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The importance of the structure of pylorus in the success of the gastric botulinum toxin injections

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ABSTRACT

Introduction: In clinical practices, our success rate proved lower in patients with hypotonic pylorus who underwent gastric botulinum toxin A (GBTA) injection. To analyze this methodologically, we researched how considering the pyloric structure contributes to the treatment success in GBTA injection.

Materials and Methods: This study included 196 patients who underwent GBTA injection between 2017 and 2018. We measured their body mass indexes (BMI) before treatment (BT) and six months after treatment (AT). Upon no contraindications in the endoscopy, we applied GBTA 200 U to the patients. During the endoscopy, we named the pylori able to strain & relax spontaneously or by a stimulus and close firmly as normotonic pylorus (NP) and patients unable to close firmly and respond to the stimulus as hypotonic pylorus (HP). The patients were analyzed under three groups: G1, G2 and G3, which included patients with NP, HP and NP (+) HP, respectively. In independent group comparisons, we used the Mann-Whitney U test. Further, we made the dependent group comparisons using the Wilcoxon paired sample test. In all tests, a level of 0.05 was considered significant.

Results: Of the patients, 63.8% (125) were female and 36.2% (71) were male. Their mean age was 32.27±9.2 years. 148 and 48 of the patients had NP and HP, respectively. The median BMIs of groups were as follows: 35.5 (27.4–48) kg/m^2 BT and 32.55 (24–44.1) kg/m^2 AT in G3 with -2.95 kg/m^2 variation (p=0.048*), 35.7 (27.4–48) kg/m^2 BT and 32.35 (24–42.8) kg/m^2 AT in G1 with -3.35 kg/m^2 variation (p=0.036*), 35.1 (29–46.2) kg/m^2 BT and 34.15 (27.9–44.1) kg/m^2 AT in G2 with -0.95 kg/m^2 variation (p=0.098).

Conclusion: We recommend administering GBTA injection therapy especially to the patients with NP.

Keywords: Bariatric endoscopy; botulinum toxin; obesity; pyloric structure

Introduction

Obesity is one of the most important public health problems of our age.[1] Its incidence is escalating to an alarming degree with each passing year.[2] The therapies for obesity control include drug therapy, surgical treatment methods and the endoscopic bariatric interventions "gastric balloon placement" and "gastric Botulinum Toxin A (GBTA) injection". Since it is a minimally invasive, reversible and affordable therapy which can be easily applied during esophago-gastro-duodenoscopy and causes

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no organ loss, GBTA injection has been widely applied over the past years. With GBTA application, temporary paralysis occurs in the gastric muscles for 4–6 months, accordingly, gastric emptying time is prolonged, thus creating a feeling of fullness and fullness for a longer time. However, no consensus has yet been reached on the GBTA injection method and dosage. In the past practices, Botulinum Toxin A (BTA) was injected to many different regions of the stomach at different dose levels, but recently it has been stated that applying 200–300 U to the distal stomach proved more effective.[3] In line with our clinical experience, we observed that the GBTA injections failed in certain patients. In view of this, we re-examined the endoscopic video recordings of the patients who did not sufficiently benefit from GBTA injection, and we observed that those patients had a low pyloric tonus and mostly had bile reflux to the stomach. We have undertaken this study by taking these observations into consideration.

Materials and Methods

The study included the patients who underwent GBTA injection treatment between 2017 and 2018. The following patient information was recorded: The patients' age, gender, height and weight before treatment (BT) and six months after treatment (AT). We contacted the patients with missing information by phone and completed the missing information. The patients who were found to have no mass lesions, active bleeding, infection or suspicious lesions during the esophago-gastro-duodenoscopy performed, underwent GBTA injection during the same session. Two bottles of BTA, each containing 100 U lyophilized "Onabotulinum Toxin A" in its sales form on the market, were diluted with 20 cc saline solution in total (0.9% NaCl). The BTA solution prepared was injected to the intramuscular distance on the stomach wall at 20 different injection points in total -each injection being 1 cc- (including 10 proximal and 10 distal points) circularly at 3 to 4 cm proximal and distal portions in reference to incisura angularis during the endoscopy performed under sedation. After the endoscopic procedure, the patients were kept under surveillance for 4 hours, and then those with normal vital signs were discharged. The study included 196 patients with complete information. During endoscopy, we named the pylori which strain and relax spontaneously or by a stimulus from endoscope and can close firmly as normotonic pylorus (NP) and those which cannot close firmly, do not respond to the stimulus and remain open as hypotonic pylorus (HP). We replayed the endoscopic video recordings of the patients, and then analyzed the data obtained. Upon replaying the video recordings, we made the necessary revisions to the file records and clarified the information on the pyloric structure. With a consideration for the pyloric structure of patients, we compared and analyzed BMI values BT and AT. The patients were analyzed under three groups: G1, G2 and G3. G1, G2 and G3 included patients with NP, HP and NP(+)HP, respectively. Informed written consent was obtained from patients.

Statistical Analysis

We examined whether the data were suitable for normal distribution by using Kolmogorov-Smirnov and Shapiro-Wilk tests based on the number of subjects. Since the data were not suitable for normal distribution, we summarized the data in median (minimum-maximum) values. In independent group comparisons, we used Mann-Whitney U test. Further, we made the dependent group comparisons using Wilcoxon paired sample test. In all tests, a level of 0,05 was considered significant.

Results

Of the patients, 63.8% (125) were female and 36.2% (71) were male. Their mean age was 32.27±9.2 years. According to the pyloric structure, the rates of those with NP and HP were 75.5% (148) and 24.5% (48), respectively. The mean ages of patients by groups were 31.51±9.23 years in G1, 34.58±8.77 in G2, 32.27±9.2 years in G3 (Table 1).

In G3, the median BMI was 35.5 (27.4–48) kg/m^2 BT and 32.55 (24–44.1) kg/m^2 AT, with a variation of -2.95 kg/m^2 (p=0.048*). In G1, the median BMI was 35.7 (27.4–48) kg/m^2 BT and 32.35 (24-42.8) kg/m^2 AT, with a variation of -3.35 kg/m^2 (p=0.036*). In G2, the median BMI was 35.1 (29–46.2) kg/m^2 BT and 34.15 (27.9–44.1) kg/m^2 AT, with a variation of -0.95 kg/m^2 (p=0.098*) (Table 2).

Discussion

Obesity is today a health problem with an incidence escalating to an alarming degree as a natural consequence of the change in the industrial production models towards automation especially after the World War II, the increased carbohydrate and fat consumption resulting from the increasing tendency to consume fast food, the acceleration of developments towards less energy consumption in housework, and the sedentary lifestyle adopted especially as a result of the increased screen dependency in the past 25

Table 1. Number and mean ages of patients by pyloric structure

	Pyloric Structure					
	Normotonic (G1)		Hypotonic (G2)		Total (G3)	
	n	%	n	%	n	%
Number of patients						
Female	98	66.2	27	56.3	125	63.8
Male	50	33.8	21	43.7	71	36.2
Total	148		48		196	
Age (year)						
Mean±SD	31.51±9.23		34.58±8.77		32.27±9.2	
Median (min.-max.)	30 (18–63)		35.5 (19–54)		30 (18–63)	

SD: Standard deviation; Min.: Minimum; Max.: Maximum.

Table 2. Body mass indexes before and after treatment

	Pyloric structure					
	Normotonic (G1)		Hypotonic (G2)		Total (G3)	
	n	(min–max)	n	(min–max)	n	(min–max)
BMI median (min.-max.) (kg/m²)						
Before treatment	35.7	27.4–48	35.1	29–46.2	35.5	27.4–48
After treatment	32.35	24–42.8	34.15	27.9–44.1	32.55	24–44.1
Variation	-3.35		-0.95		-2.95	
p	0.036*		0.098		0.048*	

BMI: Body mass index; Min.: Minimum; Max.: Maximum.

years. Therefore, we need to first consider obesity as a public health problem, and accordingly, keep the preventive medicine at the forefront. However, if dietary practices remain useless after the development of obesity, it should be treated properly. The treatment methods most frequently used for obesity include drug therapy, surgical treatment methods, gastric balloon placement and the GBTA injection. Though, there is still no standardized method in GBTA injection applications, which makes it extremely difficult to evaluate the treatment results objectively. Although it is stated in some studies that the application is successful, there are still a few studies reporting negative opinions on its success. Sanchez Torralvo et al.[1] suggest in their meta-analysis that IGBTA injection may be a useful and safe method in the treatment of obesity, however there is a need for more well-designed, placebo-controlled and long-term studies with a sufficiently large sample size. In their study, Gui et al.[4] report that GBTA injection causes weight loss but this is not statistically significant.

Having evaluated the BMI results before and six months after the treatment of the patients who underwent GBTA injection, we concluded that the difference therebetween was significant. Nonetheless, our success rate was high in some patients, yet there were patients in whom we achieved only limited success. We observed that those patients had a low pyloric tonus, of whom pylorus remained constantly open and who had significantly alkaline reflux gastritis. Although GBTA injection caused weight loss in each of the groups, namely G1, G2 and G3, the success rate was relatively higher in G1. Park et al.[5] report in their study that applying BTA to the gastric antrum is an effective treatment for obesity and may help improve lipid profile by increasing gastric emptying time. Also, Li et al.[6] point out in their study that BTA injection was successful in weight loss. Foschi et al.[7] show in their study that Botulinum Toxin A facilitates weight loss in obese patients.

On another note, Coskun et al.[8] report in their experimental study that a significant weight loss was achieved when they applied BTA to gastric antrum in obese rats.

Today, we experience difficulties in analyzing the data due to the lack of standardized practices in GBTA treatment. Topazian et al.[9] report that the results would be successful if GBTA injection is performed under the guidance of endoscopic ultrasonography (EUS). However, the EUS method is not used in all practices, and the regions and doses used for BTA injection may vary. Under any circumstances, the vast majority of studies on the subject show that a significant weight loss has been achieved.

Conclusion

GBTA injection procedure offers significant advantages from ease of application to short duration of application, reasonable treatment efficiency, being reversible and causing no organ loss. However, our results need to be supported by more detailed and extensive studies. When applied to normotonic patients, GBTA injection treatment may produce more favorable results.

Disclosures

Ethichs Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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