



Comparison of the short-term effects of intragastric balloon and botulinum toxin injection on weight loss

İntragastrik balon ve botulinum toksin enjeksiyonunun kilo kaybı üzerine kısa dönem etkilerinin karşılaştırılması

Muzaffer Al¹

Abstract

Aim: To compare the effects of endoscopic intragastric balloon (IGB) placement and intragastric botulinum toxin-A (BTX-A) injection in terms of weight loss among patients with non-morbid obesity.

Methods: This retrospective cohort study was conducted between 01.08.2020 and 01.01.2022. A total of 39 patients with a body mass index (BMI) of <40 without comorbidities were included in the study. Nineteen underwent intragastric BTX-A injection and 20 underwent IGB placement. Patients were evaluated 1 month and 6 months after the procedures.

Results: Mean age was 39.4 ± 8.6 in the BTX-A group and 37.3 ± 10.4 in the IGB group ($p = 0.496$). 78.9% of the BTX-A group and 75.0% of the IGB group were female ($p = 1.000$). In both groups, the median weight 1 month after the procedure was significantly lower than before the procedure, and the median weight 6 months after the procedure was significantly lower than 1 month after the procedure ($p < 0.001$ for both groups). The median weight loss in the IGB group at both the 1st and 6th months was significantly greater than the corresponding values of the BTX-A group ($p < 0.001$ for both).

Conclusion: IGB insertion appears to be a more successful endoscopic bariatric procedure than intragastric BTX-A injection, as measured by weight loss at post-intervention 1 month and 6 months. IGB may be preferred in patients with a BMI below 40 without obesity-related comorbidity.

Keywords: Obesity, endoscopic bariatric procedures, intragastric balloon placement, intragastric botulinum toxin-A injection, weight loss.

¹ Near East University, Faculty of Medicine, Department of Surgery, Nicosia, Cyprus.



MA: 0000-0002-0187-3247

Ethics Committee Approval: This study was approved by Ethical Committee of Buyuk Anadolu Hospital (21.05.2020/05-218614).

Etik Kurul Onayı: Bu çalışma Büyük Anadolu Hastanesi Etik Kurulu tarafından onaylanmıştır. (21.05.2020/05-218614).

Conflict of Interest: No conflict of interest was declared by the author.

Çıkar Çatışması: Yazar çıkar çatışması bildirmemiştir.

Financial Disclosure: The author declared that this case has received no financial support.

Finansal Destek: Yazar bu çalışma için finansal destek almadığını beyan etmiştir.

Geliş Tarihi / Received: 30.08.2022

Kabul Tarihi / Accepted: 17.10.2022

Yayın Tarihi / Published: 20.10.2022

Sorumlu yazar / Corresponding author:
Muzaffer Al

Adres/Address: Department of Surgery, Near East University, Faculty of Medicine, Nicosia, Cyprus.

e-mail: drmuzaffer61@hotmail.com

Tel/Phone: +90542 262 7500

Copyright © ACEM

Öz

Amaç: Morbid obez olmayan hastalarda endoskopik intragastrik balon (IGB) yerleştirme ve intragastrik botulinum toksin-A (BTX-A) enjeksiyonunun kilo kaybı açısından etkilerini karşılaştırmak.

Yöntemler: Bu retrospektif kohort çalışması 01.08.2020 ile 01.01.2022 tarihleri arasında gerçekleştirildi. Beden kitle indeksi (BKİ) <40 olan ve komorbiditesi olmayan toplam 39 hasta çalışmaya dahil edildi. Olguların 19'una intragastrik BTX-A enjeksiyonu ve 20'sine IGB yerleştirilmesi yapıldı. Hastalar işlemlerden 1 ay ve 6 ay sonra değerlendirildi.

Bulgular: Ortalama yaş BTX-A grubunda $39,4 \pm 8,6$ ve IGB grubunda $37,3 \pm 10,4$ idi ($p = 0,496$). BTX-A grubunun %78,9'u ve IGB grubunun %75,0'ı kadındı ($p=1.000$). Her iki grupta da işlem öncesi ile karşılaştırıldığında işlemden 1 ay sonra ve işlemden 1 ay sonrası ile karşılaştırıldığında işlemden 6 ay sonra ortanca ağırlık anlamlı düzeyde azaldı (her iki grup için $p<0,001$). BTX-A grubu ile karşılaştırıldığında hem 1. hem de 6. ayda medyan kilo kaybı IGB grubunda anlamlı düzeyde daha fazlaydı (her ikisi için $p < 0,001$).

Sonuç: Çalışmamızda müdahale sonrası 1. ve 6. ayda kilo kaybı ile ölçüldüğü üzere, IGB yerleştirilmesi intragastrik BTX-A enjeksiyonundan daha başarılı bir endoskopik bariatrik prosedür gibi görünmektedir. Obezite ile ilişkili komorbiditesi olmayan BKİ 40'ın altında olan hastalarda IGB tercih edilebilir.

Anahtar Kelimeler: Obezite, endoskopik bariatrik prosedürler, intragastrik balon yerleştirme, intragastrik botulinum toksin-A enjeksiyonu, kilo kaybı.

Introduction

Obesity is a significant threat to human health owing to the high prevalence of morbidity and mortality caused by the condition itself and associated comorbidities [1]. Current guidelines suggest bariatric surgery as the most potent treatment tool for patients with class-3 obesity or those with class-2 obesity compounded by an obesity-related comorbidity [2-4]. However, although treating obesity in early stages is advised before the development of comorbidities, bariatric surgery is not a first-line option [2, 4-6]. Endoscopic bariatric procedures (EBPs) are more effective than pharmacotherapy and lifestyle changes and offer a lower rate of side effects compared to bariatric surgery [7, 8]. Therefore, EBPs have evolved tremendously in last decade and can be applied to patients in all the stages of obesity [6, 9].

EBPs can be categorized as follows: space-occupying devices, gastric restrictive methods, malabsorptive procedures, regulating gastric emptying, and others [6]. Intra-gastric balloon (IGB) placement, defined as the insertion of a space-occupying device into the stomach with the aid of endoscopy, is a reversible nonsurgical bariatric procedure available since the 1980s [6, 10, 11]. It was designed to reduce food intake by inducing early satiety [10, 11]. Its safety and efficacy has been reported in various publications [12, 13]. IGB can be applied both as a bridge procedure before surgery in severely obese patients and as a primary procedure for less-severe patients [4, 14, 15]. Close follow-up with a dedicated dietitian and surgeon increases the likelihood of success, yielding comparable outcomes to surgery [4, 9]. However, with this procedure, it has been reported that maintaining weight loss is difficult in the long-term [16].

Endoscopic intra-gastric botulinum toxin-A (BTX-A) injection is a procedure which primarily regulates gastric emptying by causing gastroparesis [6]. BTX-A injection allows early satiety, extends the duration of satiety, inhibits the release of acetylcholine (delaying gastric emptying), and inhibits ghrelin release (a potent hunger-stimulating hormone) [1, 6, 17]. Although its application as an EBP is known to be safe, results concerning weight loss are inconsistent, particularly in the long-term [2, 7, 18, 19].

The number of studies in the literature comparing the success of these two EBPs, whose indications are similar to each other, is quite limited. Overall, the literature suggests greater bariatric success and fewer procedural complaints from IGB placement [20-22]; however, as mentioned, there are various inconsistencies. Thus, we aimed to compare the success in weight loss of both modalities with a follow-up of 6 months, and additionally, to assess short-term bariatric effects.

Material and methods

Study design and ethical issues

This retrospective cohort study was initiated after the local ethical committee approval (Ethical Committee of Buyuk Anadolu Hospital, 21.05.2020/05-218614) and conducted according to the principles of the Declaration of Helsinki and its later amendments at our bariatric surgery Center of Excellence (COE), Department of General Surgery, Büyük Anadolu Hospital, Samsun, Turkey between 01.08.2020 and 01.01.2022.

Participants and data collection

A total of 39 patients who were overweight or had class 1 or class 2 obesity without comorbidity underwent EBPs during the study period. Nineteen underwent endoscopic intra-gastric BTX-A injection, and 20 underwent endoscopic IGB placement.

Patients younger than 18 years, patients with obesity related comorbidities, individuals whose treatment was terminated and/or switched to another treatment protocol as a result of intolerance or complications, those who had undergone EBP for other purposes (before other operations, such as orthopedic surgery or bariatric surgery), patients with any psychiatric disorder, and subjects in whom follow-up data were unavailable or missing were excluded from the study.

Retrospective data including sociodemographic, anthropometric, surgical and weight loss at follow-up were obtained from a prospectively-maintained database.

Endoscopic procedures

The indication for EBP was defined in overweight or obese patients who did not respond positively to diet, exercise, and lifestyle modification for at least 6 months and met the following criteria: (i) having a body mass index (BMI) of <40 and (ii) not being diagnosed with any obesity-related comorbidity [6, 15]. The advantages and disadvantages and possible complications of the procedures were explained to the patients and the procedure to be applied was determined according to the patient's preference. Written informed consent forms were obtained from each patient before the procedure.

Endoscopic intra-gastric botulinum toxin-A injection: The procedure was applied in an outpatient endoscopy care unit under sedation anesthesia (midazolam 0.05 mg/kg, propofol 1 mg/kg). First, the patients underwent routine gastroscopy procedure. The patients were checked for any gastric or duodenal pathology. A total of 500 IU [7] Clostridium botulinum type-A toxin hemagglutinin complex (Dysport™; Ipsen Biopharm Ltd., UK) diluted with 20 ml of saline solution [21] was injected into the muscular layer of the stomach. Injections were made as follows: 10 spots (250 IU) at the antrum relatively close to the incisura angularis and 5 spots (125 IU) each to the corpus and fundus through a sclerotherapy needle (Interject™ 23G; Boston Scientific, USA). Each spot received 1 ml of injection volume. In the fundus, meticulous care was taken to not penetrate the diaphragm or myocardium. After checking for bleeding, patients were monitored for 1 hour after the procedure for any possible complication. A low-calorie liquid diet (1200 calories) was administered during the first week, a soft-solids diet in the second week, and a low-carbohydrate diet in the third week was provided for the patients under the follow-up of a dedicated dietitian. Feeling of satiety and weight loss were monitored in follow-up visits. Moderate physical activity was recommended for the patients.

Endoscopic intra-gastric balloon placement and removal: The procedure was applied in an ambulatory endoscopic care unit under sedation anesthesia (midazolam 0.05 mg/kg, propofol 1 mg/kg), in the left lateral decubitus position, and the removal procedure was done in the same way. Firstly, a routine gastroscopy procedure was performed to exclude any pathologies. Then, an intra-gastric fluid-filled balloon (Bariglobe™; Russia) was applied through the oropharyngeal route with the help of endoscopy according to the manufacturer's instructions. Under direct gastroscopic view, the balloons were filled with 500 ml of saline mixed with 10 ml of methylene blue. Tubing of the balloon was removed and the patient was monitored for 1 hour after the operation. A proton pump inhibitor (PPI) (pantoprazole 20 mg oral, once daily) and an antiemetic agent (ondansetron 8 mg oral, twice daily) were prescribed after the procedure. Patients were advised to continue PPI medication for the entire 6 months of follow-up. All patients were advised to adhere to a low-calorie liquid diet (1200 calories) in the first week, a soft-solid diet in the second week, and a normal diet in the third week after the

ACEM

procedure. All subjects were continuously monitored by a dedicated dietician until the IGB was removed. Moderate physical activity was recommended for the patients. At 6–12 months after placement, IGB was removed through upper gastrointestinal endoscopy under sedation anesthesia.

Follow-up

As a routine practice, patients are called for follow-up evaluations after surgery in the 1st week, 1st month, 3rd month and 6th month when these procedures are applied in our department. The 1st month and 6th month information recorded in these follow-up evaluations were obtained from the hospital records and were included in the analyses of this study.

Outcomes

The primary outcome was to compare weight loss success of two procedures and the secondary outcome was to compare the two approaches with regard to their efficacy in treating non-morbid obesity.

Statistical analysis

Data collected quantitatively were evaluated with IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Continuous data of groups were analyzed using the Mann-Whitney U test for non-parametric data, while the independent samples t-test was used for parametric data. The Chi-square test was used for categorical comparisons. Quantitative values were summarized with mean \pm SD values and median (minimum-maximum) values, depending on normality of distribution. Categorical values were reported with frequency and percentage. A p value less than 0.05 was regarded to show statistical significance.

Results

The overall mean age of patients was 38.3 ± 9.5 years. In the BTX-A group, mean age was 39.4 ± 8.6 years, while this value was 37.3 ± 10.4 years in the IGB group ($p = 0.496$). 78.9% of the BTX-A group and 75.0% of the IGB group were female ($p = 1.000$). The baseline median BMI of the IGB group [31.2 (29.2 - 33.3)] was significantly higher than that of the BTX-A group [32.5 (30.1 - 38.9)] ($p = 0.016$) (Table 1).

Table 1. Distribution of demographic, height and BMI characteristics by groups

	Total	IGB group	BTX-A group	p
Gender				
Male	9 (23.1%)	5 (25.0%)	4 (21.1%)	1.000
Female	30 (76.9%)	15 (75.0%)	15 (78.9%)	
Age (year)	38.3 ± 9.5	37.3 ± 10.4	39.4 ± 8.6	0.496
Height (m)	1.6 (1.5 - 1.9)	1.6 (1.5 - 1.8)	1.6 (1.5 - 1.9)	0.687
BMI (kg/m ²)	31.6 (29.2 - 38.9)	32.5 (30.1 - 38.9)	31.2 (29.2 - 33.3)	0.016

Normally distributed numerical data are presented as mean \pm standard deviation, non-normally distributed numerical data are presented with median (minimum - maximum) values, categorical data are presented as number (percentage) values.

Abbreviations; BMI: Body-mass index, BTX-A: Botulinum toxin-A, IGB: Intragastric balloon.

The median weight of the EBP groups at baseline and comparisons of weight loss (within-group and intergroup) during the post-procedure follow-up studies are summarized in Table 2 and Figure 1. In both groups, the median weight 1 month after the procedure was significantly lower than before the procedure, and the median weight 6 months after the procedure was significantly lower than both before the procedure and 1 month after the procedure ($p < 0.001$ for both groups). The median weight loss of the IGB group at both the 1st and 6th months was significantly higher than the BTX-A group ($p < 0.001$ for both times). No

severe complications were observed during the administration of either of the EBPs. Of note, although various mild, self-limiting side effects including nausea, vomiting, abdominal pain and abdominal discomfort were reported by some of the patients, none of these side effects required therapeutic intervention.

Table 2. Comparison of pre- and post-intervention weight values between the groups.

	Total	IGB group	BTX-A group	p*
Pre-procedural weight (kg)	84.0 (72.0 - 111.0) ^a	84.0 (74.0 - 106.0) ^a	80.0 (72.0 - 111.0) ^a	0.283
Post-procedural 1st month weight (kg)	78.0 (63.0 - 103.0) ^b	77.0 (63.0 - 97.0) ^b	78.0 (64.0 - 103.0) ^b	0.876
Post-procedural 6th month weight (kg)	69.5 (51.0 - 93.0) ^c	66.0 (51.0 - 83.0) ^c	72.0 (55.0 - 93.0) ^c	0.330
p**	<0.001	<0.001	<0.001	
Weight loss at 1st month (kg)	7.0 (2.0 - 12.0)	9.0 (5.0 - 12.0)	6.0 (2.0 - 8.0)	<0.001
Weight loss at 6th month (total weight loss) (kg)	16.0 (1.0 - 30.0)	19.0 (13.0 - 30.0)	13.0 (1.0 - 19.0)	<0.001

Data are presented with median (minimum - maximum) values.

a,b,c: There is a statistically significant difference between consecutive measurements shown with different letters.

* Inter-group comparison, ** Intra-group comparison.

Abbreviations; BTX-A: Botulinum toxin-A, IGB: Intragastric balloon.

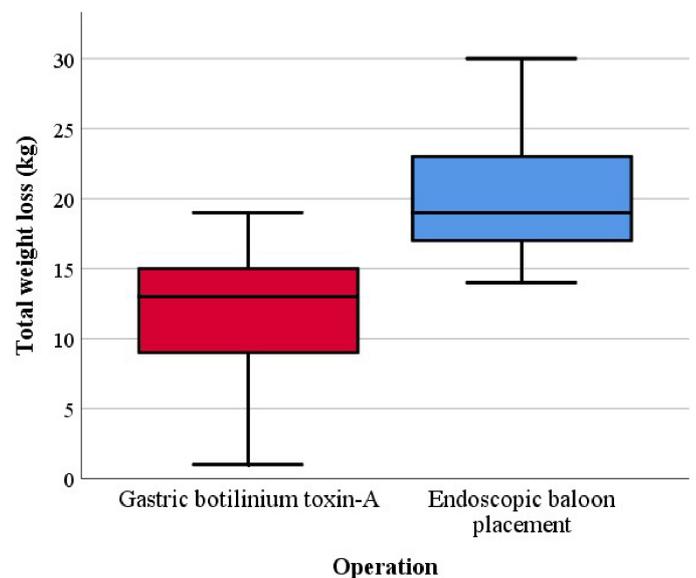


Figure 1. Comparison of weight loss at 6 months (total weight loss) between the two procedures.

Discussion

We found that the median weight loss values of IGB recipients at both 1 month and 6 months were significantly greater compared to BTX-A recipients. Although IGB appears to be superior in terms of short-term weight loss among patients with non-morbid obesity, it should also be noted that both interventions yielded significant weight loss from baseline to 1 month and from 1 month to 6 months.

Lifestyle changes and bariatric surgeries are both effective in the treatment of obesity; however, the former approach is often difficult for patients and the expensive bariatric surgeries may result in complications. These possible problems demonstrate the importance of EBP procedures and highlight the underlying reasons of their rising popularity [6, 10, 11, 14, 23, 24].

ACEM

IGB placement and intragastric BTX-A injection have the advantages of being reversible in the great majority of subjects, lower risks, and being feasible in patients who are not suitable for laparoscopic or open bariatric surgery or are at high surgical risk [6, 11, 14]. In this study, the bariatric success of these commonly used EBPs were compared. It was observed that the weight loss values in the 1st and 6th months of the patients who underwent IGB placement were significantly greater. There are very few results that have compared endoscopic IGB placement with endoscopic intragastric BTX-A injection in terms of weight loss success. In one of them, it was reported that IGB insertion was more successful than intragastric BTX-A injection (100 IU) in weight change (compared to baseline) at 1 week, 1 month, and 3 months [20]. In another study from Turkey, the success of BMI reduction after 6 months was compared in patients who received only IGB (group 1), only intragastric BTX-A injection (group 2), and the combination of the two procedures (group 3). While the decrease in BMI was significant in all three groups, it was reported that the amount of improvement was highest in group 3 and lowest in group 1 (group 3 > group 2 > group 1), and the same ranking was also valid for treatment tolerance [21]. In a systematic review and meta-analysis, the effects of some bariatric procedures (including both of these procedures) on gastric emptying and weight loss were investigated. As a result, IGB placement was found to be more effective than intragastric BTX-A injection in gastric emptying and gastric emptying-related weight loss. In addition, an interesting result of this study was that fluid-filled balloons delayed gastric emptying to a greater degree compared to air-filled balloons, and injections of >300 IU BTX-A also delayed gastric emptying more than lower doses [22].

The two methods have similarities such as being endoscopically applicable, being less invasive than bariatric surgery, having similar indications, and inferior long-term weight loss success [2, 7, 16]. Although both methods are safe and effective, BTX-A injection is reportedly more reliable which is an important advantage despite the fact that IGB placement has better short-term bariatric success, regardless of BTX-A dosage. IGB insertion may cause self-limiting side effects such as nausea, vomiting, generalized abdominal pain and/or discomfort, back pain, and acid reflux, and more severe side effects such as partial or complete gastrointestinal obstruction, injury to the lining of the digestive tract, stomach or esophagus; and gastric perforation [10, 16, 25, 26]. One review reported the adverse event rate of IGB as 28.5% [27]. In another study, it was reported that at least 1 device-related adverse event was seen in 98% of the patients undergoing IGB placement [28]. Otherwise, no significant side effects or neurophysiologic changes were reported after BTX-A injection [18, 29]. On the other hand, the efficacy of BTX-A is suggested to demonstrate a gradual decrease after surgery, especially towards the 6th month [2, 30]. Although the same BTX-A injection procedure was applied for each patient in the study, procedure standardization may not have been achieved, as BTX-A injection is a relatively more complex and operator-dependent procedure than IGB placement, and this may have affected the results.

In this study, the median weight loss at 1 month and 6 months after IGB placement was 9 and 19 kg, respectively. In two randomized clinical trials, some of the patients with a BMI between 30 and 40 underwent 12-month lifestyle modification only (control group), while other patients received an IGB for the first 6-month period in addition to this 12-month lifestyle modification. In both studies, it was reported that significantly more weight loss was achieved in the IGB group in the second 6-month period [28, 31]. In another RCT comparing air-filled IGB to a non-balloon sham capsule (placebo), patients undergoing IGB

placement had twice as much weight loss as the control group and sustained high weight loss at 48 weeks [32]. In some studies, IGB placement is applied before bariatric surgery as a pre-surgical bridging procedure [4, 6, 14, 15]. In this regard, Ashrafian et al. [14] presented their 16-year experience. They reported that short-term effective weight loss success of IGB placement alone was temporary, while long-term effects were much more pronounced when combined with bariatric surgery. Ball et al. [4] also showed that the use of IGB as the first step before definitive bariatric surgery significantly contributed to weight loss. Studies also show that the IGB should be removed 6-12 months after insertion [33]. A recently published meta-analysis of 20 RCTs reported significant results on short-term weight loss with the IGB procedure, but the sustainability of this weight loss could not be demonstrated [16]. Although we did not encounter any serious intraoperative or postoperative complications, more studies are needed to clarify potential complications.

Injection of BTX is widely used in patients with gastrointestinal smooth muscle disorders such as achalasia, diffuse esophageal spasms, gastroparesis, and Oddi sphincter dysfunction. In recent years, intragastric BTX-A injection has gained considerable popularity [34]. In the present study, after intragastric BTX-A injection, the median weight loss was 6 kg in the 1st month and 13 kg in the 6th month. However, available literature is exceedingly inconsistent [2, 7, 18, 19]. In a double-blind RCT, patients who underwent intraparietal endoscopic gastric BTX-A injection had significantly greater weight loss (11 vs 5.7 kg) and BMI reduction (4 vs 2 kg/m²) compared to placebo at 8 weeks [18]. Bang et al.'s meta-analysis also showed that intragastric BTX-A injection was effective for the treatment of obesity [7]. However, in another meta-analysis comparing the results of BTX-A versus saline injection, it was concluded that intragastric BTX-A injection was ineffective [2]. Also, other studies reported that BTX-A had no significant effect on weight loss [19, 30]. Methodological differences such as total toxin dose, the number of injections, the injection site, the distance between injections, injection needle gauge, auxiliary method (endoscopy only or combined endoscopy and ultrasound) may play a role in these conflicting findings [7, 22, 30, 34, 35]. The presence of other factors that may affect gastric emptying, such as pyloric tonus [36], and the high probability that the success of this procedure may be affected by the operator seem to be other such factors [36]. Another important issue is that intragastric BTX-A injection is a self-reversing procedure since effects disappear around 3 to 6 months after injection [2, 30]. Although this is an advantage with respect to the ease of terminating / changing intervention, it is also a considerable disadvantage since patients often expect such procedures to have long-lasting effects.

Some limitations of the study should be considered when evaluating the results. Since this was a single-center study and the number of participants was small, the generalizability of the results is limited. Another limitation regarding generalizability is the fact that the results are procured from a set of patients with non-morbid obesity who did not have comorbidities. Although data was collected from a prospectively-maintained database, the effects of additional possible factors such as adherence to diet, exercise or drug use, which may affect weight loss, could not be investigated. The absence of a control group can also be considered as a limitation. It has not been investigated whether weight loss is sustained after 6 months following either procedure (after balloon removal in the IGB group).

In conclusion, IGB insertion was found to be more successful than intragastric BTX-A injection in terms of weight loss both 1 month and 6 months after the procedures. It was

observed that both IGB placement and intragastric BTX-A injection continued to yield weight loss until the 6th month. Since only a specific subset of obese patients were included in this study, there is an apparent need for comprehensive studies involving obese patients with different characteristics in order to be able to draw definitive conclusions regarding the efficacy of these two bariatric procedures as primary treatment tools in obesity.

References

1. Stavrou G, Shrewsbury A, Kotzampassi K. Six intragastric balloons: Which to choose? *World J Gastrointest Endosc.* 2021;13:238-59.
2. Bustamante F, Brunaldi VO, Bernardo WM, De Moura DTH, De Moura ETH, Galvão M, et al. Obesity treatment with botulinum toxin-A is not effective: a systematic review and meta-analysis. *Obes Surg.* 2017;27:2716-23.
3. Emile SH, Mahdy T, Schou C, Kramer M, Shikora S. Systematic review of the outcome of single-anastomosis sleeve ileal (SASI) bypass in treatment of morbid obesity with proportion meta-analysis of improvement in diabetes mellitus. *Int J Surg.* 2021;92:106024.
4. Ball W, Raza SS, Loy J, Riera M, Pattar J, Adjepong S, et al. Effectiveness of intra-gastric balloon as a bridge to definitive surgery in the super obese. *Obes Surg.* 2019;29:1932-6.
5. Barrichello S, Badurdeen D, Hedjoudje A, Neto MG, Yance R, Veinert A, et al. The effect of the intra-gastric balloon on gastric emptying and the deemeester score. *Obes Surg.* 2020;30:38-45.
6. Behary J, Kumbhari V. Advances in the endoscopic management of obesity. *Gastroenterol Res Pract.* 2015;2015:757821.
7. Bang CS, Baik GH, Shin IS, Kim JB, Suk KT, Yoon JH, et al. Effect of intragastric injection of botulinum toxin A for the treatment of obesity: a meta-analysis and meta-regression. *Gastrointest Endosc.* 2015;81:1141-9. e7.
8. Lopez-Nava G, Asokkumar R, Lacruz T, Rull A, Beltran L, Bautista-Castaño I. The effect of weight loss and exercise on Health-Related Quality of Life (HRQOL) following Endoscopic Bariatric Therapies (EBT) for obesity. *Health Qual Life Outcomes.* 2020;18:130.
9. De Castro ML, Morales MJ, Martínez-Olmos MA, Pineda JR, Cid L, Estévez P, et al. Safety and effectiveness of gastric balloons associated with hypocaloric diet for the treatment of obesity. *Rev Esp Enferm Dig.* 2013;105:529-36.
10. Trang J, Lee SS, Miller A, Cruz Pico CX, Postoev A, Ibikunle I, et al. Incidence of nausea and vomiting after intragastric balloon placement in bariatric patients - A systematic review and meta-analysis. *Int J Surg.* 2018;57:22-9.
11. Barrichello Junior SA, Ribeiro IB, Fittipaldi-Fernandez RJ, Hoff AC, De Moura DTH, Minata MK, et al. Exclusively endoscopic approach to treating gastric perforation caused by an intragastric balloon: case series and literature review. *Endosc Int Open.* 2018;6:E1322-e9.
12. Zheng Y, Wang M, He S, Ji G. Short-term effects of intragastric balloon in association with conservative therapy on weight loss: a meta-analysis. *J Transl Med.* 2015;13:246.
13. Genco A, Cipriano M, Bacci V, Cuzzolaro M, Materia A, Raparelli L, et al. BioEnterics Intragastric Balloon (BIB): a short-term, double-blind, randomised, controlled, crossover study on weight reduction in morbidly obese patients. *Int J Obes (Lond).* 2006;30:129-33.
14. Ashrafian H, Monnich M, Braby TS, Smellie J, Bonanomi G, Efthimiou E. Intragastric balloon outcomes in super-obesity: a 16-year city center hospital series. *Surg Obes Relat Dis.* 2018;14:1691-9.
15. Telem DA, Ghaferi AA. Gastric Balloons for Weight Loss in 2020. *JAMA.* 2020;324:2206-7.
16. Saber AA, Shoar S, Almadani MW, Zundel N, Alkuwari MJ, Bashah MM, et al. Efficacy of first-time intragastric balloon in weight loss: A systematic review and meta-analysis of randomized controlled trials. *Obes Surg.* 2017;27:277-87.
17. Peeters TL. Potential of ghrelin as a therapeutic approach for gastrointestinal motility disorders. *Curr Opin Pharmacol.* 2006;6:553-8.
18. Foschi D, Corsi F, Lazzaroni M, Sangaletti O, Riva P, La Tartara G, et al. Treatment of morbid obesity by intraparietogastric administration of botulinum toxin: a randomized, double-blind, controlled study. *Int J Obes.* 2007;31:707-12.
19. Topazian M, Camilleri M, Enders FT, Clain JE, Gleeson FC, Levy MJ, et al. Gastric antral injections of botulinum toxin delay gastric emptying but do not reduce body weight. *Clin Gastroenterol Hepatol.* 2013;11:145-50. e1.
20. Durmus A, Durmus I, Akbas H, Tinkir NS. A456 The Efficacy of intragastric balloon versus botulinum toxin injection in obese patients. *Surg Obes Relat Dis.* 2019;15:S187-S8.
21. Kanlioz M, Ekici U, Tatli F, Karatas T. Efficacy of intragastric balloon placement and botulinum toxin injection in bariatric endoscopy. *Surg Laparosc Endosc Percutan Tech.* 2020;30:500-3.
22. Vargas EJ, Bazerbachi F, Calderon G, Prokop LJ, Gomez V, Murad MH, et al. Changes in time of gastric emptying after surgical and endoscopic bariatrics and weight loss: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2020;18:57-68. e5.
23. Kakarla VR, Nandipati K, Lalla M, Castro A, Merola S. Are laparoscopic bariatric procedures safe in superobese (BMI ≥ 50 kg/m²) patients? An NSQIP data analysis. *Surg Obes Relat Dis.* 2011;7:452-8.
24. Ribeiro IB, Gestic MA, Utrini MP, Chaim FDM, Chaim EA, Cazzo E. Drain amylase levels may indicate gastrojejunostomy leaks after roux-en-y gastric bypass. *Arq Gastroenterol.* 2018;55:66-72.
25. Charalambous MP, Thompson J, Efthimiou E. Late gastric perforation after insertion of intragastric balloon for weight loss—video case report and literature review. *Surg Obes Relat Dis.* 2012;8:121-3.
26. Al-Subaie S, Al-Barjas H, Al-Sabah S, Al-Helal S, Alfakharani A, Termos S. Laparoscopic management of a small bowel obstruction secondary to Elipse intragastric balloon migration: A case report. *Int J Surg Case Rep.* 2017;41:287-91.
27. Tate CM, Geliebter A. Intragastric balloon treatment for obesity: Review of recent studies. *Adv Ther.* 2017;34:1859-75.
28. Courcoulas A, Abu Dayyeh BK, Eaton L, Robinson J, Woodman G, Fusco M, et al. Intragastric balloon as an adjunct to lifestyle intervention: a randomized controlled trial. *Int J Obes (Lond).* 2017;41:427-33.
29. Kaya B, Esen Bulut N, Fersahoglu M. Is intragastric botulinum toxin A injection effective in obesity treatment? *Surg Res Pract.* 2020;2020:2419491.
30. Gui D, Mingrone G, Valenza V, Spada P, Mutignani M, Runfola M, et al. Effect of botulinum toxin antral injection on gastric emptying and weight reduction in obese patients: a pilot study. *Aliment Pharmacol Ther.* 2006;23:675-80.
31. Fuller NR, Pearson S, Lau NS, Włodarczyk J, Halstead MB, Tee HP, et al. An intragastric balloon in the treatment of obese individuals with metabolic syndrome: a randomized controlled study. *Obesity (Silver Spring).* 2013;21:1561-70.
32. Sullivan S, Swain J, Woodman G, Edmundowicz S, Hassanein T, Shayani V, et al. Randomized sham-controlled trial of the 6-month swallowable gas-filled intragastric balloon system for weight loss. *Surg Obes Relat Dis.* 2018;14:1876-89.
33. Keren D, Rainis T. Intragastric balloons for overweight populations—1 year post removal. *Obes Surg.* 2018;28:2368-73.
34. Wang TJ, Ryou M. Emerging endoscopic therapies for weight loss. *Gastrointestinal Interventional Endoscopy: Springer; 2020.* p.199-210.
35. Bang CS, Baik GH, Kim HS, Park SH, Kim EJ, Kim JB, et al. Upper GI Tract: Effect of intragastric injection of botulinum toxin a for the treatment of obesity: A systematic review and meta-analysis. *Korean Society of Internal Medicine Fall Conference Proceedings.* 2014;(PS 0770) 513-513.
36. Kanlioz M, Ekici U. How taking into account the pyloric tonus contributes to treatment success while administering gastric “botulinum toxin A” for weight loss. *Obes Surg.* 2020;30:3365-9.