Semi-Mechanistic Model to Characterize Effects of Gastric Emptying on Glucose Absorption in Obese and Non-Obese Adults

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Objectives: To develop a semi-mechanistic model that can be used to characterize and compare effects of gastric emptying on glucose absorption jointly in obese and non-obese healthy adults.

Methods: Glucose, insulin and gastric emptying data from 36 obese and 24 non-obese healthy adults were available. Oral glucose tolerance tests (OGTTs) were performed in each study subject with 10g, 25g or 75g of glucose. Blood samples and gastric emptying rates were collected at different time-points until 180 min. A semi-mechanistic model was developed to characterize gastric emptying effects on glucose absorption. A population analysis was performed using NONMEM7.3.

Results: Glucose kinetics after OGTTs was characterized by a one-compartment model. The complex absorption profile of glucose was adequately described using individual gastric emptying profiles as time-varying covariate on glucose absorption rate. Observed insulin profiles affected both glucose production and clearance. Differences between obese and non-obese subjects were identified: (i) faster glucose absorption rate in obese subjects (Ka_{Obese} = 10 \times Ka_{Non-obese}), (ii) different gastric emptying effect on glucose absorption and (iii) different insulin effect on glucose clearance, linear effect in non-obese and saturable effect in obese subjects. According to goodness-of-fit plots, glucose absorption and kinetics was properly fitted in both obese and non-obese healthy adults. Visual predictive check demonstrated good predictive performance of the developed model; Fig.1.

Conclusion: This is the first semi-mechanistic model that characterizes interactions between gastric emptying, glucose absorption and glycemic control in both non-obese and obese adults. Such model can be applied to investigate effects of bariatric surgery on glucose kinetics, identify differences in glucose absorption between adults and pediatrics and quantify drug effects on gastric emptying and glucose absorption.

Fig.1- Visual Predictive Check