

Inhaled Technosphere® Insulin in Comparison to Subcutaneous Regular Human Insulin: Time Action Profile and Variability in Subjects with Type 2 Diabetes

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Abstract

Background:

This study assessed time action profile and within- and between-subject variability of inhaled Technosphere® Insulin (TI) compared with subcutaneous regular human insulin (sc RHI).

Methods:

Thirteen subjects with type 2 diabetes (age 56 ± 7 years, body mass index 30.4 ± 3.0 kg·m⁻²; hemoglobin A1c $6.9 \pm 0.9\%$; mean \pm SD) participated in this six-period crossover isoglycemic glucose clamp study. In randomized order, each subject received three single doses of TI and sc RHI on separate study days.

Results:

Inhalation of TI resulted in a higher maximum serum insulin concentration (858 vs 438 pmol·liter⁻¹; $p = 0.0001$) and shorter intervals to maximum insulin concentration (17 vs 135 minutes; $p = 0.0001$) than sc RHI. Overall, 48 units of TI and 24 units of sc RHI provided comparable 3-hour insulin exposure (INS area under the curve_{0-3 h} 55.8 vs 60.0 nmol·min·liter⁻¹, respectively). Time to maximum metabolic effect was shorter (79 vs 293 minutes; $p < 0.0001$), and percentage of glucose disposal during the first 3 hours was higher for TI compared with sc RHI (59 vs 27%). Within-subject variabilities of insulin exposure following inhalation of TI for 2 and 3 hours and end of study period were 19, 18, and 16% as compared with 27, 25, and 15% after sc RHI injection ($p =$ not significant).

Conclusion:

Technosphere Insulin has a more rapid onset of action than sc RHI. About 60% of the glucose-lowering effect of TI occurs during the first 3 hours after application. In contrast, <30% of the glucose-lowering effect of sc RHI occurs in this period. Technosphere Insulin demonstrated a lower intrasubject variability during the 3-hour postprandial period, without reaching statistical significance.

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Abbreviations: (AUC) area under the curve, (BMI) body mass index, (C_{max}) maximum plasma concentration, (CV) coefficient of variation, (FDKP) fumaryl diketopiperazine, (GIR) glucose infusion rate, (HbA1c) hemoglobin A1c, (INS) insulin, (sc RHI) subcutaneous regular human insulin, (TI) Technosphere Insulin, (TIU) Technosphere Insulin unit

Keywords: absorption, diabetes, inhaled insulin, postprandial glucose, Technosphere Insulin, variability

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