

Oral Presentations

1 Insulin Detemir and Insulin Glargine: Similar Time-Action Profiles in Subjects with Type 2 Diabetes Mellitus

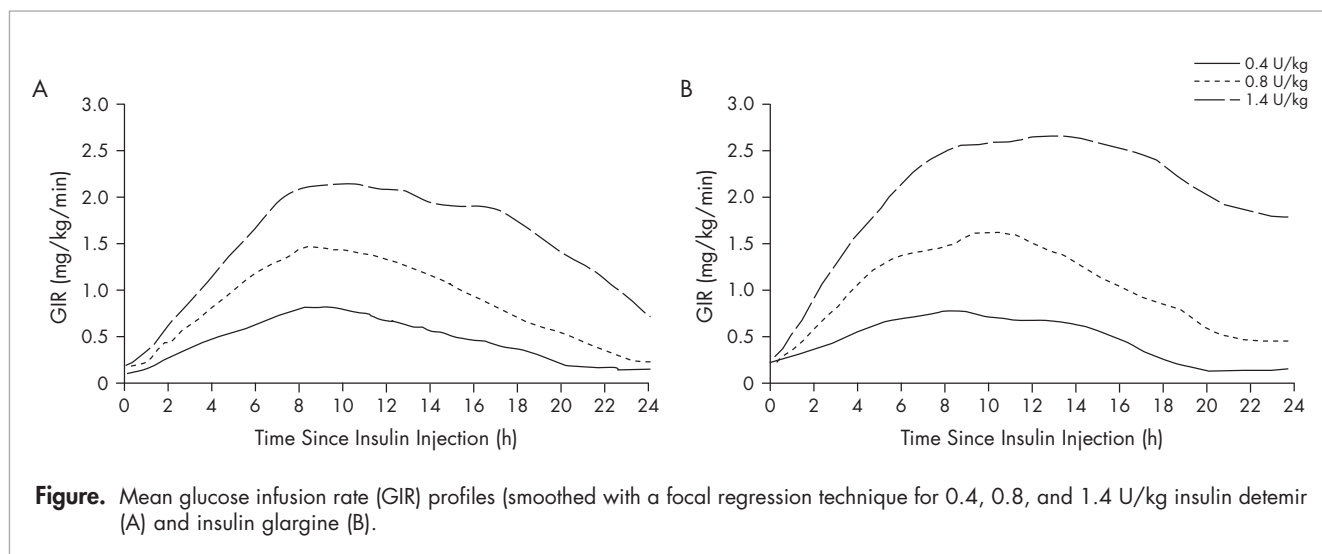
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Objective: To compare the pharmacodynamic and pharmacokinetic properties of insulin detemir (IDet) and insulin glargine (IGlar) in subjects with type 2 diabetes mellitus (DM).

Methods: In this randomized, double-blind, parallel trial, 27 insulin-treated male subjects with type 2 DM (body mass index, 30.8 ± 2.6 kg/m² [mean \pm SD]; glycosylated hemoglobin level, $7.6 \pm 1.1\%$) received 0.4, 0.8, and 1.4 U/kg of IDet or IGlar under glucose-clamp conditions: target blood glucose (BG) level 90 mg/dL; IV insulin infusion (rate, 0.3 mU/kg/min 3 ± 0.5 hours before dosing); clamp duration 24 hours or until BG level was >200 mg/dL.

Results: Mean glucose infusion rate (GIR) profiles for IDet and IGlar were similar in shape/flatness (**Figure**) and showed increasing effect with increasing dose. The dose-response relationship (log-effect versus log-dose) was similar for both insulin preparations in intercept and slope (*P* values: slope = 0.23, intercept = 0.84). Within-subject variability was lower for IDet than for IGlar (*P* values: within-subject < 0.0001 ; between-subject = 0.38). Duration of action (time from dosing to GIR of <0.5 mg/kg/min) increased with rising doses for both IDet and IGlar without major difference between the 2 preparations for the clinically relevant doses of 0.4 and 0.8 U/kg (IDet, 719 ± 512 , 1007 ± 408 ; IGlar, 613 ± 443 , 1162 ± 413 minutes) and was >24 hours in most subjects with the highest dose (1328 ± 154 vs 1440 ± 0 minutes).

Conclusion: This comparison confirmed lower within-subject variability for IDet and showed no substantial differences in GIR profile shape, duration of action, and dose-response relationship between the 2 analogues in patients with type 2 DM.



2 Pramlintide Therapy in Intensively Treated Patients with Type 1 Diabetes Mellitus Improved Markers of Cardiovascular Disease Compared with Placebo

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Background: Elevated plasma concentrations of high-sensitivity C-reactive protein (hsCRP) and decreased concentrations of adiponectin (ADPN) have been related to risk of cardiovascular disease in patients with diabetes mellitus (DM).

Objective: To assess the effects of pramlintide, an analogue of the β -cell hormone amylin that flattens glucose excursions and reduces markers of oxidative stress during the postprandial period, on hsCRP and ADPN concentrations.

Methods: This was a post hoc analysis of a randomized, double-blind, placebo-controlled study that included 187 subjects with type 1 DM treated with intensive insulin therapy (mean \pm SD for pramlintide vs placebo: age, 42 ± 14 years vs 42 ± 12 years; duration of DM, 20 ± 12 years vs 21 ± 12 years; weight, 81.0 ± 17.8 kg vs 80.6 ± 16.8 kg). Eighty-four patients received 30 or 60 μ g of pramlintide with major meals, and 103 patients received placebo, with both groups targeting similar glycemic goals. Plasma samples were assayed for hsCRP and ADPN at baseline and week 25. Baseline metabolic measures (pramlintide vs placebo: glycosylated hemoglobin [A1C] level, $8.0 \pm 0.8\%$ vs $8.1 \pm 0.9\%$; hsCRP, 2.0 ± 1.9 mg/L vs 1.7 ± 1.7 mg/L; ADPN, 12.9 ± 7.6 μ g/mL vs 14.4 ± 9.5 μ g/mL) were similar.

Results: At 25 weeks, pramlintide improved postprandial glucose (152 ± 4 mg/dL vs 174 ± 4 mg/dL, $P < 0.001$, mean \pm SE) and reduced body weight (-0.93 ± 0.4 kg vs $+1.38 \pm 0.3$ kg, $P < 0.001$) compared with placebo; reductions in A1C level were similar in the 2 groups ($-0.4 \pm 0.1\%$ vs $-0.6 \pm 0.1\%$). Subjects given placebo had a significant increase in hsCRP compared with pramlintide-treated subjects ($+0.66 \pm 0.2$ mg/L vs

-0.06 ± 0.2 mg/L, $P < 0.01$), while ADPN increased significantly in pramlintide-treated patients compared with those receiving placebo ($+0.69 \pm 0.5$ μ g/mL vs $+0.43 \pm 0.3$ μ g/mL, $P < 0.05$) at week 25.

Conclusion: Adjunctive pramlintide therapy in intensively treated patients with type 1 DM increased ADPN and attenuated increases in hsCRP compared with insulin alone, despite similar levels of overall glycemic control.

3 Reduction of Length of Stay and Postoperative Infections with an Insulin Protocol at a Community Heart Hospital

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Objective: To assess how an insulin protocol affected clinical benefits and hospital expenditures in patients admitted to a community heart hospital.

Methods: In this insulin protocol, patients with blood glucose (BG) levels >125 mg/dL received insulin infusions and were then switched to insulins glargine and lispro (basal-bolus regimen). Hospital electronic-database analysis identified 2470 patients (median age, 65 years; 40% female; 80% white; 12% black) with 3047 admissions from February 2003 to March 2004.

Results: Patients receiving insulin upon admission ($n=1007$) had an average length of stay (LOS) of 5.9 days compared with 2.6 days for those receiving no insulin ($n=2040$), an Acute Physiology And Chronic Health Evaluation (APACHE) score of 14 versus 11, and a BG level of 193 vs 142 mg/dL during the first 24 hours after admission. We evaluated outcomes in the 614 patients in whom insulin was started from day 1 compared with patients who did not receive insulin. Insulin therapy was associated with a 0.5-day reduction ($P < 0.0001$) in LOS, independent of BG variability; the LOS benefit increased with APACHE score (interaction, $P = 0.001$) and reached 1 day ($P < 0.0001$) at an APACHE score of 23 points. Postoperative infections were 2-fold higher ($P < 0.0001$) in the no-insulin group. Adverse discharges increased more rapidly with APACHE score for the no-insulin group in patients with acute myocardial infarction and coronary artery bypass (interactions, $P = 0.005$ and 0.029 , respectively). There was no adjusted difference in hospital charges between patients receiving and not receiving insulin.

Conclusion: In addition to stabilizing BG level, insulin therapy may decrease LOS and reduce postoperative infections and adverse discharges without additional hospital costs.

4 A Computerized Patient Record System–Based Decision-Support System for Subcutaneous Insulin Administration in the Inpatient Setting

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Background: Hyperglycemia is an important predictor of morbidity and mortality in hospitalized patients. Aggressive treatment of hyperglycemia is known to improve clinically important outcomes. Effective protocols for continuous insulin infusion in intensive care units have been described, but there are no specific protocols for management of inpatient blood glucose (BG) levels with SC insulin.

Objective: To determine if implementation of a computerized patient record system (CPRS)–based decision-support system improves inpatient BG management.

Methods: A CPRS-based decision-support system for SC insulin administration was developed and introduced at the Indianapolis Veterans Administration Medical Center (VAMC) in 2004. The system uses a series of windows with recommendations for insulin strategies and dosage calculations in common clinical situations. It also provides links to evidence-based quick orders for insulin administration. Resident physician teaching sessions covering basic aspects of inpatient diabetes management and explaining the CPRS-based decision-support system were also provided. Two months of inpatient BG data at the Indianapolis VAMC were examined both before (2003) and after (2005) implementation of the decision-support tool. Both bedside and laboratory BG determinations were included. Data were analyzed by hospital day to ascertain the impact of using the tool over time.

Results: Average BG levels at the Indianapolis VAMC before introduction of the CPRS-based decision-support system increased slightly from 166 mg/dL on day 1 to 171 mg/dL on day 10. In contrast, BG levels after implementation of the system declined steadily from 175 mg/dL on day 1 to 148 mg/dL on day 10. There was no evidence for an increase in the incidence of low BG levels. Feedback from providers and nursing staff was positive. Barriers to using the CPRS-based decision-support system for writing the insulin orders and reasons for failure to administer insulin were identified.

Conclusion: Implementation of the first version of our CPRS-based decision-support system improved inpatient BG management at our institution. The system will be updated based on experience and feedback.