Obesity is a worldwide health problem, particularly in Western countries. In Mexico, about 50% of the population is obese according to some studies [1]. Obesity increases the risks of morbidity and mortality, as metabolic diseases, diabetes, hypertension, cardiovascular and hepatobiliary diseases are frequent in obese individuals [2, 3]. Dietary, pharmacological and behavioral treatments have partial results and are of short duration [4]. Surgical treatments (gastric banding and by-pass), even though they are effective in some patients, are invasive and may have severe complications [5]. Botulinum toxin (BT) is a powerful, long-acting inhibitor of muscular contractions in both striated and smooth muscles [6]. This pharmacological property has been used in treating some spastic gastrointestinal diseases [7, 8]. Recently, it was observed that intramuscular injections of BT type A into the gastric antrum of laparatomized rats induced a reduction in food intake and body weight [9]. These effects might be mediated by inhibition of gastric emptying. Alternatively, in a recent report, one patient who was injected with BT type A into the gastric antrum by endoscopy had a reduction of 9 kg of body weight and a 32.5% of daily caloric intake 4 months after application of BT [10]. This prompted us to carry out a pilot study aimed at evaluating the effects of endoscopic antral injections of BT on gastric emptying and body weight of obese patients. This is the first such study carried out in human beings.

Materials and methods

Design of the study

This is a prospective non controlled clinical trial. It was approved by the Research and Ethics Committee of the Faculty of Medicine of the Autonomous University of Nuevo Leon.

Patients

Patients were included in the study according to the following criteria: (1) either sex; (2) over 18 years of age; and (3) a body mass index (BMI) over 30 kg/m².

Criteria for exclusion were: (1) clinical gastroparesis and abnormal gastric emptying at scintigraphy (more than 50% of gastric retention at

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90 min after a solid meal ingestion); (2) hypothyroidism; (3) clinical gastroesophageal reflux disease; (4) current treatment with prokinetic drugs; (5) gastric damage demonstrated by endoscopy (peptic ulcers, gastric cancer); and (6) previous gastric surgery.

**Botulinum toxin injections**

Upper endoscopy was performed with a Pentax videoendoscope under intravenous sedation with midazolam. A dose of 100 U of BT type A (Allergan, Irvine, Mexico DF) was diluted in 8 mL of saline solution. It was injected circularly through an sclerotherapy injector needle (Wilson Cook Medical Inc., Mexico DF) into the prepyloric antral gastric wall at eight sites. Each injection contained 1 mL volume and 12.5 U of BT.

**Evaluations**

Before treatment the following parameters were evaluated: (1) complete clinical history; (2) upper endoscopy with Pentax videoendoscope (endoscopic procedures were recorded on VHS videocassettes); (3) body weight measurement and (4) solid gastric emptying scintigraphy. Patients consumed a test meal consisting of an egg sandwich and water. The scrambled eggs were labeled with 500 μCi of Technetium Tc99m-DTPA. Scintigraphic images were obtained at 30, 60, 90 and 120 min after meal ingestion. The percentage of gastric retention at 90 min after meal ingestion was determined. In our laboratory, normal solid phase gastric emptying was considered to be ≤ 50% of gastric retention at 90 min for Tc-labeled solids.

After treatment, the following evaluations were performed: (1) clinical symptoms of gastroparesis (nausea, vomiting, early satiety, abdominal distension) were recorded at 1, 4, and 12 weeks after treatment; (2) body weight was measured 4 and 12 weeks after treatment and (3) solid gastric emptying scintigraphy was performed 4 and 12 weeks after the treatment.

**Statistical analysis**

Results are presented using descriptive statistical median values. The analysis of changes after the treatment (body weight and gastric emptying) was performed using the non-parametric Wilcoxon test and Student T test for dependent samples. Statistical significance was set at a 5% two-tail level.

**Results**

**Patient characteristics**

Fifteen patients were evaluated for entry into the study. Three of them were excluded because they presented abnormal gastric emptying at scintigraphy.

In this preliminary report, the results of twelve patients are described. The group included eight females (66%) and four males (34%). The median age was 29 years (range: 21 – 39), the median body weight was 83.5 kg (range: 71.8 – 100.0) and the median of gastric solid retention at 90 min was 30.5 % (range: 0 – 49%).

**Body weight**

The median body weight values 4 and 12 weeks after treatment were: 83 and 82.5 kg, respectively. They were not significantly different to baseline values (P > 0.05). Changes 4 and 12 weeks after treatment did not show significant differences as compared to baseline values : - 0.5 and – 1.0 kg, respectively, P > 0.05. Individual values are shown in figure 1.

**Gastric emptying**

The median values of solid gastric retention at 90 min 4 and 12 weeks after treatment were: 35 and 41% respectively (P > 0.05 compared to baseline values ). Changes 4 and 12 weeks after treatment did not show significant differences as compared to baseline values (+ 4.5 and + 10.5%, respectively, P > 0.05). Individual values of gastric retention at 90 min are shown in figure 2. Abnormal gastric retention for solids at 90 min > 50% was observed in only 22% and 25% of patients 4 and 12 weeks after BT injections.

**Symptoms of gastroparesis**

Five patients reported early satiety, abdominal distension or transient anorexia after treatment. None of these symptoms were severe enough to require symptomatic treatment administration.

**Side effects**

No side effects attributed to treatments were observed. Generally, treatments were well tolerated in all patients.

**Discussion**

Since we injected BT into gastric antral muscle layer we expected to observe an induced pharmacological gastroparesis in our patients. In fact this effect has never been previously

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**Fig. 1** – Individual values of body weight in 12 patients before and 4 and 12 weeks after endoscopic gastric antral injections of botulinum toxin.

**Fig. 2** – Individual values of solid gastric retention at 90 min in 12 patients before and 4 and 12 weeks after endoscopic gastric antral injections of botulinum toxin.
described. Therefore, we hypothesized that delayed gastric emptying induced by BT might contribute to a reduction in food intake and consequently reducing body weight in our patients. Nevertheless, we did not observe significant changes of either gastric emptying or body weight after treatment. Although we did not calculate the daily caloric ingestion of patients our impression is that it did change. In the reported patient in whom a beneficial effect of BT injections in the gastric antrum was suggested, gastric emptying was not evaluated and therefore factors other than BT may have been responsible for outcome and may explain these beneficial results [10]. Otherwise, changes in gastric emptying and alterations in food intake may not be strongly related. Finally, increased gastric outlet resistance due to pyloric dysfunction or pylorospasm has been observed in gastroparesis [11]. Inhibition of the pyloric sphincter muscle by means of BT injections accelerates gastric emptying in these patients [12].

Although these preliminary results are not in favor of a beneficial effect BT injections into the gastric antrum, several factors should be analyzed and taken into account.

In this study, 100 U of BT was used because it is a safe dose that has been previously used for the treatment of achalasia and anal fissure [8,13]. However, it is necessary to emphasize that the antral muscle is a more voluminous structure than the lower esophageal and anal sphincters. The use of higher doses in the gastric antrum may be necessary to obtain a pharmacological effect.

Sclerotherapy injection needles (Wilson Cook Inc.) were used because of their wide availability. By this approach, BT injections were blindly performed, so we cannot confirm as to whether BT injections were sufficiently deep enough to impregnate the antral muscle. Larger tip needles or the use of guided-injections by endoscopic ultrasonography may solve this problem. In addition, multiple injections in several endoscopic sessions may be more effective.

Our study included few patients, and the power of statistical tests may be insufficient for analysis. The use of controls for comparison is important and it should be taken into account in future studies.

On the other hand, the effect of BT is reversible. Previous studies carried out in patients with achalasia have shown that the effects of BT injections last for a mean of seven months [14]. This fact may certainly limit the utility of BT for long-term treatment of obesity. Nevertheless, transitory lost of body weight in patients requiring abdominal surgery or in individuals motivated to change their dietary and physical exercise habits after losing body weight may be beneficial. Periodic reinjections of BT may be considered in some individuals.

Taking into account the above factors, we think that the investigation of BT for the treatment of obesity merits further evaluation. If higher doses of BT (> 200 U) are used, the cost–benefit relationship has to be taken into account because of the high cost of the overall procedure.

In conclusion, BT at a dose of 100 U circularly injected at eight sites into the gastric antrum using a sclerotherapy injection needle does not seem to reduce body weight or induce changes in gastric emptying in obese patients. Studies using a higher dose of BT administered by endoscopic EUS-guided injections are currently being carried out in our hospital.

REFERENCES