

## Intermediary Variables and Algorithm Parameters for an Electronic Algorithm for Intravenous Insulin Infusion

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### Abstract

#### Background:

Algorithms for intravenous insulin infusion may assign the infusion rate (IR) by a two-step process. First, the previous insulin infusion rate ( $IR_{\text{previous}}$ ) and the rate of change of blood glucose (BG) from the previous iteration of the algorithm are used to estimate the maintenance rate (MR) of insulin infusion. Second, the insulin IR for the next iteration ( $IR_{\text{next}}$ ) is assigned to be commensurate with the MR and the distance of the current blood glucose ( $BG_{\text{current}}$ ) from target. With use of a specific set of algorithm parameter values, a family of iso-MR curves is created, each giving IR as a function of MR and BG.

#### Method:

To test the feasibility of estimating MR from the  $IR_{\text{previous}}$  and the previous rate of change of BG, historical hyperglycemic data points were used to compute the “maintenance rate cross step next estimate” ( $MR_{\text{csne}}$ ). Historical cases had been treated with intravenous insulin infusion using a tabular protocol that estimated MR according to column-change rules. The mean IR on historical stable intervals ( $MR_{\text{true}}$ ), an estimate of the biologic value of MR, was compared to  $MR_{\text{csne}}$  during the hyperglycemic iteration immediately preceding the stable interval. Hypothetically calculated  $MR_{\text{csne}}$ -dependent  $IR_{\text{next}}$  was compared to  $IR_{\text{next}}$  assigned historically. An expanded theory of an algorithm is developed mathematically. Practical recommendations for computerization are proposed.

#### Results:

The  $MR_{\text{true}}$  determined on each of 30 stable intervals and the  $MR_{\text{csne}}$  during the immediately preceding hyperglycemic iteration differed, having medians with interquartile ranges 2.7 (1.2–3.7) and 3.2 (1.5–4.6) units/h, respectively. However, these estimates of MR were strongly correlated ( $R^2 = 0.88$ ). During hyperglycemia at 941 time points the  $IR_{\text{next}}$  assigned historically and the hypothetically calculated  $MR_{\text{csne}}$ -dependent  $IR_{\text{next}}$  differed,

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**Abbreviations:** (BG) blood glucose, (C6R) rate of exposure to carbohydrate, (CR) correction rate, (CVVHD) continuous venovenous hemodialysis, (DKA) diabetic ketoacidosis, (FEBG) fractional elevation of BG, (FCABG) fractional completeness of ascent of BG, (FRROA) fractional reduction of ROA, (G-per-DIEM) glucose per daily dose of insulin exogenously mediated, (HR) hypoglycemic action of insulin delivery rate, (ICU) intensive care unit, (IR) infusion rate, (ISF) insulin sensitivity factor, (IV) intravenous, (MR) maintenance rate, ( $MR_{\text{csne}}$ ) MR cross step next estimate, (ROA) rate of ascent, (ROD) rate of descent, (SICU) surgical intensive care unit, (TDDI) total daily dose of insulin, (TPN) total parenteral nutrition

**Keywords:** algorithm, critical care, decision support, diabetic ketoacidosis, hypoglycemia, insulin, intravenous insulin

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**Abstract cont.**

having medians with interquartile ranges 4.0 (3.0–6.0) and 4.6 (3.0–6.8) units/h, respectively, but these paired values again were correlated ( $R^2 = 0.87$ ). This article describes a programmable algorithm for intravenous insulin infusion. The fundamental equation of the algorithm gives the relationship among IR; the biologic parameter MR; and two variables expressing an instantaneous rate of change of BG, one of which must be zero at any given point in time and the other positive, negative, or zero, namely the rate of change of BG from below target (rate of ascent) and the rate of change of BG from above target (rate of descent). In addition to user-definable parameters, three special algorithm parameters discoverable in nature are described: the maximum rate of the spontaneous ascent of blood glucose during nonhypoglycemia, the glucose per daily dose of insulin exogenously mediated, and the MR at given patient time points. User-assignable parameters will facilitate adaptation to different patient populations.

**Conclusions:**

An algorithm is described that estimates MR prior to the attainment of euglycemia and computes MR-dependent values for  $IR_{next}$ . Design features address glycemic variability, promote safety with respect to hypoglycemia, and define a method for specifying glycemic targets that are allowed to differ according to patient condition.

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