Obesity Surgery
https://doi.org/10.1007/s11695-023-06736-7

BRIEF COMMUNICATION

Treatment with Antiobesity Drugs in Weight Regain After Bariatric Surgery: a Retrospective Cohort Study

Bibiana S. Boger[1] · Nara L. Queiroz[1] · Paulo E. P. Noriega[1] · Maicon C. Canuto[1] · Matheo A. M. Stumpf[1] · Cintia Cercato[1] · Marcio C. Mancini[1] · Maria E. de Melo[1]

Received: 2 June 2023 / Revised: 12 July 2023 / Accepted: 14 July 2023

Abstract

Background Bariatric surgery is the most efficient treatment for obesity. However, in some cases, weight regain can occur. Currently, it is unknown the best antiobesity medication (AOM) for such clinical situation. This study aims to evaluate the effect of AOM in patients with weight regain after bariatric surgery.

Methods A retrospective cohort study from December 2010 to July 2019 with patients submitted to bariatric surgery that had weight regain and received AOM for at least 2 years.

Results Of 96 patients that had weight regain in the analyzed period and received AOM, 16 were excluded from the analysis due to non-compliance ($n = 7$), treatment failure ($n = 5$), intolerable side effects with all available AOM ($n = 2$), or interaction with other medications ($n = 2$). Eighty patients were included in the analysis. The mean age was 59.0 ± 10.1 years, 88.8% were female, 91.2% white, and most of them were submitted to gastric bypass (87.6%). The mean preoperative and nadir weight after surgery were 127.9 ± 25.5 kg and 84.7 ± 22.8 kg, respectively. At the initiation of AOM, the mean baseline weight was 99.4 ± 23.1 kg. After 2 years of follow-up, there was significant weight loss in the groups treated with topiramate-alone (− 3.2 kg), topiramate plus sibutramine (− 6.1kg), and orlistat-alone or in combination (− 3.9kg). No statistical difference was observed in the sibutramine-alone group.

Conclusion Topiramate (alone or associated with sibutramine) and orlistat (alone or in combination) promoted significant weight loss after 2 years of use in patients submitted to bariatric surgery with weight regain.

Keywords Bariatric surgery · Weight regain · Obesity · Topiramate · Orlistat · Sibutramine

Introduction

Currently, bariatric surgery is the most efficient treatment, achieving in some surgical techniques more than 60% of excess weight loss. In almost 37% of patients, however, weight regain can occur, especially in late postoperative period [1].

It is controversial which antiobesity medication (AOM) should be preferable since there is a lack of evidence concerning medical treatment for weight regain. In the few studies published, topiramate is usually the most commonly prescribed option due to experience and security profile [2].

In this retrospective study, the aim was to evaluate weight loss with AOM used in patients with weight regain following bariatric surgery.

Key Points
– Weigh regain can occur in almost one-third of patients submitted to bariatric surgery
– Few studies evaluated this population and is unclear which should be the drug of choice for treatment
– In the present study, the combination of topiramate plus sibutramine had the most significant potency for weight loss (– 6.1 kg, 5.9%)

Extended author information available on the last page of the article

Methods

This is a retrospective cohort study carried out in a single academic tertiary care service. The inclusion criteria consisted of patients > 18 years who underwent bariatric surgery; had regained weight despite dietary counseling

Published online: 19 July 2023

and lifestyle changes; had no identifiable anatomic cause for regain; and were treated with AOM for at least 2 years. Although there is no consensus on weight regain definition, we included patients that regained at least 5% of their nadir weight.

Data were obtained from medical records during follow-ups between December 2010 and July 2019. Demographic data, medical history, and surgical technique were collected. Patients were divided into four groups, based on AOM prescription: topiramate-alone, topiramate plus sibutramine, sibutramine-alone, and orlistat (alone or in combination). The choice of drug was individualized based on eating patterns (hyperphagia, binge, craving), presence of comorbidities, and on-label contra-indications. If the patient had good tolerability, the AOM was increased to the maximum dose: topiramate up to 300 mg daily, sibutramine 15mg daily, and orlistat 120 mg three times a day. If no weight loss was achieved, an association could be made or the initial drug was switched. Participants had to maintain the same drug or the combination for up to 2 years to be eligible for the study. Of note, as obesity is a chronic condition, AOM was not withdrawn after the minimum 2 years of use, and it was continuously maintained in responders. Treatment failure was defined as when no weight was lost after testing all three drugs, even with combinations between them.

Weight was evaluated during several periods: before surgery; postoperatively; at the beginning of AOM treatment; and after 6, 12, and 24 months of AOM use. All four groups received hypocaloric diet orientation, were encouraged to participate in physical activities (150 minutes or more per week), and maintained mineral and vitamin supplementations. The hypocaloric diet was empirically orientated to a maximum of 1200–1500 kcal per day. For participants that had performed bioelectrical impedance analysis (InBody 770), a 600-kcal deficit from basal metabolic rate was prescribed. The patients also had regular follow-ups with a multidisciplinary team composed of endocrinologists, nutritionists, and surgeons. The frequency of visits was individualized. Patients could also be scheduled for psychiatric and psychologic appointments if clinically indicated.

A total of 96 patients participated in this study, but 16 were excluded from the analysis due to non-compliance ($n = 7$), treatment failure ($n = 5$), intolerable side effects with all available AOM ($n = 2$), or interaction with other medications ($n = 2$).

Data were summarized as mean ± standard deviation for continuous variables and as counts and percentage for categorical variables. Difference between groups was performed by analysis of variance (ANOVA) for repeated measures. The p-value < 0.05 was considered statistically significant. Statistical analysis of the data was performed using Statistical Package for Social Science (SPSS) version 18.0. The study was approved by the local Ethics Committee.

Results

Eighty patients were included in the analysis. The baseline demographic and clinical data are available in Table 1. Most of the sample was composed of white (91.2%), women (88.8%) submitted to gastric bypass (87.6%). For weight regain, topiramate was the most commonly used drug, in 37 (46.3%) patients.

Table 2 describes weight evolution after the initiation of AOM. The weight at the beginning of treatment did not differ between groups ($p = 0.914$). There was a significant reduction in weight after 2 years of treatment in the groups treated with topiramate ($p = 0.040$), topiramate plus sibutramine ($p = 0.004$), and orlistat ($p = 0.032$). Absolute body weight loss after 2 years of follow-up was 3.2 kg (3.3%) in the topiramate-treated group, 6.1 kg (5.9%) in the topiramate plus sibutramine, and 3.9 kg (4.0%) in the orlistat. No significant difference in weight evolution was observed in the sibutramine group ($p = 0.330$).

Discussion

The present study represents real-world data for AOM in weight regain following bariatric surgery. The three drugs used are available in our Public Health System, have low cost, and have extensive literature experience for security and tolerability when prescribed as primary treatment for obesity. Moreover, the potency of weight loss reached was comparable to the reported in previous studies for weight regain [2, 3].

For some AOM, such as sibutramine, the weight loss achieved in cases of regain is less than the observed when used as primary treatment for obesity. The negative impact that bariatric surgery has on intestinal absorption could justify the lower weight loss potency. Topiramate, on the other hand, appears to be safely absorbed [4].

In recent trials [5, 6] with glucagon-like peptide-1 receptor agonists (GLP-1 RA) for weight regain, semaglutide achieved greater results than liraglutide, as expected. Interestingly, the weight loss observed is similar to the reported in pivotal obesity-focus trials, such as SCALE [7]. The subcutaneous route probably does not have impairment after bariatric surgery. In these retrospective studies, liraglutide 3 mg daily had a weight loss of 7.3% [5] and 8.77% [6], similar to our combination of topiramate plus sibutramine (almost 6%). The mechanism of action of this combination is comparable to topiramate plus phentermine (currently unavailable in Brazil).

It should be highlighted that although the weight potency of classical AOM is more modest than new GLP-1 RA (i.e.,

Table 1 Demographic and clinical characteristics of the patients

Age, years	59.0 ± 10.1
Female sex, no. (%)	71 (88.8)
Male sex, no. (%)	9 (11.2)
Race or ethnic group, no. (%)	
White	62 (91.2)
Black	1 (1.5)
Asian	1 (1.5)
Other	4 (5.9)
Pre-op maximum weight, kg	137.8 ± 31.9
Pre-op weight before surgery, kg	127.9 ± 25.5
Pre-op BMI before surgery, kg/m^2	49.4 ± 7.5
Comorbidities, no. (%)	
Hypertension	54 (67.5)
Type 2 diabetes	37 (46.3)
Dyslipidemia	16 (20)
Obstructive sleep apnea	12 (15)
Nonalcoholic fatty liver disease	5 (6.3)
Techniques, no. (%)	
Gastric bypass	41 (51.3)
Ringed or banded gastric bypass	29 (36.3)
Sleeve gastrectomy	7 (8.7)
Biliopancreatic diversion	2 (2.5)
Vertical banded gastroplasty	1 (1.2)
Post-op nadir weight, kg	84.7 ± 22.8
Baseline weight at initiation of AOM, kg	99.4 ± 23.1
Baseline BMI at initiation of AOM, kg/m^2	38.3 ± 7.3
Medications, no. (%)	
Topiramate-alone	37 (46.3)
Topiramate plus sibutramine	18 (22.5)
Sibutramine-alone	15 (18.8)
Orlistat	10 (12.5)
Orlistat-alone	5 (6.3)
Orlistat plus topiramate	2 (2.5)
Orlistat plus sibutramine	1 (1.3)
Orlistat plus topiramate and sibutramine	2 (2.5)

Table 2 Weight evolution during follow-up after initial drug prescription

Medication group	Period	Mean ± SD (kg)	*p**
Topiramate-alone	Baseline	96.0 ± 20.9	0.040
	6 m	94.2 ± 20.3	
	12 m	94.1 ± 19.5	
	24 m	92.8 ± 18.3	
Topiramate plus sibutramine	Baseline	102.0 ± 17.3	0.004
	6 m	98.2 ± 17.5	
	12 m	96.4 ± 17.2	
	24 m	95.9 ± 18.2	
Sibutramine-alone	Baseline	95.0 ± 19.3	0.330
	6 m	92.7 ± 19.5	
	12 m	92.0 ± 19.8	
	24 m	92.3 ± 18.0	
Orlistat (alone or in combination)	Baseline	97.1 ± 24.7	0.032
	6 m	97.1 ± 22.2	
	12 m	94.2 ± 25.0	
	24 m	93.2 ± 25.6	

*ANOVA test

semaglutide), a weight loss of 5–10% can already have several health benefits [8].

In the present study, the sibutramine-alone group did not significantly reduce weight after 2 years of treatment. However, in some cases of regain, the main objective with AOM could be achieving at least a weight plateau and not necessarily weight loss. In general, these patients are still at a much lower weight than their maximum lifetime weight. Therefore, it is possible that sibutramine prevented an even greater weight regain.

Some studies demonstrate that more significant weight loss occurs when AOM is introduced during the phase of weight plateau compared to waiting for weight regain occurrence [9]. Unfortunately, the present study did not aim to evaluate this strategy, and AOM was started when weight regain was detected, which is the most usual approach. Nevertheless, the use of a "prophylactic" AOM may be appropriate in patients with severe obesity and stable weight that remained with a high BMI even after significant post-surgery weight loss [2].

This study has some limitations. It has a single center data and the majority of the participants was white, female, and submitted to gastric bypass. The results might not be extrapolated for other populations. Furthermore, patients using orlistat were grouped, half of them in combined treatment, which difficult the interpretation of the isolated effect of this drug. The dropout rate was also high (16 of 96 patients, 16.7%), mostly due to non-compliance ($n = 7$). However, our study provides more evidence with classical AOM for treating patients with weight regain after bariatric surgery.

Conclusion

In patients with weight regain, topiramate (alone or associated with sibutramine) and orlistat (alone or in combination) promoted limited but significant weight loss in a 2-year follow-up study. Sibutramine-alone group, on the other hand, did not have significant weight loss. More studies are needed to define the best timing to initiate AOM and which would be the most effective treatment for weight regain.

Declarations

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent For this type of retrospective study, informed consent does not apply.

Conflict of Interest The authors declare no competing interests.

References

1. Cooper TC, Simmons EB, Webb K, et al. Trends in weight regain following Roux-en-Y gastric bypass (RYGB) bariatric surgery. Obes Surg. 2015;25:1474–81.
2. Lucas E, Simmons O, Tchang B, et al. Pharmacologic management of weight regain following bariatric surgery. Front Endocrinol. 2023;13:1043595.
3. Noria SF, Shelby RD, Atkins KD, et al. Weight regain after bariatric surgery: scope of the problem, causes, prevention, and treatment. Curr Diab Rep. 2023;23:31–42.
4. Brown CS, Rabinstein AA, Nystrom EM, et al. Antiseizure medication use in gastric bypass patients and other post-surgical malabsorptive states. Epilepsy Behav Rep. 2021;16:100439.
5. Jensen AB, Renström F, Aczél S, et al. Efficacy of the glucagon-like peptide-1 receptor agonists liraglutide and semaglutide for the treatment of weight regain after bariatric surgery: a retrospective observational study. Obes Surg. 2023;33:1017–25.
6. Murvelashvili N, Xie L, Schellinger JN, et al. Effectiveness of semaglutide versus liraglutide for treating post-metabolic and bariatric surgery weight recurrence. Obes. 2023;31:1280–9.
7. Pi-Sunyer X, Astrup A, Fujioka K, et al. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. N Engl J Med. 2015;373:11–22.
8. Halpern B, Mancini MC, de Melo ME, et al. Proposal of an obesity classification based on weight history: an official document by the Brazilian Society of Endocrinology and Metabolism (SBEM) and the Brazilian Society for the Study of Obesity and Metabolic Syndrome (ABESO). Arch Endocrinol Metab. 2022;66:139–51.
9. Edgerton C, Mehta M, Mou D, et al. Patterns of weight loss medication utilization and outcomes following bariatric surgery. J Gastrointest Surg Off J Soc Surg Aliment Tract. 2021;25:369–77.

Authors and Affiliations

Bibiana S. Boger[1] · Nara L. Queiroz[1] · Paulo E. P. Noriega[1] · Maicon C. Canuto[1] · Matheo A. M. Stumpf[1] · Cintia Cercato[1] · Marcio C. Mancini[1] · Maria E. de Melo[1]

✉ Matheo A. M. Stumpf
matheoaugusto@hotmail.com
https://orcid.org/0000-0002-6465-0972

Bibiana S. Boger
bibiana.boger@hc.fm.usp.br

Nara L. Queiroz
nara.queiroz@hc.fm.usp.br

Paulo E. P. Noriega
pauloenriquepeinado@gmail.com

Maicon C. Canuto
maicon.canuto@hc.fm.usp.br

Cintia Cercato
cintia.cercato@hc.fm.usp.br
https://orcid.org/0000-0002-6181-4951

Marcio C. Mancini
mmancini@usp.br
https://orcid.org/0000-0003-1278-0406

Maria E. de Melo
maria.edna@hc.fm.usp.br
https://orcid.org/0000-0002-1216-7532

[1] Unidade de Obesidade, Disciplina de Endocrinologia e Metabologia, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), R. Dr. Ovídio Pires de Campos, 225 - Cerqueira César, São Paulo, SP 05403-010, Brazil