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

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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.

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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.