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SYMPOSIUM

Blood Glucose Controller for Neonatal Intensive Care: Virtual Trials Development and First Clinical Trials

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Abstract

Background:

Premature neonates often experience hyperglycemia, which has been linked to worsened outcomes. Insulin therapy can assist in controlling blood glucose (BG) levels. However, a reliable, robust control protocol is required to avoid hypoglycemia and to ensure that clinically important nutrition goals are met.

Methods:

This study presents an adaptive, model-based predictive controller designed to incorporate the unique metabolic state of the neonate. Controller performance was tested and refined in virtual trials on a 25-patient retrospective cohort. The effects of measurement frequency and BG sensor error were evaluated. A stochastic model of insulin sensitivity was used in control to provide a guaranteed maximum 4% risk of BG < 72 mg/dl to protect against hypoglycemia as well as account for patient variability over 1–3 h intervals when determining the intervention. The resulting controller is demonstrated in two 24 h clinical neonatal pilot trials at Christchurch Women's Hospital.

Results:

Time in the 72–126 mg/dl BG band was increased by 103–161% compared to retrospective clinical control for virtual trials of the controller, with fewer hypoglycemic measurements. Controllers were robust to BG sensor errors. The model-based controller maintained glycemia to a tight target control range and accounted for interpatient variability in patient glycemic response despite using more insulin than the retrospective case, illustrating a further measure of controller robustness. Pilot clinical trials demonstrated initial safety and efficacy of the control method.

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Abbreviations: (BG) blood glucose, (CDF) cumulative distribution function, (IQR) interquartile range, (LBG-P) low blood glucose to performance, (NICU) neonatal intensive care unit

Keywords: blood glucose, hyperglycemia, insulin, neonatal intensive care unit, premature birth

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Abstract cont.

Conclusions:

A controller was developed that made optimum use of the very limited available BG measurements in the neonatal intensive care unit and provided robustness against BG sensor error and longer BG measurement intervals. It used more insulin than typical sliding scale approaches or retrospective hospital control. The potential advantages of a model-based approach demonstrated in simulation were applied to initial clinical trials.

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