Protocol GA-18

Title: The role of endogenous GIP in glucose metabolism during fasting

Introduction

The incretin hormone, glucose-dependent insulinotropic polypeptide (GIP), is secreted is secreted from enteroendocrine K cells in the small intestine following food. GIP have a powerful effect on glucose-induced insulin secretion from pancreatic beta cells, the incretin effect. GIP accounts for about 45 % of insulin secretion after food intake. Exogenous GIP during fasting stimulates glucagon secretion in low blood glucose and has an anabolic effect in/on fat and bone metabolism in healthy individuals. However, we do not fully understand the physiological role of GIP and with this study, we will investigate how endogenous GIP affects the body during fasting.

Purpose

The purpose of this project is to investigate the effects of endogenous GIP in healthy, obese individuals. With the infusion of the GIP receptor antagonist (GIP(3-30)NH_2) is it possible to describe the effects of endogenous GIP, by comparing with what happens during a saline infusion (placebo)

Hypothesis

We hypothesize that endogenous GIP has physiological effects in fasting and that we will see a decrease in glucagon levels during GIP(3-30)NH_2 infusion compared to placebo.

Study design

In a randomized, placebo-controlled, double-blind, crossover design comprising two experimental days, 12 participants will receive 180-minute infusions of GIP(3-30)NH2 (800 pmol/kg/min) and placebo (saline) in a randomized order respectively, after observed 10 hours fast. An *ad libitum* meal be serves at time 180 min, during continuous infusion. To keep the infusate content hidden for the investigator and the participants, the preparation of the infusate during the experimental days will be handled by an employee otherwise not involved in the study. During the trial, the participant assesses and records current appetite and thirst on standardized VAS forms. Blood pressure and heart rate are measured at time: -30 min, 0 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min. Blood samples (0,2 ml) are taken at time: -30 min, -20 min, 0 min, 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min. Brown adipose tissue activity is measured with thermal camera, and resting metabolic rate is determined with indirect calorimetry.

Calculations and statistics

Data will be processed and presented using standard descriptive statistics. Baseline-substracted and absolute values for AUC will be calculated using numerical integration. The GIP(3-30)NH_2 effect is calculated for a given endpoint as a percentage of the placebo infusion: Effect = 100 – (GIP(3-30)NH_2 / placebo)