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REVIEW

Overview on the endoscopic treatment for obesity: A review

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Abstract

Obesity rates have increased, and so has the need for more specific treatments. This trend has raised interest in non-surgical weight loss techniques that are novel, safe, and straightforward. Thus, the present review describes the endoscopic bariatric treatment for obesity, its most recent supporting data, the questions it raises, and its future directions. Various endoscopic bariatric therapies for weight reduction, such as intragastric balloons (IGBs), aspiration therapy (AT), small bowel endoscopy, endoscopic sleeve gastroplasty, endoluminal procedures, malabsorption endoscopic procedures, and methods of regulating gastric emptying, were explored through literature sourced from different databases. IGBs, AT, and small bowel endoscopy have short-term effects with a possibility of weight regain. Minor adverse events have occurred; however, all procedures reduce weight. Vomiting and nausea are common side effects, although serious complications have also been observed.

Key Words: Overweight; Gastric bypass; Malabsorption; Intragastric balloons

Core Tip: To enhance endoscopic intervention effectiveness and patent satisfaction, the research recommends device design, procedures, patient selection, and personalized therapy. Endoscopists, bariatric surgeons, and researchers must collaborate to solve problems, improve patient comfort, and reduce treatment risks. Effective weight maintenance through endoscopic methods and patient education requires comprehensive and long-term follow-up. Robotic-assisted endoscopy and tissue-engineered implants may revolutionize obesity treatment and patient outcomes in five to ten years.

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INTRODUCTION

Obesity prevalence has increased dramatically over the last thirty years, now approaching 35% in men and 40% in women[1]. Obesity affects 39 million children, 340 million teenagers, and 650 million adults worldwide. This figure is still rising; by 2025, 167 million children and adults will have suffered as a result of being obese or overweight[2]. As a multifaceted illness with pandemic proportions, obesity is prevalent nowadays. Since 1975, obesity prevalence has virtually tripled during the last three decades globally, primarily due to an increase in sedentary behavior and intake of less nutrient-dense foods[3]. There are severe public health issues with obesity[4]. Such as diabetes, hyperlipidemia, mortality all-causes, and all-cause cardiovascular mortality[5]. In 2015, the World Obesity Federation established World Obesity Day as a day of commitment and action to promote an integrated, cross-sector approach to combating obesity[6]. A new index for Obesity-Non-Communicable Disease Preparedness is presented in the World Obesity Federation report; worries about the consequences of inactivity for already vulnerable people have grown. The top 30 most prepared countries are all high-income countries, whereas the least prepared 30 are all lower-middle and low-income countries[7]. Obesity-related yearly healthcare costs are predicted to total 1.2 trillion USD globally by 2025[6].

A bio-socio-ecological framework, in which biological predisposition, environmental factors, and socioeconomic factors interact to promote the deposition and proliferation of adipose tissue, can explain the process of persistence and development of obesity[8]. In wealthy nations, poverty and obesity appear to be related. However, a more thorough examination of the empirical literature leads one to believe that the relationship between income and obesity is more nuanced because it can be either positive or negative, or it can alter as nations grow older[9]. Among the numerous therapies for obesity, pharmaceutical substances, surgical procedures, and lifestyle changes can be used[10] as shown in Figure 1.

Despite being the least invasive and expensive approach, lifestyle changes have been demonstrated to be the least effective[11]. Adults with obesity can lose > 5% of their body weight with many sessions of intensive behavioral interventions, such as identification of different barriers, peer support, and self-monitoring of weight, combined with dietary plans, lifestyle modifications, and increased exercise[12]. The central nervous system, adipose tissue, gastrointestinal hormones, liver, kidney, and skeletal muscle are only a few of the systems and tissues that are now modulated by some anti-obesity drugs under investigation[13]. Bariatric surgery is currently the only treatment that causes significant and long-lasting decrease in body weight[14]. However, even if there are clinically significant comorbidities (metabolic, psychological, *etc.*), patients with a body mass index (BMI) of 35 kg/m^2 or over are not suitable for bariatric surgery. Only a small number of eligible patients can potentially benefit from bariatric surgery[15]. This may be due to various reasons, such as a less favorable risk-benefit profile, as higher BMI levels often correlate with increased surgical complications, postoperative mortality, and reduced success rates[16]. Additionally, the potential benefits of surgery, such as weight loss and improvement in comorbidities, might be outweighed by the surgical risks and associated challenges in this specific BMI range. Moreover, alternative interventions, including lifestyle modifications, pharmacotherapy, and non-surgical interventions, might be considered more appropriate due to the complexities posed by the patient’s heightened obesity levels. However, carefully assessing individual risks and benefits remains essential in determining the most suitable treatment approach[17]. Lastly, advanced studies have questioned the longevity of bariatric surgery due to the regular occurrence of weight regain and adverse effects[17].

Endoscopic procedures can be used in a multidisciplinary approach to managing obesity. Endoscopists should become familiar with the gastrointestinal pathology that might develop after bariatric surgery, such as malnutrition, anastomotic stenosis, acid reflux, gallstone disease, leaks, fistulas, and weight gain[17]. The creation of new obesity treatment modalities without a high operational risk is the current area of research; thus, obesity endoscopic management is garnering major attention. Endoscopy has an indisputable role in the assessment and management of bariatric surgery complications as well as the evaluation of patients in the preoperative stage of the procedure[18]. Additionally, in order to lower the risks associated with surgery connected to obesity, endoscopic techniques have been employed as a “bridge to surgery”[19]. Thus, the present review describes the present endoscopic treatment for obesity, the most recent data supporting it, the questions, and the future directions the field will face in the next ten years.

BARIATRIC ENDOSCOPY

Endoscopic weight loss therapies have been developed as a result of increased interest and innovation in the fields of gastroenterology and endoscopy, as well as the proven results of bariatric surgery for weight loss[20]. Although surgery is a successful approach for weight loss, it is constrained by its high resource requirements and low patient acceptance [21]. However, endoscopic bariatric therapy (EBT) may be more effective than anti-obesity medicines[22]. Endoscopic weight loss procedures are becoming more popular in Western countries where obesity has escalated rapidly[23]. Indeed, EBT has demonstrated outstanding results in the treatment of obesity and associated surgical consequences[24], therefore, must be included in the arsenal in the battle against obesity[25]. In fact, EBT has evolved into a significant tool for exami-

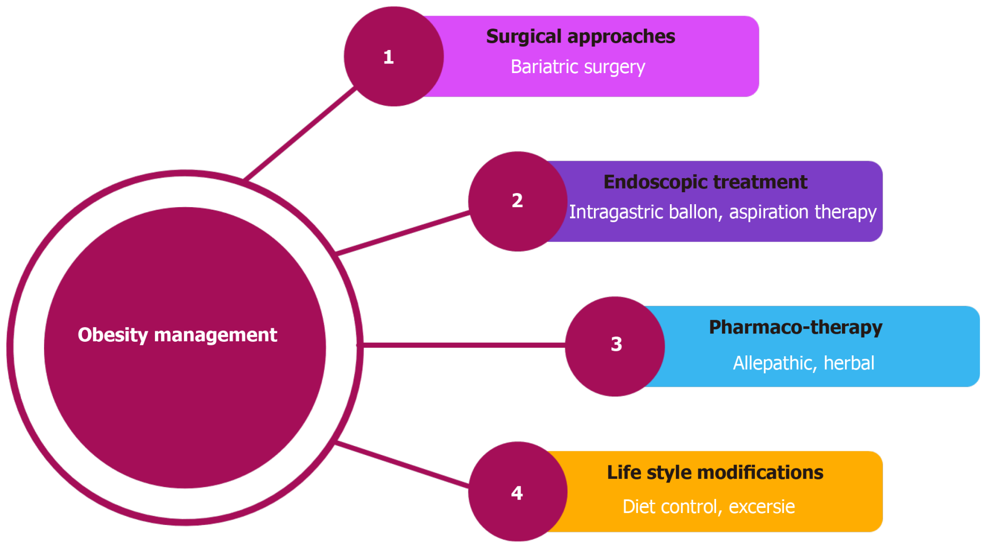

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Figure 1 Different approaches for the management of obesity.

nation, diagnosis, surgical complication management[26] and even primary bariatric therapies[27]. It can also be a more effective alternative than dietary and lifestyle changes[28]. Additionally, EBTs are being used increasingly as a treatment therapy option for obesity in different settings due to their minimally intrusive nature and ease of administration. These treatments induce weight loss primarily by reducing meal volume and promoting early satiety[29]. Currently, a wide range of endoscopic procedures, based on the principles of stomach volume reduction, small bowel or gastric bypass, and size restriction, are being investigated, with a few being used in daily practice[30]. Innovative endoscopic therapies, such as double-pigtail stents, septostomy, and endoscopic vacuum therapy, have been developed[31]. Newer endoscopic approaches, such as intragastric balloons (IGBs), aspiration therapy (AT), small bowel devices, and endoscopic plication and suturing techniques, have been developed[32] and show significant effects.

Space occupying techniques

Space-occupying devices limit stomach capacity, thus reducing hunger and food intake as a result. There are various versions of silicon-made balloons that can be filled with liquid or air. Because of its reduced likelihood for issues, the most popular type is the non-adjustable liquid-filled balloon. The mechanism of action is multifaceted, with neurohormonal and physiological alterations involved[33]. Generally, there are two types of space-occupying techniques: Intragastric fluid filled balloons, and intragastric air or gas filled balloons.

IGBs (fluid filled)

Over 20000 papers have been published in the previous 20 years covering a wide range of topics connected to the effects of the IGBs, including weight reduction outcomes, complications, hormonal impacts, quality of life (QoL), and other aspects[34]. IGBs are invasive therapies that are used to enhance satiety by neuroendocrine and mechanical mechanisms [35] as well as limiting stomach capacity as a space-occupying device, resulting in decreased food intake and hunger[33]. The Bubble (Garren-Edwards) was the first-developed IGB in 1985. The Food and Drug Administration (FDA) of the United States approved it as a temporary weight loss device[36]. IGB therapy is helpful in decreasing weight and improving depression, anxiety, symptoms of eating disorders, and overall QoL in obese individuals primarily within 6 mo of device placement and when used in tandem with conventional therapies[37] and found to be more effective in pre-obese individuals[38]. Although significant morbidity is possible, it is a useful way to lose weight when implemented in conjunction with dietary modifications and physical exercise[39]. However, due to the consequent regain of weight, different methods are now favored in adults. Balloons may be an option for less reversible operations in teens, who are more open to lifestyle modification[40]. The drawbacks of IGBs, such as risks during insertion and removal, and unknown long-term weight loss benefits, prevent their widespread use[41]. Considering conscious sedation *vs* general anesthesia during balloon withdrawal, with or without anesthetic intubation, is pivotal due to its potential implications for procedural complications[42]. The choice between these approaches hinges on patient health status, procedure complexity, and anticipated discomfort. Utilizing conscious sedation may offer benefits like reduced risks associated with intubation but could lead to patient discomfort or inadequate sedation levels, potentially increasing complications[43]. In contrast, employing general anesthesia with intubation might mitigate patient discomfort but could introduce intubation-related risks. Balancing these considerations is essential to optimize patient comfort and procedural safety during balloon withdrawal, and a comprehensive understanding of the relationship between sedation choices and associated complications is critical for informed decision-making. Meanwhile, utilizing a dual-channel gastroscope, specialized foreign body forceps, and a symmetrical snare designed for polyp removal enables a secure, efficient, and straightforward extraction of the balloon. This approach ensures the balloon is removed without any misplacement risk while maintaining patient comfort throughout the procedure[44].

Endoscopically-placed balloons are normally placed in the stomach for no longer than 6 mo, after which they are removed, as they can cause complications[45]. A meta-analysis of 5668 participants found there was moderate indication of improvement in most metabolic markers in participants (IGB therapy *vs* standard non-surgical therapy)[46]. In another review, the total body weight loss (TBWL) of the IGBs after 6-mo implantation was 6.8%-13.2% at 12 mo *i.e.*, 7.6%-11.3% TBWL[47]. Furthermore, 20 randomized controlled trials (RCTs) were used in a meta-analysis involving 1195 patients, indicating significant effects following IGB use[48]. Another similar meta-analysis was comprised of thirteen RCTs with a total of 1523 subjects. At follow-up, the difference in mean % excess weight loss (EWL) was 17.98% [total weight loss (TWL) was 4.40%] and was substantially larger in the IGB group. This concluded that, in overweight and obese individuals, IGB therapy is more effective than lifestyle change alone for weight loss[49]. Additionally, in the RCT, 288 patients were assigned at random to one of two groups: IGB or control group. At 32 wk, the mean TWL in the IGB group was 15% [95% confidence interval (CI): 13.9-16.1] against 3.3% (2-4.6) in the second group which remained as a control without any intervention (P < 0.0001). Seven (4%) patients experienced major adverse events (AEs) associated with the device, with no deaths. When therapy was combined with lifestyle changes, substantial weight loss was obtained and sustained for 6 mo after IGB removal[50]. A 10-year review was performed and initially, 49 patients (IGB *vs* control group) were included with a 51.6% follow-up rate. TBWL favored the IGB group at 6 mo [9.75 *vs* 7.48 kg (P = 0.03)], at 12 mo [6.52 *vs* 4.42 kg (P = 0.05)], at 18 mo [5.42 *vs* 3.57 (P = 0.32)], and 24 mo [4.07 *vs* 2.93 kg (P = 0.56)]. TWL at 10 years was 0.03 *vs* -2.32 kg (P = 0.05) and %TWL was -0.16% ± 12.8% *vs* -2.84% ± 5.6% (P = 0.39), which were not statistically different between groups. BMI at follow-up [30.97 ± 1.6 *vs* 30.38 ± 1.8 kg/m^2 (P = 1.00)] was comparable and it was concluded that IGB provides weight loss for up to two years and is superior to the control[51]. In contrast, in one of the studies only 2910 (0.4%) of the 652927 individuals identified received IGB treatment. Patients who received IGB therapy were older, had a lower BMI at baseline (37.0 ± 6.2 kg/m^2 *vs* 45.3 ± 7.8 kg/m^2), and had a greater rate of early non-operative re-intervention (7.7% *vs* 1.1%; P < 0.0001). Between 2016 and 2019, according to the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program the number of IGB procedures reported decreased considerably [953 (0.62%) *vs* 418 (0.25%); P < 0.0001]. Given the safety and efficacy of current bariatric surgery and novel pharmaceutical treatments for weight loss, the function of IGBs in treating obesity remains uncertain[52]. In another study, the mean preoperative BMI for all 20680 IGBs, encompassing 12 distinct models, was 34.05 kg/m^2. On average 17.66% ± 2.5% of TBWL was noted. There were 3.62% early removals because of intolerance. Consensual management had an AE rate of 0.70% and 6.37% for major and mild problems, respectively. Only one death was reported[53]. In short, many patients have benefited from the IGBs, which bridges the gap between clinical management of obesity, medications, and bariatric surgery while also helping thousands of patients lose weight and improve their comorbidities[34]. A summary is also described in Table 1.

The United States FDA has approved three IGBs. Orbera is an endoscopically implanted single balloon[54]. ReShape is a duo balloon system, connected in the middle by a tube. The third balloon, Obalon (Figure 2), is filled with nitrogen gas and is part of a three-balloon treatment. All systems require endoscopic placement and removal after 6 mo[55].

A single balloon (Orbera IGB)

The Orbera IGB (OIB) is a single fluid filled IGB authorized for weight loss induction and obesity treatment[56]. The FDA-approved Orbera is a single 13 cm silicone-made balloon that arrives commercially deflated and is inflated at the end by a filling tube connected to a radiopaque self-sealing valve. Following a diagnostic endoscopy, the balloon implantation assembly is inserted directly into the stomach, and a volume of 500 to 700 mL saline solution [this volume range (500 to 700 mL) is chosen based on optimal balloon expansion and effective positioning within the stomach] with 5 mL of methylene blue used for balloon inflation *via* a closed infusion system, with the entire procedure being performed under direct endoscopic observation[57,58]. The FDA has approved Orbera for a 6-mo placement in people with a BMI of 30-40 kg/m^2. To rule out contraindications, such as a big hiatal hernia or a stomach ulcer, an endoscopy should be performed before or concurrently with placement[54].

Orbera® meets the obesity therapy "preservation and incorporation of valuable endoscopic innovations" thresholds of 5% TBWL and 15% EWL over control, respectively[59]. Similarly, a review of a database of individuals who had the OIB endoscopically placed revealed that it was effective, safe at inducing weight loss, and reduced complications related to obesity[56]. There were no spontaneous deflations observed in employing the OIB system. In this device, deflation can be detected through weight changes or patient-reported loss of satiety; however, current practice mandates a very simple method of detection through observing any irregular change in urine output[60].

A double balloon system (ReShape Integrated Dual Balloon System)

The ReShape IGB is a temporary implantation of a fluid-filled balloon that is designed to encourage weight loss by occupying space in the stomach. Endoscopy is utilized to deliver the balloon trans-orally. After positioning, inflation is done with saline (sterile) and methylene blue, which is used as an indicator in case the balloon mistakenly leaks or deflates. The balloon can remain in the stomach for six months[61].

In one study, total body weight was found to be lowered by 6.8% ± 7.3% (P < 0.001) and BMI was reduced by 2.7 ± 2.9 kg/m^2 (P < 0.001) in all patients who had the ReShape IGB implanted, with completed follow-up of 6 mo. According to subgroup analyses, patients with > 40 kg/m^2 BMIs reported significant reductions in TBWL and BMI[61].

A three-balloon system

The three-balloon system is made up of three distinct balloons. These are placed through the mouth and subsequently filled with gas nitrogen to a capacity of roughly 250 mL by a connected catheter. One balloon is implanted monthly, with a maximum of three balloons. All balloons are removed endoscopically six months after the placement of the first balloon. The anticipated TBWL is 7.1%[62]. In one study, a swallowable gas-filled IGB device was deemed safe after six months

Table 1 A summary of endoscopic procedures for reducing weight in obese patients

Method	Indication (BMI)	Duration	Efficacy	Adverse events	Limitations	Ref.
IGBs	30-40 kg/m^2	6 mo	IGB therapy is a successful short-term weight loss strategy	Nausea/vomiting and stomach pain were the most common consequences, but mortality and gastric perforation were unusual. Other serious problems included dehydration, which required hospitalization, and intestinal obstruction due to balloon deflation, which required surgery	Short-term effects and weight regain	[45,48,50,54,87]
AT	35-55 kg/m^2	Long term usage	AT is an implantable device that drains a portion of the stomach contents after each meal, removing up to 30% of the calories consumed	Postoperative peristomal granulation tissue and peristomal irritation, cardiac arrhythmias, hypokalemia, hypochloremic hypokalemic metabolic alkalosis, rather than gastric botox and eating problems	It cannot be used for patients with eating disorders. For this technology to be effective and long-lasting, significant patient commitment, motivation, and adherence are necessary. In addition to adhering to correct device operation, chewing food thoroughly is a significant crucial aspect in attaining successful weight reduction using this device; thus, patients who fail to stick to thoroughly chewing their meal are unlikely to get ideal outcomes	[91,94,99]
Small bowel endoscopic procedures	41.5 kg/m^2	6-12 mo	10.6% TBWL and 40.2% EWL after one year	There were no AEs, and the nausea and diarrhea were self-limiting	Short-term efficacy, no small bowel EBTs are currently FDA-approved	[32,83,102,103,150]
Endoscopic sleeve gastroplasty	> 30 kg/m^2	6-24 mo	%TBWL 12%-19% [150]	Leaks, perforation, hemorrhage, improved depth perception, improved visualization, severe stomach discomfort, and perigastric collection are all possible AEs	Required expertise and skills	[105,111,119,150]
Endoluminal procedures	30-40 kg/m^2	6-12 mo	41.5 kg/m^2, which reduced to 33.1 kg/m^2	Pain, nausea, and vomiting	N/A	[129,130]
DJBS	> 35 kg/m^2	6-12 mo	Effective patients lost 15% of their body weight at 12 mo, compared to 4% of controls	Nausea, vomiting, pancreatitis, GI bleeds, hepatic abscess, obstruction of the sleeve	As the common channel length shortens, so do diarrhea and severe vitamin A and D deficits	[132,135,137-139]
GJBS	30-40 kg/m^2	N/A	Patients reduced 39.7% of their excess	N/A	N/A	[140,141]
Regulation gastric emptying	N/A	N/A	Weight loss was within 10% of their optimum weight	N/A	Hormonal imbalance and weight regain	[148,149]

IGBs: Intragastric balloons; AT: Aspiration therapy; TBWL: Total body weight loss; EWL: Excess weight loss; N/A: Not applicable; GJBS: Gastroduodenal jejunal bypass sleeve; DJBS: Duodenal-jejunal bypass sleeve; GI: Gastrointestinal; AEs: Adverse events; EBT: Endoscopic bariatric therapy; FDA: Food and Drug Administration; BMI: Body mass index.

and resulted in double the weight loss than a sham control, with significant weight loss maintenance at 48 wk[63]. However, a study with 87 individuals who were successfully implanted with IGBs (gas-filled IGB; fluid-filled IGB) showed no differences in %TBWL between balloon systems at removal and 12 mo (P = 0.39). Although both gastric balloon systems were equally effective, the gas filled IGB had fewer significant side effects[64].

Orbera 365 balloon

The revolutionary ORBERA 365® balloon, made by Apollo Endosurgery, can remain within the stomach for a full year, hence its name[65,66]. Up to this point, limited studies with clinical data have been published. In one study, 97 individuals had an Orbera365 implanted. Prior to the treatment, the average weight and BMI of participants were 93.8 kg and 35.2 kg/m^2, respectively. After the procedure, these values decreased to 80.6 kg and 29.8 kg/m^2 after 8.2 mo and to 82.4 kg and 30.4 kg/m^2 on the last day of follow-up after 12.9 mo[62]. In another study, the weight reduction at IGB (Orbera) removal after 6 mo and at IGB (Orbera 365) removal after 12 mo was retrospectively examined. Mean TBWL was 15.2 and 15.8 kg in patients undergoing IGB placement for 6 and 12 mo, respectively. In patients receiving IGB placement for 6 or 12 mo, there was no discernible change in the mean %TBWL (15.3% *vs* 14.7%, P = 0.7)[67].

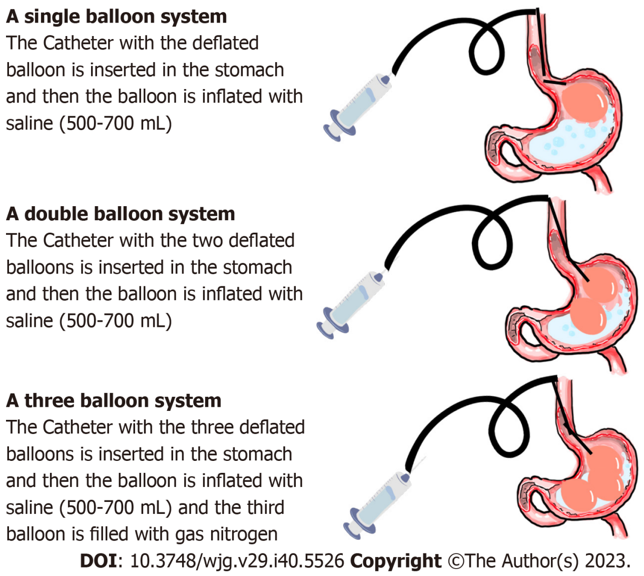

Figure 2 Different types of intra-gastric balloon system.

IGBS (AIR-FILLED)

IGBs, like air-filled balloons, as a temporary endoscopic treatment for obesity, have the potential to play an important role for the obese population[54]. They can also be used as a preoperative test before doing restricted bariatric surgery on patients. Furthermore, an intragastric device can be used as a "bridge treatment" before major surgery in individuals with severe obesity to lower the risk of operation-related complications[68]. Furthermore, IG balloons play a pivotal role as a transitional measure before bariatric surgery by serving as a bridge to reduce BMI and potentially mitigate the associated surgical risks. IGBs help patients achieve a lower BMI by facilitating initial weight loss, which may lead to improved overall health and decreased comorbidities. This reduction in BMI can also contribute to decreased surgical complications during subsequent bariatric procedures. Acting as a preoperative intervention, IGBs offer a safer trajectory for individuals with high BMI, allowing them to undergo bariatric surgery with potentially reduced morbidity and an enhanced surgical outcome. According to research, the air-filled balloon is effective and well tolerated, with weight reduction comparable to other types of balloons[69].

The air-filled IGB has not been shown to be harmful. It appears to have the same effect on weight loss as other balloons. After removal of the balloon, 30% of the patients in one study sustained a weight decrease of more than 10%[70]. However, in a comparative study, patients undergoing saline-filled balloon therapy (4.66 ± 4.75) lost considerably more weight than patients undergoing air-filled balloon surgery ($P < 0.001$). The variation in early withdrawal rates between the two groups, on the other hand, was minor ($P = 0.21$)[71]. With the air-filled IGB, the balloon is inflated with a specific gas, such as air or a mixture of air and nitrogen, using a catheter or a small tube connected to the balloon. The gas inflates the balloon, causing it to expand and take up space within the stomach[41].

Obalon

The United States FDA approved Obalon for the treatment of obesity[72]. This device, which is swallowed as a gel at the end of thin tubing, can be used anywhere. The device is then filled with a gas, and fluoroscopy is used to ensure proper installation. As a result, removal requires only one endoscopic treatment[73].

In one study, patients were randomly assigned to receive 3 balloon capsules (Obalon) or three sugar filled dummy capsules in a RCT with 15 facilities in the United States. A licensed dietician provided lifestyle advice to all subjects every three weeks. The treatment group's %TBWL was 6.81% ± 5.1%, while the control group's TBWL was 3.59% ± 5.0%. In the therapy group, the responder rate was 64.3%, defined as %TBWL > 5%. Minor AEs, such as abdominal pain and nausea, occurred in most patients, with only one serious AE, which was a gastric ulcer in a patient who violated the research protocol by using a nonsteroidal anti-inflammatory medicine[71]. Mion *et al*[74] reported a prospective feasibility study, and all balloons were retrieved *via* upper gastrointestinal (GI) endoscopy 12 wk after the ingestion of the first balloon. Of the 44 balloon swallowing attempts, 43 (98%) were successful. Nausea and stomach pain were the most common AEs. Significant weight reduction was reported as well[64].

Heliosphere

The Heliosphere Bag is a silicone-encased air-filled polymer balloon[74]. When compared to fluid-filled balloons, this endoscopy-inserted device weighs less than 30 g, shows a 30-fold weight reduction, and it is certified for 6-mo use[41]. This device demonstrates a high effectiveness and tolerance profile. Loss of weight seems to be comparable to that of other types of balloons. In contrast, technical issues, particularly during removal, are most likely related to the device's substance and create a low safety profile[74].

In one study, the average weight reduction and BMI drop were 14.5 ± 8.2 kg and 5.3 ± 2.8 kg/m², respectively (P < 0.001). During the first week after Heliosphere Bag implantation, 7.4% of patients experienced nausea and vomiting[75]. Even though mid/long-term follow-up may result in some weight gain, Heliosphere® BAG allows for short-term loss of weight with few AEs[76]. Furthermore, De Castro *et al*[77] showed comparable weight reduction outcomes. Meanwhile, fluid-filled balloons are found to be more beneficial for weight loss[77]. In addition, a life-threatening complication was also reported in a patient using Heliosphere Bag[78].

Elipse

The Elipse balloon is a unique non-endoscopic weight loss approach[79]. At 16 wk, the Elipse IGB is naturally excreted out as it is a swallowable balloon[80]. Although Elipse has a shorter residence period in the stomach than other standard IGBs that need endoscopy, the procedure appears to have identical results[81]. Vomiting and nausea are the most common AEs. There were no major AEs[82].

In prospective research, 51 Elipse insertions were performed, and the patients' total weight reduction was 8.84 kg, %EWL 40.84%, %TBWL 10.44%, and change in BMI 3.42 kg/m². The device was proven to be effective; however, several limits were discovered that must be overcome for improved results[83]. Furthermore, a meta-analysis showed that the Elipse IGB is effective in weight reduction, safe, and is an efficient obesity technology with a low AE profile. A study conducted in Italy found early results after 4 mo with a mean %EWL of 26%. There were no balloon passage issues in the included patients[84].

COMPLICATIONS WITH IGBS

Despite the extremely low rates of difficulties and death linked with IGBs, AEs and complications can occur, and they can range from mild to severe[85]. The most prevalent AEs reported were vomiting, nausea, and stomach pain, while fatalities and gastric perforation were uncommon[86]. However, a 58-year-old Pakistani female presented with 2 wk of vomiting and abdominal bloating. While the external pigtail catheter and blue clasp for retrieval were stretching into D1/D2, the balloon was impacted at the antrum and pylorus. This is a relatively uncommon IGB complication[87]. Other severe complications included dehydration, which necessitated hospitalization, and intestinal blockage induced by balloon deflation, requiring surgery[88].

In conclusion, fluid-filled balloons are much more likely to result in weight loss than gas-filled balloons. They may, however, be associated with a higher likelihood of intolerance and removal. This data will assist clinicians in selecting devices and engaging patients in collaborative decision-making[89].

AT

The AspireAssist AT is the first FDA-approved device for the treatment of class II and III obesity[90]. AT comprises an endoscopic placement of a gastrostomy tube (A-tube) and an AspireAssist siphon component to aspirate gastric contents 20 min after meal consumption[91] (Figure 3), in conjunction with lifestyle modifications and an external device to allow drainage of around 30% of the calories taken in a meal[92]. It is approved for long-term usage in persons with BMIs of 35-55 kg/m² in the United States[93].

Studies show 14.2% to 21.5% TBWL in participants who complete one year of treatment and weight loss maintenance when treated for two years[94]. A pilot study was conducted, and patients in the AT group dropped 18.6% ± 2.3% of their body weight with 49.0% ± 7.7% EWL after one year, while in the lifestyle therapy group patients lost 5.9% ± 5.0% and 14.9% ± 12.2% EWL (P < 0.04). AT was found to be effective and safe as a long-term obesity weight loss therapy[95]. Similarly, a multicenter study with 82 individuals was carried out where the patients' average baseline BMI was 41.6 ± 4.5 kg/m². At the conclusion of the first year, participants had 34.1 ± 5.4 kg/m² BMI and 18.3% ± 8.0% TWL. Patients experienced 15.3% TWL after 2 years, 16.6% after 3 years and 18.7% TWL after 4 years with a significant difference (P < 0.01). The safety profile of AT was found to be satisfactory, effective, and approved for long-term weight loss treatment. Additionally, AT was found to be a safe and effective therapy for reducing weight as the mean percent total weight reduction was 18.2% ± 9.4%, 19.8% ± 11.3%, 21.3% ± 9.6%, and 19.2% ± 13.1%, at 1, 2, 3, and 4 years, respectively[96]. Similarly, a study with 25 obese participants was undertaken, and after 2 years of AT, BMI was 31.0 ± 5.1 kg/m², P < 0.01, and EWL was 61.5% ± 28.5%, P < 0.01. It was concluded that AT is a safe and efficient treatment for obesity, and weight loss enhances QoL[97]. Furthermore, the effects were not limited to obesity; comorbidities related to obesity, such as diabetes, blood pressure, triglycerides, and lipoproteins, were significantly improved with AT[98].

However, the most commonly observed AEs with AT were perioperative discomfort and stomach pain as well as postoperative peristomal granulation tissue and peristomal irritation[91]. This can cause more serious hypokalemia, cardiac arrhythmias, and hypochloremic hypokalemic metabolic alkalosis than gastric botox. Some eating disorders can also be caused by AT[99]. Indeed, gastric irrigation and aspiration may result in persistent loss of chloride and hydrogen ions. The physiologic response is renal potassium ion secretion and hydrogen ion resorption; hypochloremic hypokalemic metabolic alkalosis may occur[100].

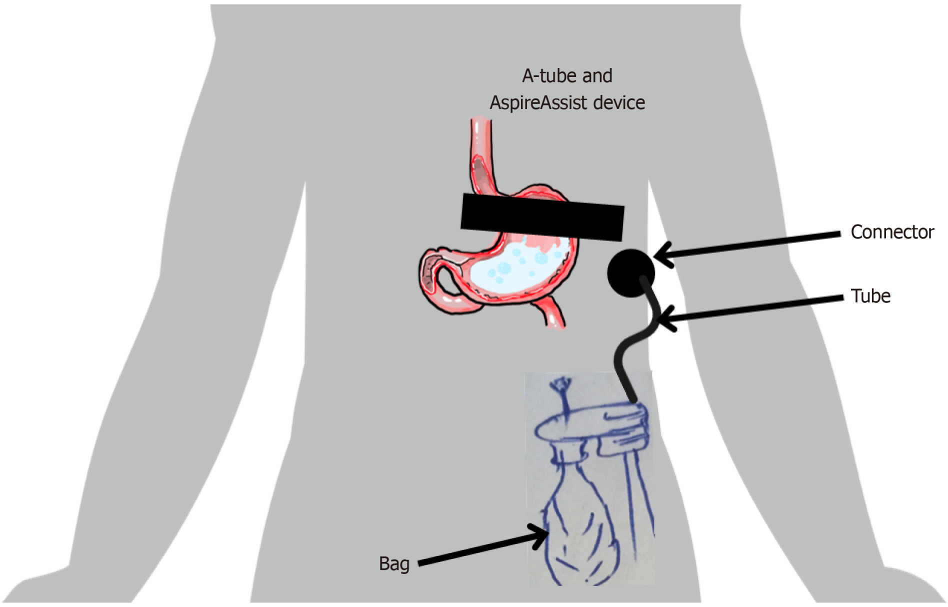

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Figure 3 Schematic illustration of aspire assist device when in place.

SMALL BOWEL ENDOSCOPIC BARIATRIC TECHNIQUE

Endoscopic bariatric therapies for the small bowel include incisionless anastomosis devices (IAS), bypass sleeves and duodenal mucosal resurfacing. Endoscopic bariatric treatments can be performed safely and efficiently for weight loss and metabolic improvement, according to clinical evidence, employing tiny intestinal devices[98]. These therapies focus on foregut and hindgut processes to achieve weight loss and enhance glucose homeostasis[101]. When fully deployed, the IAS magnets form an octagonal shape. Pairs of IAS magnets are inserted into distinct segments of the small bowel, *via* simultaneous enteroscopy and colonoscopy, and are connected under endoscopic and fluoroscopic view[102].

In a research pilot, ten patients with a 41 kg/m^2 mean BMI had the operation. Laparoscopy was performed in this pilot study to establish appropriate magnet coupling and to validate limb lengths. The anastomosis developed in about a week, and the magnets were ejected without any pain or hindrance. At the 2 and 6-mo follow-up endoscopies, all anastomoses were patented. After six months, the patient had a 10.6% TBWL and 40.2% EWL after one year, and all anastomosis endured a patent[103]. There were no AEs. Diarrhea and nausea were self-limiting[102], as shown in Table 1.

ENDOSCOPIC SLEEVE GASTROPLASTY

Endoscopic sleeve gastroplasty (ESG) is a newer type of noninvasive weight loss procedure that uses a suturing device [104]. The endoscopist uses sutures to form a tube-like configuration in the stomach to promote restriction. If diet and exercise are not working and one is extremely overweight (BMI of 30 or higher), this treatment may be possible (Table 1). The technique is minimally invasive, which reduces the risk of operational impediments and allows for a speedy return to normal activities[105]. Additionally, the overstitch system also includes a double-channel endoscope with a suturing platform attached to it. A tissue grasper device is used to mobilize and capture the desired position of the suture on the stomach wall, after which the tissue is retracted into the device's suturing arm [106].

A recent study discovered that a customized running suture adopting a Z-pattern had a good effect on producing a homogeneous distribution of the suture's disruptive force across all stitch positions[107] and a "U" stitch pattern was also used[108]. Furthermore, a review of seven of the eight trials with adequate data revealed a weight loss which was statistically significant (P < 0.05). In an RCT, for the ESG group, the primary endpoint of mean %EWL was 49.2%, and for the control group, it was 32% at 52 wk (P < 0.00001). ESG had a significant weight loss, which was sustained at 104 wk and is also safe, with significant improvements in metabolic comorbidities[109]. Similarly, in another study, 435 patients from various obesity classes were included. At all-time intervals, ESG had a significantly higher %TBWL, TBWL, and BMI decrease in class III obesity compared to obesity of classes I and II (P < 0.001). In all types of obesity, ESG causes considerable weight loss[110]. Furthermore, efficacy was well established in a multicenter study conducted with 91 patients, and after treatment, BMI reduction after 3 mo was 7.3, after 6 mo 9.3, and after 12 mo 8.6 from baseline. EBWL was 17.3% after one month, 29.2% after three months, and 35.6% after six months with significant difference (P < 0.000)[111]. In addition, a meta-analysis was performed, the ESG resulted in around 15% TBWL or 58% EWL at 6-mo, and there was sustainability in weight loss at 12, 18, and 24 mo[112]. However, a study found laparoscopic sleeve gastrectomy (LSG) to be more efficient than ESG as it improved weight related QoL significantly[113]. Seven studies in a meta-analysis encompassed 6775 patients, with 3413 undergoing ESG and 3362 undergoing LSG procedures. Notable disparities were observed in the percentage of %TBWL, all of which favored LSG over ESG. While there was a tendency towards a decreased occurrence of AEs with ESG compared to LSG, this distinction did not achieve statistical significance [risk ratio (RR) = 0.51, 95%CI: 0.23-1.11, P = 0.09]. The frequency of new-onset gastroesophageal reflux disease was markedly lower following ESG as opposed to LSG, at 1.3% compared to 17.9%, respectively (RR = 0.10, 95%CI: 0.02-0.53, P = 0.006)[114]. Moreover, a total of 2188 patients (1429 for LSG and 759 for ESG) from sixteen studies were included in another meta-analysis. The mean percentage of %EWL was 80.32% (± 12.20%; 95%CI; P = 0.001; I^2 = 98.88) for the LSG group and 62.20% (± 4.38%; 95%CI; P = 0.005; I^2 = 65.52) for the ESG group. This represents an absolute difference of 18.12% (± 0.89%; 95%CI, P = 0.0001) between the two groups. The variation in the average rate of AEs was 0.19% (± 0.37%; 95%CI; χ^2 = 1.602; P = 0.2056)[115]. Similarly, ESG results in weight loss comparable to LSG, with similar improvements in comorbidity resolution and safety profiles was shown in another study[116].

Meanwhile, around 2.3% of patients had serious post-procedure issues; nevertheless, no deaths were documented [117]. Leaks, perforation, bleeding[112], better depth perception, better visualization[118], severe abdominal pain and a perigastric collection[119] have all been reported. Intraabdominal collection, refractory symptoms requiring ESG reversal, hemorrhage requiring transfusion or endoscopic intervention, pneumoperitoneum and pneumothorax and pulmonary embolism[120] are among the serious AEs that have been documented.

In conclusion, as with any weight loss intervention, the success of the ESG procedure can be influenced by factors such as patient adherence to lifestyle changes, dietary habits, and individual metabolic factors. Comparing the lasting utility of ESG with LSG, a surgical procedure, the latter has a longer track record and more established data on long-term outcomes. LSG has demonstrated sustained weight loss and metabolic improvements over several years. However, it is essential to note that LSG is a more invasive procedure with potential surgical risks and complications. When evaluating the choice between ESG and LSG, patients and healthcare providers should consider the balance between the invasiveness of the procedure and the expected long-term outcomes, as well as individual patient preferences and medical considerations.

ENDOLUMINAL PROCEDURES

Endoluminal procedures performed exclusively using gastrointestinal flexible endoscopy provide safer and more cost-effective alternatives to currently used surgical techniques for obesity management. However, endoscopic gastroplasty is one of the promising applications of endoluminal procedures in the field of metabolic obesity disorder[121]. Several endoluminal treatments for the loss of weight in obese patients have been developed, claiming to be as effective as surgery but safer[122]. Endoluminal obesity treatments show promise, and recent technology breakthroughs have been amazing. However, new therapies have had to meet the same requirements as present surgical treatments[123]. In fact, until the success of endoluminal treatments was proven, most surgeons were unwilling to consider them for their patients [124].

The transoral gastroplasty (TOGA) method conducts a vertical gastroplasty along the smaller curvature of the stomach using transoral endoscopy[125]. As a result, a gastric pouch forms, which restricts the food quantity or liquids that the patient can intake, resulting in an early feeling of fullness[126]. Another technique is the incisionless operating platform (IOP) which is used in primary obesity surgery endoluminal (POSE). The IOP is a four-part device used to regulate a full-thickness plication system endoscopically. It delivers a series of anchors into the stomach to encourage gastric imbrication [127].

In a systematic review, it was concluded that endoluminal plication devices were more successful in 91.8% of patients with 5.02% lower recurrence rates than sclerotherapy and Argon Plasma coagulation, which also had 46.8% success and 21.5% recurrence rates, respectively[128]. The same findings were reported in a multicenter trial with a one-year follow-up that included 67 patients with a mean BMI of 41.5 kg/m^2, which decreased to 33.1 kg/m^2 at 6 mo after TOGA treatment, with consequences including respiratory insufficiency and an asymptomatic pneumoperitoneum[129]. In a 12-mo multicenter RCT in the United States, 221 patients got the POSE surgery in conjunction with low-intensity lifestyle interventions. They attained a TBWL of 4.95% ± 7.04% against 1.38% ± 5.58% in the sham group with complications such as pain, nausea, and vomiting also reported[130].

The POSE and ESG methods are distinct endoscopic approaches for obesity control. Meanwhile, the POSE method involves the creation of tissue folds within the stomach to reduce its size and restrict food intake without removing tissue. In contrast, the ESG method involves suturing and narrowing the stomach's capacity, resembling a sleeve, to induce weight loss. While both methods are minimally invasive and avoid surgical incisions, the POSE method focuses on tissue folding, while the ESG method centers on suturing, leading to different mechanisms of action. The choice between these techniques depends on individual patient characteristics, preferences, and specific weight loss goals.

MALABSORPTIVE ENDOSCOPIC PROCEDURES

Malabsorptive endoscopic procedures may potentially provide an opportunity for an ambulatory technique that is both safer and less expensive than laparoscopic surgery. Endoscopic malabsorptive treatments can result in weight loss and have improved metabolic parameters associated with obesity[131].

Duodenal-jejunal bypass sleeve

The Duodenal-jejunal bypass sleeve (DJBS), known as DJBS is introduced using endoscopic and fluoroscopic methods. This implant consists of a non-porous fluoropolymer sleeve, temporarily anchored within the duodenal bulb and extending approximately 80 cm into the small intestine, typically ending in the proximal jejunum[132,133]. It allows chyme to move from the stomach to the jejunum without contacting the duodenum. By not allowing mixing with pancreatic exocrine secretions and bile in the jejunum, it replicates a duodenal-jejunal bypass and promotes weight reduction through malabsorption[123]. Which has similarities to Roux-en-Y gastric bypass (RYGB) and this combined mechanism aims to achieve weight loss by reducing calorie intake and altering nutrient absorption patterns. The DJBS procedure offers a potentially reversible option for individuals with obesity seeking to manage their weight and improve metabolic health[134].

In a cohort trial, after 6 mo of DJBS treatment, there was a substantial rise in EWL and a drop in weight[135]. Similarly, a blinded, randomized, prospective clinical trial was carried out to assess the safety and efficacy of a new device for obese weight loss. The DJBS device was successfully implanted. At the end of the three-month research period, the device was removed endoscopically. The patient's TBWL was 9.09 kg[136]. Additionally, in another multicenter study, RCT was conducted with 41 patients and the EndoBarrier Gastrointestinal Liner device was implanted. After 3 mo, the mean EWL for the intervention group was 19% *vs* 6.9% for control patients ($P < 0.002$). The BMI absolute change was 5.5 and 1.9 kg/m^2, respectively. The device was discovered to be a practical and safe noninvasive weight loss device with outstanding short-term weight loss results[133]. Similar to previous research, in a multicenter open-label RCT, 24% of DJBS patients lost 15% of their body weight at 12 mo, compared to 4% of controls (odds ratio = 8.3, 95%CI: 1.8-39; $P = 0.007$). The inclusion of the DJBS to intense medical care was linked to greater weight loss and improvements in QoL[137]. However, significant weight recovery happens during long-term follow-up after device removal, particularly in people with BMIs larger than 35 kg/m^2[138].

In total, 3.7% of patients experienced serious AEs such as pancreatitis (2 cases), GI bleeds (7 cases), hepatic abscess, obstruction of the sleeve, and esophageal tears[139]. There were no reported fatalities. Mild AEs primarily comprised nausea, vomiting, and anchor ulceration. Meanwhile, the attachment point of the DJBL was responsible for inducing or potentially inducing 85% of the SAEs[140].

Gastroduodenal-jejunal bypass sleeve

The gastroduodenal jejunal bypass sleeve (GJBS) treatment can help patients lose weight while also managing comorbidities such as diabetes, hypertension, and obstructive sleep apnea[15]. In theory, this device is the same as the EndoBarrier®. Its sleeve, on the contrary, is attached at the esophagogastric junction and continues about 120 cm through the stomach into the small bowel, imitating the ultimate anatomical structure in RYGB surgery. As a result, food passes immediately from the esophagus to the intestine, with no nutritional absorption occurring in the stomach, duodenum, or jejunum[141].

In one study, the GJBS was implanted in 24 patients. These patients reduced 39.7% of their excess weight by the end of the study. AEs were limited and resolved after the endoscopic device was removed[142]. Similarly, the implementation and retrieval were both safe. It is generally tolerated and has a favorable safety profile. It provides effective weight loss results, with more than 70% of all comorbidities cured or improved[143].

REGULATING GASTRIC EMPTYING

Changes in gastrointestinal motility, which are critical in food absorption and digestion in the gastrointestinal tract, may be one of the reasons why obesity develops[144]. The functions of incretins, particularly glucagon-like peptide-1, gastric inhibitory polypeptide, peptide tyrosine-tyrosine, glucagon, the duodenal and pancreatic hormones motilin, amylin, motilin, and the gastric orexigenic hormones ghrelin have the greatest impact on stomach emptying. Except for ghrelin and motilin, which accelerate stomach emptying, all these hormones delay gastric emptying[144]. The vagus nerve regulates the change in fundic compliance (also known as accommodation) once food enters the stomach, allowing the stomach to develop a reservoir with just a slight increase in intragastric pressure, boosting food intake[145,146]. Changes in circulating gut hormone concentrations activate a variety of pathways, especially in the brain stem and hypothalamus, which influence eating behavior and a variety of metabolic progressions[147]. In addition, gastric emptying inhibition may contribute to a decrease in energy intake. Mechanoreceptor activation caused by stomach distension may restrict additional food intake *via* neuronal reflex arcs[148]. However, diet-induced weight reduction causes long-term alterations in gut hormones for appetite, which are thought to favor increased desire and weight regain[149].

In an experimental study, the subjects were all subjected to quantitative fluid/solid gastric emptying experiments using a dual radionuclide method. In the solid phase, obese patients had a faster emptying rate than nonobese subjects ($P < 0.05$). Repeat gastric emptying investigations on four obese participants whose weight loss was within 10% of their optimum weight found no change in liquid or solid emptying rates. Obese patients have an abnormally fast rate of solid stomach emptying[150].

FUTURE DIRECTIONS

The future directions as follows: (1) A customized step-up approach aimed at improving and sustaining health performance is ideal, such as lifestyle therapies, nutrition modification, psychiatric treatment, medication and, if necessary, bariatric surgery; (2) In obese patients, EBTs successfully control metabolic comorbidities, improve overall weight loss and lower adverse risk events; (3) There should be some proper peer-reviewed guidelines for the implementation of

EBTs; (4) Studies should be conducted to increase the efficacy of EBTs as they are effective for a short time, and the problem of weight regain is also observed in EBTs, which should also be addressed; (5) Due to the vast variety of accessible therapies, the majority of which are not FDA-approved, first, there is a need to follow FDA and other quality control organizations to get approval; (6) There is a lack of a consistent therapeutic strategy, as well as a lack of training programs, which has limited their distribution and usage, short training programs should be organized and, if possible, should be added in the curriculum of medical schools; (7) Sophisticated endoscopy is now becoming a major component of minimally invasive fellowships, preparing surgeons to take on the role of bariatric endoscopists; (8) Cost benefits analysis should be made for a better understanding of the total expenditure on the use of therapy; and (9) Longer follow-up and larger multicenter RCTs are required to confirm current outcomes and improve the standardization process of these procedures.

CONCLUSION

Obesity is a chronic systemic disease that requires a multidisciplinary approach for prevention, treatment, and management. Proper treatment must be personalized and tailored to the degree of the patient's obesity and the combination of comorbidities. According to different studies, lifestyle changes and medicines can only achieve moderate weight loss results. Despite the fact that bariatric surgery has been shown to be a game-changing strategy in obesity, many patients find it unappealing due to its adverse effect profile and potential long-term difficulties. Compared to standard surgical treatments, bariatric endoscopic therapies may offer a valuable armamentarium in the therapy of obesity because their success in loss of weight is accompanied by being less intrusive, reversible, cost-effective and having a positive safety profile. It may become increasingly popular in the coming years because, when compared to surgery, it has a lower chance of AEs. Long-term efficacy is unknown at this moment. Additional research on long-term efficacy, metabolic disease outcomes, and RCTs is required. However, the future of obesity treatment lies in a multidisciplinary strategy requiring various treatment methods.

FOOTNOTES

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