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Original article

Satiety and gastrointestinal hormones during a Mixed Meal Tolerance Test after gastric bypass surgery: association with plasma amino acid concentrations^{1,2}

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Abstract

Background: Circulating amino acids have been associated with both appetite and the secretion of anorexigenic hormones in healthy and obese populations. This effect has not been investigated in subjects having undergone Roux-en-Y gastric bypass surgery (RYGB).

Objective: To investigate the association between postprandial plasma concentrations of amino acids and the anorexigenic hormones glucagon-like peptide-1 (GLP-1) and peptide tyrosine tyrosine (PYY), the orexigenic hormone ghrelin, and satiety and hunger in post-RYGB subjects.

Setting: A Dutch surgical department.

Methods: Participants after primary RYGB were studied during a Mixed Meal Tolerance Test (MMTT). Satiety and hunger were assessed every 30 minutes on visual analogue scales. Blood samples were collected at baseline, every 10 minutes during the first half hour and every 30 minutes until 210 minutes after the start. The samples were assessed for 24 amino acids and 3 gastrointestinal hormones. Incremental areas under the curve (iAUCs) were calculated. Exploratory analyses were performed in which subjects were divided into high and low responders depending on the median iAUC.

Results: 42 subjects, aged 48 ± 11 (mean \pm SD) years, 31 to 76 months post-RYGB and with total weight loss of $30 \pm 9\%$ completed the MMTT. Subjects with high satiety scores had more than a 25% higher net iAUC of PYY and GLP-1 and at least a 10% higher net iAUC of 10 amino acids compared to subjects with low scores ($P < 0.05$). The net iAUC of five of these

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amino acids (i.e. arginine, asparagine, histidine, serine and threonine) was more than 10% higher in subjects with high responses on GLP-1 and/or PYY ($P < 0.05$).

Conclusions: Certain postprandial amino acids were associated with satiety and anorexigenic hormones and could therefore play a role in appetite regulation after RYGB; either by a direct effect on satiety, indirectly through gastrointestinal hormones, or both. (Surg Obes Relat Dis 2018;000:1–12.) © 2018 American Society for Bariatric Surgery. Published by Elsevier Inc. All rights reserved.

Keywords: Amino acids; Appetite; Roux-en-Y gastric bypass; Gastrointestinal hormones; Glucagon-like peptide-1; Hunger; Peptide tyrosine tyrosine; Protein; Satiety

Introduction

Bariatric surgery is currently the most effective treatment to achieve and maintain long term weight reduction in a morbidly obese population. It has gained high popularity, with more than half a million procedures performed worldwide in 2014 [1–3]. Unfortunately, the desired weight loss can be accompanied by loss of fat free mass and bone mineral density [4,5]. Furthermore, nutritional deficiencies can develop [6–9] and there is a risk of weight regain over time [3,10].

The Roux-en-Y gastric bypass (RYGB) was the most frequently performed bariatric procedure worldwide in 2013 [11] and the second most in 2014 [1]. This procedure involves anatomic alterations which cause orally ingested food to bypass major parts of the stomach and duodenum. As a result, food is delivered more rapidly to the jejunum. After RYGB, accelerated and increased elevations of postprandial plasma concentrations of the anorexigenic gastrointestinal hormones active glucagon-like peptide-1 (GLP-1) and peptide tyrosine tyrosine (PYY) [12–15], as well as of amino acids [16], have been reported.

Anorexigenic hormones may contribute to better treatment success of gastric bypass surgery [13,17,18]. In non-bariatric populations, increased plasma concentrations of GLP-1 and PYY contribute to the feeling of satiety [19,20], while several amino acids are associated with the secretion of these hormones [21–25]. Furthermore, in 1956, Mellinkhof et al. introduced the aminostatic hypothesis by suggesting an association between circulating serum amino acids and fluctuations in appetite [26]. In subsequent studies this theory was explained by two pathways; an indirect pathway in which protein and amino acids may induce a neural effect and a direct humoral pathway [27]. This effect could be potentiated in patients after RYGB through rapid and increased absorption of amino acids.

The aim of this study was to investigate the association between the postprandial plasma concentration of total and a broad range of individual amino acids and the anorexigenic gastrointestinal hormones GLP-1 and PYY, the orexigenic gastrointestinal hormone ghrelin, and feel-

ings of satiety and hunger in patients undergoing a Mixed Meal Tolerance Test (MMTT) after primary RYGB.

Methods

Subjects

Subjects were recruited in 2014 and 2015 at a Dutch hospital. All patients who underwent a bariatric procedure between 2008 and 2011 were prospectively included in a database. The inclusion criteria for the present study were primary RYGB between the age of 18 and 75 years. Subjects were excluded if they had diabetes mellitus as general treatments could influence the variables of interest. A random sample of 140 patients was drawn and they were approached by phone. Those who expressed interest in participating then received full information in the mail. After a consideration period of one week patients, who were willing to participate were scheduled for the MMTT. Written informed consent was obtained from all subjects and the study was approved by the regional medical ethics committee.

Initially, a total of 51 subjects were enrolled in the study. Due to unsuccessful blood collection ($n=7$), voluntary withdrawal from the study ($n=1$) and secondary surgical procedure ($n=1$), 9 subjects were excluded from all analyses. The flow diagram is presented in Supplemental Fig. 1.

Surgical procedure

The primary RYGB surgery was performed at the Department of Surgery of the hospital as described in Emous et al. [28]. The biliopancreatic limb was measured at 80 cm, the alimentary limb at 150 cm with an estimated pouch volume of 30–60 cc. All subjects received the standard post-bariatric dietary recommendations and were advised to take daily multivitamin supplements.

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