Model of the Glucose-Insulin-Glucagon Dynamics after Subcutaneous Administration of a Glucagon Rescue Bolus in Healthy Humans

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In healthy individuals, insulin and glucagon work in a complex fashion to maintain blood glucose levels within a narrow range. This regulation is distorted in patients with diabetes. The hepatic glucagon response to an intravenous glucose load depends on the current insulin concentration and thus endogenous glucose production (EGP) can be non-modelled without knowledge of the pancreatic concentrations of both hormones in plasma [2]. The new model of the glucose-insulin-glucagon dynamics in man including secretion effect of EGP.

Ten healthy subjects received a 4 mg subcutaneous (SQ) glucagon bolus (Glucagon, Plasma Diagnostic, Henningsen, Denmark). Glucagon, insulin, and glucagon concentrations. All observations were used to fill a physiological model of the glucagon-insulin-glucagon dynamics using the flyvbjerg model with a novel multiplicative description of the effects of insulin and of glucagon on EGP.

Bayesian estimation by Maximum a Posteriori using prior knowledge reported in literature was used to estimate the model parameters for each subject. Profile likelihood plots were used to investigate parameter identifiability. Underidentifiable parameters were fixed at their prior mean values.

The new model enables simulations of the glucose-insulin-glucagon dynamics in humans at both low and high glucagon concentrations (100-8000 pg/mL) and physiologically realistic concentrations of plasma insulin and glucagon. The model can be used for simulation of glucagon bolus strategies for treatment of hypoglycemia and for in silico simulation of dual-hormone artificial pancreas algorithms.

1 Background

2 Data

Ten healthy males weighing 76.4±7.4 kg (mean±SD) received 1.0 mg subcutaneous (SQ) Glucagon bolus (Glucagon, BBI, 2016). Fasting plasma samples were collected until 300 minutes post dose and analyzed for glucagon, insulin, and glucose. The model can be used for simulation of glucagon bolus strategies for treatment of hypoglycemia and for in silico simulation of dual-hormone artificial pancreas algorithms.