

ABSTRACT

Poster Presentation 952

Technosphere® Insulin Suppresses Endogenous Glucose Production Earlier Than a Rapid-Acting Analog (Lispro) and an Inhaled Insulin (Exubera)

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Background and aims: Available insulins are unable to replicate normal hepatic glucose suppression, presumably due to slow absorption. Technosphere® Insulin (TI) is an ultra rapid-acting insulin generating peak insulin levels within 12 to 14 minutes of dosing. We conducted a study to determine whether the unique pharmacokinetic profile of TI resulted in a more rapid suppression of endogenous glucose production (EGP).

Materials and methods: We compared 45 U TI administered by inhalation with 12 IU sc insulin lispro and 4 mg inhaled Exubera (EXB) in an open-label, single-dose, three-way crossover study incorporating a meal challenge (nutritional energy drink [12 fl oz] enriched with U13-C-glucose) in 18 insulin-treated subjects with type 2 diabetes and normal pulmonary function. A continuous glucose infusion enriched with 6,6-²H₂ glucose was used to assess EGP. Prior to the meal, subjects' blood glucose was adjusted to 90 mg/dL using an individual continuous low-dose iv insulin infusion, which was fixed 90 minutes before dosing. If necessary, glucose was infused to maintain blood glucose at ≥ 90 mg/dL.

Results: EGP suppression occurred markedly earlier with TI, followed by insulin lispro and EXB (40, 75, and 130 minutes postdose of the median EGP-time profiles, respectively). Significant differences between insulin lispro and EXB were observed up to 40 minutes compared with TI ($p < 0.002$) and up to 2 hours for the EXB-TI comparison ($p < 0.05$). Median total areas over the EGP curve were comparable across groups (1,938, 1,842, and 2,294 $\mu\text{mol}/\text{min}$). Median postprandial blood glucose AUCs were 53,343, 50,608, and 54,598 $\text{mg}/\text{dL}\cdot\text{min}$ for TI, insulin lispro, and EXB, respectively.

Conclusion: EGP was suppressed earlier following TI administration compared with sc insulin lispro and inhaled EXB, which suggests that treatment with TI may result in a more physiologic EGP suppression.

