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Devices and Endoscopic Bariatric Therapies for Obesity

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Abstract

Purpose of Review In this review, we describe the FDA-approved and investigational devices and endoscopic bariatric therapies for the treatment of obesity. We focus on literature published in the past few years and present mechanisms of action as well as efficacy and safety data.

Recent Findings Devices and endoscopic procedures are emerging options to fill the significant treatment gap in the management of obesity. Not only are these devices and procedures minimally invasive and reversible, but they are potentially more effective than antiobesity medications, often safer for poor surgical candidates and possibly less expensive than bariatric surgery.

Summary As many patients require a variety of management strategies (medications, devices, procedures, and/or surgery) in addition to lifestyle modifications to achieve clinically significant weight loss, the future of obesity treatment involves a multidisciplinary approach. Combinations of advanced treatment strategies can lead to additive or synergistic weight loss. This is an area that requires further investigation.

Keywords Obesity · Devices · Endoscopic bariatric therapy · Intragastric balloon · Aspiration therapy · Vagal blockade

Introduction

Lifestyle interventions including diet, exercise, and behavioral modifications are the foundation of weight management [1••]. Many patients cannot achieve and maintain clinically significant weight loss with lifestyle interventions alone, however, because adaptive physiologic responses counteract changes in caloric intake and energy expenditure [2–5]. In order to treat the resulting increased appetite and reduced resting metabolic rate, a multidisciplinary approach is often required.

Pharmacotherapy for obesity can be considered for patients with a body mass index (BMI) ≥ 30 kg/m^2 or a BMI ≥ 27 kg/m^2 with weight-related comorbidities [1••, 6••]. Antiobesity medications are generally well tolerated and patients can achieve 4.5–10.9% total body weight loss (TBWL) at 1 year [7]. Barriers to use include poor insurance coverage for new agents, inadequate training of healthcare professionals, and low reimbursement for office visits to address weight management [8]. In addition, some patients cannot achieve sufficient weight loss with lifestyle modification and medication alone.

Surgery results in greater weight loss outcomes and improvement in weight-associated comorbidities compared with non-surgical interventions [9]. For the two most commonly performed procedures, sleeve gastrectomy and Roux-en-Y gastric bypass, percent excess weight loss (EWL) at 1 year is 52–70% and 63–72%, respectively [10]. Bariatric surgery can be considered for patients with a BMI of 40 kg/m^2 or a BMI ≥ 35 kg/m^2 with weight-related comorbidities [1••]. However, only 1% of patients eligible for bariatric surgery ultimately undergo a procedure. Barriers to surgery include low referral rates from primary care physicians, limited access to bariatric surgeons, and high cost of procedures.

Patients who cannot achieve clinically meaningful weight loss with medications and who do not undergo bariatric surgery (either because they do not meet eligibility criteria, they are not surgical candidates, or they choose not to) fall into a "treatment gap." In this review, we describe the emerging devices and endoscopic procedures which may help to address this unmet need in obesity treatment. We focus on literature

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published in the past few years and present mechanisms of action as well as efficacy and safety data. Table 1 presents the efficacy of the five Food and Drug Administration (FDA)-approved devices.

Gastric Devices

Intragastric Balloons

The intragastric balloon is a space-occupying device, which is deployed within the stomach and expands, thus reducing functional gastric volume. The first commercialized device was the Garren-Edwards Gastric Bubble approved by the US FDA in 1984 [19]. The hollow cylindrical device was inserted endoscopically, filled with 200–220 mL of air, and designed to be left in place for 4 months. Mean weight loss was 7–10 kg; however, there were many reported complications including gastric erosions and ulcers, and the device could spontaneously deflate causing bowel obstruction [19–21]. Therefore, the device was removed from the market in 1992. Since then, multiple intragastric balloons have been developed including Orbera (Apollo Endosurgery, Austin TX), ReShape (ReShape Lifesciences, San Clamente CA), Obalon (Obalon Theraputics Inc., Carlsbad CA), Elipse (Allurion Technologies, Wellesley MA), and Spatz3 (Spatz Medical, Great Neck NY). At this time, only the Orbera, ReShape, and Obalon balloons have been approved by the FDA.

The multiple proposed mechanisms of action for the intragastric balloon include delayed gastric emptying and hormonal alterations [22, 23]. The contraindications to use of these devices include history of gastrointestinal surgery, history of clotting/bleeding disorder, large hiatal hernia or other structural abnormalities, gastric mass, and pregnancy [24]. To prevent rebound weight gain and maintain weight loss after removal of the balloons, patients must continue diet and lifestyle modifications. A few studies have evaluated serial intragastric balloon placement and demonstrated additional weight loss; however, these protocols are not currently approved [25–27].

Orbera

The Orbera Intragastric Balloon (formally the BioEnterics Intragastric Balloon) was approved by the FDA in 2015 for patients with a BMI of 30–40 kg/m^2. The balloon is attached to a catheter and advanced into the stomach. The endoscope follows the catheter to ensure the balloon is inflated in the stomach and filled with 400–700 mL of saline. After 6 months, the balloon is punctured to aspirate the saline and removed

Table 1 Efficacy of FDA-approved devices

Device	Description	Trial	Trial arms	Total body weight loss (%)	FDA approval
Orbera Intragastric Balloon	Endoscopically placed intragastric balloon filled with 400–700 mL saline, removed endoscopically after 6 months	Orbera U.S. Pivotal Study [11, 12] Weight loss at 6 months	Orbera Sham	10.2 3.3	2015 BMI 30–40 kg/m^2
ReShape Integrated Dual Balloon (IDB) System	Endoscopically placed balloons (2) attached via a silicone tube and filled with 750–900 mL of saline (total), removed endoscopically after 6 months	REDUCE [13, 14] Weight loss at 6 months	ReShape Sham	6.8 3.3	2015 BMI 30–40 kg/m^2 + at least one weight-related comorbid condition
Obalon Balloon System	Sequentially swallowed balloons (3) filled with 250 mL of gas each, removed endoscopically 6 months after 1st balloon placed	SMART [15, 16] Weight loss at 6 months	Obalon Sham	6.6 3.4	2016 BMI 30–40 kg/m^2
AspireAssist	Endoscopically placed percutaneous gastrostomy aspiration tube	PATHWAY [17] Weight loss at 12 months	AspireAssist + lifestyle Lifestyle alone	12.1 3.5	2016 BMI 35–55 kg/m^2
vBloc Therapy	Laparoscopically implanted device providing intermittent vagal blockade	ReCharge [18] Weight loss at 12 months	vBloc Sham	9.2 6.0	2015 BMI 40–45 kg/m^2 or 35–40 kg/m^2 + at least one weight-related comorbid condition

BMI, body mass index; *lifestyle*, lifestyle counseling (diet + exercise)

through the mouth with a grasping device. A meta-analysis of 1683 patients demonstrated an 11.5% TBWL and a 25.4% EWL at 12 months after balloon placement [28]. Weight loss from the Orbera is also associated with improvement in weight-related comorbid conditions such as hypertension, type 2 diabetes, and hyperlipidemia [29]. The most commonly reported adverse events (AEs) included abdominal pain (33.7%), nausea (29%), early explantation (7%), migration (1.4%), and perforation (0.1%) [28]. As expected, some weight regain occurs after device removal. In a study of 500 patients with obesity who had the balloon in place for 6 months, 53% of patients achieved > 20% EWL loss at 1 year post-removal whereas 23% of patients achieved > 20% EWL at 5 years post-removal [24].

ReShape

The ReShape Integrated Dual Balloon (IDB) System was also approved by the FDA in 2015 for patients with a BMI of 30–40 kg/m^2 and at least one weight-related comorbid condition. ReShape consists of two balloons attached to a silicone tube, which is inserted over a guidewire and filled with a total of 750–900 mL of saline. The balloons are sealed with mineral oil and remain in place for a maximum of 6 months. After 6 months, a catheter is used to aspirate saline and the balloons are removed endoscopically with a snare. A prospective trial demonstrated a TBWL of 15.4% and an EWL of 47.1% at 6 months post-removal among participants who had the balloons in place for at least 6 months (mean duration 6.9 months) [30]. In a randomized sham-controlled trial (REDUCE), patients who had the ReShape IDB for 6 months demonstrated a significant decrease in EWL of 25.1 versus 11.3% in the sham endoscopy group 6 months post-removal [13]. The REDUCE trial also demonstrated improvement in weight-related comorbid conditions. ReShape is generally well tolerated with similar adverse events to the Orbera balloon, including nausea, vomiting, intolerance, gastric ulcers, deflation, and perforation [13, 30].

Obalon

The Obalon Balloon System was approved by the FDA in 2016 for patients with a BMI of 30–40 kg/m^2 as the first intragastric balloon that does not require endoscopic placement. The balloon is encapsulated, attached to a tube, and swallowed in a provider's office under fluoroscopic guidance. Once confirmed in the stomach, the balloon is inflated with 250 mL of a nitrogen-sulfur-hexaflouride gas mixture. If the first balloon is well tolerated, then a second and third balloon can be sequentially swallowed. After 3 to 6 months, the balloons are removed endoscopically. Initial feasibility studies demonstrated up to 36.2% EWL at the end of a 12-week study period [31]. Successful weight loss was confirmed by the SMART trial, a randomized sham-controlled trial of 387 patients who swallowed at least one balloon. All balloons were removed 6 months after the first balloon was placed. The authors demonstrated a 6.81% TBWL compared to 3.59% TBWL with diet and exercise alone 6 months after removal [15]. Similar to the other intragastric balloons, the main AEs with the Obalon balloons mainly include intolerance (abdominal pain, nausea, vomiting, heartburn, bloating) and gastric ulcers [15].

Elipse (Not FDA Approved)

The Elipse Balloon also does not require an endoscopic procedure for placement. Similar to the Obalon, the Elipse is folded inside a capsule, attached to a catheter, and swallowed in a provider's office. It is visualized via fluoroscopy and filled with 550 mL of the supplied filling fluid once inside the stomach. The balloon remains in the stomach for about 4 months until the balloon spontaneously degrades and is passed through the intestinal tract. Initial small observational studies demonstrate a mean 10.0% TBWL at 16 weeks and 5.9% TBWL at 12 months post-balloon placement [32, 33]. Complications during balloon passage can occur. There is a case report of a small bowel obstruction, which was managed successfully by laparoscopy [34].

Spatz3 (Not FDA Approved)

The Spatz3 Adjustable Balloon System is attached to a catheter and inserted endoscopically. The end of the balloon contains a valve connected to an inflation tube that can periodically be accessed through the mouth to alter the volume. During initial placement, the balloon is inflated with 400 mL of saline. During follow-up procedures, the volume can be adjusted based on clinical symptoms. The Spatz3 is the only system designed to remain within the stomach for 1 year. Initial feasibility studies with a previous version of the Spatz balloon demonstrated a mean EWL of 26.4% at 24 weeks and 48.8% at 52 weeks post-placement [35, 36].

Aspiration Therapy

Aspiration therapy involves placement of a percutaneous gastrostomy tube, allowing partial aspiration of each meal after ingestion. AspireAssist (Aspire Bariatrics, King of Prussia, PA) is currently the only FDA-approved aspiration device. It was approved by the FDA in 2016 for patients with a BMI of 35–55 kg/m^2. A percutaneous gastrostomy aspiration tube is placed endoscopically, with an external aspiration port created at the abdominal surface. An aspiration device is attached to the port after meal ingestion to perform an initial flushing (infusion of water) followed by aspiration of a portion (~ 30%) of the meal [23]. In addition to direct calorie

extraction, food particles must be 5 mm or less in diameter and in a slurry to flow through the gastrostomy tube. To achieve this, patients must take extra time to chew thoroughly and drink sufficient liquid with each meal to ensure food will successfully aspirate, frequently leading to smaller meal portions [37].

In the Pivotal Aspiration Therapy with Adjusted Lifestyle (PATHWAY) Study, 207 patients with a BMI 35–55 kg/m^2 were randomized in a 2:1 ratio to AspireAssist plus lifestyle counseling vs. lifestyle counseling alone [17]. At 1 year, AspireAssist resulted in a mean 31.5% EWL (12.1% TBWL), compared to 9.8% EWL (3.5% TBWL) with lifestyle counseling alone. In the AspireAssist arm, 58.6% of patients lost at least 25% of excess body weight, compared to 15.3% of patients in the lifestyle counseling arm. The AspireAssist group also demonstrated significant improvements in hemoglobin A1c (HbA1c), lipid profile, and blood pressure. Notably, there was no evidence of an increase in food intake during or between meals to compensate for the aspirated calories. The most frequently reported AEs included postoperative abdominal pain, nausea, vomiting, peristomal granulation tissue, and peristomal irritation. No evidence of eating disorder development or device overuse was observed.

Hydrogels (Not FDA Approved)

Gelesis100 (Gelesis, Boston, MA) is a hydrogel composed of greater than 99% carboxymethylcellulose cross-linked with citric acid. Gelesis100 is contained within, and administered in, standard gelatin capsules that can absorb up to 100 times their weight in water. When capsules are taken with water prior to a meal, the capsule particles release and expand in the stomach by absorbing water. The particles mix with food and enhance the volume and elasticity of the stomach contents, thereby increasing post-meal satiety and decreasing caloric intake. In this setting, gastric emptying into the small intestine is also delayed, which slows glucose absorption. Gelesis particles partially degrade in the large intestine where water is released and reabsorbed, and the particles are subsequently excreted [38].

The First Loss of Weight (FLOW) study found that administration of Gelesis100 (2.25 g twice daily) over 12 weeks significantly decreased body weight in patients with overweight and obesity, especially those with baseline impaired fasting glucose. The multicenter study enrolled 128 patients who were randomized into three arms: Gelesis100 2.25 g, Gelesis100 3.75 g, and placebo. At 12 weeks, body weight decreased significantly in patients receiving Gelesis100 2.25 g, with TBWL of 6.1%, compared to 4.1% with placebo. TBWL was more pronounced (10.9%) in patients receiving Gelesis100 2.25 g who had baseline impaired fasting glucose and prediabetes, compared to placebo patients with impaired fasting glucose and prediabetes (5.6%). Patients receiving Gelesis100 2.25 g had higher rates of weight loss, and lower rates of weight gain than those receiving Gelesis100 3.75 g. Lower tolerability and compliance may account for this finding. Thirty-one patients (74%) receiving Gelesis100 2.25 g, 35 patients (85%) receiving Gelesis100 3.75 g, and 36 subjects (84%) receiving placebo reported at least one AE during the study. AEs were mainly gastrointestinal and mild in intensity, including bloating, flatulence, abdominal pain, and diarrhea [38].

TransPyloric Shuttle (Not FDA Approved)

The TransPyloric Shuttle (TPS; BAROnova Inc., San Carlos, CA) is a device comprised of a large spherical bulb attached to a small cylindrical weight connected by a flexible tether. The bulb, which remains above the pylorus, prevents migration of the device out of the stomach while the weight moves freely into the duodenum. The TPS is placed through an overtube, which facilitates coiling of a silicone cord into the bulb. The device moves with peristaltic contractions resulting in intermittent gastric outlet obstruction and delayed gastric emptying. This results in prolonged satiety and reduced caloric intake.

A feasibility study published in 2014 evaluated efficacy and safety of the TPS among 20 participants (mean BMI 36.0 kg/m^2) [39]. Mean TBWL was 8.9% at 3 months and 14.5% at 6 months. The device was removed early from two patients due to symptomatic gastric ulcerations. The device was subsequently modified to reduce the risk of ulceration and it is currently being investigated in the ENDObesity II Study, a 12-month multicenter randomized sham-controlled trial [40].

Gastric Procedures

Endoscopic Sleeve Gastroplasty (FDA-Approved Device, Off-Label Use for Obesity)

Endoscopic sleeve gastroplasty (ESG) is a procedure that utilizes the Overstich device (Apollo Endosurgery, Austin, TX) to create full-thickness sutures and reduce gastric volume. The cap-based device is attached to an endoscope and contains a needle driver, a suture anchor, and an actuating handle to transfer the suture. A tissue helix grasps the stomach to allow for sequential sutures of the anterior wall to the posterior wall of the stomach, thereby creating a tubular sleeve [41, 42]. The plications are potentially reversible, and the procedure can be repeated to attempt additional weight loss [43]. Proposed mechanisms for weight loss include delayed gastric emptying, increased satiation and insulin sensitivity, and decreased ghrelin and caloric intake [44].

Multiple case series have demonstrated successful weight loss after ESG. In addition to feasibility studies [41, 43], large case series demonstrate TBWL of 17.6 to 19.0% at 12 months or EWL of 54% at 12 months [44–47]. The largest multicenter study of 213 patients who underwent ESG demonstrated a TBWL of 18.5% at 24 months with improvement in weight-related comorbid conditions including type 2 diabetes, hypertension, and hypertriglyceridemia [48, 49].

The most commonly reported AEs include abdominal pain and nausea ranging from 20 to 80% of patients [44, 45, 47–49]. Reported major complications include bleeding, pneumoperitoneum/pneumothorax, perigastric leak/collection, and pulmonary embolism [44, 49, 50]. The Overstich device is FDA approved for tissue approximation in the gastrointestinal tract, but currently, there is no specific FDA approval for the ESG procedure. Future randomized controlled trials are needed to confirm successful weight loss from the ESG.

Primary Obesity Surgery Endoluminal (Not FDA Approved)

The Primary Obesity Surgery Endoluminal (POSE) procedure uses the Incisionless Operating Platform (USGI Medical, San Clemente CA) to create eight to 10 full-thickness tissue plications along the gastric fundus and distal body of the stomach. The tubular device contains four working channels: one accommodates a slim endoscope and the other three accommodate the procedure instruments – tissue grasper, helical probe tissue grasper, and suture anchoring delivery catheter. The plications prevent expansion of the fundus resulting in increased satiety and decreased caloric intake. Delayed gastric emptying is observed immediately after POSE, but function subsequently normalizes after 6 months [51]. Hormonal changes after POSE include decreased ghrelin and increased peptide YY (PYY).

A prospective case series reported EWL and TBWL at 1 year after the procedure of 44.9–49.4% and 15.1–15.5%, respectively [52, 53]. In the MILEPOST study, a randomized multicenter trial of 43 patients in Europe, POSE with lifestyle modification was compared to lifestyle modification alone [54]. Mean EWL and TBWL were 45.0 and 13.0%, respectively, in the POSE group compared to 18.1% and 5.3% in the lifestyle modification group, respectively. In the ESSENTIAL trial, a randomized sham-controlled trial of 332 patients comparing POSE to lifestyle modification, participants who underwent POSE achieved a 4.9% TBWL while control patients achieved 1.38% TBWL [55]. Though the study did not achieve the primary endpoint of greater than 5% TBWL, self-reported results of decreased perceived hunger, earlier satiety and decreased food craving were significantly higher in the POSE group. The major AEs reported include bleeding and hepatic abscess requiring hospitalization, and minor AEs include abdominal pain, nausea, vomiting, chest pain, sore throat and fever [51, 52, 55]. Additional studies are necessary to determine the safety and efficacy of POSE.

Botox (FDA-Approved Device, off-Label Use for Obesity)

Endoscopically injecting botulinum toxin in key points along the stomach wall can delay gastric emptying and inhibit ghrelin secretion [56]. The technique varies, ranging from five to 20 injections of 100 to 500 IU of botulinum toxin A using antrum-only injection sites versus sites throughout the antrum, body and fundus. Results from small case series in the early 2000s ranged from no weight loss to a statistically significant decrease in weight [57–59]. Randomized controlled trials have been similarly mixed. One double-blind controlled study of 24 patients with obesity who underwent injection of 200 IU into the fundus and antrum demonstrated a statistically significant reduction in weight as well as decreased gastric emptying 8 weeks after treatment [60]; however, another randomized double-blind trial of 10 patients demonstrated no significant reduction in weight or difference in feeling of early satiety [61]. A third double-blind randomized controlled trial of 60 patients demonstrated a significant difference in gastric emptying after 2 weeks, but no significant difference in weight loss after 16 weeks [62]. Meta-analyses of intragastric injection of botulinum toxin A also differ. One study suggested that botulinum toxin injection was associated with successful weight loss if performed in multiple sites including the fundus, body, and antrum whereas another meta-analysis suggested that botulinum toxin injection was not associated with successful weight loss [63, 64]. Botulinum toxin injection is associated with minimal AEs including a decrease in blood pressure after treatment, gastroesophageal reflux, loose stools, and mild nausea [58, 60, 62]. Given the low rate of AEs, the technique is an attractive option for the treatment of obesity, but it remains to be seen whether this technique will garner widespread use given the variable success reported in the literature.

Small Bowel Devices

Duodenal-Jejunal Bypass Liner (Not FDA Approved)

The EndoBarrier (GI Dynamics, Boston, MA) is a duodenal-jejunal bypass liner, which is placed endoscopically and mimics the biliopancreatic limb of the Roux-en-Y gastric bypass (RYGB) by preventing food from contacting pancreatobiliary secretions until the jejunum. The impermeable sleeve is anchored in the duodenal bulb and extends to the proximal jejunum. It is designed to stay in place for 12 months. The mechanisms leading to weight loss and potential blood sugar improvement are not clear and a few small studies examining the effects of the device on gut hormones including ghrelin and glucagon-like peptide 1 reported conflicting findings [65, 66].

A recent meta-analysis evaluating 11 randomized controlled trials (10 of which were outside of the USA) reported

EWL of 35.3% in three studies where the EndoBarrier was implanted for 12 months (mean %EWL difference compared with a control group was significant at 9.4%) [67] Although the EndoBarrier was associated with an improvement in HbA1c of 1.5% after 52 weeks implantation (additional 1% improvement in HbA1c compared with the control group), another recent meta-analysis examining five randomized controlled trials reported no significant reduction in HbA1c or fasting plasma glucose [68].

The ENDO trial, a multicenter, randomized, sham-controlled trial examining the efficacy and safety of the EndoBarrier among 325 participants with obesity and inadequately controlled type 2 diabetes, was terminated early in 2014 due to seven hepatic abscesses in the treatment group ($n = 216$) (https://clinicaltrials.gov/ct2/show/NCT01728116). Device modifications to reduce the risk of adverse events are currently being evaluated.

Gastroduodenojejunal Bypass Sleeve (Not FDA Approved)

The gastroduodenojejunal bypass sleeve (GJBS) (ValenTx, Inc., Maple Grove, MN) is designed to mimic all three components of the RYGB: (1) restriction of food intake due to the small gastric pouch, (2) exclusion of food from the stomach and proximal bowel, and (3) exposure of undigested food to the jejunum. The 120-cm sleeve is initially secured at the esophagogastric junction with endoscopic and laparoscopic techniques and it extends to the jejunum. It is designed to be retrieved endoscopically after 12 months.

In a 2011 prospective single-center trial, 22 patients (mean BMI 42 kg/m^2) had the GJBS implanted. Five participants required early explantation due to dysphagia. Among the 17 participants who completed the 12-week trial, the mean EWL was 39.7% [69]. In a second prospective single-center trial designed to evaluate the device for 1 year, 12 participants (mean BMI 42 kg/m^2) had the device implanted. Two participants required explantation within the first few weeks due to dysphagia and odynophagia. The EWL among the remaining 10 participants was 35.9%. Four patients had partial cuff detachment and, as a result, lower EWL. Among the six participants with attached and functional devices throughout the study, EWL at 1 year was 54% [70].

Small Bowel Procedures

Self-Assembling Magnets (Not FDA Approved)

The Incisionless Magnetic Anastamosis System (IMAS) (GI Windows, Inc., West Bridgewater MA) was designed to create a dual-path enteral bypass from the jejunum to the ileum. The anastomosis is formed by a pair of self-assembling octagonal magnets, which are delivered into the terminal ileum and proximal jejunum via simultaneous colonoscopy and enteroscopy, respectively. The position of the magnets is confirmed by laparoscopy and abdominal radiograph. The magnets cause necrosis of the intestinal tissue, which leads to a permanent anastomosis, and they are subsequently passed through the intestinal tract. Following the procedure, some ingested food and digestive enzymes are diverted directly to the ileum. This leads to increased secretion of glucagon-like peptide-1 (GLP-1), PYY, and other gut hormones.

In a recently published single-arm pilot study, a permanent partial jejunal diversion (PJD) was created in 10 patients with obesity (mean BMI 41 kg/m^2) with no device-related serious adverse events. The anastomosis remained patent in all patients at 1 year. Average TBWL was 14.6% (40.2% EWL at 12 months). Among the four participants with type 2 diabetes (mean HbA1c 7.8%) and the three participants with prediabetes (mean HbA1c 6.1%), there were significant reductions in HbA1c of 1.9 and 1.0%, respectively [71].

Duodenal Mucosal Resurfacing (Not FDA Approved)

The Revita duodenal mucosal resurfacing (DMR) device (Fractyl Laboratories, Inc., Lexington, MA) involves hydrothermal ablation of the duodenal mucosa via a balloon catheter. Although this procedure is not associated with significant weight loss, it has been shown to improve glycemic control. The hypothesis is that modification of the duodenal mucosa can lead to reduced insulin resistance and improved glycemic control.

In a recently published first-in-human, open-label, nonrandomized, single-arm proof-of-concept study performed at a single center in Chile, 39 patients (mean BMI 31 kg/m^2) with type 2 diabetes (mean HbA1c 9.6%) underwent the procedure [72]. Twenty-eight participants had a long duodenal segment ablated (LS, ~ 9.3 cm treated) and 11 had a short segment ablated (SS, ~ 3.4 cm treated). Three patients experienced duodenal stenosis treated successfully by balloon dilation. After 3 months, there was a mean HbA1c improvement of 2.5 and 1.2% in the LS and SS cohorts, respectively. After 6 months, the mean HbA1c improvement was 1.4 and 0.7% (difference between groups not statistically significant), respectively. Among the 8 patients in the LS group with a screening HbA1c 7.5–10% and on stable antidiabetic medications following the procedure, HbA1c was reduced by 1.8% and weight reduction was 2.5 kg at 6 months. There was no correlation between magnitude of weight loss and glycemic improvement. A prospective double-blind sham-controlled multicenter trial is ongoing in South America and Europe.

Nerve Blockade

Vagal Blockade

The vagus nerve plays an essential role in weight regulation via effects on appetite, satiety, metabolism, and autonomic control of the upper gastrointestinal track. Intermittent vagal blockade using a device (Maestro Rechargeable System, ReShape Lifesciences, San Clamente, CA) was approved by the FDA in 2015 for patients with BMI 40–45 kg/m^2, or 35–40 kg/m^2 with at least one weight-related comorbidity. The device is implanted laparoscopically and provides electrical blockade to both trunks of the vagus nerve (vBloc). The Maestro Rechargeable System consists of two leads placed around the anterior and posterior vagal trunks near the gastroesophageal junction, and a rechargeable neuroregulator which is placed subcutaneously on the thoracic wall. The device is recharged transcutaneously [18].

This device was studied in the ReCharge trial [18, 73, 74]. In this study, the vBloc Maestro system was programmed to deliver at least 12 h of therapy daily, and study investigators adjusted daily therapy duration and/or strength based on weight loss and therapy tolerability. The 239 patients with BMI 40 to 45 kg/m^2, or 35 to 40 kg/m^2 with at least one weight-related comorbidity, were randomized 2:1 to either vBloc therapy ($n = 162$) or sham intervention ($n = 77$) for 12 months. After 12 months, patients randomized to vBloc were offered the option to continue open-label therapy. At 12 months, the vBloc group demonstrated a mean 24.4% EWL (9.2% TBWL) compared to 15.9% EWL (6.0% TBWL) in the sham group. At 24 months, 123 (76%) vBloc patients remained in the trial and demonstrated a mean EWL of 21% (8% TBWL). At 24 months, 58% of vBloc participants had lost ≥ 5% total body weight and 34% had lost ≥ 10% total body weight. Quality of life and eating behaviors in the vBloc patients were significantly improved, demonstrating substantial reductions in hunger and improved food-related cognitive restraint. Significant improvements in obesity-related cardiovascular and metabolic parameters were observed, including HbA1c, lipid profile, and blood pressure. Heartburn, dyspepsia, and implant site pain were the most frequently reported AEs. Most AEs were mild or moderate in severity, and there were no serious long-term side effects, such as nutritional deficiencies [18, 73, 74].

Conclusions

Devices and endoscopic bariatric therapies are emerging options to fill the significant treatment gap in the management of obesity. Not only are these devices and procedures minimally invasive and reversible, but they are potentially more effective than anti-obesity medications, often safer for poor surgical candidates and possibly less expensive than bariatric surgery. In addition, clinical trials have demonstrated improvements in a variety of weight-related end points including HbA1c so they could be attractive options for patients with poorly controlled type 2 diabetes and other comorbid conditions. Currently, the proportion of eligible patients using these devices and undergoing these procedures is lower than for bariatric surgery given inadequate insurance coverage, high cost, limited knowledge among potential referring healthcare providers, and lack of access to providers performing the procedures.

The future of obesity medicine involves a multidisciplinary approach as many patients are likely to require a variety of treatment strategies (medications, devices, procedures, and/or surgery) in addition to lifestyle modifications to achieve clinically significant weight loss. Combinations of these advanced treatment strategies are an area that requires further investigation. While the addition of antiobesity medication after bariatric surgery can be an effective tool to counteract recidivism and enhance weight maintenance [75], the use of devices and endoscopic revisional procedures following bariatric surgery is another potential tool to counteract weight regain and produce further weight loss. Finally, the use of medications in combination with devices and procedures is an attractive new approach to weight management. By employing multiple mechanisms simultaneously, combination therapy may have an additive or even synergistic effect on weight.

Compliance with Ethical Standards

Conflict of Interest Katherine H. Saunders declares that she has no conflict of interest.

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Papers of Particular Interest, Published Recently, Have Been Highlighted as:
• Of Importance
•• Of Major Importance

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