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Endoscopic botulinium toxin-A application in the treatment of obesity: The effect of dose and application area on treatment success

Ismail Ozsan[a,*], Ahmet Yekta Tuzun[b]

[a] *Okan University, Faculty of Medicine, Department of General Surgery, Istanbul, Türkiye*
[b] *Izmir Economy University, Medicalpoint Hospital, Department of Gastroenterology, Izmir, Türkiye*

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Abstract

Aim: In this study, it was aimed to examine the effect of dose and region on the effectiveness of Endoscopic botulinum toxin A application in the fight against obesity.

Materials and Methods: A total of 446 patients who applied to our clinic with the complaint of weight were included in the study. Endoscopic botulinum toxin A was administered at doses of 300 U (n=74), 400 U (n=172) and 500 U (n=200) according to the weight and Body Mass Index (BMI) values of the patients. Patients were divided into three groups in the Preploric, Cardia and Fundus regions, after 125 U of Endoscopic Botulinum toxin A application to each region, and 125 U application to one region.

Results: Initial BMI, weight difference, last BMI and BMI differences were statistically significant between patient groups according to dose and area (p=0.000). All BMI differences between paired dose and area groups were statistically significant (p=0.000). BMI difference was significantly correlated with gender (r=0.108; p=0.023), Initial BMI (r=0.266; p=0.000), weight (r=0.219; p=0.000), dose (r=0.834; p=0.000), and area (r=0.200; p=0.000). Effects of initial BMI (B=0.031; p=0.031), dose (B=1.423; p=0.000) and area (B=0.316; p=0.000) on BMI difference were statistically significant.

Conclusion: Optimum results are obtained in the application of fundus region with a density of 500 U in total, but at levels or values below this, the results may not be effective. Weight loss with the Endoscopic botulinium toxin-A method with the appropriate dose and area is an effective and usable method in the fight against obesity.

Introduction

Obesity is an increasing problem today and constitutes an important part of not only individuals but also public health and global health problems [1,2]. Obesity is an important public health problem not only because of the health conditions it causes primarily, but also because it is secondary to other chronic diseases such as pulmonary diseases, high pressure, or cardiovascular diseases [3,4]. Obesity is also a health problem that significantly affects the fight against diseases, especially the treatment process, surgical processes, and significantly affects and reduces the quality of life of the individual. For this reason, many methods have been developed to combat obesity, and new studies are being conducted on the effectiveness of these methods and the factors affecting these activities.

Although medicated treatment methods, diet and invasive procedures are mainly used in the fight against obesity, surgical methods are used in cases with advanced obesity and emergency health conditions [4,5]. Gastric Sleeve, Gastric Bypass and other fat removal methods are the leading surgical methods. Although the effectiveness of these methods has increased greatly and the risk levels have decreased significantly in recent years, it is still seen as an important cause of mortality today [6,7]. Even in operations performed with the highest quality materials and experience, all deficiencies have been eliminated, there may be situations that result in mortality or, at best, require intensive care, albeit in a small number of cases. Therefore, non-invasive or non-surgical methods, especially Endoscopic botulinum toxin A, have become increasingly common in recent years.

Botulinium toxin A is a neurotoxin, produced from the fermentation of Clostridium botulinum type A, and is mostly used in the field of cosmetics. Botulinium toxin A, which has a widespread effect in reducing wrinkles on the face temporarily, has been applied to the stomach wall with

*Corresponding author:
Email address: dr_ozsanozsan@yahoo.com (Ismail Ozsan)

various doses and methods in recent years, and has been used effectively in weight loss and in the fight against obesity [8,9].

Endoscopic botulinum toxin A application is a method that has come to the fore in the fight against obesity in recent years and its effectiveness has been demonstrated both clinically and in various studies. However, due to the fact that the application of Endoscopic botulinium toxin A is new compared to other obesity control methods and the studies on the subject are limited, there are not enough studies on dose and region in practice. Therefore, in this study, it was aimed to examine the effect of dose and region on the effectiveness of Endoscopic botulinium toxin A application in the fight against obesity.

Materials and Methods

Research sample

In this retrospective cross-sectional study, a total of 446 patients who applied to our clinic with the complaint of weight were included in the study attempting to İzmir İsmail Özsan clinic between May 2022 and May 2023. Ethics committee approval was received for the study from Izmir Bakırçay University Non-Interventional Clinical Research Ethics Committee (date: 07.12.2022, decision no: 799). Endoscopic botulinum toxin A was administered at doses of 300 U (n=74), 400 U (n=172) and 500 U (n=200) according to the weight and BMI values of the patients according to Topazian et al [10]. Patients were divided into three groups in the Preploric, Cardia and Fundus regions, after 125 U of Endoscopic botulinum toxin A application to each region, and 125 U application to one region. Accordingly, 195 patients were included in the Preploric dense group, 126 patients in the Cardia dense group, and 125 patients in the fundus dense group. Dose groups were defined as total 300 U, total 400 U and total 500 U botox groups. Area groups were defined as Preploric, Cardia and Fundus dense groups.

Age, gender, Ursactive usage, hormone, hunger, medicine, diet, illness parameters were recorded. Hormone parameter means hormone usage for weight loss. Hunger means periodic feast, medicine means usage of medicine for weight loss. Diet and illness parameters shows comorbidity with obesity. Cohen et al [11] reported that the representative power of 384 or more samples is sufficient for the population between 1-5 million. According to this, since the research was population based and there was no similar study, power analysis was not performed and random sampling method was used.

Application

Endoscopy and botox procedures were performed by a single surgeon. Before the procedure, the stomach was evaluated with endoscope in terms of benign and malignant diseases. cancer patients, ulcer patients and patients with other diseases were not included in the study. Pyloric tone was evaluated with endoscopy before the procedure. No manometric measurements were made in the study; it was decided by the visual experience of the endoscopist. Afterwards, under surgical sedation, Clostridium botulinum toxin was administered to 500 units of the antrum according to the surrounding groups. After the procedure, the patient was kept under observation for one hour. The patients were followed up once a week for 6 months by a single dietitian. After the procedure, a liquid diet was applied for the first week, followed by a carbohydrate-restricted and protein-based diet.

Statistical analysis

Nominal and ordinal data were defined with frequencies, measurement values with mean and standard deviation values. Since it is a cross-sectional observational study, data were not subjected to pre-processing. Because of retrospective structure of the study, patient files including extreme/outlier values were excluded from the study. Only patient files having not extreme values were subjected to the study. Kolmogorov Smirnov Test was performed for normality test. The Kruskal Wallis test was used for the difference between the groups of the parameters that did not fit the normal distribution, and the Mann Whitney U test was used for the post hoc tests of the paired groups. Spearman's rho correlation was used for correlation. Since regression models include linearization deviations [12], Generalized Linear Model (Logit Model) analyzes were used in relational screening analysis. Since Generalized Linear Model (Logit) includes nominal and ordinal parameters, a function type model was not used, relationship model was used. In retrospective studies, validity of models are based on general statistical approach, and no further validation methods used in prospective studies are used. Thus, general statistical approach was used in the study [13]. All analyzes were performed with the SPSS 25.0 program at 95% confidence interval and 0.05 significance level.

Results

Age, gender, Ursactive usage, hormone, hunger, medicine usage, diet, illness and last weight differences between dose groups were statistically insignificant (p=0.000). BMI, initial weight, weight difference and BMI differences were significant between patient groups (p=0.000). Post Hoc test results showed that all BMI differences between paired dose groups were statistically significant (p=0.000) (Table 1). Age, gender, Ursactive usage, hormone, hunger, medicine usage, diet, illness, initial weight and last weight differences between area groups were statistically insignificant (p>0.05). Initial BMI, weight difference, last BMI and BMI differences were significant between patient groups (p=0.000). Post Hoc test results showed that all BMI differences between paired area groups were statistically significant (p=0.000) (Table 2). Spearman's rho correlation analysis results showed that BMI difference was significantly correlated with gender (r=0.108; p=0.023), Initial BMI (r=0.266; p=0.000), weight (r=0.219; p=0.000), dose (r=0.834; p=0.000), and area (r=0.200; p=0.000) (Table 3). Although gender was a correlated factor at univariate level, its effect on BMI difference was insignificant at multivariate level (p>0.05). Effects of initial BMI (B=0.031; p=0.031), dose (B=1.423; p=0.000) and area (B=0.316; p=0.000) on BMI difference were statistically significant (Table 4). BMI difference mean was higher in both 500 U dose and fundus are groups with a wider range (Figure 1).

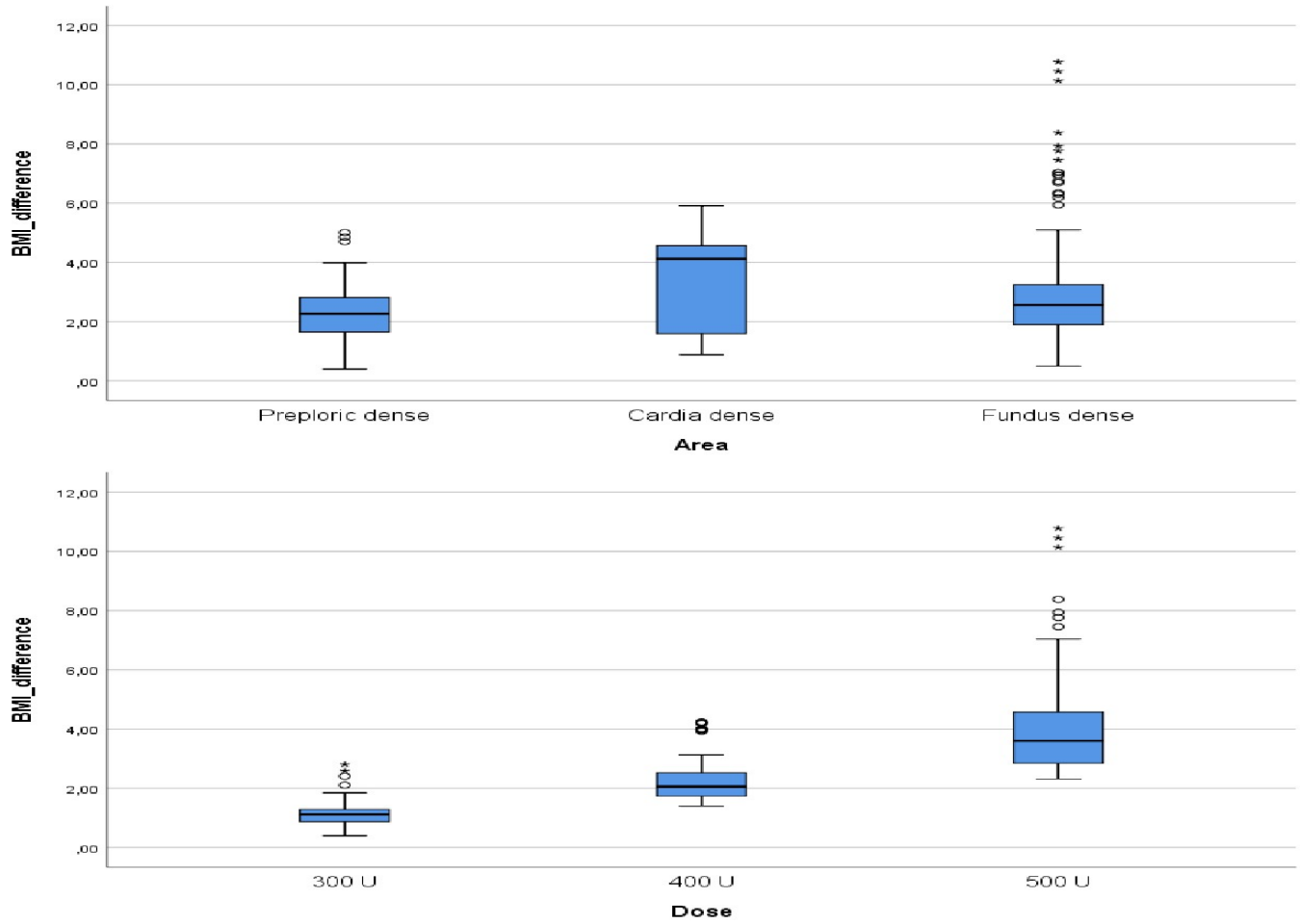

Figure 1. Ranges and BMI difference changes based on dose and area

Table 1. Baseline and progress parameters of patients according to dose groups and difference analysis results.

Dose	300 U (1)	400 U (2)	500 U (3)	p value
Age	36.07±10.81	35.18±8.99	35.27±9.24	0.950[a]
Gender, females, n (%)	68 (91.9)	147 (85.5)	162 (81.0)	0.079[b]
Ursactive, n (%)	2 (2.7)	4 (2.3)	7 (3.5)	0.792[b]
Hormone, n (%)	2 (2.7)	3 (1.7)	9 (4.5)	0.296[b]
Hunger, n (%)				
Low		2 (1.2)	4 (2.0)	
Moderate	22 (29.7)	56 (32.6)	69 (34.5)	0.072[b]
High	44 (59.5)	80 (46.5)	107 (53.5)	
Very high	8 (10.8)	34 (19.8)	20 (10.9)	
Medicine, n (%)	31 (41.9)	61 (35.5)	64 (32.0)	0.308[b]
Diet, n (%)	54 (73.0)	126 (73.3)	154 (77.0)	0.650[b]
Illness, n (%)	28 (37.8)	61 (35.5)	77 (38.5)	0.827[b]
Initial BMI	28.90±3.40	30.66±3.54	31.57±3.75	0.000[a] 2>1, 3>1, 3>2
Initial Height	166.96±6.16	167.49±7.59	167.64±8.60	0.940[a]
Initial Weigh	80.52±10.16	86.15±12.68	89.21±15.19	0.000[a] 2>1, 3>1
Last weight	77.37±9.91	79.91±12.40	77.78±13.82	0.125[a]
Weight difference	3.15±1.30	6.24±1.95	11.43±4.95	0.000[a] 2>1, 3>1, 3>2
Last BMI	27.77±3.37	28.43±3.55	27.58±3.74	0.039[a] 2>3
BMI difference	-1.12±0.43	-2.22±0.67	-3.99±1.46	0.000[a] 2>1, 3>1, 3>2

[a]: Kruskal Wallis Test, [b]: Chi-Square Test, [c]: Mann Whitney U Test (Post Hoc), SD: Standard Deviation, BMI: Body Mass Index, U: Unit.

Table 2. Baseline and progress parameters of patients according to area groups and difference analysis results.

Dose	Preoploric dense (1)	Cardia dense (2)	Fundus dense (3)	p value
Age	36.04±9.45	34.31±9.46	35.38±9.26	0.241[a]
Gender, females, n (%)	168 (86.2)	107 (84.9)	102 (81.6)	0.541[b]
Ursactive, n (%)	4 (2.1)	5 (4.0)	4 (3.2)	0.591[b]
Hormone, n (%)	6 (3.1)	6 (4.8)	2 (1.6)	0.345[b]
Hunger, n (%)				
Low	1 (0.5)	1 (0.8)	4 (3.2)	
Moderate	63 (32.3)	47 (37.3)	37 (29.6)	0.479[b]
High	103 (52.8)	62 (49.2)	66 (52.8)	
Very high	28 (14.4)	16 (12.7)	18 (14.4)	
Medicine, n (%)	69 (35.4)	47 (37.3)	40 (32.0)	0.670[b]
Diet, n (%)	141 (72.3)	100 (79.4)	93 (74.4)	0.359[b]
Illness, n (%)	77 (39.5)	47 (37.3)	42 (33.6)	0.568[b]
Initial BMI	30.28±3.64	30.73±3.08	31.60±4.29	0.013[a] 3>1
Initial Height	167.22±7.46	167.56±8.52	167.77±7.75	0.828[a]
Initial Weigh	84.78±12.46	86.76±13.58	89.24±15.64	0.072[a]
Last weight	78.50±11.84	76.57±12.45	80.56±14.04	0.093[a]
Weight difference	6.28±2.43	10.19±4.84	8.68±6.32	0.000[a] 2>1, 3>1, 2>3
Last BMI	28.04±3.55	27.17±3.02	28.56±4.14	0.037[a] 3>2
BMI difference	2.24±0.84	3.56±1.44	3.04±2.06	0.000[a] 2>1, 3>1, 2>3

[a]: Kruskal Wallis Test, [b]: Chi-Square Test, [c]: Mann Whitney U Test (Post Hoc), SD: Standard Deviation, BMI: Body Mass Index, U: Unit.

Table 3. Spearman's rho correlation between BMI difference and related parameters.

BMI difference	r	p
Gender	0.108*	0.023
Age	-0.013	0.779
Initial BMI	0.266**	0.000
Height	0.011	0.811
Weigh	0.219**	0.000
Ursactive	0.062	0.195
Hormone	0.052	0.272
Hunger	-0.057	0.232
Medicine	-0.063	0.185
Diet	0.075	0.112
Illness	0.016	0.739
Dose	0.834**	0.000
Area	0.200**	0.000

*p<0.05 **p<0.01 BMI: Body Mass Index.

Table 4. Generalized Linear Model (Logit Model) for BMI difference and correlated factors at multivariate level.

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	p
(Intercept)	-1.830	0.48	-2.771	-0.89	14.52	1	0.000
[Gender=Female]	-.134	0.14	-0.412	0.14	0.90	1	0.343
[Gender=Male]	0	.	.	.	.	.	.
Initial BMI	.031	0.01	0.003	0.06	4.68	1	0.031
Dose	1.423	0.07	1.286	1.56	416.91 2	1	0.000
Area	.316	0.06	0.199	0.43	7.88	1	0.000
(Scale)	1.082	0.07	0.949	1.23			

BMI: Body Mass Index, B: Regression Coefficient, df: Degree of freedom.

Discussion

In this study, the effect of dose and region on the effectiveness of Endoscopic botulinium toxin A application in the fight against obesity and weight loss was included, and in this context, the six-month weight change results of the patients who were treated at different doses and regions were examined. In the study, it was seen that the dose and application site had a significant effect on weight loss with Endoscopic botulinium toxin A.

Although botulinium toxin A is widely used in the field of cosmetics and aesthetics in the literature [14-16], it has been used in the fight against obesity in recent years, as well as in various gastrointestinal system diseases endoscopically [17-20]. Botulinium toxin A, which is applied in various doses to various parts of the stomach, can achieve much more effective and lower-risk results in weight loss compared to other methods of combating obesity [21-23].

In the literature, there are studies reporting that Endoscopic botulinium toxin A is effective in weight loss [21-24] as well as studies reporting that it is not effective [25]. Although the application and method are similar in these studies, the difference in the application area and dose draws attention. Although there was a significant weight reduction in all three dose groups in our study, the most effective weight gain was achieved in a total dose of 500 U and fundus-weighted applications. This application was in the form of 125 U Preoploric 250 U Fundus and 125 U Cardia. Although the dose given is related to the baseline BMI and the patient's weight, the insignificance of the difference between the final weights indicates that the 500 U value may be applicable for all patients.

Although great progress has been made in the fight against obesity, these methods still have side effects such as serious mortality or infection, and require revision surgery or reapplications in the long term. Therefore, the application of Endoscopic botulinum toxin A provides an important and safer comfort during the weight loss phase, especially in patients whose BMI value has not exceeded 35. Compared to gastric balloon, which is one of the closest invasive methods, Endoscopic botulinium toxin A has a similar effect on appetite suppression and stomach volume reduction, and can be used in combination with gastric balloon in advanced BMI values [26].

The most important limitation of the research is that there are still reservations about the application of the Endoscopic botulinium toxin A method to the stomach by certain authorities, and therefore there are no domestic studies in the field. However, studies published in scientific and peer-reviewed journals today clearly reveal that the administration of Endoscopic botulinium toxin A to the stomach for weight loss is now a scientific method. In addition, the low-cost and short-term application of the method with the least harm shows its suitability in terms of medical ethics and science. In this respect, we think that these studies will increase in the future.

The most important contribution of the research to the field and the literature is that the previous studies examined the application of Endoscopic botulinium toxin A only with and without application, and there were no studies that looked at both the dose and the effect of the region. In this respect, the research makes an important contribution both for clinical applications and for future studies.

Conclusion

The results obtained in the study reveal that the differences in the literature on whether Endoscopic Botulinium toxin A application is effective in weight loss are related to the application area and dose. While optimum results are obtained in the application of fundus region with a density of 500 U in total, the results may not be effective at levels or values below this. Weight loss with the Endoscopic Botulinium toxin A method with the appropriate dose and area is an effective and usable method in the fight against obesity.

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Ethical approval

Ethics committee approval was received for the study from Izmir Bakırçay University Non-Interventional Clinical Research Ethics Committee (date: 07.12.2022, decision no: 799).

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