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ORIGINAL ARTICLES

Combining Basal–Bolus Insulin Infusion for Tight Postprandial Glucose Control: An *in Silico* Evaluation in Adults, Children, and Adolescents

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Abstract

Background:

Achieving good postprandial glycemic control, without triggering hypoglycemia events, is a challenge of treatment strategies for type 1 diabetes subjects. Continuous subcutaneous insulin infusion, the gold standard of therapy, is based on heuristic adjustments of both basal and prandial insulin. Some tools, such as bolus calculators, are available to aid patients in selecting a meal-related insulin dose. However, they are still based on empiric parameters such as the insulin-to-carbohydrate ratio and on the physicians' and patients' ability to fit bolus mode to meal composition.

Method:

In this article, a nonheuristic method for assessment of prandial insulin administration is presented and evaluated. An algorithm based on set inversion via interval analysis is used to coordinate basal and bolus insulin infusions to deal with postprandial glucose excursions. The evaluation is carried out through an *in silico* study using the 30 virtual patients available in the educational version of the Food and Drug Administration-accepted University of Virginia simulator. Results obtained using the standard bolus strategy and different coordinated basal–bolus solutions provided by the algorithm are compared.

Results:

Coordinated basal–bolus solutions improve postprandial glucose performance in most cases, mainly in terms of reducing hypoglycemia risk, but also increasing the percentage of time in normoglycemia. Moreover, glycemic variability is reduced considerably by using these innovative solutions.

Conclusions:

The algorithm presented here is a robust nonheuristic alternative to deal with postprandial glycemic control. It is shown as a powerful tool that could be integrated in future smart insulin pumps.

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Abbreviations: (3D) three dimensional, (AUC) area under the curve, (CGM) subcutaneous continuous glucose monitoring, (CSII) continuous subcutaneous insulin infusion, (FDA) Food and Drug Administration, (I:C) insulin-to-carbohydrate ratio, (MPC) model predictive control, (OED) optimal experiment design, (PID) proportional-integral-derivative, (SIVIA) set inversion via interval analysis, (T1DM) type 1 diabetes mellitus, (UVa) University of Virginia

Keywords: blood glucose control, insulin pump therapy, interval analysis, set inversion, type 1 diabetes mellitus

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