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SYMPOSIUM

Glucose Clamp Algorithms and Insulin Time-Action Profiles

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Abstract

Motivation:

Most current insulin pumps include an insulin-on-board (IOB) feature to help subjects avoid problems associated with "insulin stacking." In addition, many control algorithms proposed for a closed-loop artificial pancreas make use of IOB to reduce the probability of hypoglycemic events that often occur due to the integral action of the controller. The IOB curves are generated from the pharmacodynamic (time-activity profiles) actions of subcutaneous insulin, which are obtained from glycemic clamp studies.

Methods:

Glycemic clamp algorithms are reviewed and *in silico* studies are performed to analyze the effect of glucose meter bias and noise on glycemic control and the manipulated glucose infusion rates. The glucose infusion rates are used to obtain insulin time-activity profiles, which are then used to generate IOB curves.

Results:

A model-based, three-step-ahead controller is shown to be equivalent to a proportional-integral control algorithm with time-delay compensation. A systematic glucose meter bias of +6 mg/dl results in a decrease in the glucose area under the curve of 3% but no change in the IOB profiles.

Conclusions:

Based on these preliminary simulation studies, a substantial amount of glucose meter bias and noise during a glycemic clamp can be tolerated with little net effect on the IOB curves. It is suggested that handheld glucose meters can therefore be used in clamp studies if the measurements are filtered (averaged) before processing by the control algorithm. Clinical studies are needed to confirm these preliminary results.

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Abbreviations: (AUC) area under the curve, (IOB) insulin on board, (PI) proportional integral, (PKPD) pharmacokinetic–pharmacodynamic

Keywords: glycemic clamp, *in silico* model, insulin on board, insulin pharmacodynamics

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