ORIGINAL ARTICLE

Neuroendocrine brake for the treatment of morbid obesity. Preliminary report

Freio neuroendócrino para o tratamento cirúrgico da obesidade mórbida. Relato preliminar

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ABSTRACT

Objectives: To demonstrate the preliminary results of a new technique named neuroendocrine brake, for surgical treatment of morbid obesity. **Methods:** In November 2003, three patients underwent the neuroendocrine brake operation performed by the laparoscopic approach. The mean age was 46.4 years; all patients were female. Mean BMI was 42.3 kg/m2. The patients selected presented some relative or absolute contraindications to the use of gastrointestinal bypass techniques, including gastric ulcer and a family history of gastric malignancy(1) and chronic anemia (2). All patients had associated diseases, including type II diabetes mellitus (2), hypertension (2), obstructive sleep apnea (1), dyslipidemia (3), cholecystolithiasis (1), gastric ulcer (1) and chronic anemia (2). The laparoscopic technique consisted of an ileal interposition at the proximal jejunum and longitudinal gastrectomy. **Results:** There was no conversion to open surgery or postoperative complications. Sixteen months later, the mean percentage of initial body weight loss was 44.6% and the mean BMI was 24.3 kg/m2. Glucose, triglyceride and cholesterol levels were normalized, and sleep apnea showed remission. **Conclusion:** In spite of the reduced number of patients and short term follow up, the good results suggest that the neuroendocrine brake may become an option for surgical treatment of morbid obesity in the near future.

Keywords: Obesity morbid; Neurosecretory systems; Gastroplasty; Gastrectomy; Diabetes mellitus type II; Hyperlipidemia

RESUMO

Objetivos: Demonstrar os resultados preliminares de uma nova técnica cirúrgica para o tratamento da obesidade mórbida. **Métodos:** Em novembro de 2003, três pacientes foram submetidos à cirurgia denominada "freio neuroendócrino", por via laparoscópica. A idade média era de 46,4 anos, sendo todos os pacientes do sexo feminino. O índice de massa corporal (IMC) médio era de 42,3 kg/m2. Os pacientes selecionados apresentavam algum tipo de contra-indicação, relativa ou absoluta, ao uso das técnicas de "bypass" gastrointestinal. As principais razões incluíam úlcera gástrica e história familiar de câncer gástrico (1) e anemia crônica (2). Todos pacientes possuíam doenças associadas como diabetes mellitus tipo 2 (2), hipertensão arterial (2), apnéia obstrutiva do sono (1), dislipidemia (3), colelitíase (1), úlcera gástrica (1) e anemia crônica (2). A técnica laparoscópica consistiu de uma interposição ileal no jejuno proximal associada a uma gastrectomia longitudinal. **Resultados:** Não houve conversão para cirurgia aberta ou complicações pós-operatórias. O percentual médio de perda do excesso de peso foi de 44% após 16 meses e o IMC médio foi 24,3 kg/m2. Os níveis séricos de glicose, triglicérides e colesterol foram normalizados e houve remissão da apnéia noturna do sono. **Conclusão:** Apesar do reduzido número de pacientes e do curto período de seguimento, os bons resultados sugerem que o freio neuroendócrino pode se tornar uma opção para o tratamento cirúrgico da obesidade mórbida em um futuro próximo.

Descritores: Obesidade mórbida; Sistemas neurossecretores; Gastroplastia; Gastrectomia; Diabetes mellitus tipo II; Hiperlipidemia

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INTRODUCTION

Obesity is a major public health problem in our community. It is estimated that about 41% of the male population is overweight and 8.9% is obese. As to women, 40% are overweight and 13.1% are obese[1]. Weight reduction achieved with diet, physical exercise and medication frequently determines compensating changes in the appetite and energy expenditure[2], preventing significant and sustained weight loss.

Surgery is the only effective treatment to achieve appropriate weight loss for longer periods[3]. The main weight loss techniques related to surgical treatment of morbid obesity include: 1 - restrictive techniques; 2 - malabsorptive techniques and 3 – a combination of the previous two. In recent years, with proven participation of leptin, ghrelin and many other peptides secreted by the digestive system, our knowledge about the peripheral signs regulating appetite and energy homeostasis expanded[4].

This current report intends to apply the concept of associating restrictive food intake mechanisms with effective neurohormone participation in the gastrointestinal tract (without bypassing it) as an agent that controls appetite and satiety, weight loss and associated diseases, such as type II diabetes mellitus, dyslipidemia and others. The title of this report, neuroendocrine brake, emphasizes the importance of participation of neuronal and hormonal mechanisms in this technique.

The objective of this report is to demonstrate the preliminary results of a new technique named neuroendocrine brake, for surgical treatment of morbid obesity.

METHODS

In November 2003, three patients underwent laparoscopic neuroendocrine brake. All patients were female, with mean age of 46.4 years (range 41-50 years). The mean body mass index was 42.3 (range 39.1-43.6). Patients were carefully selected, since the current approach in our services at Hospital de Especialidades de Goiânia and Hospital Israelita Albert Einstein, involves the use of different laparoscopic techniques, such as gastric bypass, duodenal switch, modified Magenstrassen & Mill gastroplasty, adjustable gastric banding and Scopinaro.

The inclusion criteria were based in the 1991 NIH Consensus Development Panel on bariatric surgery[5]. The exclusion criteria included previous major abdominal surgery in the upper abdomen, such as gastric resection, age under 18 or above 65 years, severe coagulopathies, pulmonary and cardiac disorders. All patients presented some kind of contraindication, either relative or absolute, to the use of gastric bypass. The main contraindications were gastric ulcer and family history of gastric malignancy (1) and chronic anemia (2).

The preoperative evaluation included the clinical history and specially history of obesity and food intake pattern, physical examination, blood and urine tests, upper abdominal ultrasonography, upper gastrointestinal endoscopy with testing for Helicobacter pylori assessment, lung function tests, blood gas analysis and cardiac examination. The patient with obstructive sleep apnea syndrome underwent polysonography. Other exams specific to some concurrent diseases were also requested, including hormone levels, such as ghrelin, leptin, cholecystokinin, GLP-1, GLP-2, adiponectin, GIP, oxyntomodulin, pancreatic polypeptide, PYY and insulin. Dietitians and endocrinologists evaluated all patients. Endocrine diseases were excluded. A visit to a psychiatrist or psychologist was liberally recommended. In the postoperative period, before hospital discharge, chest films and iodine-contrast radiograph of the upper digestive tract were made.All patients presented associated diseases, including type II diabetes mellitus (2), arterial hypertension (2), obstructive sleep apnea (1), dyslipidemia (3), cholecystolithiasis (1), gastric ulcer (1) and chronic anemia (2).

The indicators of a successful procedure were related to weight loss (expressed as BMI and percentage of weight loss compared with baseline), resolution or improvement of associated diseases, morbidity and mortality, re-operation and quality of life.

This study was preceded by evaluation of the technique in eight dogs, which had good clinical evolution, with no complications. Informed consent and hospitals ethics committee approval were also obtained.

TECHNIQUE

A 5-port laparoscopic technique was used. The gastric reservoir (longitudinal gastrectomy) was prepared with the operating table at 30-degree head-up. It was followed by devascularization of the greater curvature initiating in the distal portion of the antrum, 5 cm apart from the pylorus, utilizing the harmonic scalpel. The anesthesiologist introduced, under laparoscopic control, a 30-Fr Fouchet calibration, which was positioned along the lesser curvature towards the pylorus. After that, gastric resection was performed starting at the antrum up to the angle of Hiss using a 45-mm linear stapler. The resected portion was removed at the end of the surgery. A silicon band was

positioned 3 cm below the cardia and adjusted to the diameter of the gastric pouch. The last step involved a running suture with PDS 3.0 over the stapling line (figure 1).

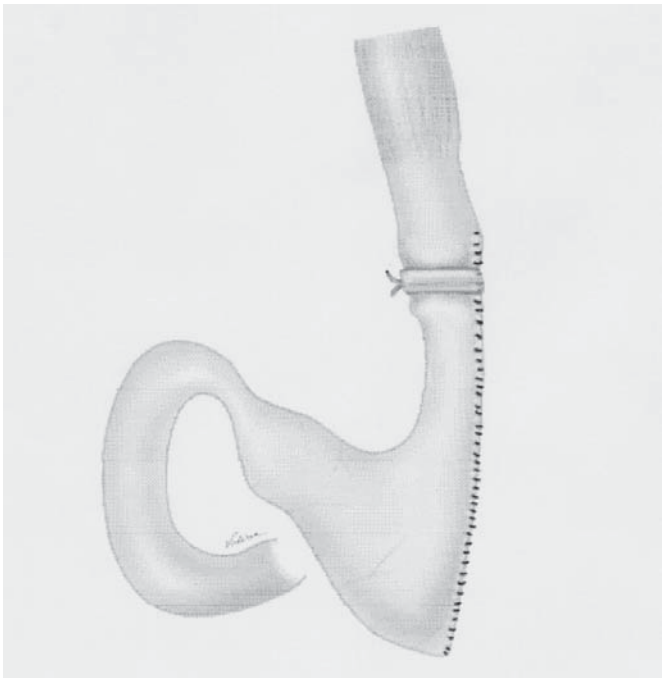

Figure 1. Vertical gastrectomy

For ileal loop interposition, the patient was placed at 15 degree Trendelenburg position. First the angle of Treitz was identified and a site was marked 50 cm distal in the jejunum. The jejunum was then sectioned with a linear stapler. Sites A (proximal) and B (distal) were marked in the sectioned jejunum. The cecum and terminal ileum were identified, and an ileal site was marked 50 cm proximal to the cecum. Ileal sectioning was performed at this site with a linear stapler. Two distal and proximal sites were denominated D' and D, in the sectioned ileum. The new ileal site was sectioned at 100 cm proximal to D with a linear stapler. These two ileal sites were denominated C' and C, proximal and distal, respectively. The next step was anastomosis of the ileal sites identified as C and D and restoration of ileal transit. Anastomosis was performed using a linear stapler and suture of the opening defect with PDS 3.0 and approximation of ileal mesentery with prolene 3-0 with continuous suture. The ileal segment C D was transposed clockwise on the right side. Jejunoileal anastomosis, connection of sites A and C and jejunoileal between D' and B were performed. Anastomoses were performed similarly to the one described above. Approximation of the two last anastomotic mesenteries with prolene 3-0 and continuous suture (figure 2). Insertion sites of trocars were revised, abdomen was deflated and the 12-mm holes had their aponeurosis sutured.

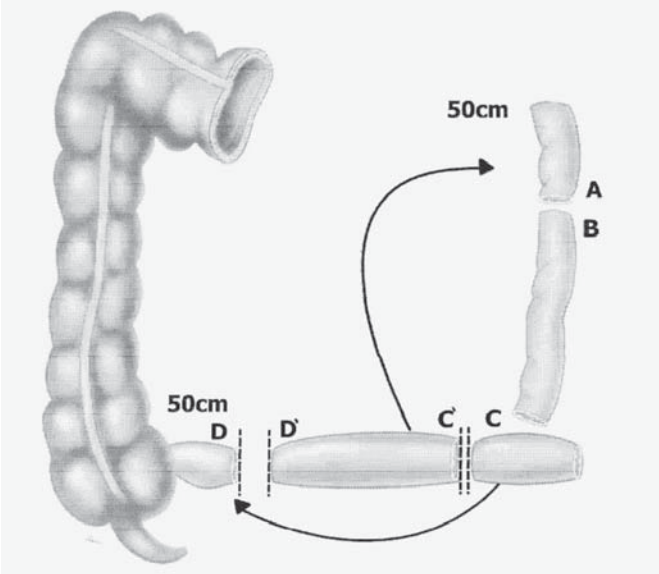

Figure 2. Ileal interposition

RESULTS

The postoperative follow-up was 17 months. There was no conversion to open surgery. One patient was simultaneously submitted to cholecystectomy and cholangiography. The mean operative time was 215 minutes, ranging from 190 to 265 minutes. Restoration of intestinal function occurred after an average of 48 hours. There were no early postoperative complications Mean hospitalization time was 3.5 days, ranging from 3 to 5 days.

The most frequent symptoms in the first 30 postoperative days were related to nausea, appetite loss, early satiety, inferior abdomen discomfort and adynamia. All patients felt ready to return to normal activities on the 8th postoperative day. There were no late postoperative complications.

The mean percentage of baseline weight loss was 9.9% after one month, 17.4% after three months, 23.4% after 6 months, 38.9% after 12 months and 44.6% after 16 months, according to figure 3. Mean postoperative BMI was 24.3 kg/m^2 after 16 months.

Blood tests after 30 days showed normalization of glucose and hemoglobin A1c in patients with type II diabetes mellitus. After 3 months, the three patients presented normal levels of cholesterol and triglycerides. Polysonography confirmed significant improvement of apnea indexes in one patient. An evaluation 6 months later showed that two patients with arterial hypertension had normalized their blood pressure or reduced the amount of drugs. Serum hemoglobin levels did not show any change.

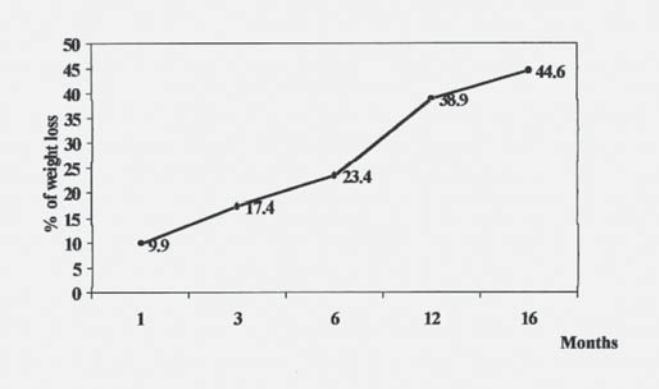

Figure 3. Percentage of baseline weight loss

DISCUSSION

The preliminary results of the three patients point to the technical feasibility of the neuroendocrine brake surgery as well as significant weight loss and remission of important associated diseases.

The most important principles of the neuroendocrine brake are integrity of the digestive tract, i.e., the absence of a bypass, and early exposure of food to the distal ileum. This mechanism determines a series of events, including motility changes in the upper gastrointestinal tract, a phenomenon called "ileal brake"[6]. Fewer contractions in the gastric antrum and slowed gastric emptying are noticed, as well as reduction of duodenal and jejunal motility[7]. According to Olitani et al.[8], in a study performed in dogs, and Strader et al.[9], in a study in rats, this phenomenon is mediated by nerves extrinsic to the ileum and by gastrointestinal polypeptides, mainly PYY and GLP-1. These peptides also present different actions associated with energy homeostasis and are considered anoretic peptides. They are found in lower blood concentrations in obese patients than in control individuals with normal weight[10]. Both Koopmans et al.[11], in studies performed in rats, and Smith et al[12], in studies in dogs, observed weight reduction after transposition of an ileal segment to the proximal jejunum.

The possibly complementary association of neuroendocrine brake with different options of gastric restriction emphasizes the importance of creating mechanically restrictive forms of food intake. Isolated longitudinal gastrectomy achieves maximum weight loss in high-risk super obese patients after one year, with roughly 45% excess weight loss[13]. Magenstrasse & Mill surgery type also achieves the maximum weight loss about one year later, with approximately 60% of excess weight loss[14]. Adjustable gastric band results demonstrate a significant excess weight loss of 50% during the first 24 months[15]. It is possible that any of the above-mentioned gastric restrictive operations may result in the same weight loss, and ultimately the ileal interposition may be in patients submitted to an isolated restrictive operation and who have failed to achieve an adequate weight loss.

The laparoscopic approach was chosen and was free of complications. Certainly, the use of this technique through an open approach is technically feasible although it will require larger incisions than the ones usually performed. The technical complexity of ileal interposition is significant and the need for three intestinal anastomoses potentially increases the risk of early dehiscence and possible late obstructions or internal herniations. The use of suture techniques, closure of all possible sites of internal herniations and oversewing of staple lines have probably been extra safety issues that prevented different complications in these first patients.

Patients were carefully selected and presented a mean BMI of 48.7, which is below the mean values in our service. In spite of the short postoperative follow-up period, the pattern and the percentage of weight loss were very similar to the levels achieved by gastric[16] and biliopancreatic bypasses[17], suggesting a complementary effect of gastric restrictive operation and ileal interposition, each procedure contributing to roughly 50% of weight loss.

The initial results in relation to regression of associated diseases were significant. Patients with type II diabetes mellitus presented complete normalization of glucose levels much earlier than effective weight loss, which was similar to the data obtained with gastric bypass surgery[18-19]. There was an early normalization of cholesterol levels and late normalization of triglycerides, corroborating the data found in studies performed in rats by Tsuchiya et al.[20].

However, according to Oria and Brolin[21], a minimum five-year postoperative follow-up is necessary for a valid analysis of any type of bariatric surgery and the final objective of weight reduction is improvement of associated conditions and better quality of life, which can possibly have an impact in longevity.

CONCLUSION

In spite of limited experience, the neuroendocrine brake may become an option for surgical treatment of morbid obesity in the near future, with selective indication. Moreover, it may represent the fourth technical variation of weight control in bariatric surgery, since it has several advantages in relation to isolated gastric restrictive operations, intestinal malabsorption or the combination of both.

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