



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

Wendt, Sabrina Lyngbye; Møller, Jan Kloppenborg; Haidar, Ahmad ; Bysted, Britta Væver; Knudsen, Carsten Boye; Madsen, Henrik; Jørgensen, John Bagterp

Publication date:
2016

Document Version
Publisher's PDF, also known as Version of record

[Link back to DTU Orbit](#)

Citation (APA):

Wendt, S. L., Møller, J. K., Haidar, A., Bysted, B. V., Knudsen, C. B., Madsen, H., & Jørgensen, J. B. (2016). *Model of the Glucose-Insulin-Glucagon Dynamics after Subcutaneous Administration of a Glucagon Rescue Bolus in Healthy Humans*. Abstract from The American Diabetes Association's 76th Scientific Sessions (ADA 2016), New Orleans, Louisiana, United States.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Abstract for ADA 2016, New Orleans.

Authors: Sabrina Lyngbye Wendt, Jan Kloppenborg Møller, Ahmad Haidar, Britta Væver Bysted, Carsten Boye Knudsen, Henrik Madsen, John Bagterp Jørgensen

Keywords (1-2): 'Pharmacodynamics modeling'

Max character count (no spaces): 1800

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

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 glucose response due to an elevated glucagon level depends on the current insulin concentration and thus endogenous glucose production (EGP) can not be modelled without knowledge of the concentration of both hormones in plasma. Furthermore, literature suggests an upper limit to EGP irrespective of glucagon levels. We build a simulation model of the glucose-insulin-glucagon dynamics in man including saturation effect of EGP.

Ten healthy subjects received a 1 mg subcutaneous (SC) glucagon bolus (GlucaGen®). Plasma samples were collected until 300 minutes post dose and analyzed for glucagon, insulin, and glucose concentrations. All observations were used to fit a physiological model of the glucose-insulin-glucagon dynamics using the Hovorka 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. Unidentifiable 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 (180-8000 pg/mL) and physiologic insulin concentrations (1.2-81.9 mIU/L). 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.

Character count: 1573