Neonatal Glycaemic Control: Model Validation and *In-Silico* Virtual Patient Trials


**INTRODUCTION**

Premature, low-birth-weight infants in the neonatal intensive care unit (NICU) can lose blood glucose homeostasis due to immaturity of endogenous regulatory systems and the stress of their condition.

Typical treatment relies on glucose restriction before insulin administration due to fear of hypoglycaemia. However, glucose restriction may adversely affect the infant’s nutrition status.

A model of the fundamental glucose regulatory dynamics can provide insight about the metabolic state of the patient. *In-silico* virtual trials can be used to design optimal insulin therapy regimes for this vulnerable patient group.

**MODELS AND METHODS**

An adult critical care metabolic system model is adapted to the unique physiological case of the neonate. Time dependent volumes of distribution, insulin clearance and central nervous system uptake are significantly different in the neonate compared to adult.

Integral-based methods identify time-varying insulin sensitivity. Optimal non-insulin mediated glucose uptake and endogenous glucose production parameters selected through grid-search.

Retrospective clinical for N=25 cases contained 1091 glucose measurements over 3567 total patient hours plus all insulin and nutritional infusion data.

**RESULTS: VIRTUAL TRIALS**

Virtual trials modulated insulin infusions utilising model-based predictions on 25 patient profiles.

Two-hourly measurement regime simulation achieved 76.1% of measurements within target 4-7 mmol/L band, compared to 30.9% for retrospective records. Median BG reduced 25% from 8.0 to 6.0 mmol/L.

More frequent BG measurement and intervention achieved greater glycaemic control performance.

Optimal measurement frequency balances control performance with clinical requirements.