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Comparison of botulinum toxin applications in the treatment of obesity

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Abstract

Obesity is a global health problem, however, there is no consensus on the treatment for patients with a BMI between 30 and 35. Intragastric botulinum toxin injection (IGBT) has been proposed as a new endoscopic treatment for obesity, with the potential to delay gastric emptying and increase satiety by temporarily paralyzing the injected area. A retrospective study was conducted on 157 patients who received antral or fundus dominant IGBT and were followed up for 6 months with a diet program from January 2020 to December 2022. The patients were divided into three groups: Group 1 consisted of patients who received more injections in the fundus during IGBT, group 2 consisted of patients who received more injections in the antrum during IGBT, and group 3 consisted of patients who were only followed up with a diet program. Group 1 patients received 10 fundus and 10 antrum injections, while group 2 patients received 18 antrum and 2 fundus injections. Group 3 patients were only followed up with a diet program. Both antral and fundus dominant IGBT were effective in reducing body weight, and there was a significant difference between the two groups in terms of weight loss. Both groups 1 and 2 had significantly greater weight loss than group 3 ($p<0.001$). Antral and fundus dominant IGBT can be considered as a potential treatment option for obese patients with a BMI between 30 and 35 who do not meet the criteria for bariatric surgery.

Keywords: Botox, intragastric botox, fundal botox, weight loss, diet

Introduction

Obesity has become a significant health problem worldwide, increasing even more in the last decade [1]. In modern medicine, the first step in combating obesity is through treatments such as diet and lifestyle changes. Bariatric surgery is recommended as the gold standard treatment for overweight patients with a body mass index (BMI) of 35 or above, along with comorbidities, or those with a BMI of 40 or above. However, there is no consensus worldwide for patients with a BMI between 30-35. Therefore, patients in this group may benefit from endoscopic treatments [2]. Excessive eating and increased appetite are the most significant problems for individuals with obesity. Injection of botulinum toxin-A (BT-A) into the gastric wall is a relatively new endoscopic treatment for obesity. This method has the potential to delay gastric emptying and increase satiety by temporarily paralyzing the injection site. BT-A works by blocking acetylcholine release in cholinergic neuromuscular connections [3]. Its effect gradually decreases in the first 3-6 months and does not leave permanent damage.

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Excessive food intake and increased appetite in individuals have been discussed in numerous studies regarding the intragastric botulinum toxin (IGBT) treatment. However, the application sites of botox and the role of incretins in this regard have not been clearly understood [4]. In our study, we evaluated three groups of patients: the first group consisted of patients who received botox injections mainly in the fundus, the second group consisted of patients who received botox injections mainly in the antrum, and the third group consisted of patients who were only monitored under the supervision of a dietitian.

Material and Methods

This retrospective study is approved by Cukurova University Ethics Committee (decision number 133, dated May 5, 2023). In the study, data of patients who underwent fundus IGBT and antral IGBT procedures and were followed up with a diet program for 6 months between January 2020 and December 2022 were retrospectively evaluated. The study sample comprised of 157 patients. Patients who did not attend follow-up appointments were excluded from the study. We evaluated three patient groups in our study: Group 1 consisted of patients who received more injections into the fundus during IGBT; Group 2 consisted of patients who received more injections into the antrum during IGBT; and Group 3 consisted of patients who were only followed up with a diet program. Patients undergoing IGBT were injected with 500 IU of the drug. Botulinum toxin was diluted with 20 cc of saline. The injection was planned to contain 25 IU of botulinum toxin in each cc. Firstly, sedation was applied to the patients and then endoscopy was performed. Intragastric botulinum toxin injection was administered with a sclerotherapy needle to patients who did not have severe gastritis, ulcer, or mass lesion that would hinder the procedure. Group 1 patients received 10 antrum and 10 fundus injections (Figure 1). Group 2 patients received 18 antrum and 2 fundus injections (Figure 2). After the procedure, patients who underwent the procedure under sedation were discharged after resting for 30 minutes. Group 3 patients were only followed up with a diet program and did not receive botulinum toxin injection. All patients were followed up by a dietician every two weeks for 6 months. T-test or Mann-Whitney U test was used for continuous data for background clinical data, and Fisher's exact test or chi-square test was used for categorical data. The data were analyzed using SPSS ver. 22.0, and descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used to evaluate study data. One-way ANOVA test was used to compare normally distributed quantitative variables between two groups. In accordance with standard statistical practice, two-tailed tests were employed for all analyses, and P values below 0.05 were deemed to be statistically significant.

Figure 1. Group 1 patients who received 10 antrum and 10 fundus injections

Figure 2. Group 2 patients who received 18 antrum and 2 fundus injections

Results

Between January 2019 and December 2021, patients who underwent fundus IGBT, antral IGBT, and were followed

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up with diet were included in the study. A total of 157 obese patients were included in the study. Fifty patients were treated with fundus IGBT, 57 with antral IGBT, and the remaining 50 patients were given a diet program. Of the patients, 129 were female and 28 were male. When we examined the demographic data of all patients, the preoperative weight was 94.17±12.79, the preoperative BMI was 35.59±5.32, the postoperative weight was 86.95±12.77, the postoperative BMI was 32.85±5.16, and the weight loss and BMI reduction after 6 months of follow-up were 7.22±4.03 and 2.73±1.56, respectively. When comparing the fundus+antral IGBT and diet groups, there was no statistically significant difference in preoperative weight and BMI ($p>0.05$) (Table 1). However, statistically significant differences were found in favor of IGBT in terms of weight, BMI, weight loss, and BMI reduction after 6 months of follow-up ($p<0.05$) (Table 2). When we evaluated the IGBT group as fundus IGBT, antral IGBT, and diet groups, there was no statistically significant difference in preoperative weight and BMI ($p>0.05$) (Table 3). When we compared the weight loss and means of the three groups after 6 months of follow-up, the analysis of variance was found to be significant ($p<0.05$) (Table 3). It appears that there is a significant difference in weight loss between at least two of these three groups. In pairwise comparisons, the mean of Group 1 was significantly higher than that of Groups 2 and 3 ($p<0.05$), and similarly, the mean of Group 2 was also significantly higher than that of Group 3 ($p<0.05$). The differences were in the order of Group 1-3>1-2>2-3. As a result, when evaluating the groups in terms of weight loss, Fundus IGBT and Antral IGBT groups were found to be statistically more effective than the diet group, and similarly, the antral group was also found to be statistically more effective than the diet group ($p<0.05$). When we compared the mean BMI reduction of the three groups after 6 months of follow-up, the analysis of variance was found to be significant ($p<0.05$) (Table 4). It appears that there is a significant difference in mean BMI reduction between at least two of these three groups. In pairwise comparisons, the mean of Group 1 was significantly higher than that of Groups 2 and 3 ($p<0.05$), and similarly, the mean of Group 2 was also significantly higher than that of Group 3 ($p<0.05$). The differences were in the order of Group 1-3>1-2>2-3. As a result, when evaluating the groups in terms of mean BMI reduction, Fundus IGBT and Antral IGBT groups were found to be statistically more effective than the diet group, and similarly, the antral group was also found to be statistically more effective than the diet group ($p<0.05$) (Table 3).

Table 1. Preoperative and postoperative data for the IGBT and diet groups

	IGBT (n=107)	Diet program (n=50)	P value
Preoperative weight (kg), Mean±SD, range	94.32±11.99 (73-113)	93.86±14.47 (72-113)	0.083
Postopeative weight (kg), Mean±SD, range	85.76±11.68 (64.8-109.7)	89.5±14.65 (66-109.9)	P<0.01
Preoperative BMI, Mean±SD, range	35.60±5.2 (25.3-46.4)	35.55±5.59 (26.4-45.7)	0.784
Postoperative BMI, Mean±SD, range	32.35±4.86 (22.9-42.4)	33.90±5.66 (24.6-32.8)	0.032
Weight loss after 6-month follow-up, Mean±SD, std error mean	8.56±4.19 (0.40)	4.35±1.19 (0.16)	P<0.01
Reduction in BMI after 6-month follow-up, Mean±SD, std error mean	3.24±1.63 (0.15)	1.64±0.44 (0.06)	P<0.01

IGBT: intragastric botulinum toxin injection, BMI: body mass index, SD: standard deviation

Table 2. Preoperative and postoperative data for the three groups

	Fundus IGBT (n=50)	Antrum IGBT (n=57)	Diet (n=50)	P value
Preoperative weight (kg), Mean±SD, range	95.94±11.86 (73-113)	92.92±12.04 (73-113)	93.86±14.47 (72-113)	0.187
Postoperative weight (kg), Mean±SD, range	85.21±11.55 (64.8-107.2)	86.24±11.88 (66-109.7)	89.50±14.65 (66-109.9)	0.074
Preoperative BMI, Mean±SD, range	36.31±4.95 (25.8-46.2)	34.98±5.41 (25.3-46.4)	35.55±5.59 (25.3-46.4)	0.325
Postoperative BMI, Mean±SD, range	32.24±4.62 (22.9-38.6)	32.45±5.11 (23.3-42.4)	33.90±5.66 (24.6-44.9)	0.076
Weight loss after 6-month follow-up, Mean±SD, std err. mean, range	10.72±4.69 (0.66) (3.2-24.5)	6.66±2.48 (0.32) (1.3-11.2)	4.35±1.19 (0.16) (2-6.5)	P<0.01
Reduction in BMI after 6-month follow-up, Mean±SD, std err. mean, range	4.07±1.83 (0.26) (1.1-10.2)	2.52±0.99 (0.13) (0.4-4.4)	1.64±0.44 (0.06) (0.77-2.49)	P<0.01

IGBT: intragastric botulinum toxin injection, BMI: body mass index, SD: standard deviation

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Table 3. Comparison of pairwise mean differences in weight loss and reduction in BMI after 6-month follow-up among three groups

	Procedure		Mean difference	Std. error	P value
Weight loss after 6-month follow-up	Fundus IGBT	Antrum IGBT	4.05	0.60	P < 0.01
		Diet	6.37	0.62	
	Antrum IGBT	Diet	2.31	0.60	
Reduction in BMI after 6-month follow-up	Fundus IGBT	Antrum IGBT	1.54	0.23	P < 0.01
		Diet	2.42	0.24	
	Antrum IGBT	Diet	0.88	0.88	

IGBT: intragastric botulinum toxin injection, BMI: body mass index

Discussion

In a meta-analysis conducted in 2015, it was reported that IGBT could play an effective role in the treatment of obesity. The meta-analysis was conducted on seven studies and a total of 115 patients. However, there was heterogeneity in the application method of the injection. It was reported that injections distributed to the fundus and corpus outside of the antrum led to better results. However, there is no clear information on the number of injections made to the fundus and corpus and the technical practice. The number of patients was low, and heterogeneity was present among the procedures [5].

In a recent study, a diet group, an IGBT group, and a bariatric surgery group were compared. The IGBT group was given 100 units of injection to the antrum and 100 units to the fundus. When the results were examined, the highest effect was observed in the bariatric surgery group. However, the group in which botulinum toxin was applied to the gastric antrum and fundus also achieved significant weight loss. The study did not detect technically different results in terms of the sensitivity of gastric sections to botulinum. However, IGBT was found to be an effective method for weight loss [6].

BT-A injection inhibits interdigestive motility complexes in the antrum, preventing the passage of solid food towards the pylorus. This blocks gastric emptying and also inhibits the secretion of ghrelin, a potent hormone that stimulates appetite [7]. Therefore, targeting both the inhibition of antral motility complexes and ghrelin inhibition improves and optimizes weight loss outcomes associated with intragastric BT-A injections (IGBT).

This article aims to evaluate the efficacy of endoscopic intragastric BT-A injection for the treatment of morbid obesity in a prospective study. Fifty-six patients participated in the study. Each patient was given 250 units of BT-A injected into the antrum. Patients' weights were measured monthly for 5 months. As a result, an average weight loss of 9 kg and a decrease of approximately 3 BMI units were observed after the procedure. Furthermore, a high number of patients reported a decrease in appetite following the application. The study indicated that larger randomized prospective studies are needed. Limitations of the study include the use of a limited number of patients and the absence of a control group. The study notes that only the antrum region of the stomach was injected with botulinum toxin A [8].

Some literature studies emphasize that IGBT is not an effective treatment. A study of 13 patients from Turkey found IGBT to be an ineffective weight loss tool [9].

Garcia-Compean and Garza (2008) published a meta-analysis comprising six studies in the format of an academic medical article. They observed positive weight loss in only one study, which was the only study that involved eight injections into the fundus, unlike the other five studies that only involved antral injections of IGBT [3]. When evaluating a total of 157 patients, IGBT was found to be superior to diet therapy, and IGBT applied to the fundal region was found to be more effective than IGBT applied to the antral region. However, there were limitations in obtaining these results. For example, the short observation period in the study may limit the determination of long-term effects of the results. Also, conducting the study on a small sample may limit the generalization of the results. Therefore, we can conclude that IGBT and botulinum toxin applied to the fundal region may be effective options for obesity treatment, but further research needs to be conducted on larger sample groups to gain a clearer understanding of their effectiveness and safety.

Conclusion

The results of the present study show that antral and fundus dominant IGBT can be considered as a potential treatment option for obese patients with a BMI between 30 and 35 who do not meet the criteria for bariatric surgery.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
The study was conducted in accordance with the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects and the protocol was approved by the Ethics Committee of Cukurova University (Date: 05.05.2023, Meeting No: 133).

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