Complications of Intragastric Balloons

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16.1 Introduction

The American Society for Gastrointestinal Endoscopy (ASGE) and the American Society for Metabolic and Bariatric Surgery (ASMBS) have defined acceptable thresholds of safety and efficacy for primary endoscopic bariatric therapies (EBTs). Specifically, a given EBT should have an incidence of serious adverse events ≤5% and should result in ≥25% excessive weight loss (EWL) at 12 months, and this EWL should be ≥15% higher than in a control group [1].

In recent decades, several intragastric balloons (IGBs) have demonstrated safety and efficacy, with broad adoption internationally. The U.S. Food and Drug Administration (FDA) has approved the Orbera Intragastric Balloon System (Apollo Endosurgery, Inc., Austin, TX, USA), the ReShape Integrated Dual Balloon System (ReShape Medical, Inc., San Clemente, CA, USA) and, more recently, the Obalon (Obalon Therapeutics, Inc. Carlsbad, CA, USA). The Spatz Adjustable balloon (Spatz Medical, Great Neck, NY, USA) is currently conducting its US pivotal trial. The Elipse Balloon (Allurion Technologies, Natick, MA, USA) has been proven to

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Table 16.1 Features of the FDA-approved IGBs and other balloons [2–5]

IGB	Orbera [2]	ReShape [2]	Obalon [2]	Elipse [3, 4]	Spatz [5]
FDA approval	2015	2015	2016	No	No
Delivery/ insertion	Endoscopy needed	Endoscopy needed	Patient swallows, X-ray	Endoscopy not needed	Endoscopy needed
Removal	Endoscopy needed	Endoscopy needed	Endoscopy needed	Endoscopy not needed	Endoscopy needed
Capacity	500–750 cc (1 balloon)	450 cc/balloon for a total of 900 cc (double balloon system)	Gas-filled balloon with a max volume of 250 cc (up to 3 balloons can be placed: 750 cc)	550 cc (1 balloon)	400–800 cc
Implantation period	Up to 6 months	Up to 6 months	Up to 6 months	16 weeks	Up to 12 months
Weight loss	29% EWL at 12 months	25% EWL at 12 months	25.2% EWL at 12 months	39 and 26% EWL at 16 weeks	34.4% EWL at 6 months

IGB intragastric balloon, *EWL* excess weight loss

be a safe and effective device in European clinical studies and the clinical study for FDA approval is still in process.

EBTs are mostly represented by intragastric balloons and the balloons we are addressing in this chapter have either been approved or are in the process of being approved by the FDA. Table 16.1 summarizes the main characteristics of each balloon [2–5].

The number of adverse events associated with IGB insertion varies across studies [6]. The most commonly reported symptoms after IGBs placement are accommodative in nature, such as abdominal pain, nausea, and vomiting. These generally tend to last only for few days after balloon insertion and are usually self-limiting. Serious adverse events described after IGB placement include dehydration, gastrointestinal ulceration, dislocation of the balloon causing intestinal obstruction, and perforation especially during balloon insertion or removal.

16.2 Orbera

The Orbera Intragastric Balloon System is the most commonly used IGB, approved for use in Europe in 1997. Clinical device surveillance based on reports from European practitioners between 2006 and 2013 revealed 3316 unspecified events/complaints representing 2.1% of 154,955 procedures. The FDA approved the use of Orbera in the USA in August 2015 on the basis of results of the Orbera FDA pivotal clinical trial and two non-US clinical trials in Australia and France [6].

The rates of adverse events after implantation of the Orbera balloon are pooled from a manual review of 67 studies (8500 implantations). Abdominal pain and nausea are frequent side effects after Orbera balloon implantation, occurring in 33.7% and

29.0% of subjects, respectively. Other rates of adverse events observed with the Orbera are: gastroesophageal disease (13.3%), erosion (12%), ulcer (2%), migration (1.4%), small bowel obstruction (0.3%), perforation (0.1%) and death (0.08%) [7]. Medications such as proton pump inhibitors, antispasmodic drugs and antiemetics are usually prescribed few weeks before, during, and after balloon placement to prevent or minimize these expected common side effects. The early removal rate of the Orbera balloon was required in 7.5% subjects. Case reports have been published about asymptomatic microbial colonization of the Orbera, though no clinical significance was noted [8, 9]. Serious side-effects with the Orbera balloon are rare with an incidence of migration and gastric perforation of 1.4% and 0.1%, respectively. Most of the reported perforations with the Orbera were in patients who had undergone previous gastric surgeries. Four deaths associated with the Orbera IGB are reported in the literature, and these were either related to gastric perforation or an aspiration event [10].

16.3 ReShape

The ReShape Duo has a favorable adverse events profile. In the pivotal Reduce US ReShape trial, which evaluated the safety and efficacy of the ReShape Duo IGB in 264 patients, abdominal pain and nausea were common symptoms and were successfully managed medically. Early retrieval was necessary in 15% of patients. Spontaneous balloon deflation occurred in 6% of subjects without balloon migration. Gastric ulcers and erosions were frequent adverse events, initially observed in 39.6% of the study subjects. However, a subsequent device design modification led to decreases in both ulcer frequency (reduced to 10.3%) and in ulcer size (from 1.6 to 0.8 cm). Most of the reported ulcers were not clinically significant, except for one ulcer-related upper gastrointestinal hemorrhage requiring blood transfusion. There were no reported deaths, balloon migrations, or intestinal obstructions. Three serious adverse events were observed with ReShape Duo retrieval, including an esophageal mucosal tear requiring hemoclip application, a contained cervical esophagus perforation managed conservatively with antibiotics, and one post-retrieval aspiration pneumonitis [11].

16.4 Obalon

In a pivotal multi-center randomized blinded clinical trial (SMART study) conducted in the US, 185 patients underwent a combination of lifestyle modifications in addition to the Obalon system, while 181 patients underwent lifestyle modifications with a sham placement procedure. All balloons were removed 24 weeks after insertion. The most common adverse effects reported in patients using the Obalon system were abdominal pain (72.6%), nausea (56.0%), vomiting (17.3%), indigestion or heartburn (16.9%), and bloating (14.6%). Most of these effects were mild in severity and resolved within 14 days. The Obalon system did not report any deflations. Early device removal due to adverse effects occurred in 3.0% of patients. Gastric, esophageal, and esophagogastric bleeding and abrasion, procedure-related

adverse effects identified at balloon removal, occurred in 5.1%, 4.2%, and 3.6% of patients, respectively. One case of bleeding gastric ulcers was seen in 0.3% [12]. Nobili et al. evaluated the effectiveness of the Obalon System as treatment of 17 morbidly obese children. Excess weight was calculated according to Cole's curves for pediatric populations. Fourteen of 15 patients (93.3%) swallowed the first balloon simply and quickly. In two patients endoscopy was planned due to slight mental retardation. In 9 of 17 children enrolled, a second balloon was placed 30–40 days after the first insertion. All devices were endoscopically removed after a mean time of 18 weeks. In the 16 patients who completed the study, the mean weight decreased from 95.8 ± 18.4 to 83.6 ± 27.1 kg ($p < 0.05$), mean BMI decreased from 35.27 ± 5.89 to 32.25 ± 7.1 ($p > 0.05$); with an %EWL of 20.1 ± 9.8 (range 2.3–35.1). As regards side effects, 5 of 18 patients reported mild to moderate epigastric pain/cramping that completely disappeared after few days, using a single dose of oral hyoscine butylbromide. Nausea, recorded in five patients, resolved spontaneously after 1 day (4 cases) to 2 days (1 case) without medication. In the group of nine children who underwent a second balloon positioning, side effects were even less common [13].

16.5 Elipse

The Elipse device (Allurion Technologies, Wellesley, Massachusetts, USA) is a procedureless, swallowable gastric balloon that can be deployed without the use of endoscopy or anesthesia. It is filled with 550 mL water via a catheter, which is then detached, and remains in the stomach for approximately 4 months before it empties and passes through the gastrointestinal tract. The Elipse IGB was approved for the European Union in December 2015. In a systematic review, two studies with Elipse placement reported nausea in 21 out of 42 patients with a meta-analytic rate of 51.42% (95% CI 46.00–57.00%) and vomiting in 23 out of 42 patients with rate of 12.48% (95% CI 8.51–16.44%) [14]. A prospective, observational, open-label, multicenter study demonstrated clinically significant weight loss with the Elipse: the mean percent total body weight loss, BMI point reduction, and waist circumference reduction were 10.0 ± 6.6%, 3.9 kg/m^2 and 8.4 cm respectively, at 16-week follow-up. There were no serious adverse events or serious adverse device effects. Among accommodative symptoms, 18 participants (64%) had vomiting, 15 participants (54%) experienced nausea, and 7 participants (25%) had abdominal pain. In particular, the rate of obstruction incidents ranged from 0.8 to 0.1% after device improvements (new release-valve closure) [14].

16.6 Spatz

The Spatz Adjustable Balloon System (Spatz Medical, Great Neck, NY, USA) is an endoscopically placed IGB that is filled with saline solution. It has an extractable inflation tube that allows for volume adjustment while the IGB remains in the stomach. The balloon volume may be decreased to improve patient tolerance or increased to enhance efficacy. Outside the United States, the Spatz IGB is approved for up to a

12-month implantation. A pivotal multicenter US trial currently is underway. Earlier generations of the Spatz Adjustable Balloon System had a non-collapsible loop with an internal metal chain that maintained a 7-cm balloon diameter within the gastric lumen to prevent or delay a deflated balloon from migrating. This design has been implicated in a higher incidence of migration complicated by balloon impaction, necessitating surgical removal [15]. The Spatz 3 balloon has been modified with removal of the metal chain and stiff catheter, thereby mitigating these unwanted effects. Recently, implantations of Spatz3 in 165 consecutive patients in two centers were retrospectively reviewed. The mean weight loss was 16.3 kg and 67.4% EWL. Down adjustments alleviated early intolerance in 80% of patients. One gastric perforation (0.6%) occurred in a patient who experienced abdominal pain for 2 weeks. Five patients with small ulcers did not require balloon extraction [16].

16.7 Potential Risks with Liquid-Filled Intragastric Balloons

Since 2016, the FDA has received reports of a total of 12 deaths that occurred in patients with liquid-filled intragastric balloon systems worldwide. Seven of these 12 deaths were patients in the U.S. (four with the Orbera Intragastric Balloon System, and three with the ReShape Integrated Dual Balloon System). The FDA, however, has also stated that the "root cause" of these case fatalities is not known, as the evidence only depicts a 1-month or less temporal relationship between balloon placement and death. It was thus uncertain if the cause of death was gastric or esophageal perforation, intestinal obstruction, or through an alternate means. On February 2017 the FDA warned medical providers about the potential risks of fluid-filled balloons after receiving several dozen reports of IGB hyperinflation (reported as "overinflation"), with air or fluid in the stomach, resulting in device removal as early as 9 days following insertion. Symptoms of hyperinflation included intense abdominal pain, abdominal distension with or without discomfort, difficulty breathing, and/or vomiting. The cause of hyperinflation was cited as unknown by the FDA. Due to incidents of hyperinflation of saline-filled silicone breast implants, IGB permeability may have resulted in fluid or air entry by osmosis. Another possibility with regard to air is that anaerobic bacteria, which have been identified in breast implants, may also have been present in IGBs and released gas within the balloon. The FDA also received several reports of acute pancreatitis associated with the Orbera and ReShape, resulting in early device removal as well as hospitalization [17].

16.8 Conclusions

To conclude, the use of intragastric balloon is now a widespread procedure all over the world both as a bridge to any surgery or to control comorbidities in patients with lower BMI no longer able to control the obese-related disease with diet alone. It is very important for any physician to know very well all the possible complications of intragastric balloon treatment in order to manage them properly and above all to prevent the complications.

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