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ORIGINAL ARTICLE

The Identifiable Virtual Patient Model: Comparison of Simulation and Clinical Closed-Loop Study Results

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Abstract

Background:

Optimizing a closed-loop insulin delivery algorithm for individuals with type 1 diabetes can be potentially facilitated by a mathematical model of the patient. However, model simulation studies that evaluate changes to the control algorithm need to produce conclusions similar to those that would be obtained from a clinical study evaluating the same modification. We evaluated the ability of a low-order identifiable virtual patient (IVP) model to achieve this goal.

Methods:

Ten adult subjects (42.5 ± 11.5 years of age; 18.0 ± 13.5 years diabetes; 6.9 ± 0.8% hemoglobin A1c) previously characterized with the IVP model were studied following the procedures independently reported in a pediatric study assessing proportional–integral–derivative control with and without a 50% meal insulin bolus. Peak postprandial glucose levels with and without the meal bolus and use of supplemental carbohydrate to treat hypoglycemia were compared using two-way analysis of variance and chi-square tests, respectively.

Results:

The meal bolus decreased the peak postprandial glucose levels in both the adult-simulation and pediatric-clinical study (231 ± 38 standard deviation to 205 ± 33 mg/dl and 226 ± 51 to 194 ± 47 mg/dl, respectively; $p = .0472$). No differences were observed between the peak postprandial levels obtained in the two studies (clinical and simulation study not different, $p = .57$; interaction $p = .83$) or in the use of supplemental carbohydrate (3 occurrences in 17 patient days of closed-loop control in the clinical-pediatric study; 7 occurrences over 20 patient days in the adult-simulation study, $p = .29$).

Conclusions:

Closed-loop simulations using an IVP model can predict clinical study outcomes in patients studied independently from those used to develop the model.

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Abbreviations: (ANOVA) analysis of variance, (CI) confidence interval, (CIR) carbohydrate-to-insulin ratio, (DIR) daily insulin requirement, (EGP) endogenous glucose production, (FCL) full closed loop, (FIR) finite impulse response, (GEZI) glucose effectiveness at zero insulin, (HbA1c) hemoglobin A1c, (HCL) hybrid closed loop, (ISF) interstitial fluid, (IVP) identifiable virtual patient, (MARD) mean absolute relative difference, (NIH) National Institutes of Health, (PID) proportional–integral–derivative, (PD) pharmacodynamic, (PK) pharmacokinetic, (SC) subcutaneous, (SD) standard deviation, (SG) sensor glucose, (UVA) University of Virginia

Keywords: algorithm, artificial pancreas, automated, closed loop, diabetes, insulin delivery, mathematical model

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