Intraperitoneal and subcutaneous glucagon delivery in pigs: Effects on circulating glucagon and glucose levels

Marte K. Åm[1,2,5], Ilze Dirnena-Fusini[1,2], Sven M. Carlsen[1,2,5], Anders L. Fougner[1,3], Sverre C. Christiansen[1,2,5]

[1]Artificial Pancreas Trondheim – The APT research group (www.apt-norway.com)
[2]Department of Clinical and Molecular Medicine
[3]Department of Engineering Cybernetics

Norwegian University of Science and Technology (NTNU), Trondheim, Norway

[5]Department of Endocrinology, St. Olav's University Hospital, Trondheim, Norway

Background

Aim:

Investigate effect of intraperitoneal (IP) glucagon boluses with respect to glucagon absorption, the effect on blood glucose levels (BGL) and compare this to subcutaneous (SC) glucagon administration.

Motivation:

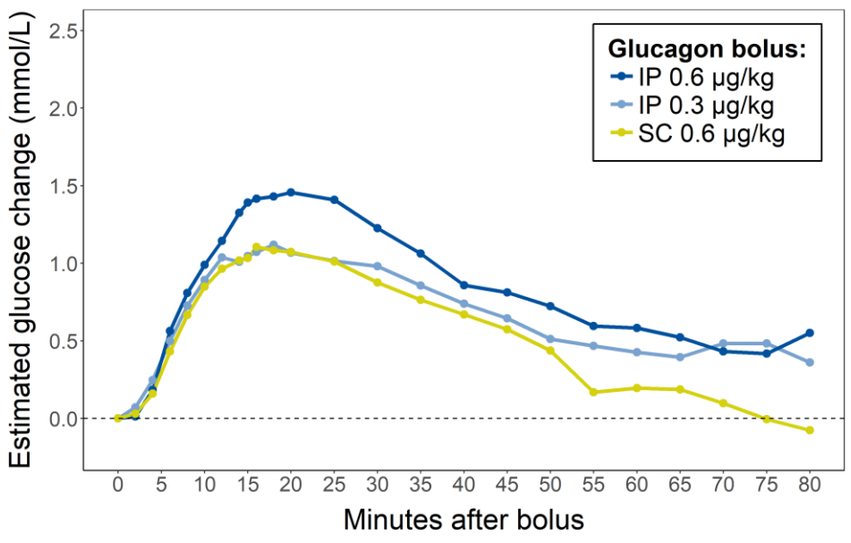
Limited available information about glucose response after IP glucagon administration. This is needed to build suitable mathematical models of IP glucagon absorption and glucose response.

Methods

- Intraperitoneal and subcutaneous glucagon boluses (GlucaGen, NovoNordisk, Denmark) administered to 10 pigs (36.0–42.6 kg).
- Three different boluses (IP 0.6 µg/kg, SC 0.6 µg/kg and IP 0.3 µg/kg).
- Endogenous insulin and glucagon production suppressed by a combination of octreotide and pasireotide.
- Blood samples collected from -10 minutes to 80 minutes after glucagon administration.
- Glucagon measured with ELISA kit (Mercodia, Sweden).

Results

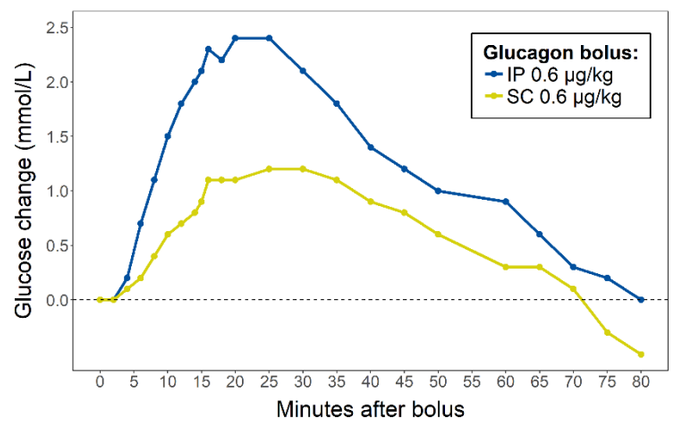
Mean glucose change from 10 pigs:



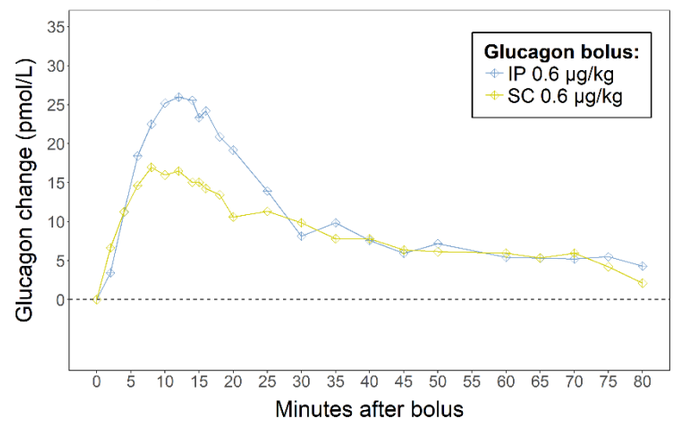
Graph shows glucose changes estimated from a mixed linear model with bolus and bolus order as fixed effects and pig ID as random effect.

Examples from pig no. 9:

Glucose measurements:



Glucagon measurements:



Discussion

- Glucose increased in seven out of 10 pigs after IP delivery of glucagon, and in nine pigs after SC delivered glucagon.
- We believe that the preceding 12 h fast did contribute to the lack of glucose response in some of pigs.
- Preliminary glucagon analysis from one pig shows comparable absorption of glucagon, but a faster glucose response after the IP bolus. Further analysis is needed to verify if this is observed for the other pigs in the study.

Conclusions

- IP administration of glucagon elevates BGL, but statistical analysis has to be performed to elucidate if IP glucagon raises glucose in a dose dependent manner, and whether the glucose peak is significantly higher after IP glucagon as compared to SC delivered glucagon.
- These results provide data for modelling of IP glucagon absorption and its effect on glucose level, necessary for the development of an IP artificial pancreas.

Acknowledgements

The animal experiments were conducted at the Comparative medicine Core Facility (CoMed), Norwegian University of Science and Technology (NTNU). CoMed is funded by the Faculty of Medicine at NTNU and Central Norway Regional Health Authority. The experiments were approved by Norwegian Food Safety Authority (FOTS no.12948).
Declaration of interest: There is no conflict of interest that could be perceived as bias in data interpretation and analysis.
Funding: This research is funded by The Norwegian Research Council (Project no.: 248872/O70), Central Norway Regional Health Authority and Johan Selmer Kvanes Endowment for Research and Combating of Diabetes.

ARTIFICIAL PANCREAS TRONDHEIM

CENTRE FOR DIGITAL LIFE NORWAY

NTNU – Trondheim Norwegian University of Science and Technology

HELSE MIDT-NORGE

marte.k.am@ntnu.no