Intragastric Balloon History

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The Rapunzel Syndrome

The concept of weight loss using an intragastric balloon (IGB) originated from the Rapunzel Syndrome – a rare psychiatric condition resulting from trichophagia or ingesting hair. The trichobezoar (hairball) occupies the stomach culminating in diminished appetite, postprandial fullness, and weight loss. This concept was used to fill the stomach with a pseudo bezoar – the intragastric balloon, a unique and innovative supposition to induce weight loss.

Minimally Invasive Philosophy: An Alternative to Surgery

The gastric bypass gained popularity in the 1980s as a restrictive and malabsorptive procedure. Even though this is a superb procedure with significant and sustained weight loss, few qualified for it and fewer underwent the procedure due to the apprehension of 'going under the knife' and fear of complications. Thus, it became imperative for surgeons and gastroenterologists to fill this void with a procedure that was easily accessible and less invasive.

The initial experiment of an IGB was conducted in dogs using a 250 ml polyethylene bottle introduced at laparotomy [1]. Subsequently, free-floating rubber balloons that were easy to insert were explored in humans and seemed to reduce hunger. There were no complications noted in the five obese women who participated in the initial 272-day study. The balloons remained inflated for an average of

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7–21 days, and though encouraging weight loss was noted during periods of inflation, researchers remained in a quandary as to how to keep the balloons from deflating [2].

Early Development

The Garren–Edwards Bubble made its debut in September 1985, after being approved by the U.S. Food and Drug Administration (FDA), as the first IGB, amidst much speculation as a weight loss measure more drastic than stomach stapling and jaw-wiring [3]. It was designed by gastroenterologists Lloyd R. Garren and his wife Mary L. Garren. The *New York Times* reported that 'severely obese Americans were now swallowing stomach balloons to help them reduce their girth'. The bubble was a novel 3 × 4 cm cylinder constructed with polyurethane and a self-sealing valve (Fig. 1.1).

Following routine endoscopy, the bubble was inserted using an introducer tube and inflated with 200 cc of room air with subsequent release into the fundus of the stomach. The exact mechanism of action was unclear and proposed theories included a placebo effect, mechanical, hormonal, or behavioral modification and neuronal pathways to name a few. It was marketed as a temporary device with removal after 4 months [4]. The initial hysteria resulted in the sale of 20,000 bubbles in less than a year. The reality in that first year of placement, based on a retrospective study by Ulicny KS Jr et al., was a mean weight loss of 10.1 kilograms with five patients developing small bowel obstruction from spontaneous deflation of the balloon. Only 33% required endoscopic removal of the balloon whilst the remainder passed the balloon per rectum [5].

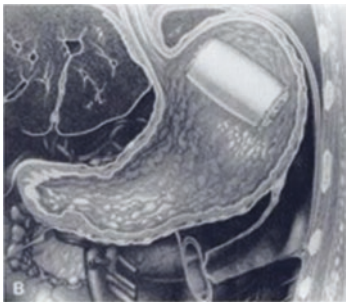

Fig. 1.1 The Garren–Edwards bubble

This was followed by a 24-week double blind crossover study of 90 patients randomized into three groups: bubble-sham, sham-bubble, and bubble-bubble with diet and behavioral modification therapy. Unfortunately, this trial did not demonstrate significantly more weight loss with the gastric balloon compared to diet and behavioral modification alone. Complications included gastric erosions and ulcers, small bowel obstruction, Mallory–Weiss tears, and esophageal laceration [6]. The safety and efficacy were compared to bariatric surgery and demonstrated inferior weight loss [7], resulting in a rather disheartening withdrawal from the market in 1992.

Europe: The Taylor Balloon and the Ballobes Bubble

There was much doubt regarding the efficacy and safety of IGBs, but there were a few that believed the suboptimal weight loss results were a design failure rather than a concept failure and thus the Taylor balloon emerged. In contrast to the Garren–Edwards Bubble, the Taylor balloon was a pear-shaped 550 ml liquid-filled silicone balloon that again remained within the stomach for 4 months. It was filled with normal saline and methylene blue so that the patient would be alerted if there was spontaneous deflation resulting in blue urine. It was introduced in the United Kingdom in 1985. A prospective, multicenter clinical trial conducted at four clinical centers in a total of 60 patients demonstrated an 11.6% decrease in mean total body weight at 16 weeks. Again, seven balloons deflated spontaneously secondary to a manufacturing defect and the design was subsequently modified with no further incidents [8].

The Ballobes bubble was developed in Denmark in 1988. It had a larger volume like the Taylor balloon but was oval in shape. However, in contrast to the Taylor balloon, the 500 ml silicone balloon was filled with air and 10 ml diatrizoate following endoscopy. A randomized double-blind trial of balloon or sham treatment of 3 months' duration did not show a significant difference in weight loss. There were less spontaneous deflations; however, 7% had intolerance secondary to esophagitis [9], likely due to its free-floating nature as it was filled with air (Fig. 1.2).

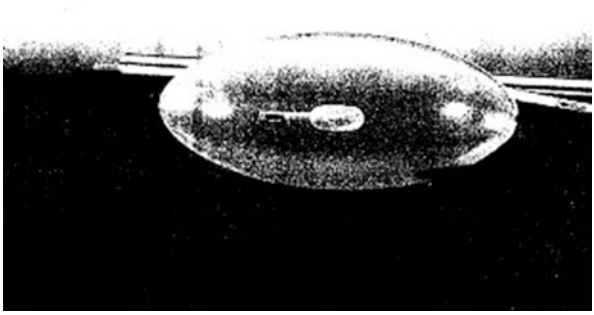

Fig. 1.2 Ballobes intragastric balloon. (Reproduced with permission from - Bariatric surgery, Edited by Nadey S Hakim, Franco Favretti, Gianni Segato and Bruno Dillemans. Copyright @ 2011 Imperial College Press)

Table 1.1 Characteristics of the 'ideal' intragastric balloon

1. Effective
2. Low ulcerogenic and obstructive potential
3. Adjustable volume
4. Soft surface
5. Constructed of durable material
6. Liquid content
7. Radiopaque marker

The Ideal Intragastric Balloon

Following the failure of the IGB in the United States, a comprehensive workshop was held in 1987 to design the ideal IGB. International experts in gastroenterology, surgery, obesity, nutrition, and behavior medicine met in Tarpon Springs, Florida. They developed guidelines for patient selection, insertion, and retrieval techniques and discussed the need for appropriate patient education on nutrition, exercise, and behavior modification [10] (Table 1.1).

In 1991, the BioEnterics® Intragastric Balloon (BioEnterics Corporation) was developed based on the ideal characteristics from the Florida conference. It was a smooth, spherical, 400–700 ml saline- and methylene blue–filled silicone elastomer with a radiopaque filling valve that was introduced endoscopically and remained in the stomach for 6 months. It was initially marketed in Europe, South America, Asia, and Middle East. A randomized controlled trial comparing IGB for 6 months with behavioral modification for 12 months, versus behavioral modification alone showed statistically significant greater weight loss at 6 months in the IGB group (−14.2 vs. –4.8) [11]. Genco A. et al. in his retrospective study of 2515 patients showed not only satisfactory weight loss, but also an improvement in comorbidities, [12] and the feasibility of a first intragastric balloon followed by a second balloon for continued weight loss [13]. Subsequent studies have established the utility of a third and fourth balloon for augmented weight loss over a 6-year follow-up period [14].

The BIB balloon continues to be marketed today as the Orbera® (Apollo Endosurgery, Inc., Austin, TX, USA) balloon. In a multicenter randomized trial of 255 adults with a body mass index of 30–40 kg m^2, Courcoulas A et al. demonstrated a superior weight loss at 3 and 6 months in subjects randomized to IGB with lifestyle intervention compared to lifestyle intervention alone. Due to the larger volume, patients experience more side effects such as nausea (86.9%), vomiting (75.6%), abdominal pain (57.5%), and early balloon removal (18.8%) [15], with a risk of erosions and ulcers (Fig. 1.3).

Gastric Balloons Regain FDA Approval

After a long hiatus, the IGB reappeared on the American market in July 2015, when the ReShape® Duo Integrated Dual Balloon System (ReShape Medical Inc., San Clemente, CA, USA) received FDA approval. It differs from other balloons in

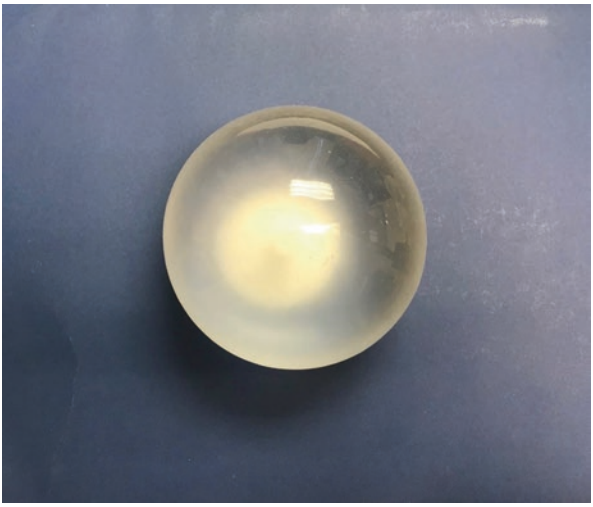

Fig. 1.3 The Orbera® Intra Gastric Balloon

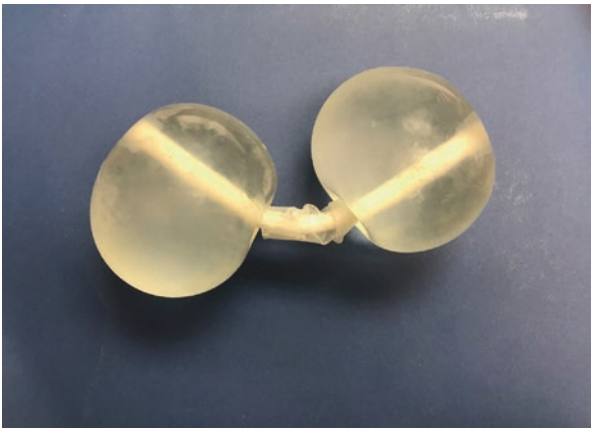

Fig. 1.4 The Reshape® Duo Integrated dual balloon system

its shape which is thought to conform to the natural curvature of the stomach. It consists of two balloons attached by a flexible silicone shaft to decrease migration into the small bowel in the event of deflation. Each balloon is filled with 450 ml of saline and methylene blue for a maximum capacity of 900 ml. It is placed endoscopically and remains in the stomach for 6 months followed by endoscopic removal. The REDUCE pivotal trial was a prospective, randomized controlled trial of the ReShape IGB. A total of 326 subjects were randomized to IGB with diet and exercise versus sham endoscopy with diet and exercise alone. IGB with diet and exercise had significantly greater %EWL at 24 weeks [16]. The Orbera gained FDA approval in August 2015 (Fig. 1.4).

South America: The Silimed Gastric Balloon (SGB)

The Silimed® gastric balloon (Silimed, Rio de Janeiro, Brazil) is a spherical, 650 ml, silicone-coated balloon with a self-sealing valve like the orbera balloon. It is filled with normal saline, 20 ml Iopamiron contrast, and 10 ml of 2% methylene blue. The balloon is lodged within a sheath that is anchored to the endoscope with a snare and thus introduced using traction. It is easier to place and remove and has superior radiopaque visualization. Mean excess weight loss at 6 months was 11.3 ± 6.2 kg with similar issues of spontaneous deflation and early removal [17].

Adjustable Volume

The Spatz® (Spatz Medical, Great Neck, NY, USA) balloon, though not FDA approved, warrants special mention as the only free-floating balloon with an adjustable volume. This is an important feature that addresses the weight loss plateau seen at 3 months. It also improves tolerance of the IGB as the volume can be increased gradually following insertion. In addition, the Spatz balloon can remain for a total of 12 months increasing additional weight loss by 7–12 kg. The downside to the Spatz balloon is that in order to change the volume an additional endoscopy is warranted (Fig. 1.5).

The adjustable totally implantable intragastric prosthesis (ATIIP)-EndogAst® (Districlass Medical, Saint-Etienne, France) is an air-filled balloon that is attached to the abdominal wall and connected to a subcutaneous totally implantable system and thus overcomes the obstacle of balloon migration. It is placed in a similar fashion as a percutaneous endoscopic gastrostomy tube. In a 1-year multicenter prospective clinical survey mean %EWL at 6 months was 28.7%, however local subcutaneous infection and port erosion have limited its use [18] (Fig. 1.6).

Fig. 1.5 The Spatz® intragastric balloon

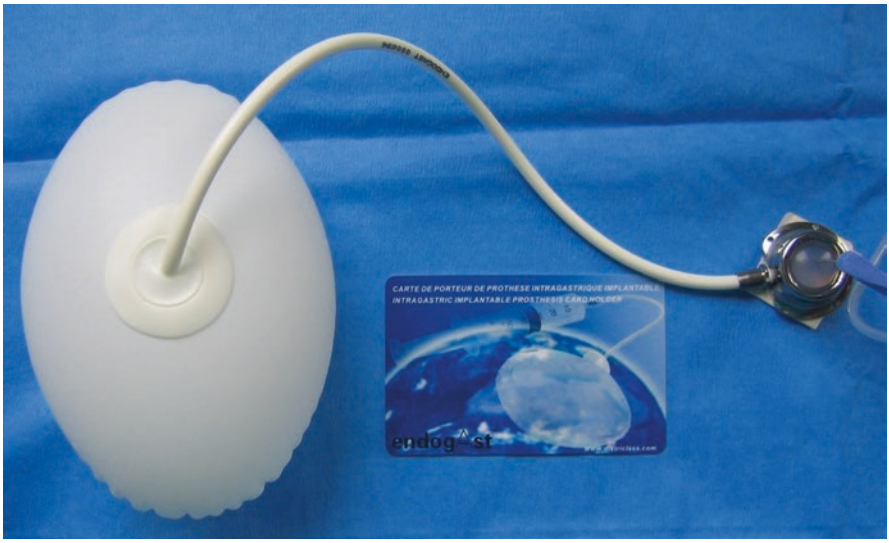

Fig. 1.6 The adjustable totally implantable intragastric prosthesis (ATIIP)-EndogAst®

Is Endoscopy De Rigueur for IGB Placement?

Since a screening endoscopy prior to IGB placement is unlikely to predict the likelihood of complications or intolerance [19], could a balloon be swallowed instead? Indeed, the Obalon® (Obalon Therapeutics Inc., Carlsbad, CA, USA) was the first FDA-approved swallowable balloon developed to circumvent endoscopic placement of the IGB. Endoscopy is expensive and drives up the cost of IGB placement. The Obalon transformed an expensive and time-consuming procedure at a surgical center into a relatively cheaper 10-minute office visit. It is a system of three balloons swallowed 2 weeks apart in the first 3 months of treatment and retrieved with endoscopy 6 months after placement of the first balloon. The 250 cc balloon is deposited in a small capsule that is attached to a 2 *Fr* catheter. Once swallowed, the location is confirmed by X-ray and then inflated with a nitrogen-based proprietary air mixture. The progressive increase in volume to a total of 750 cc over 4 weeks decreases intolerance and early removal secondary to nausea, vomiting, and abdominal pain [20] (Fig. 1.7).

An 'Easy-to-Swallow' Treatment for Weight Loss

The Elipse® (Allurion Technologies Inc., Natick, MA, USA) balloon does not need endoscopy for placement or retrieval. Like the Obalon®, it is swallowed within a capsule and filled with saline during a brief office visit and then months later passes per rectum. It has revolutionized endoscopic IGB placement, to the simplicity of

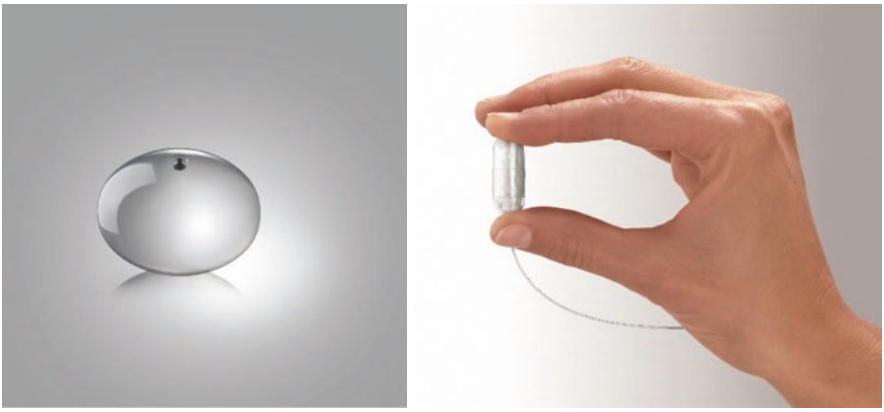

Fig. 1.7 a) The Obalon® Intra Gastric Balloon after inflation b) The capsule containing the Obalon Intragastric Balloon

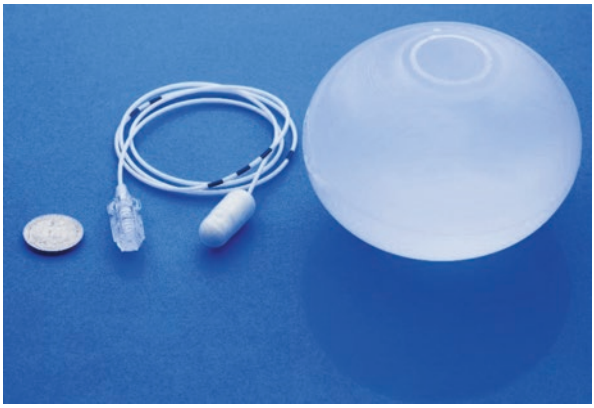

Fig. 1.8 The Elipse® gastric balloon is folded into a vegetarian capsule and attached to a thin catheter (left). After it is swallowed, the balloon is filled with liquid (right). A US quarter is shown for size comparison purposes

swallowing a pill. It has also eliminated the issue of patients not returning for planned balloon removal [21] (Fig. 1.8).

Balloon-Like Devices: The Semistationary Antral Balloon (SAB) and the Transpyloric Shuttle (TPS)

The semistationary antral balloon is also a pear-shaped saline-filled balloon with a 30 cm silicone duodenal stem for anchorage into the antrum and a 7 g metallic counterweight at the tip. Unlike the Taylor balloon, it is only filled with 150–180 cc saline as the mechanism is believed to be intermittent occlusion of the pyloric opening versus a space-occupying device. In a pilot study of 26 patients, the median weight reduction was 6.5 kg (range 3.7–19.9) at 4 months. Even though the balloon

Fig. 1.9 The Transpyloric Shuttle®

was well tolerated due to its relatively smaller volume distal migration was seen in three patients [21].

The BARONova Transpyloric Shuttle® (BARONova, Goleta, CA, USA) is a novel balloon-like weight loss device that is inserted and removed via standard endoscopy. Unlike the conventional balloons, the mechanism of weight loss is delayed gastric emptying. It consists of a large spherical bulb with a mechanical fill connected to a smaller cylindrical bulb by a flexible tether. The larger bulb prevents migration from the stomach, while the cylindrical bulb migrates into the duodenum during peristalsis to enable intermittent obstruction across the pylorus. An initial feasibility study of 20 patients demonstrated 25.1% and 44% excess weight loss at 3 and 6 months, respectively. The ENDObesity II study is a multicenter, randomized, and sham-controlled clinical trial of 270 patients with TPS insertion for 12 months, that demonstrated a mean %TBWL of 9.5% at 12 months (95% C.I. 8.2 to 10.8) in the TPS group compared to 2.8% (95% C.I. 1.1, 4.5) for the Control Group, with an observed difference of 6.7 (95% C.I. 4.5 to 8.8, $p < .0001$) [22, 23] (Fig. 1.9).

Experimental Devices: Balloon to Butterfly

The butterfly technique is an experimental technique that involves the use of a small butterfly-like, gastric space-occupying device. It consists of an 18-mm × 15-mm, double polyethylene ribbon folded into loops and introduced through an overtube. Upon entry into the stomach, the knot holding the wings together are cut, and the butterfly is released [23].

Comparison of IGBs

Intragastric balloons can be compared based on shape, construction material, volume, filling material, and method of insertion/removal (Table 1.2).

Table 1.2 The comparison of intragastric balloons

	Shape	Material	Volume	Contents	Duration	Method of placement	Method of removal
The Garren-Edwards bubble	Cylindrical	Polyurethane	200 ml	Air	3 months	EGD	EGD
The Taylor balloon	Pear shaped	Silicone	550 ml	Liquid	4 months	EGD	EGD
The Ballobes bubble	Oval	Silicone	500 ml	Air and 10 ml diatrizoate	3 months	EGD	EGD
BIB/Orbera	Spherical	Silicone	400–700 ml	Saline ± methylene blue	6 months	EGD	EGD
Reshape	Bi-lobed	Silicone	450 ml × 2	Liquid	6 months	EGD	EGD
Silimed gastric balloon	Spherical	Silicone	650 ml	Saline, 20 ml Iopamiron contrast and 10 ml of 2% methylene blue	6 months	EGD	EGD
Obalon	Spherical	Silicone	250 ml × 3	Gas mixture	6 months	Swallowed	EGD
Elipse	Spherical	Silicone	550 ml	Saline	4 months	Swallowed	Passed per rectum
Spatz	Spherical	Silicone	700 ml –adjustable	Saline ± methylene blue	12 months	EGD	EGD
Semi stationary antral balloon	Pear shaped	Silicone	150–180 ml	Saline	4 months	EGD	EGD

Conclusion

IGBs earned themselves a credible spot on the armamentarium of short-term weight loss devices and are here to stay. In the future, we anticipate innovative modifications of the IGB that will address side effects such as nausea and gastroesophageal reflux resulting in early removal, technical improvements that will prevent complications including spontaneous deflation, migration, and hyperinflation and solutions for the weight loss plateau seen with current iterations. Balloon placement and removal will be simplified, and duration will progressively lengthen with development of more permanent devices.

However, it is also likely that we will see a shift in gears from space-occupying devices to implantable ones that mimic surgery. Future innovations will be competing with other endoscopic weight loss solutions such as sleeve gastroplasty, and thus will need to be more effective in a shorter duration of time with lasting results. The evolution of the IGB over the last 30 years has been sluggish, to say the least, but has gained momentum in the last few years. This is only a glimpse into the future, which is certain to offer more effective and less invasive solutions than currently available therapy. New device development and research will likely continue until it is possible to deliver custom creations based on subject BMI, comorbidities, weight loss goals, tolerability, and side effect profile. It is unquestionably an exciting time in device development.

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