

Other

25 Diabetes Treatment Satisfaction as an Independent Factor Contributing to Glycemic Control in Patients with Type 2 Diabetes Mellitus

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Objective: To determine whether self-reported outcomes (ie, treatment satisfaction, health-related quality of life) independently contribute to glycemic control in patients with type 2 diabetes mellitus (DM).

Methods: This 24-week study compared glycemic control in 273 patients with type 2 DM receiving basal insulin glargine (GLAR) and pre-meal insulin glulisine (GLU) doses based on either carbohydrate counting (Carb Count, n=137) or weekly adjustments using a simple algorithm based on preprandial glucose patterns (ALG, n=136). Patients were assessed with the Diabetes Treatment Satisfaction Questionnaire, Audit of Diabetes Dependent Quality of Life scale, and the Well-Being Questionnaire.

Results: Mean adjusted baseline glycosylated hemoglobin (A1C) level was 8.16% in both groups, although patients in the ALG group had a higher body mass index (37.73 kg/m²) than patients in the Carb Count group (35.6 kg/m²). Patients in both groups achieved study-end target A1C levels (ALG, 6.70%; Carb Count, 6.54%). Patients in the ALG group used higher daily doses of GLU (110.2 vs 94.3 U; $P = 0.04$) and GLAR (103.4 vs 87.0 U; $P < 0.0001$) and had fewer episodes of symptomatic hypoglycemia (blood glucose <50 mg/dL) (4.9 vs 8.0 events/patient-year, $P = 0.02$). Self-reported treatment satisfaction improved in both groups ($P < 0.0001$). At study midpoint, treatment-dissatisfied patients were significantly more likely than satisfied patients to have higher A1C values ($P = 0.0073$), an effect independent of demographic characteristics, baseline A1C level, and other clinical variables. Patients in the ALG group with a history of healthy diet and carbohydrate counting had the lowest mean A1C level (6.46%, $P = 0.0174$).

Conclusion: Satisfaction with insulin therapy was independently related to glycemic control. Greater treatment satisfaction was associated with improved A1C level in patients receiving basal-prandial insulin therapy. Concern for patient satisfaction may increase insulin treatment efficacy and the likelihood of attaining glycemic control.

26 Effect of Technosphere® Inhaled Insulin on Glycemic Control, Quality of Life, and Treatment Satisfaction

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Objective: To assess the impact of Technosphere® insulin delivered via the MedTone inhaler on glycemic control, quality of life, and treatment satisfaction in adults with type 2 diabetes mellitus.

Methods: The study population, as specified by protocol, included 90 insulin-naive subjects with a starting glycosylated hemoglobin (A1C) level of $>6.5\%$, 48 in the active inhaled insulin group and 42 in the inhaled placebo group. All subjects completed a measure of quality of life (the SF-36 health survey) and a measure of treatment satisfaction before starting insulin treatment and ~12 weeks later. A1C level was assessed at the same times.

Results: Subjects in the active insulin group showed significantly ($P < 0.005$) greater improvement in A1C level than those in the placebo group (pre/post means = 7.74/6.97 active, 7.75/7.43 placebo). For 2 of the 8 SF-36 factors (vitality, social functioning), quality of life improved significantly ($P < 0.05$) more in the active insulin group than in the placebo group; all SF-36 factors improved more in the active insulin group than in the placebo group. For all treatment-satisfaction items assessing use of the MedTone inhaler, the majority of subjects rated their experience positively (median = 92% positive ratings). Subjects' attitudes toward insulin treatment improved significantly after they used inhaled insulin (effect size = 0.38; $P < 0.005$). There was no significant change in patients' level of worry about hypoglycemia.

Conclusion: Treatment with inhaled insulin improved glycemic control, quality of life, and treatment satisfaction.

27 Efficacy of the Bonabi IV Insulin Infusion Protocol in the Community Hospital Setting

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Background: In community hospitals, physician rounds may be less frequent than in larger teaching hospitals, and the insulin infusion titration process may thus depend largely on nurses' calculations and comfort level. Evidence-based treatment of hyperglycemia in the intensive care unit (ICU) calls for standardized protocols that nurses can easily understand and follow, with minimal error in titration.

Objective: To determine the efficacy of a nurse-driven, 4-tiered, insulin infusion protocol in the community hospital setting.

Methods: This was a retrospective study of 131 hyperglycemic patients admitted to the ICU at Providence Health Systems Holy Cross Medical Center, a community hospital in Mission Hills, California. Target blood glucose (BG) level for this protocol was first 110 to 150 mg/dL and was subsequently decreased to 90 to 120 mg/dL.

Results: With this protocol, average time to target BG level was 8.2 hours, average time in target was 12.75 hours, and average percentage of hypoglycemic events (ie, <50 mg/dL) was 2%. Based on the results cited here, the current BG target is 85 to 110 mg/dL.

Conclusion: This protocol, designed for the community hospital setting, provided safe, effective glycemic control in the ICU.

28 Switching Patients to Insulin Detemir from Insulin Glargine as Basal Insulin in a Basal-Bolus Regimen Improves Glycemic Control, without Increasing Weight or Hypoglycemic Risk: Data From a German Cohort of the PREDICTIVE Study

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Background: Insulin detemir, a long-acting insulin analogue, provides less variability in absorption and effect on blood glucose level than insulin glargine.

Objective: To assess the safety and efficacy of insulin detemir in clinical practice in patients with type 1 and type 2 diabetes mellitus (DM).

Methods: This report presents data from a cohort of patients who were switched from insulin glargine to insulin detemir as basal insulin in a basal-bolus regimen in the large, multicenter, prospective, observational Predictable Results and Experience in Diabetes through Intensification and Control to Target: An International Variability Evaluation (PREDICTIVE) study. Analysis included mean baseline and 12-week follow-up data from 1457 patients with type 1 DM (n = 775, 58% female, age 46.0 years, weight 74.8 kg, body mass index [BMI] 25.6 kg/m², duration of DM 18.6 years) and type 2 DM (n = 654, 52% female, age 63.2 years, weight 88.3 kg, BMI 31.0 kg/m², duration of DM 13.3 years). Twenty-eight patients had DM other than type 1 or type 2.

Results: Hypoglycemia rates (events per patient/year) decreased when patients were switched to insulin detemir (type 1 DM: all hypoglycemia, 46.8 vs 13.4; major, 0.9 vs 0.1; nocturnal, 15.6 vs 2.1; and type 2 DM: all hypoglycemia, 11.4 vs 3.1; major, 0.7 vs 0; nocturnal, 4.4 vs 0.4). Glycosylated hemoglobin level decreased from baseline (type 1 DM, 7.9% to 7.5%; type 2 DM, 8.0% to 7.4%). Fasting blood glucose (FBG) and within-subject variability in FBG also decreased. Weight was stable (type 1 DM, 0.2 kg; type 2 DM, 0.5 kg).

Conclusion: Switching patients with type 1 or type 2 DM to insulin detemir from insulin glargine as basal insulin in a basal-bolus regimen improves glycemic control without causing weight gain and lowers the incidence of hypoglycemia.

29 Pharmacokinetic and Pharmacodynamic Characteristics of Therapeutic Doses of the Insulin Analogues Glargine and Detemir at Steady State in Patients with Type 1 Diabetes Mellitus

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Objective: To compare the pharmacokinetic and pharmacodynamic characteristics of the long-acting insulin analogues glargine (GLA) and detemir (DET) in patients with type 1 diabetes mellitus (DM).

Methods: In this randomized, double-blind, crossover study, 24 GLA- and DET-naïve subjects with type 1 DM were studied twice. Plasma glucose (PG) was clamped at 5.5 mmol for 24 hours after SC injection of 0.35 U/kg of GLA or 0.35 U/kg of DET after 2 weeks of treatment with either GLA or DET.

Results: With GLA, PG remained at 5.7 ± 0.2 mmol/l until 24 hours (all 24 subjects completed the study). With DET, PG started to increase after 16 hours; only 33% of subjects completed the study because PG increased >11.1 mmol/l before 24 hours. Onset of insulin action (time at which IV glucose was initiated after SC injection) did not differ between treatments. Glucose infusion rate (GIR) was almost constant over 24 hours with GLA but decreased markedly with DET. Total activity (GIR AUC_{0-end of GIR}) was 1412 ± 662 mg/kg and 915 ± 225 mg/kg, whereas the end of GIR was 23 ± 2.1 hours and 15 ± 3.3 hours for GLA and DET, respectively (P < 0.05). In particular, mean values of GIR AUC_{0-12h} were not different, whereas AUC_{12-end of GIR} were, on average, 80% lower after DET than GLA (142 ± 196 and 605 ± 390, P < 0.05). GIR C_{max} was not different between GLA and DET, whereas GIR T_{max} was reached at a median time of 7 hours with DET and 4 hours with GLA (P < 0.05).

Conclusion: At steady state, GLA and DET have different total activity despite identical nominal units, as well as different pharmacodynamic characteristics that should be considered in the dosing, number, and timing of daily injections in patients with type 1 DM.

30 Standardized Subcutaneous Insulin Orders Affect Hospital Glycemic Control on Adult Medicine and Surgery Units

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Objective: To assess the use of the standardized subcutaneous insulin order (SQIO) to enable safe, effective insulin therapy and targeted blood glucose (BG) control in the hospital.

Methods: The SQIO was implemented in a teaching hospital. Education stressed BG targets, insulin-action profiles, and scheduled basal-bolus SQ insulin. Outcomes were tracked using COMPAS software. All non-intensive care unit fingerstick and laboratory BG values were included in the analysis.

Results: A 24% decrease in first-morning hyperglycemia in patients with known diabetes mellitus (DM) or hospital-related hyperglycemia was observed from fiscal year 2005 (19%, n = 6655) to the second quarter of fiscal year 2006 (14%, n = 1639). Basal (glargine, neutral protamine Hagedorn, 70/30) insulin orders for hyperglycemia increased from 18.5% to 83.6%. Severe hypoglycemia declined concurrently. Accurate documentation of uncontrolled DM improved from 13% to 26% of patients (Table).

Conclusion: The SQIO and an accompanying education initiative successfully changed basal-insulin prescribing patterns, lowered first-morning hyperglycemia, and improved documentation accuracy for uncontrolled DM, supporting the increasingly widespread practice of using SQIO for hospital management of hyperglycemia.

Table.

Performance Indicator	2005	2006 Q2	Improvement, %
Patient days first morning day 2 (5 AM to 9 AM) with BG >180 mg/dL, %	19.0	14.5	24.0
Patient days with BG ≤40 on 2+ days, %	1.3	0.7	46.1
Patient days receiving basal insulin when 2 BG in day >180 mg/dL, %	18.5	83.6	352.1
Patients with documented uncontrolled DM, %	12.7	26.1	105.4

BG = blood glucose.

31 Initiation of Biphasic versus Basal Analogue Insulin in Patients with Type 2 Diabetes: A Health Economic Comparison

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Background: Published data reveal comparative clinical benefits of initiating biphasic insulin aspart 70/30 (BIAsp) versus insulin glargine (glar) in patients with type 2 diabetes mellitus (DM) in whom oral therapy does not achieve glycosylated hemoglobin (A1C) goals.

Objective: To project the intermediate- and long-term cost-utility of BIAsp vs glar as add-on treatment to metformin (met) and glimepiride (gli), respectively, from a US Medicare perspective.

Methods: Treatment-effect data were derived from a 26-week randomized controlled trial (age: 61.2 years; baseline A1C level, 9.1%) that demonstrated significant A1C reduction favoring BIAsp (−0.5% between groups; $P = 0.0036$) without significant differences in body mass index or major hypoglycemia, although minor hypoglycemic episodes increased with BIAsp ($P < 0.05$). A series of interrelated Markov sub-models employing Monte Carlo simulation and combining published data on risk of DM-related complications with associated quality-of-life utilities were used to measure life years gained (LYG), quality-adjusted life years gained (QALY), and cumulative incidences of complications over 12, 20, and 35 years. Treatment costs were calculated (annual pharmacy plus complication; US Medicare perspective), and outcomes were discounted at 3% per annum. Sensitivity analyses were performed.

Results: Incremental gains in QALYs (0.09 ± 0.07 to 0.17 ± 0.16) favoring BIAsp versus glar were calculated with improved A1C level as the primary driver. Reduced incidences of neuropathic, retinal, and renal complications were also observed. Incremental cost effectiveness ratios (ICER) ranged from \$36,715 to \$30,265 per QALY, and an acceptability curve (willingness to pay = \$50,000/QALY) revealed BIAsp to be 58% to 71% cost effective.

Conclusions: Improved efficacy and simulated reductions in DM-related complications in patients with type 2 DM initiating BIAsp + met were estimated to increase quality-adjusted life expectancy and generate ICERs within established standards of cost effectiveness versus glar + gli.

32 Medication Adherence, Hypoglycemia, and Related Economics of Conversion to an Insulin Analogue Pen

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Objective: To evaluate whether switching from a vial/syringe to an insulin analogue pen affects adherence, hypoglycemic events, and health care costs in patients with type 2 diabetes mellitus (DM).

Methods: This before-and-after, intrasubject evaluation used an integrated medical and pharmacy claims database from >50 managed care health plans. Adults with an ICD-9 diagnosis of type 2 DM converting to pen therapy (FlexPen[®]) from human or analogue insulin vials from July 2001 to December 2002 with no prior use of FlexPen were retrospectively analyzed. End points included adherence (medication possession ratio [MPR]), follow-up time adjusted odds ratio (OR) of hypoglycemic events, association between adherence and hypoglycemic events in a Poisson multivariate context, and diabetes-attributable (DA) and hypoglycemia-attributable (HA) costs.

Results: A total of 1156 identified subjects (mean age 45.4 ± 13.7 ; 51.5% previously using human insulin vials) significantly improved MPR after switching (69% vs 62%; $P < 0.01$). Additionally, less hypoglycemia was observed [OR: 0.50 (CI: 0.37-0.68); $P < 0.05$] and such events requiring emergency department and physician visits decreased 56% (OR: 0.44 [CI: 0.21-0.29] and 61% (0.39 [CI: 0.24-0.46]), respectively ($P < 0.05$). Subjects with MPR >70% reduced hypoglycemic incidence by nearly two thirds (0.35 [0.11-0.81]; $P < 0.05$), confirmed by multivariate regression. Total annual HA costs decreased 56% (\$1415 vs \$627; $P < 0.01$), and DA costs decreased 7% (\$8827 vs \$8227; $P < 0.01$).

Conclusion: Patients with type 2 DM who switch to pen therapy from a vial/syringe may improve medication adherence, reduce hypoglycemia, and decrease treatment costs.

33 Basal Insulin Analogue Initiation in Patients with Type 2 Diabetes Mellitus: A Health Economic Assessment

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Objective: To evaluate the potential clinical and economic outcomes in routine clinical practice of adding insulin detemir (IDet) to treatment of patients with type 2 diabetes mellitus (DM) taking oral antidiabetic drugs (OADs) alone.

Methods: Baseline and treatment-effect data were derived from a 12-week observational trial in which 1321 insulin-naive patients with type 2 DM (mean age: 62.2; glycosylated hemoglobin [A1C] level, 8.49%; body mass index, 29.5 kg/m²) initiating IDet (mean daily dose, 19.1 U) demonstrated a 1.29% reduction in A1C value and a mean weight loss of 0.9 kg. Fasting blood glucose was more tightly controlled without significant increase in hypoglycemia (no major episodes). Most patients received metformin (73.5%) ± sulfonylurea (SU) (61.3%), and most continued OADs at initiation of IDet (86.9%). Interdependent Markov submodels (15 complication states) based on published risk progressions and associated quality-of-life utilities incorporated Monte Carlo simulation to measure differences in total treatment costs (annual pharmacy plus complication), life years gained (LYG), quality-adjusted life expectancy (QALE), and complication incidences in patients starting IDet versus those modeled to continue OAD-only therapy. Outcomes were discounted at 3% annually (US Medicare perspective) over 10 years. Sensitivity analyses were performed.

Results: IDet initiation corresponded with extended LYG (0.156) and QALE (0.173 years). Reduced relative risks of major complications were estimated (eg, 38.5% less peripheral vascular disease, 38.9% less macular edema, 36.1% less microalbuminuria). Total annual patient pharmacy costs increased \$361 with IDet, although this increase was offset by reduced complication costs.

Conclusion: Insulin-naive patients with type 2 DM may benefit over short-term periods when IDet is initiated. Over longer periods, IDet was projected to increase quality-adjusted outcomes and reduce diabetic complications in a cost-effective manner.

34 Impact of Nursing Diabetic Educational Programs on Patient Management

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Background: Recent evidence has shown that instituting nurse-driven protocols for glycemic control can improve overall outcomes for hospitalized patients with diabetes mellitus (DM). To implement these protocols, however, nurses require knowledge of the DM disease process to understand the rationale and treatment goals for oral and insulin therapy. Many institutions have not adopted nurse-driven protocols because of the challenges in developing appropriate educational programs on DM for nurses.

Objective: To determine whether extensive DM education for hospital nursing staff before initiation of nurse-driven glycemic protocols helps ensure successful and safe implementation.

Methods: Nurse managers, nurse practitioners, nurse educators, and a clinical nurse specialist collaborated to develop educational programs on the following topics: overview of DM, the correct use of oral antidiabetic drugs and insulin, transitioning patients from IV insulin, managing patients with newly diagnosed DM, and discharge planning. All staff nurses and nursing assistants were required to attend the educational sessions. Additional staff training was provided by pharmaceutical and glucometer device representatives.

Results: The education provided to the nursing staff allowed successful initiation and appropriate patient management using a nurse-driven glycemic protocol for cardiothoracic surgical patients.

Conclusion: Education for hospital nursing staff before initiation of nurse-driven glycemic protocols helps ensure appropriate patient management.

35 A Regular Human Insulin Formulation with a More Rapid Onset of Action than Rapid-Acting Insulin Analogues

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Background: Insulin in most commercial formulations exists as 6-molecule aggregates (hexamers) stabilized by 2 zinc atoms. Once injected into SC tissue, the hexamers must first dissociate into complexes of 2 molecules (dimers) and then into single molecules (monomers) before significant absorption of insulin into the bloodstream can occur. Viaject™, a new formulation of recombinant human insulin, contains ingredients that are generally regarded as safe that support the dissociation of insulin hexamers and increase its rate of absorption.

Objective: To determine the efficacy of Viaject, a new formulation of recombinant human insulin.

Methods: Phase I and II clinical trials using the euglycemic clamp technique in healthy volunteers and patients with type 1 diabetes mellitus have demonstrated that Viaject insulin is absorbed and exerts its action significantly faster than insulin lispro and regular human insulin.

Results: Pharmacodynamic data in 10 healthy volunteers are as shown in the Table. Clinical trials show that Viaject insulin has a faster onset of action, which suggests that less insulin is required to adequately cover a meal. During the trials Viaject demonstrated an excellent safety profile.

Conclusion: Patients treated with Viaject may have fewer hypoglycemic episodes and fewer emergency department visits, making Viaject insulin a safe, efficacious, and cost-effective choice for a mealtime insulin.

Table.

Early 1/2 Glucose Infusion Rate T _{max}	Mean ± SD (min)
12 U RHI	66 ± 15
12 U L	51 ± 13 *(RHI)
Viaject	
12 U	33 ± 17 *(L,RHI)
6 U	35 ± 18 *(L,RHI)
3 U	31 ± 14 *(L,RHI)

L = insulin lispro; RHI = regular human insulin.

*(comparator) Duncan's multiple range test, P < 0.05.

36 Assessment of Insulin's Microvascular Action in Human Skeletal Muscle: The Application of Contrast-Enhanced Ultrasound

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Background: Skeletal muscle is the primary site of insulin-mediated glucose disposal in humans. In addition to the well-described effects of insulin at the level of the myocyte, data suggest that insulin acts on the vasculature to facilitate its own delivery to skeletal muscle interstitium. Approximately 25% of skeletal muscle microvasculature is perfused at rest. Expanding the microvascular surface area within muscle, a process termed *recruitment*, significantly increases the opportunity for insulin and glucose exchange across the endothelium. However, assessment of human microvasculature has been difficult due to lack of noninvasive techniques. Contrast-enhanced ultrasound (CEU) allows quantification of the rate (microvascular flow velocity) and area (microvascular blood volume) of microbubble replenishment from contrast intensity produced by intravenously infused microbubbles as they traverse the capillary bed.

Objective: To observe skeletal muscle microvascular recruitment with physiologic doses of insulin in both animals and humans.

Methods: CEU was used to quantify microvascular perfusion.

Results: Capillary recruitment occurs earlier and at lower insulin concentrations than changes in total blood flow, is impaired by nitric oxide synthase inhibition and free fatty acid infusion in rodents, and is blunted by obesity in humans. However, the timing and extent of insulin delivery to skeletal muscle in response to microvascular recruitment have yet to be defined (Figure).

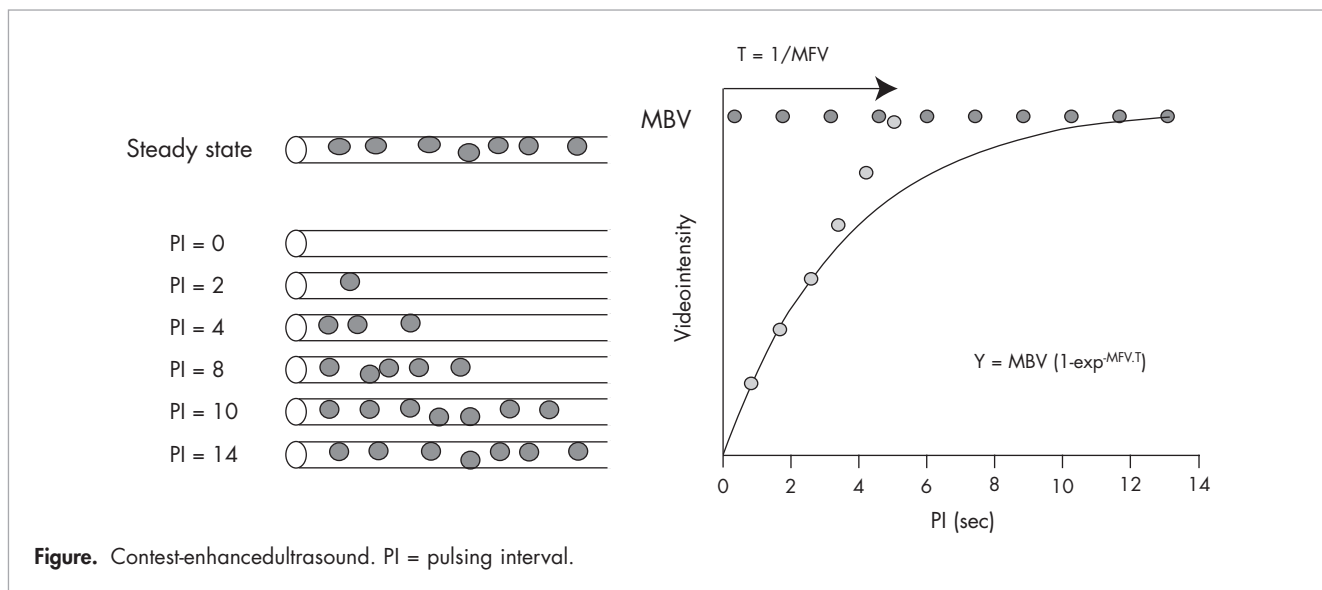


Figure. Contrast-enhanced ultrasound. PI = pulsing interval.

Conclusion: Preliminary data from an ongoing study in healthy control subjects suggest that the flux of insulin into skeletal muscle can be accurately measured during euglycemic hyperinsulinemic (1 mU/min/kg) clamp and that changes in microvascular perfusion can be assessed using CEU for ≤ 40 minutes.

37 Effect of Polyunsaturated and Monounsaturated Fatty Acids on Insulin Resistance in Polycystic Ovarian Syndrome

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Background: Polycystic ovary syndrome (PCOS) is characterized by ovarian dysfunction, androgen excess, and, frequently, insulin resistance. Although treatment of insulin resistance with either insulin sensitizers or weight loss/exercise improves ovarian function and increases fertility, insulin sensitizers can have hepatic and renal side effects, and their long-term use can be a concern. The long-term success of weight loss and exercise regimens has been somewhat disappointing.

Objective: To determine whether modulating fatty acid composition of the diet can improve insulin resistance without restricting energy intake.

Methods: This research focuses specifically on the changes of insulin resistance and secretion. We hypothesized that polyunsaturated fatty acid (PUFA)-rich walnuts and fish oils would improve insulin sensitivity and alleviate hyperinsulinemia in patients with PCOS but that monounsaturated fatty acid-rich almonds would have no effect. This ongoing study is evaluating 96 women with PCOS aged 14 to 45. Patients continue their regular diet during a 4-week lead-in period and record their meals in a 7-day food diary that is analyzed by a registered dietician. Patients are then randomized to 1 of 4 groups for 6 weeks: almonds, walnuts, walnut oil, or fish oil. The nuts and oils replace the fat in patients' regular diet. This is accomplished by exchanging 31 g of the fat in the regular diet with either 48 g of almonds or walnuts or 31 g of walnut oil. The fish-oil supplementation group receives 6 capsules of fish oil per day. Anthropometric data will be collected at weeks 1, 4, and 10. Waist circumference will be used to assess central obesity, and body composition will be assessed by bioelectrical impedance. A

5-hour oral glucose tolerance test (OGTT) is conducted during weeks 3 and 9. A frequently sampled IV glucose tolerance test will also be done during weeks 4 and 10 (1 week apart from the 5-hour OGTT). Data will be analyzed by the MINMOD Millennium computer software of Dr. Richard Bergman to calculate the acute insulin response to glucose, the glucose disappearance constant (kg), the insulin sensitivity index, and glucose effectiveness at zero insulin.

Conclusion: The long-term effects of PCOS put young women at risk for diabetes mellitus, hypertension, obesity, and infertility. Further study is needed to ascertain whether PUFA can be beneficial, by reducing insulin resistance and hyperinsulinemia, or harmful, by increasing blood glucose levels.

38 Insulin-like Growth Factor Binding Protein 3 Inhibits Adipocyte Differentiation

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Background: Adipocytes are emerging as an important endocrine source of adipokines (eg, leptin, adiponectin, resistin, tumor necrosis factor- α and interleukin-6) and as a target tissue for various cytokines that modulate adipocyte differentiation and function, as well as insulin sensitivity. A key adipocyte pathway involves peroxisome proliferator-activated receptor- γ and retinoid X receptor (RXR). Interfering with their activity has been shown to decrease adipocyte maturation and adipocytokine production. Insulin-like growth factor (IGF) binding protein 3 (IGFBP-3) is an important binding protein for insulin-like-growth factor-1 and has also been shown to be internalized into the nucleus and bind to RXR. The IGF-axis plays an important role in glucose metabolism and insulin action, and we have recently shown that IGFBP-3 leads to the induction of insulin resistance in vitro in 3T3L1 adipocytes and in vivo in rats.

Objective: To explore whether IGFBP-3 exerts its effects on adipocytes by its nuclear actions.

Methods: We treated maturing 3T3-L1 adipocytes with IGFBP-3. We then assayed cells for lipid production with Oil Red staining as a marker for differentiation. We then reemulsified the stain and examined the degree of optical absorbance at 490 nm.

Results: IGFBP-3-treated adipocytes showed a marked decrease in lipid droplets and Oil Red staining on examination by optic absorbance.

Conclusion: IGFBP-3 inhibits adipocyte differentiation.

39 Failure of Multiple Therapies in the Treatment of Insulin Allergy in a Patient with Type 1 Diabetes Mellitus: A Case Report

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Background: Allergic hypersensitivity to insulin, although uncommon, is a well-documented adverse effect. Various cutaneous and systemic reactions have been reported, but the underlying mechanisms are unclear. Multiple treatment options have been proposed.

Objective: To present a case of an insulin allergy that has not responded to multiple therapies.

Methods: An 18-year-old woman with type 1 diabetes mellitus (DM) was referred with a 3-year history of cutaneous reactions to insulin. Environmental allergies had been treated with allergy shots from age 10 to 17. DM was diagnosed when the patient was 11 years of age and was well controlled with multiple daily injections and, later, an insulin pump.

Results: At age 16 the patient developed sporadic maculopapular lesions at the insertion site of her pump catheter. Antihistamines and local steroids were not helpful. The lesions worsened, and glycemic control has been poor ever since. Skin testing showed immediate reactions to multiple insulin preparations (+3, insulin aspart and regular human insulin; +2, insulins glulisine and lispro; +1, insulins glargine and neutral protamine Hagedorn). She had no delayed hypersensitivity reactions, and her initial insulin immunoglobulin E (IgE) levels were undetectable. She did not respond to 2 attempts at formal desensitization with insulin. After several therapeutic trials, the combination of insulins glargine and glulisine appeared to cause the least prominent reactions. Oral methotrexate was not effective, and the addition of dexamethasone to insulin preparations (4 to 8 μ U) provided only transient improvement.

Conclusion: On repeat testing, the patient's insulin IgE antibody levels are elevated. She is now considering a third desensitization procedure due to worsening lesions on her current regimen.

40 Could a Long-Acting Insulin Analogue Overdose Cure Certain Forms of Diabetes Mellitus?

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Background: Recent advances in the study of the gene defects of neonatal diabetes mellitus (NDM) have shed light on alternatives to insulin (ie, sulfonylureas) in the treatment of patients with specific variants of NDM. There are no reports in the literature of megadoses of insulin "curing" any form of DM.

Objective: To describe a case of NDM that was complicated by an insulin glargine overdose of >100 times the prescribed amount.

Methods: This case report evaluates the literature to date.

Results: This 3-month-old boy presented to our neonatal intensive care unit with perinatal asphyxia. He was a 37-week gestation, 2.5-kg infant born by emergent cesarean section for questionable fetal heart tracings and poor variability. The pregnancy was complicated by lack of prenatal care, smoking and alcohol use, and amphetamines in maternal urine and infant meconium screens. The boy had no heart rate or spontaneous respirations at delivery, with Apgar scores of 0, 1, 3, 7, and 8 at 1, 5, 10, 15, and 20 minutes, respectively. He exhibited signs of perinatal asphyxia, with transient kidney and liver insults, a grade 3 intraventricular hemorrhage with possible seizure activity, and initial hypoglycemia requiring increased dextrose delivery. At 3 days old he became hyperglycemic (blood glucose [BG] level of >200 mg/dL) and

required insulin infusion. As he was weaned off intravenous fluids and increased his PO intake to goal, he continued to have hyperglycemia requiring insulin. He was initially transitioned to an insulin lispro correction factor based on his premeal BG level, but on this regimen he experienced marked hypoglycemia after nearly every feeding. His insulin regimen was changed to glargine 2 U/24 hr. This caused his BG level to drop to ~20 mg/dL 3 to 5 hours after administration, yet still he had a BG level of >300 mg/dL 18 hours after administration. The insulin regimen was changed to glargine 1 U/12 hr. BG levels dropped to ~30 mg/dL 3 to 5 hours after administration, yet the boy still had a BG level of >250 mg/dL 10 hours after administration. After several days of adjustments, the patient's BG level became fairly stable with a regimen of insulin glargine 0.25 U/8 hr, and he was prepared for discharge to home. A dose of insulin glargine 25 U (in place of his scheduled 0.25 U) was inadvertently given the day before scheduled discharge. The boy was noted to be lethargic, and his BG level was 3 mg/dL. IV dextrose infusion was required for 5 days, in addition to regular formula feeding. BG levels after cessation of dextrose and insulin have been within normal limits since discharge >2 months ago.

Conclusion: Although our infant may have had a transient form of NDM that would have resolved without the insulin glargine overdose, it seems reasonable to test the following hypothesis in animal models: "Could a long-acting insulin analogue overdose cure certain forms of DM?"
