



Liquid-Filled Balloon

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Introduction

In 1985 the United States Food and Drug Administration (FDA) approved the Garren–Edwards Gastric Bubble (GEGB) as the first endoscopically implanted gastric balloon for the treatment of obesity [1]. In an era where procedures such as the Roux-en-Y gastric bypass and vertical banded gastroplasty predominated, the GEGB provided a novel, reversible, and less invasive alternative to complex bariatric surgery. Although the adoption of the first intragastric balloon was widespread across the world, the outcomes were less than optimal [2–4]. Weight loss was minimal, and the frequency of serious complications such as gastrointestinal obstruction and gastric ulceration was notable, leading to discontinuation of the device in 1988 [2–4]. Around the same time, different intragastric balloons were introduced (none of which were approved for use in the U.S.), such as the Taylor balloon (Mill-Rose Technologies, Cleveland, Ohio 1985) and the Ballobes bubble (DOT ApS Company, Denmark 1988). These devices varied in synthetic material (polyurethane *vs.* silicone), fill substance (air *vs.* saline), shape, size, and implantation duration. Despite

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these variations, weight loss outcomes remained suboptimal and similar complications to the GEGB were reported [5–8]. The disappointing clinical results of intragastric balloons set the stage for the convergence of international experts in a scientific meeting (the “Obesity and the Gastric Balloon: A Comprehensive Workshop”) in 1987 aiming to identify a patient population that would benefit most from IGBs and to design the ideal balloon [9]. The conclusion of the conference set the standard for the ideal balloon, which would be spherical in shape, designed from silicone, filled with saline rather than air, up to a volume of 400–500 ml. Importantly, prior gastric surgery was to remain a contraindication to balloon insertion, and the device would be kept in place for 4–6 months.

The clinical application of IGBs was also established at the “1987 Obesity Congress”, and these indications remain today. The balloons were to be used (1) in patients with a BMI between 30 kg/m² and 35 kg/m² as an adjunct to conservative weight loss measures, primarily in the form of diet and exercise; (2) in patients with a BMI greater than 40 kg/m² or a BMI greater than or equal to 35 kg/m², with at least one obesity-related comorbidity, who lack reasonable access to a bariatric center or are excluded based on increased intraoperative risk secondary to cardiovascular disease or other severe obesity-related comorbidities; and (3) in patients who are super-obese (BMI >50 kg/m²) as a bridge to bariatric surgery to reduce surgical morbidity.

History and Outcomes of ORBERA

The Orbera® (Apollo Endosurgery, Inc., Austin, TX, USA) intragastric balloon (IGB), formerly BioEnterics Intragastric Balloon (Inamed, Santa Barbara, CA, USA), is an endoscopically placed spherical balloon that remains in the stomach for 6 months to induce weight loss, and is subsequently removed. It was first introduced in 1991 after the “1987 Obesity Congress” [1]. The conference aimed to develop the ideal gastric balloon while identifying a target population. Although not approved for use in Canada or the United States at the time, utilization of the BioEnterics Intragastric Balloon quickly spread across countries from South America to the Eastern hemisphere. Currently, there has been over 15 years of clinical experience with the Orbera® IGB, and it has been implemented in more than 80 countries worldwide with over 200,000 devices used [2].

In August 2015, the FDA approved the Orbera® device for use in the United States. The pivotal study was a multicenter, randomized, non-blinded trial that included 448 subjects to assess the safety and efficacy of the device. In addition, changes in weight and obesity-related comorbidities were compared in patients randomized to Orbera® IGB for 6 months with behavioral modification versus behavioral modification alone. Overall, mean % total body weight loss (% TBWL) was significantly higher in the Orbera® group at 6 months (10.1% vs. 3.3%), 9 months (9.1% vs. 3.4%), and 12 months (7.6% vs. 3.1%). There was no difference in the improvement of obesity-related comorbidities between the two groups. The rate of device and procedure-related serious adverse events was 10%, although there were no unanticipated adverse device effects or deaths.

Literature suggests that the combination of Orbera® IGB with lifestyle and dietary changes provides superior short-term weight loss relative to behavioral and dietary modification alone [3]. The Italian experience reported a mean percent excess weight loss of 33.9 after 6 months in 2515 patients that had undergone treatment with Orbera® IGB [4]. In a recent randomized trial by Courcoulas et al., improved weight loss outcomes were demonstrated in patients who underwent Orbera® and lifestyle change in comparison to those who underwent lifestyle change alone [2]. Their study showed significantly higher weight loss at 6 months (10% TBWL vs. 3.3% TBWL, $P < 0.001$) in the Orbera® treatment arm. Improved weight loss was maintained at 3 and 6 months post balloon removal. Similar results have been reported in other prospective studies [5–7]. Despite this, long-term data on weight loss maintenance is unknown [8, 9].

The Device

The Orbera® balloon is made of an inert, non-toxic, and soft silicone viscoelastic polymer. The outer surface of the balloon is resistant to friction against the gastric mucosa, limiting focal point irritation. Unlike previous balloons, which were filled with air, the Orbera® balloon is filled with saline allowing it to float freely within the gastric lumen and preferentially remain in the body of the stomach. The expansible design can hold a wide volume of saline ranging from 400 cc (diameter of 9.14 cm) up to 700 cc (diameter of 11 cm). The volume of the balloon cannot be adjusted once it has been filled. Additionally, it is radiopaque and easily identified on radiography.

Although the mechanism of action of the Orbera® IGB has not been fully elucidated, it appears to be multifactorial and related to both physiological and neurohormonal factors. First, the inflated balloon acts as an artificial bezoar preloading the stomach and decreasing the size of the gastric reservoir to induce early satiety [10]. A second mechanism involves alterations in gut hormones and gastric motility. In a study by Mion et al., plasma ghrelin levels decreased and gastric emptying time was delayed in patients following IGB placement [11]. Other studies have demonstrated a similar effect on gastric motility [12, 13]. Despite this, the data is inconsistent, and it remains unclear whether these potential changes in gut hormone levels and gastric emptying actually correlate with weight reduction.

Indications

Indications for the use of Orbera® IGB differ in the US and internationally. In the United States, implantation is indicated as an adjunct to weight reduction for patients with a BMI of ≥ 30 Kg/m² or ≤ 40 Kg/m² in conjunction with an intensive supervised diet and lifestyle modification program. The presence of obesity-related comorbidities is not required. A failed attempt at conservative weight loss measures including supervised diet, behavior modification regimens, and exercise programs

should precede placement of the Orbera[®] IGB. Body mass index requirements are less stringent internationally. In Europe, Canada, Brazil, and Australia, Orbera[®] use is expanded to overweight patients with a BMI > 27 Kg/m².

Contraindications

Knowledge of absolute and relative contraindications of Orbera[®] IGB implantation is important in optimizing patient safety and minimizing risk. Common absolute contraindications include:

- Presence of more than one intragastric balloon simultaneously
- Prior gastrointestinal or bariatric surgery
- Presence of a large hiatal hernia (>5 cm) or a smaller hiatal hernia with intractable gastroesophageal reflux (GERD) symptoms
- Severe esophagitis (Los Angeles Grade C and D)
- Structural esophageal or pharyngeal abnormalities such as esophageal stricture or diverticulum
- Esophageal motility disorders (i.e., achalasia)
- Severe coagulopathy, hepatic insufficiency, or cirrhosis
- Presence of a gastric mass
- Inflammatory conditions of the gastrointestinal tract (i.e., esophagitis, gastric ulceration, duodenal ulceration)
- Conditions predisposing to potential upper gastrointestinal bleeding (including esophageal/gastric varices, congenital or acquired intestinal telangiectasias)
- Pregnancy or desire to become pregnant
- Patients with known or suspected allergies to materials contained in Orbera[®]
- Any contraindication to endoscopy
- Psychiatric illness or disorder, which prevents the patient from complying to follow-up visits and removal of the device after 6 months

Relative contraindications include Crohn's disease, previous abdominal surgery, presence of a hiatal hernia, use of nonsteroidal and anti-inflammatory medication, uncontrolled psychiatric disease, or inability/unwillingness to comply with prescribed anti-secretory medications.

Procedure and Patient Management

All patients who are being considered for Orbera[®] IGB placement should undergo a thorough evaluation of medical history and a full physical examination. Assessment for any swallowing dysfunction/disorders or esophageal disorder should be performed. Pre-procedure workup includes appropriate blood tests (basic metabolic panel, liver function panel, lipid studies, coagulation function) and an electrocardiogram. Patients with gastroesophageal reflux require anti-secretory medications prior

to Orbera[®] implantation. With respect to preoperative counseling, it is important to establish realistic patient expectations and stress the critical role of lifestyle change and dietary modification in conjunction with the IGB for successful outcomes.

The Orbera[®] balloon is supplied attached to the Placement Catheter Assembly (PCA), a silicone catheter that is connected on one end to a sheath containing the collapsed balloon and on the other end to a Luer-Lock connector that attaches the filling system. The filling system includes a fill tube, filling valve, and an IV spike. If the device has any evidence of damage, it should not be used, and a new device should be obtained.

The procedure begins with upper gastrointestinal endoscopy to evaluate gastroesophageal anatomy and possible contraindications to intragastric balloon placement. The endoscope is then removed upon completion. The Placement Catheter Assembly (PCA) with the internal guidewire is carefully inserted into the esophagus and ideally positioned in the stomach. The endoscope is then reinserted alongside the catheter and the PCA is guided beyond the lower esophageal sphincter and into the stomach. Once the catheter is positioned, the guidewire is removed. The following step is filling of the balloon with sterile saline. It is important to maintain the position of the catheter alongside the endoscope, so it is not pulled back during inflation of the balloon. The filling system spike is inserted into a sterile saline bag. A 50 cc syringe and the fill tube (using the Luer-Lock connector) is then attached to the filling system valve. The Orbera[®] balloon can be filled with 400 cc to a maximum of 700 cc of saline. It should not be filled with any less volume than 400 cc or more volume than 700 cc, as this can lead to serious and life-threatening complications.

In a meta-analysis of 44 studies (5549 patients) by Kumar et al., there was no significant correlation between balloon-filling volumes and % total body weight loss at 6 months although larger filling volumes were less likely to migrate [14]. All the included studies used filling volumes of 500–700 cc. The current recommendation is filling volumes of 500 to 650 cc. Once the balloon is filled with the desired volume of saline, the fill kit is removed from the fill tube. The balloon valve is sealed by drawing back on the fill tube with the syringe to produce suction on the placement catheter. Finally, the balloon is separated from the fill tube by gently pulling the tube against the lower esophageal sphincter or tip of the endoscope.

Knowledge of the anticipated physiological responses to the Orbera[®] device allows the clinician to optimize patient tolerability while minimizing adverse symptoms. Common post-procedure side effects include nausea, vomiting, and abdominal pain. The majority of patients (59.7%) have mild symptoms, while 5.8% may experience severe symptoms. To aid in management of typical postoperative symptoms a treatment protocol including anti-emetics, proton-pump inhibitors, and close patient monitoring is recommended. Proton-pump inhibitors should be started 2 weeks prior to IGB placement and continued through the removal of the device. Aggressive management of nausea with anti-emetics and anticholinergics should be planned on the day of the procedure and continued for 2–5 days, then used on an as needed basis for 1 week following placement of the balloon. Adequate hydration is of utmost importance during and after the procedure. Goal fluid intake is 1.5 liters over a 24-hour period. The clinician is expected to contact the patient at 24 hours

and daily for 1 week to assess both fluid intake and symptoms. If a patient is experiencing severe symptoms and unable to maintain adequate fluids, prompt evaluation of the patient and intervention is crucial.

Although IGB placement is a relatively low risk procedure, rare serious complications including visceral perforation, major gastric hemorrhage, bowel obstruction, pancreatitis, and resulting mortalities have been reported [15–17]. Five deaths related to the Orbera balloon were reported to the FDA in 2016 although the true incidence rate of patient death is unknown. In a systematic review of mostly fluid-filled IGBs, the rate of gastric perforation and mortality was 0.1% and 0.05%, respectively [18]. Recently, in February 2017, an updated FDA-issued alert was published describing the phenomena of spontaneous balloon over-inflation and pancreatitis shortly following IGB placement. Thus, knowledge of proper insertion, filling, and removal techniques in addition to its possible complications is critical.

In the U.S., The Orbera[®] device is designed to remain in place for a maximum of 6 months. Use of Orbera[®] beyond 6 months increases the risk of balloon deflation with subsequent morbidity, including gastrointestinal obstruction and mortality. Earlier removal is recommended in patients who become pregnant after balloon placement, are undergoing planned surgery, or develop intolerance to the device and those with a deflated balloon. Removal of the balloon is done under sedation with endoscopy according to general hospital protocol. The filled balloon is visualized endoscopically, and a needle instrument is guided down the working channel of the endoscope. The balloon is then punctured, and suction tubing is pushed through the balloon shell. Once the needle is removed, suction is applied and the fluid from the balloon is evacuated. The suction tubing is subsequently removed from the working channel, and a two-pronged grasper is inserted and used to grasp the balloon. With a firm grip on the balloon, it is slowly extracted up to the esophagus and removed.

Aftercare Platform

Following payment for the procedure, which at this time is not covered by insurance, patients are provided personalized aftercare education for up to 6 months after device removal. A unique aftercare platform that functions to provide post-procedure support to patients is the Orbera[®] COACH. This is a mobile application that provides patients with live personal and group sessions with dietitian coaches, motivational strategies, educational content, and a means to record and track dietary information. For example, the Orbera[®] COACH allows online and app-based weight tracking and picture-based meal tracking to give patients up-to-date and comprehensive data regarding their progression. Furthermore, among other things, the platform contains detailed nutritional content, meal recipes, and lifestyle tips. Primary providers are also able to access the platform and monitor a patient's weight loss trends. Other options include having the practice dietitian follow the patient with a year of aftercare.

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