İKÇÜSBFD

SİSTEMATİK DERLEME / SYSTEMATIC REVIEW

A Systematic Review on Intragastric Balloons and TransPyloric Shuttle in Obesity Treatment

Obezite Tedavisinde İntragastrik Balonlar ve TransPyloric Shuttle Üzerine Sistematik Bir İnceleme

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Abstract

Endoscopic bariatric procedures in the treatment of obesity have become widespread in recent years. In this systematic review, it was aimed to assess the role of intragastric balloons and transpyloric shuttle in the treatment of obesity. A comprehensive search was conducted using the search terms "Intragastric Balloon" and "TransPyloric Shuttle" in PubMed, Cochrane Library and Web of Science databases from 1st of December to 25th of December in 2020. Twenty-seven clinical studies (24 studies on intragastric balloons and 3 studies on transpyloric shuttle) were assessed. It is clear that both methods have significant positive effects on obesity-related comorbidities and weight loss. These techniques also have potential to reduce comedications in patients with type 2 diabetes mellitus and obesity. The most important differences between intragastric balloons and transpyloric shuttle are in the severity and frequency of the complications they cause. While the most common complications related to intragastric balloons are vomiting, nausea, bloating, and abdominal pain, the most common complications due to transpyloric shuttle are gastroduodenal ulcers, gastroesophageal reflux disease, and sore throat. In addition, one of the most important finding is that the type and structure of the balloon, as well as the application period and position of the balloon in the stomach, may cause changes in the adverse and practical effects of intragastric balloons. As a conclusion, intragastric balloon application is a relatively effective short term treatment and relatively safe endoscopic technique used in patients with obesity to improve comorbidities accompanying obesity, but with risks of adverse events. On the other hand, the safety profile of the transpyloric shuttle still needs to be improved.

Anahtar Kelimeler: Gastric balloon, obesity management, endoscopic gastrointestinal surgery.

Öz

Endoskopik bariatrik prosedürlerin obezite tedavisinde kullanımı son yıllarda yaygınlaşmaya başlamıştır. Bu sistematik derlemede, obezite tedavisinde intragastrik balon ve transpilorik shuttle uygulamalarının rolünün değerlendirilmesi amaçlanmıştır. 1 Aralık 2020 – 25 Aralık 2020 tarihleri arasında PubMed, Cochrane Library ve Web of Science veri tabanlarında "Intragastric Balloon" ve "TransPyloric Shuttle" arama terimleri kullanılarak kapsamlı bir arama yapılmıştır. Toplam yirmi yedi klinik çalışma (intragastrik balonlarla ilgili 24 ve transpilorik shuttle ile ilgili 3 çalışma) değerlendirilmiştir. Her iki yöntemin de ağırlık kaybı ve obeziteye bağlı komorbiditeler üzerine önemli olumlu etkilerinin olduğu açıktır. Bu tekniklerin ayrıca tip 2 diyabet ve obezitesi olan hastalarda ilaç kullanımını azaltma potansiyeli de bulunmaktadır. İntragastrik balon ve transpilorik shuttle uygulamaları arasındaki en önemli fark, neden oldukları komplikasyonların sıklığı ve şiddetidir. İntragastrik balonlar ile ilişkili en sık görülen komplikasyonlar bulantı, kusma, karın ağrısı ve şişkinlik iken, transpilorik shuttle ile ilişkili en sık görülen komplikasyonlar gastroduodenal ülserler, gastroözofageal reflü hastalığı ve boğaz ağrısıdır. Tüm bunlara ek olarak elde edilen en önemli bulgulardan birisi de balonların tipinin ve yapısının yanı sıra, balonun uygulama süresi ve midedeki pozisyonunun da intragastrik balonların olumsuz ve pratik etkilerinde değişikliklere neden olabileceği sonucudur. Sonuç olarak, intragastrik balon uygulaması, obeziteye eşlik eden komorbiditeleri iyileştirmek için obez hastalarda kullanılan, ancak yan etki riskleri olan ve nispeten kısa süreli etkili bir endoskopik tekniktir. Diğer yandan, transpilorik shuttle tekniğinin güvenlik profilinin iyileştirilmesi gerekmektedir.

Keywords: Gastrik balon, obezite yönetimi, endoskopik gastrointestinal cerrahi.

1. Introduction

Obesity is characterized by an excessive accumulation of body fat and defined as a multi-factorial, relapsing, chronic, neurobehavioral disease. Obesity has reached epidemic proportions in the world and this complex disease is interconnected with impaired quality of life, a multitude of adverse health outcomes, and reduced life expectancy. However, obesity, which has a high incidence not only in adults but also in adolescents and children, is a preventable health problem. Treatment modalities for obesity include therapeutic lifestyle modifications (diet, physical activity etc.), pharmacotherapy, and bariatric surgery (1). Non-surgical methods, such as dietary interventions and lifestyle changes, may be insufficient to provide permanent and effective weight loss in some cases, and therefore, surgical interventions may become necessary in those circumstances (2).

A number of endoscopic techniques in obesity surgery have been used in recent years, and the developments in this area are closely followed by both physicians and patients with obesity. Endoscopic techniques include space-occupying techniques (transpyloric shuttle and intragastric balloons), gastric plication and suturing techniques (endoscopic sleeve or vertical gastroplasty, transoral gastroplasty, primary obesity surgery endoluminal, and transoral endoscopic restrictive implant system), gastrointesinal bypass sleeves (duodenal jejunal bypass liner), intragastic Botulinum Toxin A injection and aspiration therapy. Among these methods, transpyloric shuttle (TPS) and intragastric balloons (IGB) have been used frequently and are touted as effective in the obesity treatment. In addition, these methods are also used as bridging interventions before laparoscopic bariatric surgery to reduce complication risk. It is obvious that such endoscopic procedures will be used more frequently in the future. In order for these techniques to become more effective and safer in the future, it is important to determine the effectiveness of, and the complications that arise from, these procedures. This paper reviews the effect of IGBs and TPS on weight loss and obesity related parameters. In addition, adverse events occurred due to the methods were also investigated.

2. Materials and Methods

2.1. Defining the Search Questions

The research questions reflecting the purpose of this systematic review are as follows;

- What are the effects of IGB and TPS applications on weight loss in people with obesity?

- What are the complications caused by IGB and TPS applications?

- What are the effects of IGB and TPS applications on obesity-related complications?

- What are the roles of extra applications (diet, physical activity, etc.) in addition to IGB and TPS in terms of the effectiveness of IGB and TPS?

2.2. Data Sources and Searches

A deep search was performed to identify available clinical studies evaluating the outcomes of IGBs and TPS in the treatment of obesity by adhering to PRISMA statements (Figure 1). Three databases including PubMed, Cochrane Library, and Web of Science were searched from 1st of December to 25th December in 2020 without language or study design restriction. A systematic search was carried out using the search terms as "Intragastric Balloon" and "TransPyloric Shuttle" by the authors. Additional eligible researches were also tried to identify by manual search and reviewing the reference list of included studies.

2.2. Eligibility Criteria

Clinical trials and observational prospective cohort studies that were published and peer reviewed were included. Editorials, reviews, retrospective studies, conference abstracts, studies using nonhuman subjects, and case reports were excluded as were articles without English translation or full text availability. Studies on IGBs were also excluded for the following reasons: [1] if there were subjects under the age of 18 years; [2] if a study was designed to evaluate endoscopic intervention's efficacy for a specific disease (non-alcoholic fatty liver disease, renal diseases etc.) other than obesity, type 2 diabetes mellitus (T2DM) or metabolic syndrome; [3] if a study's outcomes were not reported as total weight loss, absolute weight loss, or excess weight loss; [4] if a study was designed primarily to evaluate the effectiveness of medication, aftercare programs, or a special diet application (ketogenic diet, low carbohydrate diet, etc.) rather than endoscopic intervention; [5] if the number of patients who were undergone an endoscopic intervention was 20 or less at the beginning or at the end of the study. The above criteria have been considered in studies on IGB and were ignored in the inclusion and exclusion of studies on TPS. In addition, only studies published from 2015 onwards on IGBs were included, while there was no restriction in terms of years in the including of studies on the TPS technique.

2.3. Data Extraction and Outcomes

Twenty-four clinical studies on IGBs and 3 studies on TPS were examined. Data for study characteristics, weight loss outcomes at follow-up, procedure technique, patient baseline characteristics, adverse/side events, and changes in any obesity-related parameters were collected for each study and organized in the tables.

3. Results and Discussion

3.1. General Characteristics of Intragastric Balloons

One of the methods considered as an alternative to laparoscopic bariatric techniques in obesity treatment is IGB application, and it is one of the most widely used endoscopic techniques today. The IGB placement, which was first used in 1980s (3), is based on the endoscopic placement of a balloon filled with liquid or gas into the stomach while the patient is under sedation or general anesthesia. Today, there are seven different types of intragastric balloons in the world market, two of them (Orbera and Obalon) have been approved by the Food and Drug Administration (FDA) and two (Elipse and Spatz) are awaiting approval. Of these FDA-approved balloons, Orbera is a single balloon filled with saline, while Obalon is filled with nitrogen gas. In addition, Obalon is a 3-balloon treatment in which a patient swallows a balloon every 4 weeks (for a total of 12 weeks). ReShape balloon which was a double balloon technique connected in the middle by a tube has been taken off

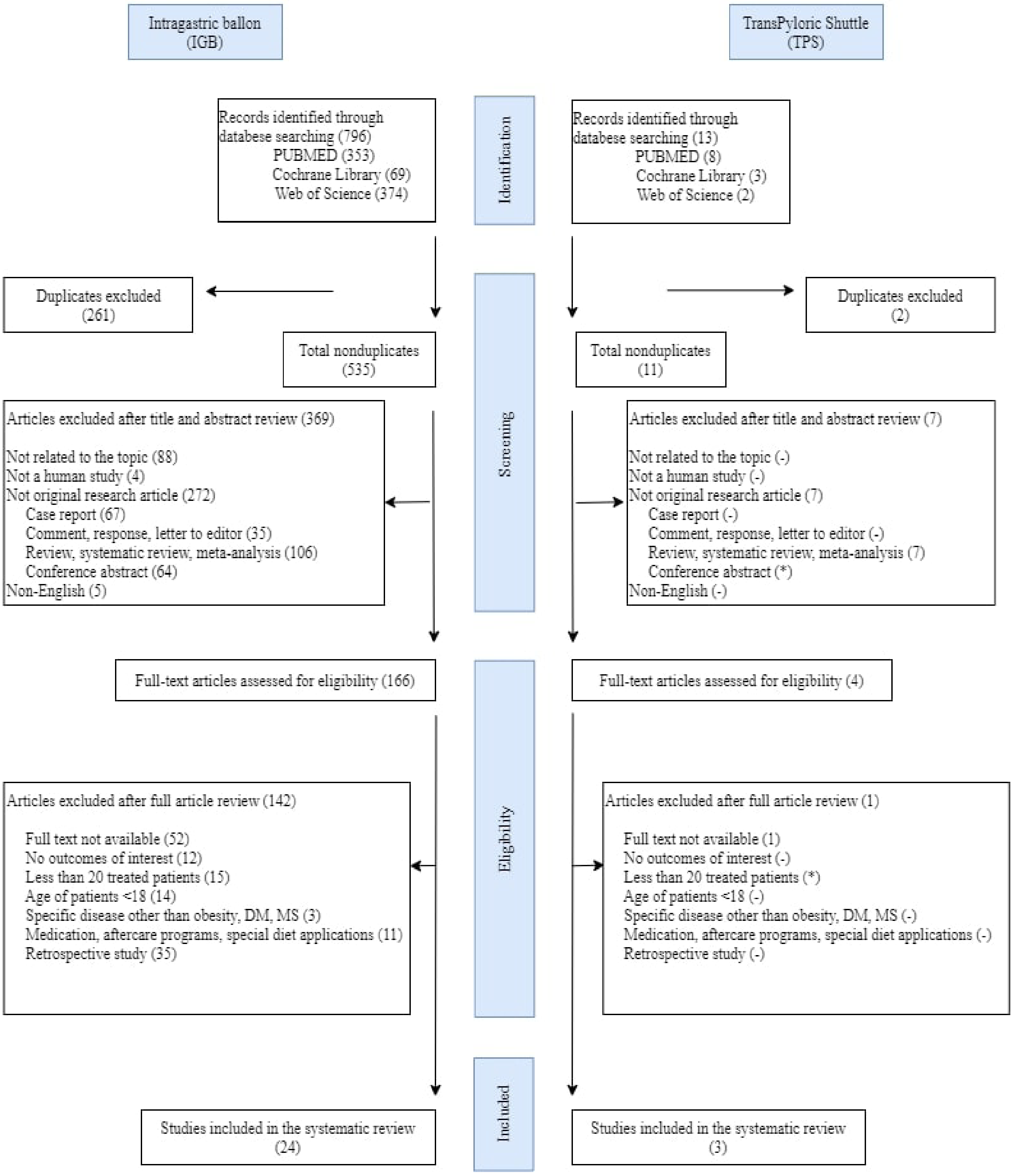

Figure 1. PRISMA Flow Diagram Detailing the Process of Study Selection

the market although it was previously approved by the FDA. On the other hand, nitrogen-filled balloons require endoscopy for removal only, while saline-filled balloons require endoscopy for both implantation and removal. In addition, all balloons stay in the stomach for up to 24 weeks/6 months (4).

Aplication of IGBs can modify the distribution of food in the stomach, leading to distention of the antrum and potentially invoking exaggerated fundic relaxation (5). The positive effects of IGB application on the gastric emptying rate (6) and the neurohormonal components that play a role in hunger and satiety provide targeted weight loss. However, there may be diversities in practical effects depending on the differences in the type and structure of the balloons. For example, it is noted that gas filled IGBs do not delay gastric emptying, unlike fluid-filled IGBs (7). In addition to the structural features of the balloon, differences in patient characteristics, position of the balloon in the stomach, and application period may also cause changes in the adverse and practical effects of IGBs. It is stated that, displacement of the IGB from fundus to antrum results in enhanced weight loss (8).

3.2. Effects of IGBs on Obesity Related Comorbidities and Weight Loss

According to the clinical studies in the literature evaluating the effectiveness of IGBs on obesity (Table 1), it is obvious that the method has significant positive effects on obesity-related comorbidities and weight loss.

Application of intragastric balloon provides significant improvements in cholesterol, triglyceride, fasting glucose, C-reactive protein, blood pressure, and HbA1c levels and significant reductions in the incidence of T2DM, non-alcoholic fatty liver, metabolic syndrome, hyperuricemia, osteoarthropathy, hypertriglyceridemia, and hypercholesterolemia (Table 1). Intragastric balloons can also be applied in adolescents with obesity and give positive results in impaired blood pressure, insulin resistance, and liver functions due to obesity. In addition to these metabolic benefits, IGB application also leads to positive changes in sleep apnea and skeletal health (9,10)

3.3. IGBs and Neurohormonal Changes

Neurohormonal changes (ghrelin, leptin, cholecystokinin, glucagon-like peptide-1 and pancreatic polypeptide) caused by IGB treatment are not yet fully understood. In the study conducted by Mathus-Vliegen and Eichenberger (11), it was stated that IGB application had no significant effect on fasting and meal-suppressed ghrelin concentrations, while Mion et al. (12) stated that ghrelin level decreased with IGB application. Konopko-Zubrzycka et al. (13) and Fuller et al. (14) stated that there was an increase in ghrelin levels with the insertion of IGB, but, a few months after the removal of the IGB, ghrelin levels returned to their baseline values. The main reason for different outcomes regarding neurohormonal changes with IGB application may be due to the heterogeneity of the methodology of IGB application in clinical studies. Generally, the application period varies between 3-6 months, while the body mass index (BMI) values of the individuals treated with IGB can vary between 27-60 kg/m^2. In other words, differences in both the application technique and the patient profile may result in different outcomes.

3.4. Advantages/Disadvantages of IGBs and Complications Related to IGBs

Advantages of intragastric balloon application include, increasing the feeling of satiety by affecting the gastric stretch receptors, and delaying the rate of gastric emptying without altering stomach or intestinal anatomy. Although the risk of severe adverse events caused by IGB treatment is low, complications, such as esophageal or gastric perforations, rupture/deflation/displacement of the balloon, acute pancreatitis, abdominal pain, and gastric ulcer, may occur. In addition, chronic nausea, vomiting, abdominal pain, and stomach cramps observed in IGB implanted patients may cause the balloon to be removed earlier than the prescribed time (6-15% of the patients cannot tolerate balloon). On the other hand, 33 deaths related to IGB treatment (ORBERA ve ReShape) were reported from 2006 to 2018 (15), while the treatment-related mortality rate was stated as 0.05% (16). Despite the complication risks reported in the literature, many reviews and meta-analyses have stated that IGB treatment is a safe and effective technique in the treatment of obesity (9,17,18). The lower complication risk of the treatment than laparoscopic bariatric surgical techniques and its provision of effective weight loss facilitate patients' compliance with the method. In this way, IGB treatment stands out as an effective method in the obesity treatment. In addition, the fact that it can be applied to individuals with lower BMI values makes the IGB method frequently used.

Table 1. Summary of Reported Outcome Data Following Intragastric Balloon Treatment (Results of Recent Studies Published Between the years of 2015-2020).

Ref.	IGB Group (I) n (II) Initial BKI (kg/m^2) (III) Extra application (IV) Treatment period (V) Device	Control Group (I) n (II) Initial BKI (kg/m^2) (III) Extra application	Main outcomes	Adverse events (n / %)
Coffin et al. (22)	(I) 55, (II) 53.9, (III) NA, (IV) 6 months, (V) BioEnterics or Heliosphere	(I) 60 (II) 54.7 (III) SMC, LCD	WL was significantly greater in the IGB group than in the SMC group. In addition, WL was similar in both types of IGB. On the other hand, WL occurred during the first three month period, and the BW then remained stable during the last three month period.	BioEnterics group; esophageal tear (1), hemorrhage (1). Heliosphere group; unsuccessful balloon removal (surgical gastrotomy was required). Early removal of the IGB (5).
Mitura and Garnysz, (23)	(I) 57, (II) 37.2, (III) LCD+PA, (IV)6 months, (V) Orbera	(I) - (II) - (III) -	Upon balloon removal 6 months later, the reduction in mean BW, BMI and EBW was 15.9 kg, 5.8 kg/m^2 and 41%, respectively. In addition, the reduction of > 10% WL, was achieved in all patients.	Vomiting (33), heartburn (27), abdominal pain (13) and other complications (11).
Ponce et al. (24)	(I) 187, (II) 35.4, (III) Diet and exercise, (IV) 6 months, (V) ReShape	(I) 139 (II) 35.4 (III) Diet and exercise	The reduction in BW, BMI and EBW was 7.6%, 2.7 kg/m^2 and 27.9% in IGB group, respectively. In addition, the mean WL in the IGB group was more than twice that of the control group.	Early deflation (6%), early retrieval for nonulcer intolerance (9%) and gastric ulcers (NA).
Lopez-Nava et al. (25)	(I) 60,(II) 38.8, (III) LCD+PA, (IV) 6 months, (V) ReShape	(I) - (II) - (III) -	The reduction in mean BW, BMI and EBW was 15.4%, 6.1 kg/m^2 and 47.1%, respectively. In addition, most patients with morbid obesity (71.4 %) decreased their BMI below 40 kg/m^2.	Early deflation (1), gastric perforation (1) and gastric ulcers or erosions (14). Early removal of the IGB (1).

Table 1. Summary of Reported Outcome Data Following Intragastric Balloon Treatment (Results of Recent Studies Published Between the years of 2015-2020) (continued)

Palmisano et al. (26)	(I) 81, (II) 39.6, (III) LCD (800-1000 kcal/day), (IV) 6 months, (V) Heliosphere and BioEnterics	(I) - (II) - (III) -	A significant reduction in BW was observed at device removal and 1 year thereafter. But most of the patients (63%) were not satisfied with the procedure, refused to perform it again, and did not deem useful to change their diet.	NA
Mariani et al. (27)	(I) 32, (II) 41.8, (III) NA, (IV) 6 months, (V) BioEnterics	(I) 10 (II) 38.9 (III) LCD	A significant reduction in BW, BMI, EBW and total fat mass was observed, together with a significant increase in sirtuins level (main regulators of energy homeostasis and metabolism) both in IGB and LCD groups. A trend toward a inflammatory and metabolic amelioration was observed with both treatments.	Nausea (3), vomiting (3), bad breath (3), discomfort (3), belching (3) and flatulence (3).
Fernandes et al. (28)	(I) 26 and 113, (II) 28.6 and 35.8, (III) NA, (IV) 6 months, (V) Silimed	(I) - (II) - (III) -	The mean EWL was 41% in the patients with obesity (*n*=113) and 96% in patients with overweigh (*n*=26).	Nausea and pain (50-95%). Early removal of the IGB (6%).
Courcoulas et al. (29)	(I) 137, (II) 35, (III) LT, (IV) 6 months, (V) ORBERA	(I) 136 (II) 35 (III) LT	The mean WL in the IGB group at the end of the 6,9 and 12 months was 10.2%, 9.1% and 7.6%, respectively and the reduction in BW and EBW in IGB group at these months was significantly higher than the control group.	Vomiting (75.6%), nausea (86.9%), abdominal pain (57.5%) and gastric abnormality (3.1%). Early removal of the IGB (18.8%).
Al-Subaie et al. (30)	(I) 51, (II) 32.1, (III) Non-standard diet program, (IV) 4 months, (V) Elipse	(I) - (II) - (III) -	The decrease in BW, EBW, BMI and WC was 10.44%, 40.84%, 3.42 kg/m^2 and 8.62 cm, respectively.	Vomiting the balloon (1) and early deflation (1). Early removal of the IGB (5).
Żurawiński et al. (31)	(I) 63, (II) 58.3, (III) NC, (IV) 6 months, (V) LexBal	(I) - (II) - (III) -	The decrease in BMI was 7.1 kg/m^2 and the highest BMI reduction was recorded in patients in the age group of 30–39, whereas the lowest value was in the patients aged 40– 49.	Nausea (57.1%), vomiting (44.4%), general discomfort (38.1%), flatulence (38.1%), upper abdominal pain (30.2%), heartburn (17.5%), dehydration and oesophageal candidiasis (7.9%).
Guedes et al. (32)	(I) 50, (II) 40, (III) NA, (IV) 6 months, (V) Silimed	(I) - (II) - (III) -	The mean reduction in BMI, BW, WC, total body fat and fat free mass was 4.4 kg/m^2, 11.7 kg, 9.3 cm, 7. 5 kg and 3.7 kg, respectively. A significant improvement was also observed in almost all aspects of health-related quality of life measured by (WHOQOL-BREF).	NA
Da Silva et al. (33)	(I) 51, (II) 35.8, (III) LCD, (IV) 6 months, (V) ORBERA®	(I) - (II) - (III) -	The mean WL and EWL were 11.9 kg and 42.2%, respectively. After removal of the IGB (at 6-12 months) the mean WL and EWL were 8.2 kg and 30.3%, respectively.	Abdominal pain (7), nausea (7), vomiting (5), and spontaneous IGB deflation (1).
Genco et al. (34)	(I) 38, (II) 38.6, (III) 1000-1200 kcal/day diet, (IV) 4 months, (V) Elipse	(I) - (II) - (III) -	The mean reduction in BW, EBW and BMI was 12.7 kg (11.6%), 26% and 4.2 kg/m^2, respectively. Significant reductions in major co-morbidities related to metabolic syndrome (HOMA-IR index, blood glucose, blood pressure, triglycerides, and WC) were observed.	NA
Reimão et al. (35)	(I) 40, (II) 32.9, (III) LCD (up to 1000 kcal/day)+PA, (IV) 6 months, (V) Orbera	(I) - (II) - (III) -	There was a significant reduction in BW (12.3 kg, 13.69%), body fat mass and fat area. Quality of life (assessed by the Short Form 36 Health Survey) improved in all eight sections analyzed: mental health, functional capacity, general health status, physical aspects, emotional aspects, social aspects, vitality, and pain.	NA
Foroutan and Ardeshiri, (36)	(I) 52, (II) 39.4, (III) 1000 kcal/day diet, (IV) 6 months, (V) BioEnterics	(I) - (II) - (III) -	The mean reduction in BW and BMI was 18.9 kg and 6.9 kg/m^2, respectively, at six months after balloon placement. Although there was an increase in BW and BMI at 6 months after the balloon removal, the decrease compared to the baseline values were 14.2 kg and 4.6 kg / m^2, respectively.	Nausea and vomiting (NA).
Sullivan et al. (37)	(I) 198, (II) 35.2, (III) LT, (IV) 6 months, (V) OBALON	(I) 189 (II) 35.5 (III) LT	The decrease in BW and BMI in the IGB group (7.1% and 2.5 kg/m^2, respectively) was significantly greater.	Nonserious adverse events (91.1%), bleeding ulcer (1) and early balloon deflation (1).
Alsabah et al. (38)	(I) 135, (II) 33.7, (III) NC, (IV) 4 months, (V) ELIPSE	(I) - (II) - (III) -	The decrease in BW and BMI was 13 kg (15.1%) and 4.9 kg/m^2, respectively.	Colicky abdominal pain (29), diarrhea episodes (18), early deflation (3), vomiting the balloon (2), and small bowel obstruction (1). Early balloon removal due to intolerance (3).

Table 1. Summary of Reported Outcome Data Following Intragastric Balloon Treatment (Results of Recent Studies Published Between the years of 2015-2020) (continued)

Guedes et al. (39)	(I) 42, (II) 35.1, (III) NC+LCD (12 kcal/kg), (IV) 6 months, (V) Orbera or Spatz	(I) - (II) - (III) -	In addition to a significant reduction in central and total body fat, there was a significant decrease in BW (15.8%), EBW (56.1%) and WC (13.3 cm). On the other hand, there was an improvement of quality of life, an increase in physical activity, and a reduction in energy intake during the IGB treatment.	NA
Jamal et al. (40)	(I) 112, (II) 34.3, (III) High protein low calorie diet, (IV) 6 months, (V) Elipse	(I) - (II) - (III) -	The mean WL at 3, 6, and at date of last follow-up was 10.7%, 10.9%, and 7.9%, respectively.	Early balloon deflation (3) and small bowel obstruction (1). Early balloon removal due to intolerance (6).
Guedes et al. (41)	(I) 42, (II) 35.1, (III) NC+LCD (12 kcal/kg), (IV) 6 months, (V) Orbera or Spatz	(I) - (II) - (III) -	The decrease in mean BMI was 5.6 kg/m^2. In addition there was a significant reduction in insulin, glucose, HOMA-IR, high-sensitivity C-reactive protein, triglycerides, and leptin levels. On the other hand adiponectin/leptin ratio increased.	NA
Madeira et al. (42)	(I) 40, (II) 39.8, (III) LCD (1200 kcal/day energy and 1000-1500 mg/d calcium), (IV) 6 months, (V) Silimed	(I) - (II) - (III) -	There was a significant decrease in BW (11.5%), and a significant increases in carboxyterminal telopeptide of type 1 collagen and vitamin D levels after 6 months. On the other hand areal bone mineral density decreased in the total femur and radius but increased in the spine. In addition, cortical bone mineral density increased in the distal radius but tended to decrease in the distal tibia.	NA
Fittipaldi-Fernandez et al. (43)	(I) 94 (600 mL IGB volume) and 86 (850 mL IGB volume), (II) 39.5, (III) 10-15 kcal/kg/day diet, (IV) 6 months, (V) Spatz3	(I) - (II) - (III) -	The mean reduction in BMI, BW and EBW was 6.7 kg/m^2, 21.5 kg and 18.6 kg, respectively. The adjustment in IGB volume (250 mL greater IGB volume) resulted in greater mean WL of 4.35 kg. The upward adjustment group did not present greater %TWL, %EWL, or BMI reduction when compared with the standart IGB volume (600 mL) group.	Spontaneous deflation (1.66%), gastric ulcer (3.32%), Mallory-Weiss syndrome (0.55%), and gas production inside the balloon (0.55%) Early balloon removal (8.32%).
Lopez-Nava et al. (44)	(I) 32, (II) 34.9, (III) LCD+LT (IV) 6 months, (V) Orbera	(I) - (II) - (III) -	The mean reduction in BW at 3, 6, and 12 months was 13.3%, 15.9%, and 16.8%, respectively. Patients in the higher gastric retention quartile at baseline had a 6.2-time higher likelihood ratio for early balloon removal secondary to intolerance.	NA
Ibrahim et al. (45)	(I) 86, (II) 42.9, (III) NC, (IV) 6 months, (V) MedSil	(I) - (II) - (III) -	The mean reduction in BMI was 5.8 kg/m^2 and 4.2 kg/m^2 at 6 and 12 months, respectively.	NA

BMI; body mass index, BW; body weight, EBW; excess body weight, EWL; excess weight loss, LCD; low calorie diet, LT; lifestyle therapy, NA; data not available, PA; physical activity, SMC; Standart medical care, WC; waist circumference, WL; weight loss.

Intragastric balloon treatment is used only as a bridge to laparoscopic bariatric surgery by many physicians due to the fact that IGB application is temporary therapeutic modality for obesity treatment, and the weight lost after IGB may be quickly regained (28-80% of the patients regain the weight they lost within one year following the removal of the balloon) (19, 20). Because of quick regain of the lost weight after removal of the gastric balloon, it has been stated that IGB application combined with laparoscopic bariatric techniques, instead of IGB application alone, may give more effective results (19,21).

3.5. General Characteristics of TransPyloric Shuttle

TransPyloric Shuttle placement is one of the minimally invasive methods intended to treat obesity by reducing the gastric emptying rate with a spherical silicone device placed endoscopically in the stomach. The TPS consists of a small and large spherical bulb connected by a flexible silicone tether. When this device positioned endoscopically, the large bulb (not as large as the gas- or water-filled balloons) repeatedly engages the pylorus during antral contractions, causing intermittent obstruction, while the other bulb (smaller bulb) passes freely into the duodenum to position the TPS across the pylorus (46). The action of large bulb prolongs gastric accommodation, delays gastric emptying, and produces early and prolonged satiety.

3.6. Effects of TPS on Obesity Related Comorbidities and Weight Loss and Complications Caused by the Technique

To date, the effect of TPS on obesity has been evaluated in some studies (Table 2). This technique was first applied by Marinos et al. (47) in 2013 and it was found that weight loss was achieved in patients in the 3-6 months period. However, in this study, it was stated that persistent gastric ulceration was observed in two patients depending on the application. In another randomized double-blind trial (48), it was observed that mean body and excess weight loss at twelve months was higher in TPS group (9.5% and 30.9%, respectively) compared to control group (2.8% and 9.8%, respectively). In addition, significant decreases in plasma insulin and insulin-resistance level (measured by HOMA-IR) and significant improvement in lipid profile and blood pressure were observed in TPS group. However, serious adverse events were occurred (none developed perforation or bleeding) in TPS group (2.5%). Because of the gastroduodenal ulcers (10.3%) and other adverse events the device was removed earlier than anticipated time. Although studies on TPS are limited, similar positive results were obtained (weight loss, improved quality of life scores) in the study conducted by Sartoretto et al. (49), and these positive results enabled the device to be approved by the FDA on April 16, 2019.

Table 2. Summary of Reported Outcome Data Following TransPyloric Shuttle

Ref.	TPS Group (I) n (II) Initial BKI (kg/m²) (III) Extra application (IV) Treatment period	Control Group (I) n (II) Initial BKI (III) Extra application	Main outcomes	Adverse events
Rothstein et al. (48)	(I) 180 (II) 30-40 (III) NA (IV) 12 months	(I) 90 (Sham-controlled) (II) 30-40 (III) NA	The mean reduction in BW in TPS and control groups were 9.5% and 2.8% at 12 months, respectively. Greater improvement in cardiometabolic risk factors (blood pressure, insulin, HOMA-IR, triglyceride, LDL, and total cholesterol) were observed in TPS group patients compared to control group patients.	Dyspepsia (NA), nausea (NA), vomiting (NA) and stomach pain (NA). Early removal of the device due to gastroduodenal ulcer (21).
Sartoretto et al. (49)	(I) 8 (II) 37.2 (III) NA (IV) 12 months	(I) - (II) - (III) -	The mean reduction in BW and EBW was 10.4% and 33.8 at 6 months. At 12 months these values further increased to 12.8% and 36.2%, respevtively. In additon, the decrease in mean BMI was 4.6 kg/m² at 12 months.	Nausea (NA), reflux (NA), cramping (NA), abdominal pain (NA), bloating (NA) and ulcer (1).
Marinos et al.(50)	(I) 20 (II) 36 (III) LCD (IV) 3-6 months	(I) - (II) - (III) -	The decrease in BW, EBW and excess BMI was 8.9%, 25.1%, and 33.1%, respectively in three-month patients (*n*=10). On the other hand in six-month patients (*n*=10) the decrease in BW, EBW and excess BMI was 14.5%, 41.0%, and 50.0%, respectively.	Nausea (9), sore throat (7), abdominal pain (6), diarrhea (5), gastroesophageal reflux disease (4), vomiting (3), constipation (3), feeling heaviness and bloating (1) Early removal of the device due to symptomatic gastric ulcerations (2).

BMI; body mass index, BW; body weight, EWL; excess weight loss, LCD; low calorie diet, NA; data not available, WL; weight loss

3.7. Overview of Both Techniques

When the studies on IGB in the literature are examined, it is thought that IGB is an effective endoscopic technique for patients with obesity to improve comorbidities accompanying obesity and to reduce the severe complication or adverse event risk of laparoscopic bariatric surgery in the preoperative period. Considering that preoperative weight loss may be the predictive factor of post-operative weight loss, IGB treatment combined with laparoscopic bariatric methods may be one of the most effective techniques in the treatment of morbid obesity. The positive effects of IGB on obesity-related comorbidities and weight loss, and the low adverse events rate compared to other techniques facilitate the patient's acceptance of the IGB treatment and highlight the technique over other methods.

Similar to IGBs, endoscopic TPS placement may be useful both for primary obesity management and as a bridge to laparoscopic bariatric surgery. However, the safety profile of device still needs improvement. The device used in this method is 85-90% smaller than intragastric balloons, and this is considered as an advantage; however, more clinical studies investigating the long term effects (especially in the period after device removal) and possible complications of the TPS method are needed.

5. Conclusion and Recommendations

The positive effects of IGB and TPS application on the gastric emptying rate and the neurohormonal components that play a role in hunger and satiety provide targeted weight loss. However, there may be diversities in practical effects depending on the differences in the type and structure of the IGBs. Common features of IGBs and TPS are: they do not alter stomach or intestinal anatomy, they are not permanent, and they provide effective weight loss. In addition, these techniques also have potential to reduce comedications in patients with T2DM and obesity. The most significant differences between IGBs and TPS are in the severity and frequency of the complications they cause. The nearly 40-year history of IGB application in obesity treatment makes it a safer and more effective approach. Because of the quick regain of lost weight within a year after the balloon removal, it should also be noted that IGB application combined with laparoscopic bariatric techniques, instead of IGB application alone, may give more effective results. However, for both IGB and TPS usage should be considered with caution as they are temporary treatments for a chronic condition. On the other hand, although TPS has some advantages over IGBs, the serious adverse events risk is higher, and, therefore, the safety profile of the TPS still needs to be improved.

6. Contributions to the Field

In this systematic review, the role of the IGB technique, which is very common in the surgical treatment of obesity, and the TPS technique, which is expected? to be used more frequently in the future, in the treatment of obesity were evaluated. All results and adverse events determined in the reviewed studies stated without any classification because of helping guide the clinical decision making and procure better treatment of obesity. The data obtained and presented may be effective in the further improvement of both methods.

Conflict of Interest

This article did not receive any financial fund. There is no conflict of interest regarding any person and/or institution.

Authorship Contribution

Consept: TGÜ, FPÇ; **Desing:** FPÇ, MT; **Supervision:** FPÇ, MT; **Funding:** - **Materials:** - **Data Collection/Processing:** TGÜ, FPÇ, MT, ÇÖ; **Analysis/Interpretation:** TGÜ, FPÇ, MT, ÇÖ; **Literature Review:** TGÜ, FPÇ, MT, ÇÖ; **Manuscript Writing:** TGÜ, ÇÖ; **Critical Review:** FPÇ, MT.

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