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ORIGINAL ARTICLE

Intragastric Botox Injection Barely to the Antrum vs. Diet: A Comparative Study

Sadece Antruma Yapılan İntragastrik Botoks Enjeksiyonu Diyete Karşı: Karşılaştırmalı Bir Çalışma

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Abstract

Introduction: In this study, we aimed to report the clinical outcomes of antral BTX-A injection in the absence of widespread injections and compare the results with the control cases who only were under a diet program without any invasive procedure.

Methods: Intragastric BTX-A injection was performed in 42 patients. Meanwhile, 38 age- and gender-matched patients who started a new diet program were included in the control group. Only the patients with a body mass index (BMI) between 30 kg/m^2 and 35 kg/m^2 were included for analysis.

Results: In total, 42 patients (11 males, 31 females) who had intragastric BTX-A injection and 38 patients (8 males, 30 females) who were under a diet program were included in this study. In the group administered with BTX-A, the minimum weight loss in this 5-month period was 7 kg, and the maximum weight lost was 19 kg with a mean of 14.48±2.20 kg; while the minimum weight loss in this 5-month period was 5 kg and the maximum weight lost was 13 kg with a mean of 10.78±2.09 kg in the control group (p=0.001).

Discussion and Conclusion: Intragastric BTX-A injection, barely to the antrum, was determined to be more effective in inducing significant weight loss in patients with grade 1 obesity than only diet and exercise. Approximately 10%–15% weight loss was achieved after antral BTX-A injection in about 3 months without any significant adverse events. In that aspect, intragastric BTX-A injection could be a promising way of inducing weight loss in obese patients.

Keywords: Antrum; Intragastric BTX-A Injection; Obesity

Obesity is a chronic disease affecting 10%–15% of people worldwide; it is one of the main risk factors of some metabolic disorders such as diabetes mellitus, hypertension, and obstructive sleep apnea. Increasing prevalence and morbidity rates make obesity an important health problem.[1] Although there has been significant progress

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recently in the development of several novel surgical and endoscopic treatment options for obesity, the success rates and long-term outcomes have remained conflicting.

Botulinum toxin (BTX) is the most powerful known inhibitor of muscular contraction by interfering with acetylcholine release in the neuromuscular plaque in both striated and smooth muscles.[2] Antral BTX-A injection was first suggested as an endoscopic treatment of obesity approximately 20 years ago.[3] With the inhibition of the acetylcholine-mediated peristalsis after BTX-A injection, gastric emptying is expected to be slowed down inducing earlier satiety. Elevated gastric emptying time resulting in weight reduction has also been demonstrated in experimental studies with antral BTX-A injection.[4] However, the clinical data are conflicting regarding the outcomes of this endoscopic treatment. Different responses of intragastric BTX-A administration have been reported in previous studies, which may be associated with the differences in injection sides or techniques or patient selections.

In this study, we aimed to compare the clinical outcomes of antral BTX-A injection in the lack of widespread injections through the fundus with the control cases who only were under a diet program without any invasive procedure.

Materials and Methods

Intragastric BTX-A injection was performed in 42 patients between June 2019 and June 2020 in Lokman Hekim Akay Hospital, Ankara, Turkey. Age- and gender-matched 38 patients who started a weight management program on the same period were included in the control group. The records of patients were evaluated retrospectively.

BTX-A injection was performed in volunteer patients, who were older than 18 years of age and having a body mass index (BMI) of over 30 kg/m^2 and lower than 35 kg/m^2. All patients were asked to come once in every 2 weeks. The body weights and adverse events were then recorded. Body weights were determined on the same scale. Exclusion criteria were as follows: pregnant or lactating women; patients with known chronic systemic diseases such as hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, chronic renal failure, or cirrhosis; patients who had prior gastric/bariatric surgery; patients with a known history of alcohol or drug abuse, and patients with a known allergy to any ingredients in botulinum toxin products

All patients were informed about BTX-A and its procedure before the injections. During the initial evaluation, before injection, patients were assessed for clinical gastroparesis, hypothyroidism, clinical gastroesophageal reflux disease, gastric ulcers or cancer, and previous gastric surgery. During endoscopy, in the presence of gastric ulcers or esophagitis, BTX-A injection was not performed. Upper endoscopy was performed with Olympos® video endoscope (Olympos® Video Gastroscope GIF-XTQ160) under intravenous sedation with propofol. A dose of 200 U of BT type A (Allergan, Irvine, Mexico DF) was diluted in 8 mL of saline solution. It was injected circularly through a sclerotherapy injector needle (TechnoCath® Disposable 23 Gauge/5 mm Sclerotherapy Needle) into the prepyloric antral gastric wall at 20 sites in a concentric ring 1 cm apart. Each injection contained 0.5 mL volume and 6.25 U of BTX-A. After BTX-A injection, all patients were recruited in a 24-week weight management program.

During follow-ups, clinical symptoms of gastroparesis (nausea, vomiting, early satiety, and abdominal distension) were recorded at 1, 4, and 12 weeks after treatment. Body weight was measured monthly after treatment. All patients were treated only with botulinum toxin injection; they were not under any other medications that may induce weight loss.

In total, 38 age- and gender-matched patients who were recruited in the same 24-week weight management program with the group injected with BTX-A on the same period were included in the control group. All patients were asked to come once in every 2 weeks. They were not under any other medications that may induce weight loss.

Patients with lacking file information or follow-up data were excluded from the study. Patients who were under any medications that may induce weight loss or patients having any chronic diseases such as diabetes mellitus, hypertension, or cardiovascular diseases were excluded from the study.

Body mass index was calculated in all participants using the formula as follows: BMI=weight/height^2. Since the study was retrospective in nature, informed consents could not be obtained, so the patients' privacy information was removed from the data analysis

Statistical Analyses

For statistical analysis, the Statistical Package for Social Sciences (SPSS) 21.0 software (SPSS Inc., Chicago, IL, USA) package program was used. The normality of the distribution of the data was analyzed using the Kolmogorov–Smirnov test. Descriptive statistical methods are then performed. Data were presented as mean±standard deviation or count (percentage). The body mass indexes of study participants at admission and on the 3rd or 6th month after the injec-

Table 1. The body mass index of study participants at admission and on the 3rd month and 6th month after the procedure

	At admission	On the 3rd month	On the 6th month	p
BMI (kg/m^2)				
Botox group (n=42)	32.17±1.20	26.93±1.26	24.22±1.14	**0.001**
Control group (n=38)	31.98±0.99	28.24±1.44	27.34±1.88	**0.001**
P	0.55	0.001	0.001	

BMI: Body Mass Index.

Table 2. Distributions of initial weight and the weights of the participants on the 5th month of follow-up

	Botox group (n=42)	Control group (n=38)	p
Initial weight			
Weight on the 1st month	86.32±5.84	84.89±5.57	**0.36**
Weight on the 2nd month	78.96±5.89	80.68±5.30	**0.29**
Weight on the 3rd month	75.64±5.92	77.46±5.27	**0.28**
Weight on the 4th month	72.96±5.64	75.90±5.79	**0.001**
Weight on the 6th month	71.02±5.71	75.18±5.97	**0.001**

tion were compared using one-sample t-test. Two-sample t-test (also known as the independent samples t-test) was performed to compare the continuous data between or among groups. Chi-square test was used to compare the categorical data between groups. The significance level was set at $p<0.05$.

Results

In total, 42 patients (11 males, 31 females) who had intragastric BTX-A injection and 38 patients (8 males, 30 females) who were under a weight management program were included in this study. No significant difference was observed between study and control groups as regards gender (p=0.178). The mean age of the patients in Botox and control groups were 38.02±4.42 years and 37.12±5.64 years, respectively (p=0.467).

Meanwhile, significant decreases were noted in terms of BMI among patients on the 3rd and 6th month of follow-up compared at admission in both groups (Table 1). Distributions of initial weights and the weights of the participants on the 6th month are summarized in Table 2. In every month, participants were noted to lose weight. The weight loss journey of the participants from the 1st month of the study is summarized in Table 3 and Figure 1. The minimum weight loss for the 6-month period was 7 kg, and the maximum weight loss was 18 kg with a mean of 14.48±2.20 kg in BTX-A group; while in the control group,

Table 3. The weight loss by study participants from the 1st month of the study

	Botox group (n=42)	Control group (n=38)	p
Δ1	7.36±1.80	5.09±1.54	**0.001**
Δ2	4.32±1.24	3.30±1.44	**0.02**
Δ3	2.68±0.90	2.09±127	0.34
Δ4	1.42±0.44	1.18±0.78	0.68
Δ6	14.88±2.26	10.24±3.49	**0.001**

Δ1: Weight loss on the 1st month; Δ2: Weight loss on the 2nd month; Δ3: Weight loss on the 3rd month; Δ4: Weight loss on the 4th month; Δ6: Weight loss throughout the 6 months after injection or starting weight management program.

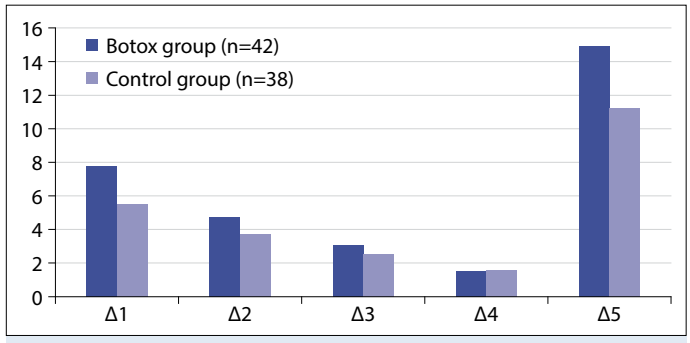

Figure 1. Distributions of the weight lost by study participants from the 1st month of the study.

the minimum weight loss in the 6-month period was 5 kg and the maximum weight lost was 13 kg with a mean of 10.78±2.09 kg (p=0.001).

Five (14.7%) patients reported early satiety, abdominal distension, or transient anorexia after BTX-A injection. None of these symptoms were severe enough to require symptomatic treatment administration.

Discussion

With the rising prevalence of obesity and its associated complications, finding new treatment options has become essential. In this study, we have determined that intragastric BTX-A injection was more effective in inducing weight loss than diet in patients with grade 1 obesity. The most important characteristic feature of this study was that we did not perform widespread injections through the fundus and compared the outcomes with the patients under diet.

Satiety and appetite control is a complex process. Gastric distention and accommodation and some hormones such as cholecystokinin, bombesin, somatostatin, glucagon-like peptide-1, and ghrelin play important roles in appetite control.[5] Gastric accommodation is the relaxation of the gastric wall in response to food intake. Impairment in gas-

tric accommodation has been associated with induced satiety and sensation of fullness. Increased gastric accommodation is positively correlated with the volume needed to suppress food intake. The speed with which the stomach empties also depends on the nature of the food, its osmolality, and its chemical composition. Small temporary increases in gastric emptying time have been reported after antral BTX-A injections.[6,7] Although we did not analyze the gastric emptying time in patients, we believe that statistically significant weight loss obtained with BTX-A injection was associated with the altered gastric accommodation. Approximately 10%–15% weight loss was achieved after antral BTX-A injection in about 3 months in the absence of significant adverse events. The degree of weight loss in a month decreased in time and after 3 months.

The data on the clinical outcomes of intragastric BTX-A injection remain controversial in the literature. In the study of Foschi et al.,[8] 24 morbidly obese patients were blindly randomized to re-ceive 200 IU BTX or placebo into the antrum and fundus of the stomach by intraparietal endoscopic administration. They reported that 8 weeks after BTX injection, in the BTX group, the patients had significantly higher weight loss and BMI reduction and a higher satiety score than controls. Further-more, BTX patients showed a significantly greater reduction in maximal gastric capacity for liquids and a greater prolongation in gastric emptying time. No significant side effects or neurophysiologic changes were found. In an experimental study, Park et al.[9] compared the following three groups: BTX group consisting of 15 obese rats which were administered with 20 U of BTX into the gastric antrum, the saline group consisting of 15 obese rats injected with 20 U of saline, and the control group consisting of 10 obese rats that did not receive any surgical intervention. As per their findings, it was determined that the bodyweight of the BTX group was significantly lower than those of the other groups at 6 weeks after the operation. They also reported that the gastric emptying time was sig-nificantly delayed in the BTX group. Meanwhile, de Moura et al.[10] compared the two groups: BTX-A, in which 200 units of BTX-A were injected into the gastric antrum and body, and control, in which the same injections were performed with 0.9% saline in the preoperative treatment of super-obese patients. They reported that the patients in both groups showed significant weight loss through-out the study, but there were not any significant differences between the groups regarding weight loss or change in BMI. The authors concluded that the intragastric injection of BTX-A was not an effective endoscopic treatment for preoperative weight loss in super-obese patients, which was also discussed further by Ribeiro IB et al.[11] We injected BTX-A to the antrum barely in patients with a BMI be-tween 30 kg/m^2 and 35 kg/m^2. We did not include the super-obese patients.

Different responses to intragastric BTX-A administration have been reported in previous stud-ies, which may be associated with the differences in injection sides or techniques.[12–14] In a meta-analysis of 8 studies on 115 patients (79 treated vs. 36 placebo), the treatment group was associated with weight loss in a pre/post-comparative approach compared to the placebo group; and the authors concluded that wide-area injection including the fundus or body rather than the antrum only was asso-ciated with weight loss.[12] Similarly, in another systematic review and meta-analysis of four studies, Bustamante et al.[13] concluded that treating obesity with BTA was not effective. However, we did not perform any injections to the fundus but achieved significant weight loss in patients with grade 1 obesity. Patient selection may be an important factor in this difference. Our patients were not super-obese, and we informed all of the patients before the treatment for at least two times. Moreover, re-garding the BMI or age distribution, our population was not a cosmopolite group which may also have some influences in our results.

Ghrelin, an appetite hormone, is mainly secreted from the fundus, and the main rationale for BTX-A injection to the fundus is to decrease the ghrelin secretion.[15] However, to the best of our knowledge, the data regarding the ghrelin levels after BTX-A injection remain limited. In their study on 20 obese patients, Li et al.[16] reported significant body weight and BMI decreases, with signifi-cantly elongated gastric emptying times after endoscopic multi-punctures of BTX-A including fundic injections. The authors also reported a significant decrease in fasting ghrelin levels 4 weeks after BTX-A administration. On the other hand, since muscle structures in the fundus are not as broad as those of the antrum, theoretically, fundus injections may be associated with more adverse events in-cluding perforations.

The main limitation of this study was the low number of patients and short follow-up periods.

Though this is not a miracle method, when asked, all patients responded that they were feeling full for a longer time, which induced the compliance of diet. However, all patients shared they were trying to have an appropriate diet for a long time, but had always failed until this time.

In conclusion, barely antral BTX-A injection was more effective in inducing significant weight loss in patients with grade 1 obesity than diet. Approximately 10%–15% weight loss was achieved after antral BTX-A injection in about 3

months without any significant adverse events. In that aspect, antral BTX-A injection may be a promising way of inducing weight loss in grade 1 obese patients. Further, larger studies with longer follow-up periods are warranted, since this is an endoscopic treat-ment method having less morbidity compared with the more invasive surgical methods.

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