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Study of the effects of transoral gastroplasty on insulin sensitivity and secretion in obese subjects

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Abstract *Background and aims:* Transoral gastroplasty (TOGA) recently emerged as a new, feasible and relatively safe technique for the surgical treatment of obesity. However, so far there are no data on the effects on insulin sensitivity in the literature. Our aim is to evaluate the effect of TOGA on insulin sensitivity and secretion.

Methods and results: Nine glucose normo-tolerant obese subjects (age:41 $\pm$ 6 years; BMI:42.49 $\pm$ 1.03 kg/m^2) were studied. Fat-free mass (FM) and fat mass (FM) were assessed by bioelectrical impedance; plasma glucose, insulin, and C-peptide were measured during an oral glucose tolerance test (OGTT) before and 3 months after the operation. Insulin sensitivity was calculated using the oral-glucose insulin-sensitivity index, and insulin secretion by C-peptide deconvolution.

Three months after surgery, a significant ($P = 0.008$) reduction of BMI to 35.65 $\pm$ 0.65 kg/m^2, with a decrease of FM and FFM from 57.22 $\pm$ 2.19 to 41.46 $\pm$ 3.02 kg ($P = 0.008$) and from 59.52 $\pm$ 1.36 to 56.67 $\pm$ 1.10 kg ($P = 0.048$) respectively, was observed. Insulinemia was significantly reduced at fast and at 120 min after OGTT; in contrast, no significant change in glucose concentration was observed. Insulin sensitivity significantly increased (348.45 $\pm$ 20.08 vs. 421.18 $\pm$ 20.84 ml/min/m^2, $P = 0.038$) and the incremental area of insulin secretion rate (total ISR) significantly decreased (from 235.05 $\pm$ 27.50 to 124.77 $\pm$ 14.50 nmol/min/m^2, $P = 0.021$). Total ISR correlated with weight, BMI and FM ($r = 0.522$, $P = 0.028$; $r = 0.541$, $P = 0.020$; $r = 0.463$, $P = 0.049$, respectively). BMI represented the most powerful predictor of ISR decrease ($R^2 = 0.541$, $P = 0.020$).

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Conclusion: Transoral gastroplasty allows a significant weight loss 3 months after the intervention as well as an amelioration of insulin sensitivity with subsequent reduction of the insulin secretion.

Introduction

Obesity has dramatically augmented in the last decades, with an increasing prevalence worldwide, especially in Western countries. Several pathologies are associated with obesity, such as heart disease, diabetes, hypertension and dyslipidemia, thus representing a serious health concern [1].

As far as the treatment of obesity and morbid obesity is concerned, diet and physical activity result in a modest body weight reduction, while the pharmacological treatment provides only limited benefits [1]. By contrast, surgery recently has emerged as a powerful tool for achieving a long-term weight loss [2].

Besides the effect on the reduction of body weight [3], we reported that a malabsorptive bariatric surgery procedure—the bilio-pancreatic diversion, BPD—resulted in a prompt reversibility of type 2 diabetes by normalizing peripheral insulin sensitivity and enhancing beta-cell sensitivity to glucose, very early after the operation, before weight loss occurred [4]. Despite the fact that the molecular mechanisms involved in the amelioration of insulin sensitivity after BPD are still unclear, it is worth mentioning the importance of BPD in the treatment of diabetes. Other bariatric procedures that are mainly restrictive or purely restrictive, such as Roux-en-Y gastric bypass (RYGB) and laparoscopic gastric banding respectively, have been reported to resolve [5] or improve [6] type 2 diabetes.

However, most of the patients undergoing BPD or RYGB develop some nutritional deficiency, justifying mineral and multivitamin supplementation postoperatively. Of course, the nutrient deficiency is proportional to the length of the bypassed absorptive area and to the percentage of weight loss. Low levels of iron, vitamin B12, vitamin D and calcium are predominant after RYGB. Protein and fat-soluble vitamin deficiencies are mainly detected after BPD [7—9].

Recently, the transoral gastroplasty (TOGA) system (Satiety Inc., Palo Alto, CA) has emerged as a new approach for the obesity treatment, allowing endoluminal restriction, without the above-mentioned complications. Only a few reports have described the use of TOGA in humans [10,11]. These preliminary results clearly indicate the feasibility and safety of TOGA, thus encouraging the use of such a technique to treat obesity. According to the literature, TOGA determines a significant weight loss 1—6 months after the intervention [10,11]. However, no data of the effects on insulin sensitivity have been reported in the literature until now.

The aim of the current preliminary study was to evaluate the effect of TOGA on insulin sensitivity and secretion in a group of nine obese subjects, 3 months after the intervention. To the best of our knowledge, our report is the first addressing this issue, in order to shed some light on the use of TOGA as a possible tool for allowing weight loss while treating insulin resistance.

Methods

Study population

Nine obese, normo-glucose tolerant subjects (8 women/1 man, mean age 41 ± 6 years) were recruited from the School of Medicine at the Catholic University in Rome. None of the subjects presented thyroid or other endocrine disease, renal or liver failure. All subjects underwent transoral gastroplasty. The study protocol was approved by the Ethical Committee of the Catholic University (School of Medicine, Rome) and all subjects gave their written informed consent.

Transoral gastroplasty (TOGA)

The TOGA system was performed according to the procedure recently reported [10]. Briefly, a 60-F bougie was introduced over the guide wire to dilate and test for any resistance. The TOGA Sleeve Stapler was introduced over the guide wire; an 8.6-mm or smaller endoscope was introduced through a channel in the device, advanced into the stomach and retroflexed. The stapler body was positioned along the lesser curvature of the stomach, the stapler jaws were opened, and a septum with attached retraction wire was deployed to spread and orient the stomach tissue. Suction was applied, and tissue from the anterior and posterior walls of the stomach was acquired into two vacuum pods in the device. The stapler was then closed and fired, delivering three rows of 11 titanium staples, thus creating a transmural staple line connecting the anterior and posterior stomach, beginning 1 cm proximal to the Z line and extending distally 4.5 cm, parallel to the lesser curvature. A second staple line was added, extending the new sleeve distally to create a sleeve approximately 8—9 cm in length. The distal sleeve outlet was then narrowed using a single-suction-pod stapler. Restrictions were placed until the outlet was less than 20 mm.

Following an overnight stay for observation, all patients underwent a plain abdominal X-ray to visualize staple orientation and Gastrografin (water-soluble contrast agent) and barium swallow to visualize the new stomach anatomy and verify the absence of any gastric leak. After the intervention, all subjects were placed on protein-rich liquid formula alone (Fortimel, Nutricia, Italy; 800 kcal/day, 80 g protein/day) in the first 2 weeks and pureed food for a further 2 weeks. After 4 weeks, patients added solid foods to their diets. The calorie content of the diet was around 1000 kcal/day (30% proteins, 25% lipids and 45% carbohydrates). The most common side effects reported after the intervention included nausea, sporadic vomiting and central chest pain after meals, which generally resolved within 3 weeks. No serious adverse events have been observed in this series of subjects.