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EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM

Research Article

Combination of Intragastric Balloon and Liraglutide: Short-Term Results

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Received: February 13, 2021; **Published:** February 26, 2021

Abstract

Introduction: As isolated therapies, intragastric balloon and liraglutide are used throughout the world to treat excess weight and obesity.

Objective: Compare the effectiveness of intragastric balloon therapy alone and combined with liraglutide.

Methods: Ninety patients (64 women) were randomly divided into two groups of 45 people with the same composition (32 women and 13 men). Group 1 underwent isolated therapy with an intragastric balloon (IGB) for a period of six months. Group 2 also received an IGB implant, along with a daily dose of liraglutide (maximum: 3.0 mg).

Results: Mean age was 34.4 years. Mean initial BMI was 33.93 kg/m^2 in Group 1 and 33.95 kg/m^2 in Group 2. Forty-two patients in Group 1 and 31 in Group 2 completed treatment. The mean reduction in BMI was significantly greater in Group 2 (7.23 ± 1.07) compared to Group 1 (6.21 ± 0.88) ($p < 0.001$). The same was found regarding percentage of total body weight loss (22.21 ± 2.94 in Group 2 vs. 18.29 ± 2.16 in Group 1), percentage of excess weight loss (86.53 ± 17.06 in Group 2 vs. 71.81 ± 14.50 in Group 1) and absolute weight loss in kg (21.71 ± 3.72 in Group 2 vs. 17.90 ± 2.87 in Group 1) ($p < 0.001$ for all comparisons).

Conclusion: Both treatments are effective at promoting weight loss. However, the combination of IGB and liraglutide seems to promote greater weight loss without increasing the occurrence of complications. Therefore, liraglutide proved to be a good adjuvant drug for IGB therapy.

Keywords: *Bariatric Endoscopy; Intragastric Balloon; Obesity; Bariatric Surgery*

Introduction

Different treatment options are available for individuals with overweight and obesity, such as medications or endoscopic and surgical procedures [1,2]. The effectiveness and safety of the widely used intragastric balloon (IGB) have been proven, as this technique achieves good weight loss results with a low rate of complications [3-6].

Liraglutide (LG) is a glucagon-like peptide-1 (GLP-1) receptor agonist that has been successfully used in the treatment of type 2 diabetes [7-9]. Among its physiological aspects, the anorexigenic and insulinotropic effects of the GLP-1 receptor are particularly important

to the treatment of obesity [10]. In the pancreas, LG increases glucose-stimulated insulin secretion and reduces levels of glucagon. The central effects on the hypothalamus delay gastric emptying and increase satiety. LG leads to a dose-dependent weight loss due to its effects on the brain and gastrointestinal tract [11]. Because of this dose-dependent effect, higher dose formulation was developed specifically for the treatment of obesity.

High-dose LG use results in significant and sustained weight loss in patients who have already lost weight with low-calorie diet [12]. This suggests that LG can be used as a pharmacological complement to bariatric procedures in cases of inadequate weight loss. However, few studies have analyzed the combined effect of IGB and LG on weight loss in non-diabetic patients [13]. Thus, the aim of the present study was to evaluate the effects of this combined treatment by comparing randomized groups.

Methods

A randomized prospective study was conducted at the Angioskope Clinic in São Jose dos Campos, Brazil. A selection of 90 patients (64 women) was randomly divided into two groups of 45 people, matched for sex and body mass index (BMI) (32 women and 13 men in each group). Patients eligible for IGB placement with a BMI above 27 kg/m^2 were included. The main exclusion criterion was a risk of baseline gastroparesis (type II diabetes and age greater than 60 years). All patients signed a statement of informed consent.

Group 1 was submitted to intragastric balloon (IGB) therapy (Orbera®, Apollo Endosurgery, Austin, TX, USA) for a six-month period. Group 2 received IGB therapy as well as a daily dose of liraglutide (maximum: 3.0 mg) (Saxenda®, Novo Nordisk, Bagsvaerd, Denmark).

The IGB was filled with 500 to 700 ml of saline with methylene blue. All procedures were performed on an outpatient basis by an experienced gastroenterologist, who performed all insertions and removals of the device. The IGBs were programmed for removal six months after placement.

A daily dose of LG was initiated one month after the placement of the IGB in Group 2. The initial dose was 0.6 mg and was increased weekly up to a maximum dose of 3.0 mg based on the symptoms presented, as recommended by the manufacturer. Both groups were counseled by a multidisciplinary team regarding lifestyle changes, physical activity and the diet prescribed by a specialized dietitian.

The patients were assessed at baseline, monthly and at the time of balloon removal (sixth month). Data on medical history, weight and BMI were collected. The occurrence of adverse events was also assessed. The reduction in mean body weight in kilograms (kg) at the end of six months was the main endpoint.

The data were analyzed using descriptive statistical methods, the Student's t-test and analysis of variance followed by Tukey's post hoc test. The level of significance was set at 5% ($p < 0.05$).

Results

Mean age was 34.4 years (range: 21 to 57 years). Mean initial BMI was 33.93 kg/m^2 in group 1 and 33.95 kg/m^2 in group 2. Regarding the dropout rate, 42 patients in group 1 completed treatment, compared to 31 in group 2 (Table 1).

Parameters	Group 1	Group 2
Mean initial BMI	33.93 kg/m^2	33.95 kg/m^2
Mean reduction in BMI	6.21 ± 0.88	7.23 ± 1.07
Percentage total body Weight Loss	18.29 ± 2.16	22.21 ± 2.94
Percentage of excess weight loss	71.81 ± 14.50	86.53 ± 17.06
Absolute weight loss in kg	17.90 ± 2.87	21.71 ± 3.72

Table 1: *Dropout rate, 42 patients in group 1 completed treatment, compared to 31 in group 2.*

The mean reduction in BMI was significantly greater in group 2 (7.23 ± 1.07) compared to group 1 (6.21 ± 0.88) ($p < 0.001$). The same was found regarding the percentage of total body weight loss (22.21 ± 2.94 in group 2 vs. 18.29 ± 2.16 in group 1), percentage of excess weight loss (86.53 ± 17.06 in group 2 vs. 71.81 ± 14.50 in group 1) and absolute weight loss in kg (21.71 ± 3.72 in group 2 vs. 17.90 ± 2.87 in group 1). Statistically significant differences were found in all intragroup and intergroup comparisons ($p < 0.0001$), with lower mean total weight, overweight and BMI in group 2 at the end of the six months of treatment (Figure 1-5).

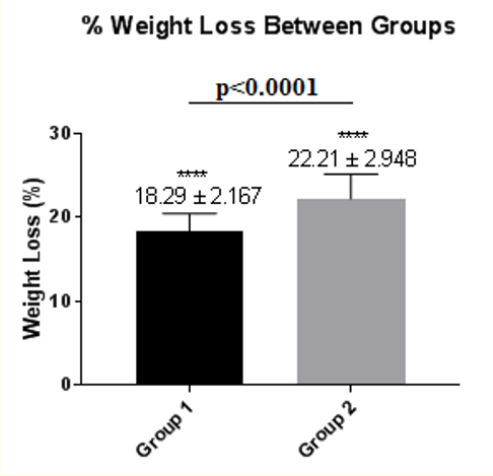

Figure 1: *Percentage weight loss between groups.*

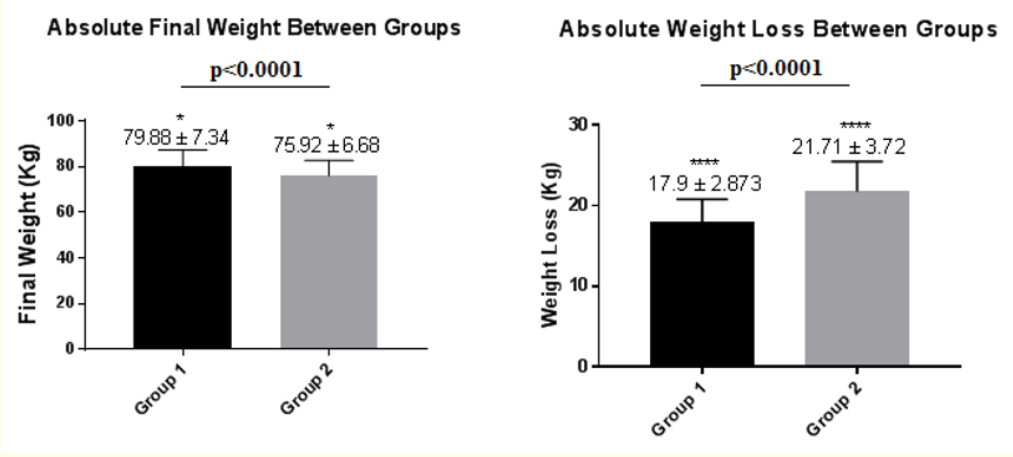

Figure 2: *Weight loss in kilograms between groups.*

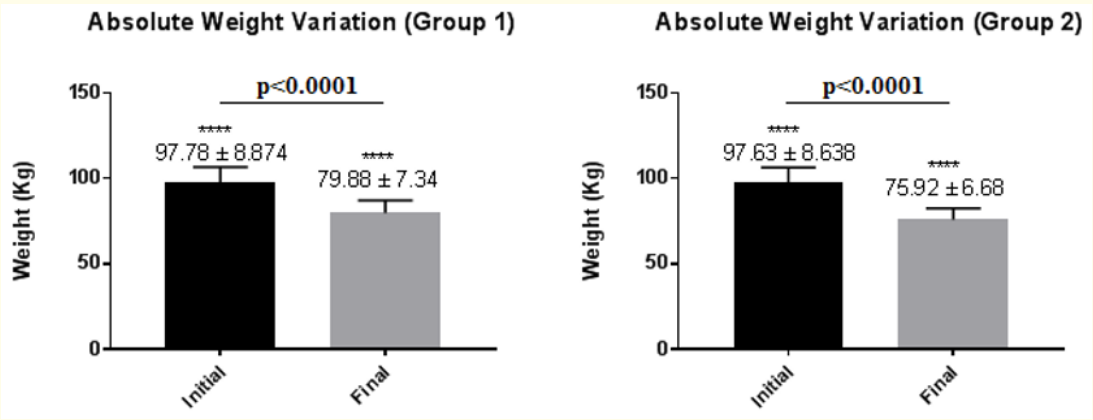

Figure 3: *Difference in weight between groups.*

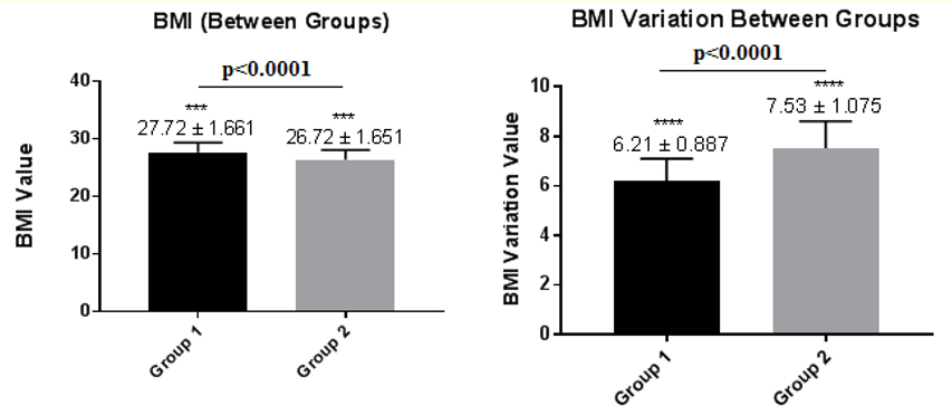

Figure 4: *Difference in BMI and BMI variation in groups.*

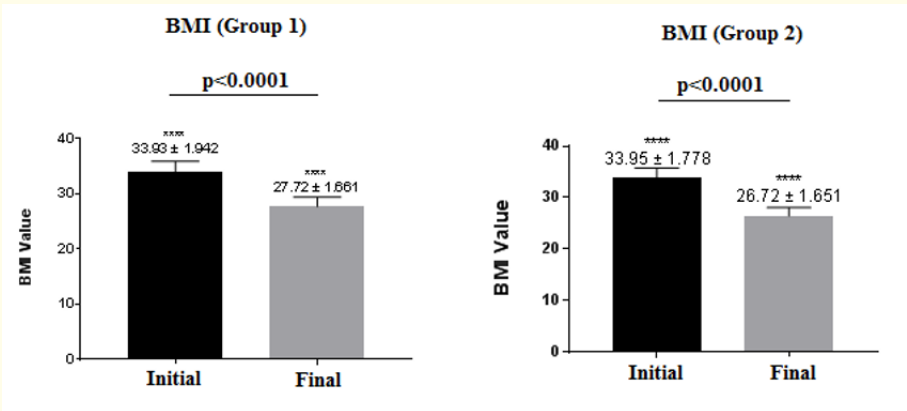

Figure 5: *Differences in BMI between groups.*

Discussion

The IGB has been used in clinical practice as an option for the treatment of overweight and obesity, especially when associated with diet therapy and exercise [14-16]. Many studies have demonstrated its effectiveness for short-term weight loss, achieving significant improvements in comorbidities related to obesity [17-20].

In a recent systematic review and meta-analysis, the use of an IGB in comparison to diet alone achieved better results in terms of final weight, with a reduction in BMI of 2.62 kg/m^2 (95% CI: 0.33 to 4.92). The quantitative analysis also showed a statistically significant difference in favor of the IGB group regarding the percentage of excess weight loss (14%, $p < 0.005$) [21].

Liraglutide (LG) is an analogue of the GLP-1 (glucagon-like peptide-1) hormone that controls glycemic levels and reduces weight in individuals with diabetes and obesity [7-9]. The GLP-1 receptor has many physiological functions on the body, the anorexigenic and insulinotropic effects of which are the most important to the treatment of obesity [10]. Centrally, GLP-1 analogs affect the hypothalamus, resulting in a reduction in appetite. Peripherally, GLP-1 analogs affect vagal sensory afferent neurons that signal the brain and have a direct effect on the stomach, delaying gastric emptying, which causes satiety. A diminished circulation of leptin has also been suggested, with an anorexigenic effect [22,23]. Thus, GLP-1 analogs cause satiety, leading to decreased food intake, a negative energy balance and weight loss.

The review by Nuffer., *et al.* demonstrated that LG can successfully achieve weight loss of 5% to 10% or more compared to baseline. The most common adverse effects are gastrointestinal, which are mild to moderate in intensity. The weight loss promoted by LG has been described as an additional benefit, leading the manufacturer to develop a higher dose formulation specifically for the treatment of obesity. LG at 3.0 mg/day was approved by the US Food and Drug Administration for this indication in December 2014 [11].

A meta-analysis found that the addition of LG 3.0 mg/day to lifestyle counseling increased weight loss by approximately 5.2 kg compared with the same counseling with a placebo [24]. According to the study by Wadden., *et al.* adding LG to intensive behavioral therapy nearly doubled weight loss compared to behavioral counseling alone (6.1% vs. 11.5%) [25]. In the study by Rye., *et al.* LG was shown to be an effective adjunct treatment for weight loss in patients with prior bariatric surgery, leading to a median reduction in BMI of 4.7 kg/m^2 after 28 weeks [26].

In a study with 564 participants, LG was tested as an adjuvant to the treatment of obesity in non-diabetic obese individuals. The participants received LG subcutaneously once daily at doses of 1.2 mg, 1.8 mg, 2.4 mg and 3.0 mg. Weight loss was reasonable, but with a high incidence of nausea in the treatment group [27].

The present findings demonstrate better effectiveness in total and excess weight loss with the combination of an IGB and LG in comparison to the IGB alone. The mean reduction in BMI was significantly greater in Group 2 (7.23 ± 1.07) compared to Group 1 (6.21 ± 0.88) ($p < 0.001$). The same was found regarding the percentage of total body weight loss, percentage of excess weight loss and absolute weight loss in kg. The percentage of total body weight loss achieved in the group undergoing IGB therapy alone (18.29 ± 2.16) was comparable to quantities generally described in the literature (18.4 ± 2.9%), as shown in the Brazilian Consensus Data.

To the best of our knowledge, this is the first prospective randomized study to compare IGB therapy to the combination of this therapy and LG. Only one previous study has been published analyzing the combined use of IGB and LG [13]. Mosli., *et al.* performed a retrospective analysis of all cases treated with IGB (combined or not with LG), totaling 108 patients, 64 of whom underwent IGB therapy alone and 44 received a combination of IGB and LG. The patients treated with IGB + LG exhibited greater mean weight loss at the end of treatment compared to those treated with IGB alone (18.5 ± 7.6 vs. 10.2 ± 6.7, $p < 0.0001$) [13]. Moreover, the patients treated with IGB and LG lost

more weight six months after the completion of treatment (4.7 ± 6 vs. 2.7 ± 4.10, p = 0.019). However, the multiple regression analysis swung the results in the opposite direction, suggesting that IGB as monotherapy is sufficient. This result may have cost-effectiveness implications. Patients treated with IGB alone appeared to have 2.98% higher odds of treatment success compared to those treated with IGB + LG. However, since patients were not randomized, the potential for selection bias should be considered. The study demonstrated no benefit of adding LG to IGB therapy with regards to weight regain six months after the removal of the IGB.

Several studies using IGB and LG separately have shown satisfactory results regarding total weight loss and BMI. Further studies are needed to prove the effectiveness of adding LG to IGB therapy. The best period for initiating this combination also needs to be tested, considering the limited period in which the IGB remains in place, the side-effects of LG and the high weight regain rates after IGB therapy. More prospective randomized clinical trials with larger samples are needed to demonstrate the cost-effectiveness of combined therapy. The major limitation of IGB insertion is weight regain after the balloon is removed, which is reported in up to 35% of patients [15,28]. LG may play a role in reducing weight regain after IGB removal and this effect needs to be analyzed further. The main limitations of this study are the small sample size and the absence of a crossover period.

Conclusion

Intragastric balloon therapy is effective at achieving weight loss and the combination of this therapy with liraglutide seems to promote a greater weight loss without increasing the rate of complications. Therefore, liraglutide proves to be a potential adjuvant drug for intragastric balloon therapy.

Financial Support and Sponsorship

None.

Conflicts of Interest

There are no conflicts of interest.

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