Journal of Diabetes Science and Technology
Volume 7, Issue 1, January 2013

ORIGINAL ARTICLE

In Silico Evaluation of an Artificial Pancreas Combining Exogenous Ultrafast-Acting Technosphere Insulin with Zone Model Predictive Control

Justin J. Lee, B.S., Eyal Dassau, Ph.D., Howard Zisser, M.D., Rebecca A. Harvey, B.S., Lois Jovanovič, M.D., and Francis J. Doyle III, Ph.D.

Abstract

Background:

Because of the slow pharmacokinetics of subcutaneous (SC) insulin, avoiding postprandial hyperglycemia has been a major challenge for an artificial pancreas (AP) using SC insulin without a meal announcement.

Methods:

A semiautomated AP with Technosphere® Insulin (TI; MannKind Corporation, Valencia, CA) was designed to combine pulmonary and SC insulin. Manual inhalation of 10 U ultrafast-absorbing TI at mealtime delivers the first, or cephalic, phase of insulin, and an SC insulin pump controlled by zone model predictive controller delivers second-phase and basal insulin. This AP design was evaluated on 100 in silico subjects from the University of Virginia/Padova metabolic simulator using a protocol of two 50 g carbohydrate (CHO) meals and two 15 g CHO snacks.

Results:

Simulation analysis shows that the semiautomated AP with TI provides 32% and 16% more time in the controller target zone (80–140 mg/dl) during the 4 h postprandial period, with 39 and 20 mg/dl lower postprandial blood glucose peak on average than the pure feedback AP and the AP with manual feed-forward SC bolus, respectively. No severe hypoglycemia (<50 mg/dl) was observed in any cases.

continued →

Author Affiliations: Department of Chemical Engineering, University of California, Santa Barbara, Santa Barbara, California; and Sansum Diabetes Research Institute, Santa Barbara, California

Abbreviations: (AP) artificial pancreas, (ARX) autoregressive with exogenous input, (BG) blood glucose concentration, (CGM) continuous glucose monitor, (CHO) carbohydrate, (CSII) continuous subcutaneous insulin infusion, (FDA) Food and Drug Administration, (GIR) glucose infusion rate, (HBGI) high blood glucose index, (HMS) health monitoring system, (IV) intravenous, (LBGI) low blood glucose index, (MPC) model predictive control, (PID) proportional-integral-derivative, (SC) subcutaneous, (SD) standard deviation, (T1DM) type 1 diabetes mellitus, (TI) Technosphere Insulin

Keywords: artificial pancreas, inhaled insulin, model predictive control, zone model predictive control

Corresponding Author: Francis J. Doyle III, Ph.D., Department of Chemical Engineering, University of California, Santa Barbara, Sansum Diabetes Research Institute, Chemical Engineering Dept., Mail Code 5080, University of California, Santa Barbara, CA 93106-5080; email address doyle@engineering.ucsb.edu

Abstract cont.

Conclusions:

The semiautomated AP with TI provides maximum time in the clinically accepted region when compared with pure feedback AP and AP with manual feed-forward SC bolus. Furthermore, the semiautomated AP with TI provides a flexible operation (optional TI inhalation) with minimal user interaction, where the controller design can be tailored to specific user needs and abilities to interact with the device.

J Diabetes Sci Technol 2013;7(1):215–226