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ORIGINAL CONTRIBUTIONS

The Efficacy and Safety of a Procedureless Gastric Balloon for Weight Loss: a Systematic Review and Meta-Analysis

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Abstract

Background Intragastric balloons have been used to bridge the obesity treatment gap with the benefits of being minimally invasive but still required endoscopy. The Elipse intragastric balloon (EIGB) is a swallowable balloon that is spontaneously excreted through a natural orifice at approximately 16 weeks. Several concerns exist, including the treatment efficacy and risk of bowel obstruction. Our meta-analysis aimed to evaluate the efficacy and safety of EIGB.

Methods A literature search was performed from several databases from database inception to November 2019. Eligible studies must report percent total weight loss (%TWL) after completion of treatment and adverse events. The pooled means and proportions of our data were analyzed using random effects model, generic inverse variance method.

Results Six studies involving 2013 unique patients met our eligibility criteria and were included. The mean baseline BMI ranged from 30.6 to 36.2. The pooled early removal rate was 2.3% (95% CI, 1.1–3.5%; I^2 31%). The pooled %TWL after completion of treatment (4–6 months) was 12.8% (95% CI, 11.6–13.9%; I^2 83%) and at 12 months was 10.9% (95% CI, 5.0–16.9%, I^2 98%). For serious adverse events, three patients had small bowel obstruction, and one patient had gastric perforation requiring surgery. Early expulsion by emesis and early deflation were seen in 3 and 9 patients, respectively.

Conclusions This meta-analysis demonstrates that EIGB is a safe device offering an effective weight loss that warrants further studies for its long-term weight loss outcomes. Severe adverse events are rare, and the rate of early removal is low.

Keywords Gastric balloon · Procedureless Gastric Balloon · Elipse Intragastric Balloon

Introduction

Obesity is becoming a highly debated topic in recent years given multiple associations with serious health conditions [1, 2] and its continuously increasing prevalence, which was already up to 40 % among US adults in 2016 [3]. Bariatric surgery is considered in patients with obesity class III or class II with obesity-related comorbidities and proven to be the most effective and sustainable treatment of obesity [4]. Multiple techniques of bariatric interventions have been introduced, including endoscopic intragastric balloon, which has emerged in recent years after several studies have been shown its satisfactory effectiveness for treatment of obesity and the possibility of being a bariatric therapy option for patients with obesity class I and II [5, 6]. However, several potential risks are unavoidably concerning while performing endoscopy, which is an invasive procedure by itself with the need of

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anesthesia and sedation that might accentuate the risks and eventually lead to unwelcoming adverse events.

The Elipse device (Allurion Technologies, Wellesley, MA, USA) is a procedureless intragastric balloon, which has been introduced in 2015 as a promising alternative to endoscopic intragastric balloon [7], and it initially demonstrated decent results from its proof-of-concept pilot study [7, 8]. It was the first and only swallowable intragastric balloon that was approved by the Conformité Européenne of the European Union [9]. The most significant advantage of Elipse intragastric balloon (EIGB) is that endoscopy is not required for both implantation and removal. This particular device eliminates the risks associated with endoscopy, sedation, and anesthesia. This biodegradable device is initially folded inside a capsule attached to a thin catheter, and a stylet can be inserted through the catheter to facilitate the swallowing process. After the placement is confirmed by an abdominal X-ray or ultrasonography, the balloon is inflated with 550 ml of fluid. The balloon is also made from an absorbable material that is automatically degraded after residing in the stomach for approximately 4 months. This subsequently triggers a self-releasing valve, which leads to balloon self-emptying and eventually natural excretion through a gastrointestinal tract.

Nonetheless, the long-term benefit is still controversial, given a short balloon residence time and risks of major complications such as gastrointestinal perforation and bowel obstruction while passing through the gastrointestinal tract during its excretion [10]. Besides, the risk of intolerance is theoretically increased, given the lack of pre-procedural endoscopic surveillance.

Due to its convenience and possibly superior safety profile, this device is becoming more popular, mainly in Europe and the Middle East. Nevertheless, it has not been used in the USA due to the lack of Food and Drug Administration (FDA) approval and scant literature data. This systematic review and meta-analysis aimed to evaluate all available evidence to better characterize the efficacy and safety of EIGB as promising nonsurgical management for weight loss.

Methods and Materials

Search Strategy and Data Sources

A comprehensive search of several databases from each database's inception to November 1, 2019, any language, was conducted. The databases included Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, and Daily, Ovid EMBASE, Ovid Cochrane Central Register of Controlled Trials, and Scopus. The search strategy was designed and conducted by an experienced librarian with input from the study's principle investigator. Controlled vocabulary supplemented with keywords was used to search for procedureless intragastric balloon for weight loss in adult patients. The actual strategy listing of all search terms used and how they are combined is available in Supplementary Item 1.

Eligibility Criteria and Quality Assessment

Eligible studies must meet all of the following inclusion criteria: (1) Participants must be adults older than or equal to 18 years who underwent Elipse intragastric balloon implantation; (2) percent total weight loss (%TWL) must be reported after completion of treatment; and (3) adverse events must be reported after completion of treatment. The quality of each study was independently evaluated by two authors (KV and VJ) using the National Institutes of Health (NIH) quality assessment. Results of the quality assessment of all included studies are shown in Supplementary Table 1.

Statistical Analysis

The pooled means and proportions of our data were analyzed using a random effects model, generic inverse variance method of DerSimonian and Laird, which assigns the weight of each study based on its variance [11]. The heterogeneity of effect size estimates across the studies was quantified using the Q statistic and I^2 ($P < 0.10$ was considered significant). A value of I^2 of 0–25% indicates insignificant statistical heterogeneity, 26–50% low heterogeneity, and 51–100% high heterogeneity [12]. Publication bias was assessed using a funnel plot [13]. Data analysis was performed using Open Meta analyst software (CEBM, Brown University, Providence, RI, USA) and Stata 16 (StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC.).

Results

Study Selection and Characteristics

The initial search yielded 160 potentially relevant articles (20 articles from Ovid MEDLINE, 89 articles from Ovid EMBASE, 9 articles from Ovid CCRCT, and 42 articles from Scopus). After the exclusion of 62 duplicated articles, 98 articles underwent title and abstract review. A total of 66 articles were excluded at this stage, as they did not fulfill the eligibility criteria, leaving 32 articles for full-length review. Twenty-eight articles were excluded after a full-length review with reasons shown in Supplementary Item 2, leaving 6 unique studies, which are all prospective cohort studies and involving 2013 patients fulfilling our eligibility criteria. The baseline characteristics of the included studies are comprehensively described in Table 1. A total of 1466 patients were women (72.8%), and the mean baseline BMI ranged from 30.6 to 36.2. All EIGBs were successfully administered except for 1 patient that had the capsule retained in the lower esophagus.

Table 1 Baseline characteristics of included studies

Study	Ienca et al. [14]	Raftopoulos et al. [15]	Espinet Coll et al. [16]	Jamal et al. [17]	Alsabah et al. [18]	Machytka et al. [19]
Year	2019	2019	2019	2019	2017	2016
Country	International	Greece	Spain	Kuwait	Kuwait	Czech and Greece
Study design	PC	PC	PC	PC	PC	PC
Inclusion	NA	NA	BMI 27–40	BMI > 27.5	BMI 25–45	BMI 27–40
No. of subjects	1623	79	30	112	135	34
Average age (years)	39.2	43	43.1	31.3	33.5	42
Female (%)	72.2	68.4	93.3	73.6	82.2	82.1
Baseline BMI (kg/m^2)	34.2	36.2	30.6	34.3	33.7	34.8
Successful administration (%)	100	100	100	100	100	96.4 (1 remained in lower esophagus)
Early removal due to intolerance	41/1623	0/79	1/30	6/106	3/135	2/28
Excretion route	NA	NA	NA	Rectum (43), oral (6), unnoticed (58)	NA	Rectum (30), oral (4)
AE	Early deflation (3), esophagitis (1)	None	Early expulsion by emesis (1)	Early deflation (3)	Early deflation (3), early expulsion by emesis (2)	None
Serious AE	Gastric perforation requiring surgery (1)	None	Small bowel obstruction requiring endoscopic removal (1)	Small bowel obstruction requiring laparoscopic removal (1)	Small bowel obstruction requiring laparoscopic removal (1)	None
Follow-up duration (months)	4	12	4	12	4	4

Abbreviations: *AE* adverse event, *BMI* body mass index, *NA* not available, *PC* prospective cohort study

Percentage of TWL

The %TWL was reported at 4 months in 4 cohort studies [14–17], 6 months in 2 cohort studies [18, 19], and 12 months in 2 cohort studies [18]. The pooled mean %TWL after completion of treatment (4–6 months) [6, 7, 14–16, 18] was 12.8% (95% CI, 11.6–13.9%; I^2 83%) and at 12 months [17] was 10.9% (95% CI, 5.0–16.9%, I^2 98%). The statistical heterogeneity was high, with I^2 of 83% at 4–6 months and 98% at 12 months (Fig. 1). A funnel plot was used for the evaluation of publication bias. The plot was symmetric and did not provide suggestive evidence of publication bias (Fig. 2).

Adverse Events

Regarding the safety of EIGB, serious adverse events were rarely observed, and there was no mortality. There was only one patient among 2013 participants who had gastric perforation requiring surgery. Also, three patients developed small bowel obstruction. One patient required colonoscopy with ileoscopy, and the other two patients underwent laparoscopic enterotomy for removal. The balloons were successfully removed in both cases without any complications, and no exploratory laparotomy was required.

For other minor adverse events, accommodative symptoms such as abdominal pain and nausea/vomiting were frequently observed and mostly successfully managed with medications. Esophagitis was seen in 1 patient. Early expulsion by emesis and early deflation were seen in 3 and 9 patients, respectively.

For excretion, it is not uncommon for the EIGB to pass unnoticed (39.7%), and passing out by emesis (6.8%) was also observed (2 studies).

Discussion

In the modern era of medical technologies, there is considerable potential to create innovative bariatric therapies. Making novel tools for bariatric patients is mandatory, given the limited efficacy of nutritional and lifestyle intervention which are the foundation of therapy for weight loss [20]. Multiple endoscopic bariatric techniques have been introduced in recent years [21], especially endoscopic intragastric balloon, which

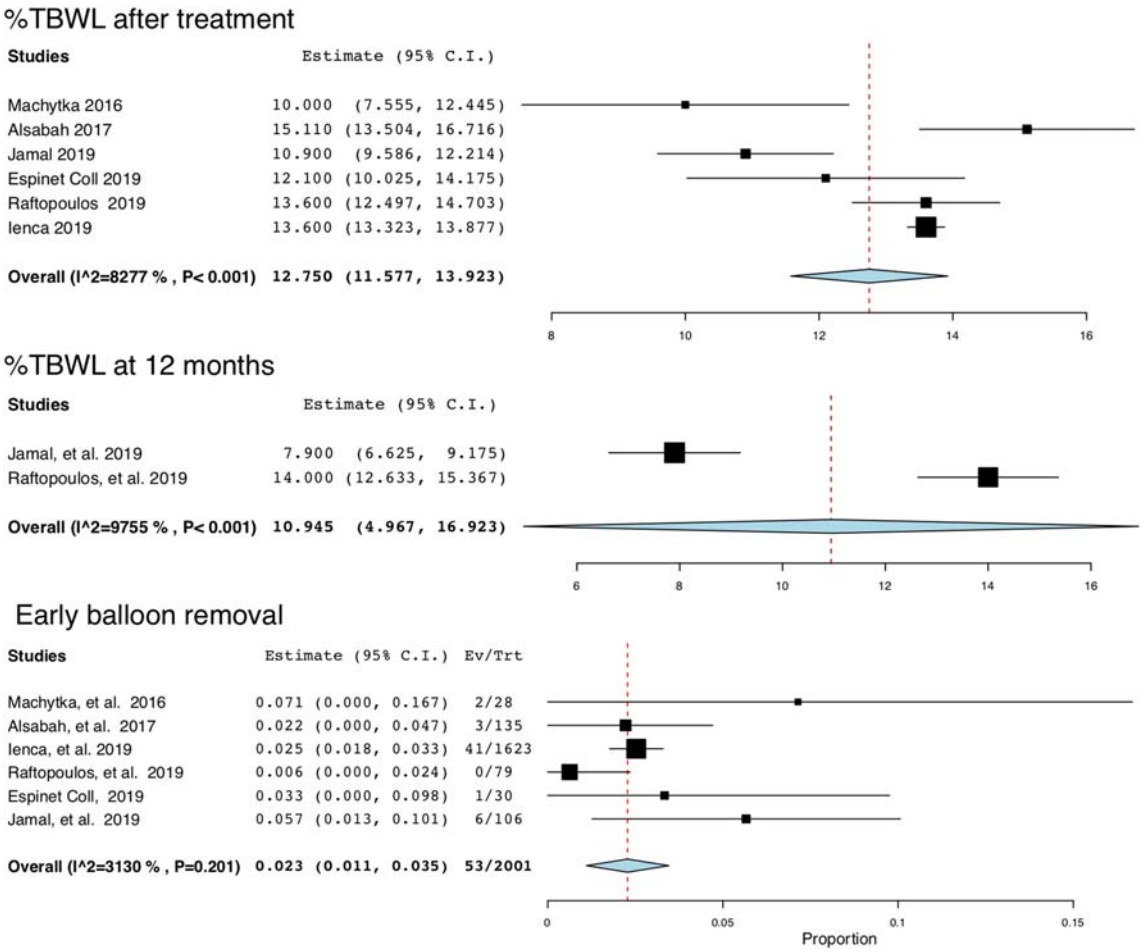

Fig. 1 Forest plots of the included studies evaluating %TWL

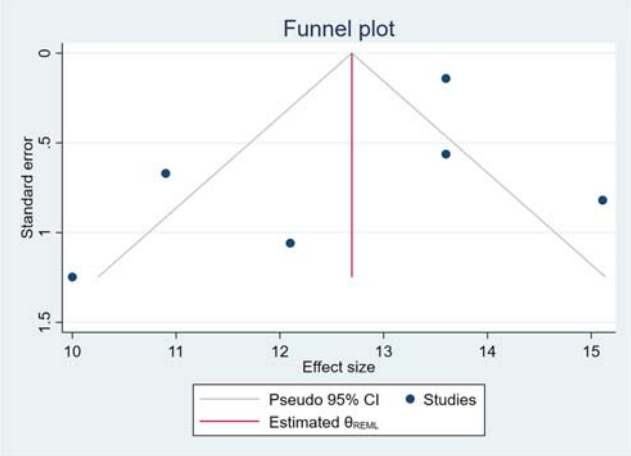

Fig. 2 Funnel plot for %TWL after treatment

has shown satisfactory results regarding its efficacy and safety in conjunction with behavioral modification [22]. Procedureless EIGB has emerged in recent years as one of the alternatives due to its convenience and perhaps superior safety profile [23]. Our study is the first systematic review and meta-analysis that summarized the efficacy and safety of EIGB.

Our study demonstrated %TWL of 12.8% and 10.9% at 4–6 months and 12 months, respectively. These weight loss outcomes are promising. However, there is no trial comparing EIGB with other intragastric balloons. Orbera (Apollo Endosurgery, Austin, TX), Obalon (Obalon Therapeutics, Carlsbad, CA), and ReShape Duo (ReShape Medical, San Clemente, CA) are the three current US FDA-approved intragastric balloons. Orbera intragastric balloon is currently the most widely used [24, 25], which offered %TWL of 13.2% and 11.3% at 6 and 12 months, respectively [26]. A randomized trial of the Obalon balloon (SMART trial) demonstrated %TWL of 7.8% and 6.9% at 6 and 12 months [27]. Another randomized trial of the ReShape Duo balloon (REDUCE trial) showed %TWL of 7.6% at 6 months [28]. Though further comparative studies with other balloons are needed, our meta-analysis showed that EIGB could be an effective weight loss tool.

Regarding its safety, EIGB showed an acceptable safety profile with 0.2% of serious adverse events according to our result, which is also comparable to Orbera intragastric balloon [26]. Furthermore, no deaths were reported. The serious adverse events from Orbera intragastric balloon were similar to EIGB, including esophageal perforation, gastric perforation, and small bowel obstruction [29], and four deaths associated with Orbera intragastric balloon were reported [29, 30]. However, the safety data of our study was available only up to 12 months after therapy, unlike the Orbera balloon, which has been utilized for a more extended period. Long-term data of EIGB is needed to better characterize its safety profile.

The cost-effective standpoint also needs to be considered. Presently, the Weight Watchers Meetings lifestyle modification program is the only evidence-based cost-effective option for nonsurgical management of weight loss when the cost-effectiveness is determined by cost per kilogram lost and quality-adjusted life years (QALY) gained [31]. The absence of endoscopy requiring sedation or anesthesia lowers the implantation and removal cost of EIGB comparing to other endoscopic intragastric balloons or bariatric surgery, and this might compensate the higher price tag of the device itself.

Our study has several limitations. First, the sample size was relatively small, with its early phase of use. Second, high between-study heterogeneity of %TWL was observed in our study. This could be from the differences in patient's baseline characteristics and treatment protocol with supplemental lifestyle intervention and dietician follow-up in some of the included studies. Moreover, modifiable risk factors of obesity, nutritional status, and other metabolic parameters could play a role in the heterogeneity but could not be further explored, as not reported in the primary studies. Subgroup analyses could technically explore this heterogeneity but could not be conducted due to the limited number of studies along with the absence of subgroup data from the primary studies. Third, the long-term effect after EIGB treatment for weight loss is still unclear, given that there were only two studies that reported results after a long-term follow-up at 12 months. Long-term studies are needed. Lastly, it should be noted that the patients in this meta-analysis were mainly mild-to-moderate obesity, not the same as the bariatric surgery population, which could limit the generalizability of our results to a bariatric surgery population.

In summary, our meta-analysis demonstrated that EIGB is a reasonably safe device and could become a practical tool for weight loss when performed by bariatric endoscopists, given its potentially severe complications. Nonetheless, the limited quality of existing literature resulted in several constraints as discussed above. Further prospective studies, preferably randomized controlled trials, could be done to determine its execution against other intragastric balloon devices with a long-term follow-up and assessment of metabolic outcomes.

Compliance with Ethical Standards

Conflict of Interests The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Informed consent does not apply.

Disclosure Statement The authors have nothing to disclose.

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