

Pharmacokinetics and Postprandial Glycemic Excursions following Insulin Lispro Delivered by Intradermal Microneedle or Subcutaneous Infusion

Elaine McVey, M.Stat.,¹ Laurence Hirsch, M.D.,² Diane E. Sutter, C.R.A.,¹ Christoph Kapitza, M.D.,³ Sibylle Dellweg, M.D.,³ Janina Clair, M.D.,³ Kerstin Rebrin, M.D., Ph.D.,⁴ Kevin Judge, M.D.,¹ and Ronald J. Pettis, Ph.D.¹

Abstract

Background:

Intradermal (ID) delivery has been shown to accelerate insulin pharmacokinetics (PK). We compared the PK and pharmacodynamic (PD) effects of insulin lispro administered before two daily standardized solid mixed meals (breakfast and lunch), using microneedle-based ID or traditional subcutaneous (SC) delivery.

Method:

The study included 22 subjects with type 1 diabetes in an eight-arm full crossover block design. One arm established each subject's optimal meal dose. In six additional arms, the optimal, higher, and lower doses (+30%, -30%) were each given ID and SC delivery, in random order. The final arm assessed earlier timing for the ID optimal dose (-12 versus -2 min). The PK/PD data were collected for 6 h following meals. Intravenous basal regular insulin was given throughout, and premeal blood glucose (BG) adjusted to 115 mg/dl.

Results:

The primary end point, postprandial time in range (70–180 mg/dl), showed no route-based differences with a high level of overall BG control for both SC and ID delivery. Secondary insulin PK end points showed more rapid ID availability versus SC across doses and meals (ΔT_{max} -16 min, $\Delta T_{50rising}$ -7 min, $\Delta T_{50falling}$ -30 min, all $p < .05$). Both intrasubject and intersubject variability for ID T_{max} were significantly lower. Intradermal delivery showed modest, statistically significant secondary PD differences across doses and meals, generally within 90–120 min postprandially ($\Delta 12$ mg/dl BG at 90 min, $\Delta 7$ mg/dl BGmax, $\Delta 7$ mg/dl mean BG 0–2 h, all $p < .05$).

Conclusions:

This study indicates that ID insulin delivery is superior to SC delivery in speed of systemic availability and PK consistency and may improve postprandial glucose control.

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Author Affiliations: ¹BD Technologies, Research Triangle Park, North Carolina; ²BD Medical - Diabetes Care, Franklin Lakes, New Jersey; ³Profil Institut für Stoffwechselforschung GmbH, Neuss, Germany; and ⁴BD Medical - Diabetes Care, Billerica, Massachusetts

Abbreviations: (%CV) percentage coefficient of variation, (ANOVA) analysis of variance, (AP) artificial pancreas, (AUC) area under the curve, (BG) blood glucose, (CGM) continuous glucose monitoring, (CHO) carbohydrate, (CSII) continuous subcutaneous insulin infusion, (GV) glycemic variability, (HbA1c) glycated hemoglobin, (ID) intradermal, (IL) insulin lispro, (JDRF) Juvenile Diabetes Research Foundation, (PD) pharmacodynamics, (PK) pharmacokinetics, (PPG) postprandial glycemic excursion, (RHI) regular human insulin, (SC) subcutaneous, (SEM) standard error of the mean, (T1DM) type 1 diabetes mellitus, (VAS) visual analog scale

Keywords: clinical research, clinical trial, insulin pharmacokinetics and pharmacodynamics, intradermal, microneedle, ultra-rapid insulin

Corresponding Author: Ronald J. Pettis, Ph.D., BD Technologies, 21 Davis Dr., Research Triangle Park, NC 27709; email address Ron_J_Pettis@bd.com