weight was 64.5 kg±1.5, BMI 23.8±3.2 kg/m^2. The mean HbA1c in the 3rd trimester was 5.7%±1.0. We observed mean gestational weight gain of 14.2 kg±1.5. During first the 6 months after delivery HbA1c increased by 0.9% ($p<0.0001$), while weight was increased by 4.7 kg compared to pre-pregnancy ($p<0.0001$) and BMI increased to 25.5 ($p<0.0001$ compared to pre-gestational level). After another 6 months HbA1c further deteriorated by 0.3%, and it was higher than in the last trimester ($p<0.0001$). The last HbA1c recorded (>12 months from delivery) was 1.5% higher than at the end of pregnancy ($p<0.0001$) and not different from the initial level (7.2% vs. 7.2%, $p=0.9$). BMI did not return to the pre-pregnancy level, and it was 1 kg/m^2 higher ($p<0.0001$). In summary, in this large clinical observation, T1DM women showed substantial post-pregnancy deterioration in glycemic control. They were also unable to return to their pre-pregnancy weight.

Supported by: Polish Ministry of Science Grant No. N N407 414436

2548-PO

WITHDRAWN

2549-PO

WITHDRAWN

2550-PO

Characteristics of Women With Recent GDM attending a Postpartum Diabetes Prevention Seminar

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Type 2 diabetes (T2DM) is a preventable condition. Women with gestational diabetes (GDM) are an identified cohort who should benefit from preventive lifestyle interventions. However, it is unknown how to best provide such a post-partum program, or whether participation is meaningful or predictable. Therefore we investigated the characteristics of women attending and not attending a post-GDM diabetes prevention seminar. In the final weeks of pregnancy, all women with GDM at a tertiary care clinic were handed a summary of T2DM prevention along with a discussion emphasizing that the risk for future T2DM. They were further informed that they would be invited to a T2DM prevention seminar at 3-4 months postpartum. An invitation was mailed to each woman one month in advance of the seminar, explicitly inviting women to bring their child(ren) as babysitting was provided. Participants were asked to do a postpartum A1C on the seminar day to minimize time pressures. Demographics of attendees vs non-attendees were recorded. 131 women were invited to the seminars: 44% attended. Attendees were slightly older than those not attending (32.5±5.08 yrs vs 30.9±4.5 yrs; $p=0.047$). However, no differences were found in any of the other characteristics of interest including: local vs non-local address; upper vs lower SES address; previous pregnancies or pregnancy losses, age of youngest/eldest child; weight, GDM diagnosis week; insulin start week; insulin dose; caucasion vs noncaucasian; number of missed clinic appointments; contacts with clinic RN, family history of diabetes. Less than 50% of women with recent GDM returned to a diabetes prevention seminar at 3-4 months postpartum despite discussion of T2DM risk, personal invitation at clinic discharge, a reminder letter, and conscious efforts to minimize known attendance barriers. Translating diabetes prevention messages to populations at risk is likely to be need to be multifaceted and go beyond individual contact.

2551-PO

WITHDRAWN

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2552-PO

Atlantic DIP: Universal vs. Selective Screening for Gestational Diabetes (GDM)

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The ATLANTIC Diabetes in Pregnancy consortium (ATLANTIC DIP) was set up to study Gestational Diabetes Mellitus (GDM) in an Irish population using a 75g oral glucose tolerance test (OGTT) at 24-28 weeks gestation and the International Association of Diabetes in Pregnancy Study Groups (IADPSG) cut off values. GDM is associated with adverse pregnancy outcomes but since universal screening is costly, we aimed to compare a universal to a selective screening strategy. The source population consisted of 41,438 women attending five obstetric centres (2007-2010). Those with a prior diagnosis of diabetes were excluded. During 2007-08, universal screening was offered while in 2009-2010 selective screening was offered. In both strategies a 75g OGTT using IADPSG cut off values was applied. 5302 women underwent universal screening and 573 (10.8%) were diagnosed with GDM. During selective screening 570 women met criteria to undergo OGTT out of a total obstetric population of 22,647, 484 (2.1%) of whom were diagnosed with GDM. The number screened by 28 weeks was significantly higher for universal screening n=335 (74%) than selective (62% n=305, P<0.001). We estimate selective screening missed 9 per 100 cases of GDM as compared to the universal approach. No important differences were found between the two groups when pregnancy outcomes were compared. Universal screening leads to earlier identification of GDM compared to selective but no differences were identified in key pregnancy outcomes between the two groups of women. However, selective screening potentially missed 9% of GDM cases and their outcomes are unknown. Further prospective research is required to assess the potential benefit of either approach using IADPSG criteria.

Supported by: Health Research Board of Ireland

2553-PO

Anatomical Adiposity & Metabolic Response in Lean and Non-Lean Pregnancies

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Maternal obesity is a risk factor for GDM and adipocyte dysregulation is thought to be a possible pathway. This longitudinal study assessed distribution of subcutaneous fat accumulation (at 15, 25 and 35 weeks gestation) in lean pregnancies (LP) and non-lean pregnancies (NLP) and whether different anatomical sites had an impact on metabolic markers (glucose, insulin, TG, NEFA). Adipose tissue accumulation was measured by skinfold thickness by the same trained operator. Plasma markers were measured by routine methodology. There was no significant difference in gestational weight gained by LP (n=27) compared to the NLP (n=8). In healthy LP there was a significant increase in abdominal skinfolds (costal, suprailiac) (28.9mm to 34.4mm p=<0.0001) and lower body peripheral (midthigh, suprapatellar) (35.0mm to 43.5mm p=<0.0001) across gestation. In NLP, upper body peripheral (biceps, triceps, subscapular) (73.2mm to 86.7mm p=0.012) and lower body peripheral skinfolds (61.4mm to 75.1mm p=0.002) were significantly increased over gestation. In LP there was significant gestational increases in insulin (3.0mU/L to 6.7 p=<0.0001) and TG (1.2mmol/l to 2.5 p=<0.0001) but not Glucose or NEFA. In LP gestational increase in fasting insulin were inversely correlated with greater deposition of fat upper body peripheral during pregnancy (r=-0.55, p=0.009). In NLP there was significant gestational increases in TG (1.8mmol/l to 3.0 p=0.003) but not insulin, glucose or NEFA. In NLP upper body skinfolds were correlated with gestational change (GC) in fasting glucose (r=0.91, p=0.002) and GC in TG (r=0.97, p=0.002). We found that LP had a significant increase in central adiposity, but this did not lead to an adverse metabolic response. Although NLP gain fat preferentially in peripheral body depots, this is associated with an exaggerated TG response. We continue to collect data on the NLP (n=16 in total) to investigate the effect of fat accumulation on endothelial function, oxidised LDL and superoxide formation in LP and NLP.

Supported by: Wellbeing of Women Training Fellowship

2554-PO

Coexistence of Insulin Resistance and Increased Glucose Tolerance in Pregnant Rats: a Physiological Mechanism of Glucose Maintenance

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The participation of insulin resistance (IR) and glucose tolerance in the maintenance of blood glucose levels in non diabetic pregnant Wistar rats (PWR) was investigated. PWR were submitted to conventional insulin tolerance test (ITT) and glucose tolerance test (GTT) in which blood were collected 0, 10 and 60 min after intraperitoneal insulin (1 U/kg) or oral (gavage) glucose (1 g/kg) administration. Moreover, ITT, GTT and the kinetic of glucose concentration in the fed and fasted state were evaluated with the real-time continuous glucose monitoring system (RT-CGMS) technique. Furthermore, the contribution of the liver glucose production was investigated. Conventional ITT and GTT from 0, 7, 14 and 20 days of pregnancy showed increased of IR and glucose tolerance after 20 days of pregnancy. For this reason this period of pregnancy was used to investigate the kinetic of glucose levels, ITT and GTT measured by RT-CGMS technique. PWR (day 20) showed lower ($p < 0.05$) glucose concentration in the fed state. In addition, we also demonstrated IR and increased glucose tolerance in the fed state (PWR-day 20 *vs.* day 0). Furthermore, in general terms our data from glycogenolysis or gluconeogenesis suggests that the liver glucose production did not contribute to the changes of insulin sensitivity and/or glucose tolerance during late pregnancy. In contrast with the general view that IR is a pathological process associated with gestational diabetes, a certain degree of IR could represent an important physiological mechanism for blood glucose maintenance during fasting.

Supported by: CNPq 563870/2010-9, FAPESP and Araucaria Foundation

2555-PO

Diabetes in Pregnancy among Hospital Deliveries in 24 States, 2007-2009

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Diabetes mellitus (DM) is currently one of the most common and fastest growing co-morbidities of pregnancy. However, state-level and race/ethnicity data for this condition are limited. This study describes the state-level rates of pre-existing DM (PDM) and gestational DM (GDM) overall and by race/ethnicity among delivery hospitalizations with available race/ethnicity data. Data on hospitalizations for delivery were obtained from the Healthcare Cost & Utilization Project State Inpatient Databases (SID) for 22 states in 2008 (Arkansas, Arizona, California, Colorado, Florida, Hawaii, Iowa, Kentucky, Maine, Maryland, Massachusetts, Michigan, North Carolina, New Jersey, Oregon, Rhode Island, South Carolina, South Dakota, Utah, Vermont, Washington, and Wisconsin), for Nevada in 2009, and for New York in 2007. Maternal deliveries were identified using diagnosis-related group codes (2007: 370, 371, 372, 373, 374, 375; and 2008-2009: 765, 766, 767, 768, 774, 775) and presence of DM was determined using ICD-9-CM diagnosis codes (648.0x, 250.xx, and 249.xx for PDM and 648.8x for GDM). Rates of hospitalizations with PDM or GDM were calculated per 100 deliveries and race/ethnicity. Age-standardized PDM ranged from 0.64/100 deliveries in Colorado to 1.18 in South Carolina (state median PDM: 0.87). Age-standardized GDM ranged from 3.20/100 deliveries in Utah to 6.59 in Rhode Island (state median GDM: 5.21). The median rate of age-adjusted PDM was higher among blacks (1.40/100 deliveries) and Hispanics (0.97/100) than among whites (0.70/100) and Asians (0.62/100). The median rate of age-adjusted GDM was higher among Asians (7.44/100 deliveries) and Hispanics (6.78/100) than among whites (4.62/100) and blacks (5.26/100). Our results suggest that effective

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diabetes prevention and control strategies among women of childbearing age will require monitoring of trends and better understanding of factors that contribute to state-level differences and to racial/ethnic disparities in the rate of DM in pregnancy.

2556-PO

WITHDRAWN

2557-PO

WITHDRAWN

2558-PO

Resources to Improve Care among Women With a History of Gestational Diabetes: A Provider Perspective

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Women with a history of gestational diabetes mellitus (GDM) are at high risk of developing type 2 diabetes. However, previous research has shown rates of postpartum glucose testing are low, partially due to discontinuity of care after delivery. The objective of this study was to identify perceived barriers to and suggested resources for improving care among women with a history of GDM. A dual mode (mail and internet) survey was sent to a random sample of licensed and practicing family practice physicians, internal medicine physicians, obstetricians/gynecologists (OB/GYN), and nurse midwives in Ohio from September through December 2010 (N= 2,035). The overall response rate was 46%. Approximately 70% of all providers felt it is important for them to increase patient knowledge of future risk of type 2 diabetes among patients with a GDM history. Over 60% of OB/GYNs and nurse midwives report always having access to a woman's GDM status, compared to less than 5% of family practice or internal medicine physicians. Over two-thirds of OB/GYNs and nurse midwives believe that increased patient responsibility for self-preventative care is necessary to help support care. The majority of all provider types reported that care can be enhanced by: (a) improving access to primary care providers and endocrinologists; (b) including an automatic reminder at postpartum visit of woman's GDM status in her chart or electronic medical record; and (c) improving patient education of their condition through increased access and availability of patient education materials. Better insurance reimbursement and extended Medicaid coverage were also identified as resources to support care. Providers recognize the importance of type 2 diabetes risk education among women with a history of GDM. Resources to support patient education for self-preventative care, enhance health care decision making, and improve insurance reimbursement and coverage are needed to facilitate this.

2559-PO

Levels of the Inflammation Marker YKL-40 in Young Adults Exposed to Intrauterine Hyperglycemia

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YKL-40 is an inflammation marker, which is increased in patients with diabetes and associated with insulin resistance and atherosclerosis. Exposure to intrauterine hyperglycemia because of maternal diabetes increases the risk of overweight, the metabolic syndrome and type 2 diabetes in adulthood. We aimed to investigate associations between exposure to intrauterine hyperglycemia and plasma level of YKL-40 in adult offspring. We studied 597 offspring, aged 18-27 years, from 4 different groups based on maternal glycemic status and genetic predisposition to type 2 diabetes: 1. Offspring of women with gestational diabetes mellitus (GDM) 2. Offspring of women with risk factors for GDM but normal glucose tolerance in pregnancy 3. Offspring of women with type 1 diabetes 4. Offspring of women from the background population. The offspring were characterized by fasting plasma levels of YKL-40, and metabolic and anthropometric measurements. Exposure variables were maternal glycemic status as well as measures of maternal glucose levels during pregnancy. The median plasma YKL-40 in the total cohort was 45 ng/ml (25-75 percentiles: 35-56) without significant dif-

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ferences between the 4 different exposure groups. Multivariate regression analysis did not show an association between maternal glucose level during pregnancy and levels of YKL-40 in the offspring. We found increasing offspring BMI at follow-up ($p < 0.0001$) to be positive predictors of YKL-40. Furthermore offspring characterized by overweight (BMI >25kg/m^2) or the metabolic syndrome (IDF criteria 2006) at follow-up had significantly higher levels of YKL-40 compared with the remaining offspring, (47 vs. 44 ng/ml, $p = 0.02$ and 49 vs. 44 ng/ml, $p = 0.003$ respectively). Conclusion: Fetal exposure to intrauterine hyperglycemia was not associated with levels of YKL-40 in adult offspring of women with diabetes. Adult offspring BMI were positively associated with YKL-40 levels.

2560-PO

Measurement of Fasting Plasma Glucose alone in the Postnatal Follow-Up of Gestational Diabetes does not Identify Continued Glycaemic Impairment in Patients who Received Medical Intervention

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Gestational diabetes (GDM) is a known risk factor for Type 2 diabetes. Clinical guidelines in the UK recommend that women with GDM are offered fasting plasma glucose (FPG) 6weeks postnatally to identify type 2 diabetes or impaired glycaemic status. Increasingly, GDM patients are being treated with metformin and/or insulin. The aim of our study was to assess the effectiveness of FPG alone at 6 week post-partum in identifying all patients at risk of diabetes after antenatal medical intervention. Our retrospective study reviewed post-natal glucose tolerance test (GTT) results in a cohort of GDM patients (n=46) who attended an antenatal diabetes clinic in a UK hospital. The groups were classified based on treatment to diet only (D, n=18) and metformin (M, n=28). Four in the M group needed additional insulin therapy. Statistical analysis between the groups was done using unpaired t-testing. The 6 weeks post-natal FPG was 4.7± 0.3 (mean±SD) in the D group and 4.86±0.4 in the M group, (D vs M, p=0.18 respectively) while the 2 hour post glucose (2hr PG) was 4.78±0.9 and 5.76±1.7 (D vs M, p= 0.03 respectively). No impaired fasting glycaemia was noted in either group. All patients in D group had normal 2 hr PG however 5 of the 28 patients in M group (18%) had impaired glucose tolerance with 2 hr PG values of 10.9, 8.4, 7.9 , 8.2, 8.8mmol/l. Two of these 5 patients had required additional insulin therapy. This study suggests that measurement of the FPG alone at the 6 week postnatal screen misses a significant number of patients at risk of developing T2DM especially if they received medical intervention therapy antenatally. This would falsely re-assure these patients and result in inappropriate delays in initiating preventative life style modification strategies. It supports the use GTT for postnatal screening in all patients especially if they required more than dietary intervention for glycaemic control during pregnancy.

2561-PO

WITHDRAWN

2562-PO

Postpartum Diabetes Testing among Women With Recent Gestational Diabetes Mellitus History

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Prevention studies suggest early detection and intervention for glucose intolerance can reduce progression to type 2 diabetes by more than 50% in women with GDM history. However, previous research shows fewer than half of these women get tested for diabetes postpartum. Therefore, the objective of this study was to examine frequency of and factors associated with postpartum diabetes testing. Data are from the 2009 Pregnancy Risk Assessment Monitoring System (PRAMS), an ongoing state- and population based survey collecting self-reported information on maternal behaviors and experiences that occur before, during, and after pregnancy. In 2009, Colorado, Minnesota, and Utah added a question about postpartum diabetes testing. Multiple logistic regression was used to determine factors associated with getting tested for diabetes postpartum. Data analyses were performed using survey procedures in SAS 9.2. Approximately 7.0% [95%CI: 6.0-7.9] of women had a history of GDM (overall n=4669). Among these women, 48.5% [95%CI: 41.5-55.5] self-reported being tested for diabetes postpartum. Adjusted for age, race, education, history of GDM, parity, and participation in The Special Supplemental Nutrition Program for Women, Infants and Children (WIC) during pregnancy, factors associated with increased likelihood of being tested for diabetes postpartum included: non-Hispanic black (adjusted odds ratio (AOR) =2.1 [1.2-3.5]) or non-Hispanic other (AOR=2.0 [1.3-3.0]) compared to non-Hispanic white; high school diploma (AOR=1.7 [1.2-2.3]) compared to having more education, nulliparous (AOR=1.5 [1.1-1.9]) compared to multiparous, and WIC participation during pregnancy (AOR=1.7 [1.3-2.3]). Although women with a history of GDM are more likely to be tested for diabetes postpartum, less than half of respondents reported being tested. Continued efforts to translate postpartum screening recommendations into practice are needed among these women at high risk for developing future type 2 diabetes.

2563-PO

The Prevalence of Metabolic Syndrome and Insulin Resistance Post Gestational Diabetes in the West of Ireland

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Metabolic syndrome (MetS) is associated with increased cardiovascular mortality and increased risk of type 2 diabetes. We examined the prevalence of MetS in a cohort of Caucasian women with previous gestational diabetes (GDM) (n=211), and those with normal glucose tolerance (NGT) during pregnancy (n=265). Fasting glucose alone (known DM/pre-diabetes post-partum patients) or 75g OGTT (other patients), lipid profile, insulin and C-peptide were performed. We calculated insulin resistance using the HOMA2-IR computer model. Results are shown in attached tables. These results show that metabolic syndrome is common, affecting 23% (49/211) of women with a history of GDM. Of these, 61% (30/49) have progressed to pre-diabetes/diabetes up to 5 years post-partum. This shows the importance of lifestyle intervention for GDM patients in the early post partum period to help prevent progression to DM. HOMA2IR measurement may identify at-risk women who may benefit from more intensive lifestyle intervention prior to the appearance of metabolic syndrome.

Metabolic Syndrome Prevalence		
	Pre-DM/DM currently	NGT currently
GDM in index pregnancy (n=211)	30/55 (54.5%)	19/156 (12.2%)
NGT in index pregnancy (n=265)	2/9 (22.2%)	15/256 (5.9%)

Prevalence of HOMA2-IR>1.7		
	Pre-DM/DM currently	NGT currently
GDM in index pregnancy (n=211)	33/55 (60%)	42/156 (26.9%)
NGT in index pregnancy (n=265)	5/9 (55.5%)	48/256 (18.8%)

2564-PO

Glycemic Control and Fetal Growth in Patients With Gestational Diabetes

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Objective: To compare the fetal growth in patients with gestational diabetes according to glycemic control. Method: retrospective study of 89 pregnant women performed between May 2005 to June 2011. We included patients with singleton pregnancies and diagnosed with GDM by the test of oral glucose tolerance of 100 grams or 75 grams. Exclusion criteria were presence of medical conditions that affect fetal growth, fetal malformations or smoking. In weekly antenatal care the patients received diet for diabetes, daily glycemic control and insulin when needed. Insulin was introduced when 30% or more of the measured values in a week were above the following values: fasting > 95mg/dl and 1 hour post-prandial > 140mg/dl. The patients were divided into two groups: when 70% or more of all the measured capillary blood glucose were within the therapeutic target they were allocated in good control group (n = 65), and otherwise in poor control group (n = 24). The patients performed ultrasound (USG) in three periods: 18 to 24 weeks (USG 0), start of treatment of GDM (USG1) and in the end of the treatment (USG 2). Results: There were no differences in maternal age and prepregnancy BMI, maternal weight gain during the prenatal, gestational age (GA) of GDM diagnosis and in the GA of ultrasound exam. The mean glicemic value were 98.7 mg/ dl in group 1 and 111.9 mg/dl in group 2 (p <0.001). The use of insulin was 16.9% in group 1 and 87.5% in group 2. The percentiles of fetal weight were similar between groups at USG 0 and USG 1, but higher in USG 2 in poor control group (p = 0.02). The fetal abdominal circumference percentiles were significantly higher in the group 2 at usg 1 and usg 2. The group 2 had a greater fetal weight gain (27,53 gr/day vs. 33,43gr/day; p=0,001) and had also a greater birth weight (3247g vs. 3499g; p = 0.025). Conclusions: The fetal abdominal circumference percentile seem to change before the percentile fetal weight and would be a better marker of fetuses at risk of large for gestational age.

2565-PO

Maternal 25 Hydroxyvitamin D Level is Inversely Associated With Fasting Plasma Glucose in Thai Gestational Diabetes

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Studies suggest that vitamin D deficiency in pregnancy may increase the risk of developing gestational diabetes(GDM). This study was to identify 25 Hydroxyvitamin D (25 OHD) level in Thai pregnant women with GDM and non-GDM. This study was conducted in 197 pregnant women at the tertiary care medical center in Bangkok, Thailand from October 2010 to July 2011. Serum 25OHD level were evaluated during the 75g OGTT in pregnancy. The 197 pregnant women had a mean age of 32.1±5.9 years and a mean maternal 25OHD level was 34.3±8.3 ng/dl. Only 3.1% of patients had 25OHD deficiency (<20ng/dl), 22.3% had 25OHD level 20to29 ng/dl and 74.6 % had 25OHD level≥30ng/dl. In our study, 70 patients (34.8%) had GDM. The patients with GDM had 25OHD levels significantly lower than non-GDM (32.3±10.3 vs 35.5±6.7ng/dl, p=0.001). In regression analysis adjusted for age, family history of diabetes and trimester, maternal 25 OHD level was inversely associated with fasting PG (β=-0.27, 95% CI; -0.503,-0.029, p=0.029) in GDM. In contrast, there were no associated of glycemic parameters with 25OHD levels in women without GDM. This study suggests that lower levels of maternal 25OHD are associated with higher fasting PG level in gestational diabetes.

2566-PO

WITHDRAWN

2567-PO

Ethnic Difference in Adiponectin Concentration in Pregnant Women With and Without Gestational Hyperglycemia

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There are ethnic disparities in obesity related diseases. Low maternal adiponectin is associated with an increased risk of gestational diabetes mellitus (GDM). It is not known if there are ethnic differences in serum adiponectin during pregnancy. A nested case-control study from a cohort of 2,379 pregnant women (African-American 35%, Hispanic 47%, Caucasian 18%) age 23.1±0.2 (yr), pregravid BMI (kg/m2) 26.3±0.2 includes cases of hyperglycemia (GDM or impaired glucose challenge test non-GDM pooled, N=208) and normoglycemic controls (N=557). Serum adiponectin was measured at entry (week 17) and week 28. The distribution of ethnicity between cases and controls was not different (p=0.66). After adjustment for several confounding variables including entry BMI, African-American cases had a significantly decreased adiponectin (µg/ml, 11.17±0.81, p<0.001 for each) compared to controls (African-Americans, 14.28±0.47, Hispanics, 14.64±0.39, Caucasians, 14.69±0.65) and to Hispanic cases (13.98±0.63, p<0.01), but not to Caucasian cases (13.03±1.1, p=0.16). During the 3rd trimester, adiponectin was significantly lower in African American cases when compared to Hispanic and Caucasian cases and to African American, Hispanic and Caucasian controls (p<0.05 for each comparison). Adiponectin also was significantly lower among African American controls in the 3rd trimester when compared to Hispanic and Caucasian controls (p<0.05 for each). We also compared the changes in adiponectin by ethnic group, pooling cases and controls. During the 3rd trimester, adiponectin decreased significantly more in African Americans (-3.2±0.49) compared to Hispanics (-2.3±0.4) and Caucasians (-1.43±0.6) (p<0.05 for each). Our data showed that there is a detectable ethnic difference in serum adiponectin levels during pregnancy. This ethnic difference is in addition to the effect of hyperglycemia and independent of maternal BMI.

2568-PO

GDM Risk Factors Are Relative to Higher Incidences of Perinatal Complications and Early Postpartum Abnormal Metabolism

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Objective: To investigate the effects of traditional risk factors of gestational mellitus diabetes (GDM) on pregnant outcomes as well as early postpartum abnormal metabolism. Methods: Data of pregnant women with GDM and data of their prenatal and newborn were collected retrospectively. Those women with GDM were recruited at 6 months to 2 years after delivery to take 75 g OGTT, have the physical examinations as well as lipid profile assessments. Pregnant women with any of the followings were considered have GDM risk factors: age ≥ 35 yr, BMI ≥ 25 kg/m^2, family history of diabetes, positive uric glucose, GDM history, and abnormal pregnancy and delivery history. Results: A total of 340 GDM data were collected. 146 of those GDM women were with GDM risk factors. Compare to those without risk factors, women with risk factors has higher pregnant complications (26.5% vs 16.1%, P< 0.05), higher premature birth rate (8.4% vs 2.3%, P< 0.05) and higher birth-weight. Also a higher 2h glucose level during 75g OGTT was observed in those with GDM risk factors (5.89 ± 1.02 mM vs 5.17± 0.64 mM, P< 0.05). Multiple logistic regressive analyze indicated that family history of diabetes and positive uric glucose were relative to the early postpartum abnormal glucose tolerance. No significant differences of body weight, BMI, waist circumferences, fasting glucose levels and lipid profiles were observed between the two group women after delivery.Conclusions: The GDM risk factors are not only the predictor of GDM, but also are relative to higher rates of perinatal complications and early postpartum abnormal glucose regulation. Among these risk factors, family history of diabetes and positive uric glucose are of greater contribution.

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