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ORIGINAL ARTICLE

Association between weight loss and reduced use of antihypertensive, hypoglycemic, psychotropic, and lipid-lowering drugs in patients undergoing bariatric surgery

Associação entre perda de peso e redução do uso de fármacos anti-hipertensivos, hipoglicemiantes, psicotrópicos e antidislipidêmicos em pacientes submetidos a cirurgia bariátrica

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KEYWORDS

Bariatric surgery
Hypoglycemic agents
Weight loss
Antihypertensive agents
Pharmaceutical preparations

ABSTRACT

Objectives: To analyze whether the weight reduction observed in bariatric surgery (Roux-en-Y gastric bypass; BGYR) is accompanied by a reduction in the use of antihypertensive, hypoglycemic, lipid-lowering, and psychotropic drugs after 6 and 12 months.
Methods: Longitudinal, retrospective study of 100 adult patients undergoing RYGB from May 2015 to January 2019, by laparotomy or laparoscopy. Data on age, body mass index (BMI), and the number of drugs used were recorded 6 and 12 months after surgery.
Results: The mean age was 39.7 ± 9.7 years, and the majority were female (n = 78). The mean preoperative BMI was 43.7 ± 5.1 kg/m^2, and the mean reduction in BMI after 6 months was 12.1 kg/m^2 and 14.9 kg/m^2 after 12 months. The reduction in antihypertensive drugs was 65.2% after 6 months and 96% after 12 months. The reduction in 6 months of hypoglycemic agents was 84.3%, and in 12 months, 98.3%. The average reduction in lipid-lowering drugs was 86.7% in 6 months, and there was no record of using this medication after 12 months. Psychotropics showed a temporary reduction in use after 6 months with a return to levels close to the baseline after 1 year. There was no correlation between the variation in BMI and the use of drugs.
Conclusions: there was a significant reduction in the use of drugs after 6 and 12 m, except for psychotropic drugs. The reduction in the use of drugs was not correlated with a reduction in BMI.

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PALAVRAS-CHAVE

Cirurgia bariátrica
Hipoglicemiantes
Perda de peso
Anti-hipertensivo
Preparações farmacêuticas

RESUMO

Objetivos: Analisar a redução de peso observada na cirurgia bariátrica (*bypass* gástrico em Y de *Roux*; BGYR) e do uso de medicamentos anti-hipertensivos, hipoglicemiantes, antidislipidêmicos e psicotrópicos, após 6 e 12 meses.
Métodos: Estudo longitudinal, retrospectivo, em 100 pacientes adultos submetidos a BGYR de maio de 2015 a janeiro de 2019, por laparotomia ou videolaparoscopia. Foram anotados dados de idade, índice de massa corpórea (IMC) e quantidade de fármacos utilizados após 6 e 12 meses da cirurgia.
Resultados: A média de idade foi de 39,7 ± 9,7 anos, e a maioria era do sexo feminino (n = 78). O IMC médio pré-operatório foi de 43,7 ± 5,1 kg/m^2 e a redução média do IMC após 6 meses foi de 12,1 kg/m^2 e de 14,9 kg/m^2 após 12 meses. A redução no uso de anti-hipertensivos foi de 65,2% após 6 meses e de 96% após 12 meses. A redução em 6 meses dos hipoglicemiantes foi de 84,3% e em 12 meses de 98,3%. A redução média dos antidislipidêmicos foi de 86,7% em 6 meses e não houve registro de uso desta medicação após 12 meses. Os psicotrópicos apresentaram redução temporária de uso após 6 meses com retorno aos níveis próximos dos basais após 1 ano. Não foi observada correlação entre a variação do IMC e o uso de fármacos.
Conclusões: houve redução significativa no uso de fármacos após 6 e 12 m, exceto pelos psicotrópicos. A redução do uso de fármacos não se correlacionou à redução do IMC.

INTRODUCTION

The obesity epidemic is a reality that has grown globally. In 2015, there were 603.7 million obese adults in the world. Over the past 25 years, the prevalence of obesity has doubled in 73 countries[1]. In Brazil, about 40% of the population is overweight: 10.1% are obese, and 28.5% are overweight. Mortality increases 12 times more in morbidly obese patients than in normal-weight patients aged 25 to 40 years[2]. Severe obesity is generally refractory to lifestyle changes, including diet and exercise. Pharmacological treatment is also of limited effectiveness. Even when lifestyle modification or drug treatments are successful, weight loss is usually completely regained in one year. Thus, bariatric surgery has become a good alternative for treating this group of patients[2,3].

The elevated body mass index (BMI) is an independent risk factor for developing systemic arterial hypertension (SAH), type 2 diabetes mellitus (DM2), dyslipidemia (DLP), chronic kidney disease (CKD), ischemic heart disease, cerebrovascular disease, dementia, neoplasms, nonalcoholic fatty liver disease, and obstructive sleep apnea. These comorbidities generate more significant disability, morbidity, and mortality among obese people and promote a relevant worsening of quality of life[3].

Recent studies have shown a reduction in total mortality, cardiovascular complications, improvement in physical and metabolic performance, and various health indexes after bariatric surgery compared to clinical treatment, contradicting the old premise of its association with high rates of morbidity and mortality[4-7]. Given the unequivocal benefits of surgically induced sustained weight loss, it is likely that bariatric surgery will continue to evolve and play an increasing role in preventing cardiovascular diseases[8].

The term "bariatric" (which originates from the Greek word for weight, *baros*) reflects the notion that gastrointestinal surgery is primarily used to induce weight loss. However, strong evidence shows that bariatric surgery not only induces dramatic weight loss but also improves the metabolic control of DM2, SAH, and DLP[9]. Metabolic control usually precedes substantial weight loss. Based on this evidence, the term "metabolic surgery" becomes more appropriate, as it refers to the effects of gastrointestinal surgery on the metabolic syndrome as a whole, in addition to capturing the metabolic nature of its mechanisms of action[10].

However, few studies have addressed reducing the routine use of drugs associated with the metabolic control of the main comorbidities, especially hypoglycemic, antihypertensive, and lipid-lowering drugs[11-13]. The aim of this study, therefore, is to analyze whether the weight reduction observed in bariatric surgery (Roux-en-Y gastric bypass; RYGB) is accompanied by a reduction in the use of comorbidity control drugs, specifically DM2, SAH, DLP, in addition to psychotropic drugs, after 6 and 12 months.

METHODS

This is a single-center, longitudinal, retrospective study of medical records analysis of patients undergoing bariatric surgery at the Hospital de Clínicas de Itajubá, located in the south of Minas Gerais, from May 2015 to January 2019. The hospital is accredited by the Unified Health System to perform bariatric surgeries and also performs surgeries for complementary and private health. The Research Ethics Committee approved the study of the Faculdade de Medicina de Itajubá under protocol number 3,517,185. Due to the characteristics of the study, the application of the Informed Consent Form was waived.

It was included for analysis all patients operated in the period, over 21 years of age, who underwent RYGB surgery by laparotomy or laparoscopy, whether or not associated with cholecystectomy, regardless of the provider. All operated patients had a formal indication by BMI (> 40 kg/m^2 or > 35 kg/m^2 associated with one or more comorbidities) after failing to attempt weight loss by noninvasive means. Psychological and nutritional assessment and monitoring were mandatory in all cases, whether in a hospital outpatient or private clinic. It was

excluded cases in which there was no adequate filling out of the medical record, loss of follow-up information as early as the first postoperative return, or death within six months. Patients with missing data in the 6 to 12-month follow-up were excluded from the sub-analysis. The use of drugs or the diagnosis of cardiovascular comorbidities was not an inclusion or exclusion criterion since it was investigated not only the reduction in medications, but the initial average of the number of drugs.

Data on age, sex, height and weight (immediately before surgery and after 6 and 12 months), type of surgery, and the number of drugs used to treat comorbidities in the above periods were recorded. It was impossible to calculate the dosage in mg/day of each drug used due to difficulties in obtaining medical record data. Data were obtained from electronic hospital and outpatient physical records.

SAH was defined as blood pressure greater than 140 × 90 mmHg or continuous use of antihypertensive drugs, DM2 as fasting glucose > 106 mg/dL or use of hypoglycemic agents, and DLP as total cholesterol > 200 mg/dL or LDL > 130 mg/dL. Due to the high prevalence in this population, the reduction in the use of psychotropic drugs was also included.

The sample calculation was based on an estimate of variance analysis (one-way ANOVA) for fixed effect, with an estimate of a 50% decrease in the use of antihypertensive drugs over a year of follow-up, with a probability of type error I of 5% and test power of 95%, requiring at least 66 patients per group. The sample was calculated using the G* Power software version 3.1.9.4[14].

The data were arranged in summary measures (mean and standard deviation) and eventually shown in graphs. The data were submitted to the Kolmogorov-Smirnov normality test. Inferential analysis was performed using Student's t-test for two-tailed independent samples and one-way ANOVA or Kruskal-Wallis test for three groups, followed by Tukey or Dunn's posthoc tests, respectively, as applied. Spearman's rank correlation coefficient was used to test the association between the mean variation of BMI and the average amount of drugs (in units) used in 6 and 12 months. For this analysis, only patients who used at least one medication in each group of drugs studied were included. Statistical significance was set at $p < 0.05$, and the 95% confidence interval (CI) was adopted. GraphPad Prism v.9 software (San Diego, CA, USA) was used.

RESULTS

One hundred sixty-two patients undergoing bariatric surgery during the study period were initially analyzed. After applying the inclusion and exclusion criteria, the final sample consisted of 100 patients, with an average age of 39.7 ± 9.7 years. Most were female (n = 78). There was no statistically significant difference between the mean ages between both sexes. The data related to the age, weight, height, and sex of the sample is shown in Table 1. Most (n = 87) of the surgeries were performed by the Unified Health System, while the remaining 13 patients were operated on by supplementary health insurance or by private hospitalization. Twelve patients underwent laparoscopic surgery, while the rest underwent laparotomy. The evolution of BMI values before surgery and after 6 and 12 months is described in Figures 1 and Table 2. It was impossible to calculate BMI in 15 patients after the first 6 months of surgery and 39 patients after 12 months due to lack of information in medical records, loss of follow-up, or reduced follow-up time. It was possible to observe significant differences in weight loss evolution in the sample and both genders over the analyzed period.

The list of drugs used by the patients under study is described in Table 3. Table 4 and Figure 2 show the average number of antihypertensive, hypoglycemic, psychotropic, and lipid-lowering drugs used by the patients during the follow-up period. It was possible to observe a significant decrease in the number of drugs used 6 and 12 months after surgery. Regarding

Table 1 — Clinical-demographic data of patients undergoing bariatric surgery at Itajubá Clinics Hospital, between 2015 and 2019 (N = 100).

Variables	Total	Male	Female	p-value
Age (years)	39.7 ± 9.7	40.6 ± 9.8	39.5 ± 9.7	0.65
Weight* (kg)	116.1 ± 19.4	135.7 ± 18.4	110.6 ± 15.6	< 0.0001
Height (m)	1.63 ± 0.08	1.71 ± 0.07	1.60 ± 0.07	< 0.0001

*weight before surgery.

Table 2 — Temporal evolution of the body mass index (mean ± standard deviation; Kg/m^2) in patients undergoing bariatric surgery, between 2015 and 2019.

Genre	Before surgery	After 6 months	After 1 year	F*; p-value
Male	46.4 ± 4.4	33.2 ± 3.1†	30.4 ± 5.1†	79.7; < 0.0001
Female	42.9 ± 5.1	31.0 ± 4.3†	28.4 ± 4.8† ‡	162.9; < 0.0001
Total	43.7 ± 5.1	31.6 ± 4.2†	28.8 ± 4.9† ‡	235.9; < 0.0001

* One-way ANOVA; Tukey's multiple comparison test: † p < 0.0001 in relation to the value before surgery, ‡ p < 0.01 in relation to the value of 6 months.

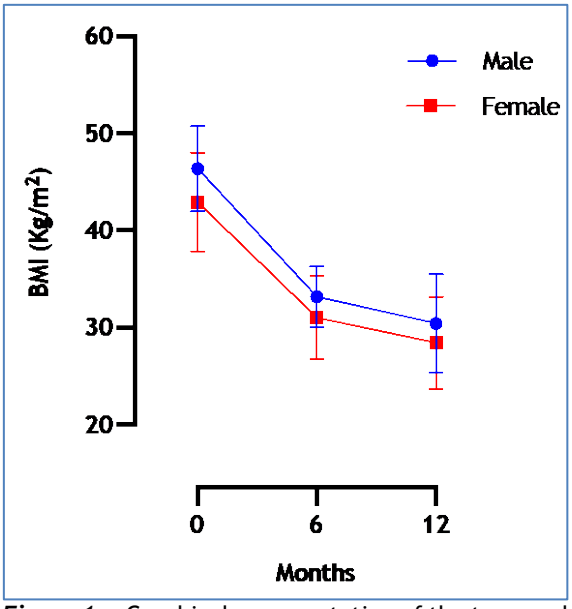

Figure 1 — Graphical representation of the temporal evolution of the BMI of patients undergoing bariatric surgery over the follow-up time (initial n = 100).

antihypertensive agents, the reduction in the average number of drugs in use per individual was 65.2% in 6 months (95% CI 43.1% - 87.3%) and 96% in 12 months (CI 95% 87.0% - 100%). For hypoglycemic agents, the reduction in 6 months was 84.3% (95% CI 72.0% - 96.6%) and 98.3% in 12 months (95% CI 94.9% - 100%). Regarding women using psychotropics, despite an initial decrease in use after 6 months, they returned to levels close to the baseline after one year, which was not observed in males. The reduction in the use of psychotropic drugs was 39.1% in 6 months (95% CI 2.8% - 75.3%) and only 10% in 12 months (95% CI 29.7% - 49.7%). For lipid-lowering drugs, the mean reduction was 86.7% in 6 months (95% CI 67.2% - 100%), and there was no record of using this medication after 12 months.

Table 5 shows the correlation coefficients between the variation in BMI and the number of drugs used, and it is not possible to observe any statistically significant correlation.

Table 3 —- List of antihypertensive, hypoglycemic, psychotropic and lipid-lowering drugs used by the patients in the study.

Antihypertensive drugs	Hypoglycemic drugs	Psychotropic drugs	Lipid-lowering drugs
Amiloride	Dapaglifozin	Alprazolan	Atorvastatin
Amlodipine	Glibenclamide	Amitriptyline	Ciprofibrate
Atenolol	Glicazide	Bromazepam	Fenofibrate
Captopril	Insulin	Bupropion	Rosuvastatin
Chlortalidone	Metformin	Citalopran	Simvastatin
Diltiazem	Pioglitazone	Clonazepam	
Enalapril		Cloxazolam	
Spironolactone		Duloxetine	
Furosemide		Escitalopran	
Hydrochlorothiazide		Fluoxetine	
Losartan		Mirtazapine	
Methyldopa		Paroxetine	
Metoprolol		Sertraline	
Nifedipine		Sibutramine	
Perindopril		Topiramate	
Propanolol		Venlafaxine	
Propatylnitrate		Zolpidem	
Valsartan			

DISCUSSION

This study showed a significant reduction in the number of drugs used for glycemic and blood pressure control in patients undergoing bariatric surgery in the short and medium-term. Although several studies have demonstrated the impact of metabolic surgeries in reducing cardiovascular risk[4,8,15,16], few studies have focused on reducing the polypharmacy observed in these patients.

YRGB is considered the gold standard for bariatric surgery and is the most performed technique. The procedure involves creating a small gastric pouch, a small intestine loop that connects to the gastric pouch

Table 4 — Average number per patient of different types of antihypertensive, hypoglycemic, psychotropic and lipid-lowering drugs used in individuals undergoing bariatric surgery, before surgery and after 6 and 12 months. Values expressed as mean ± standard deviation.

Drug class	Male	Female	Total	p-value *
Antihypertensive				
Before	1.64 ± 1.26	1.03 ± 1.14	1.16 ± 1.19	
After 6 months	0.35 ± 1.09	0.21 ± 0.61	0.24 ± 0.73	< 0.0001
After 1 year	0	0.02 ± 0.14	0.01 ± 0.12	
Hypoglycemic				
Before	0.45 ± 0.60	0.36 ± 0.53	0.38 ± 0.55	
After 6 months	0	0.08 ± 0.27	0.06 ± 0.24	< 0.0001
After 1 year	0	0.02 ± 0.14	0.02 ± 0.12	
Psychotropic				
Before	0.23 ± 0.69	0.37 ± 0.61	0.34 ± 0.62	
After 6 months	0.05 ± 0.22	0.19 ± 0.54	0.16 ± 0.49	0.041
After 1 year	0.06 ± 0.25	0.34 ± 0.69	0.28 ± 0.62	
Lipid-lowering				
Before	0.23 ± 0.53	0.15 ± 0.40	0.17 ± 0.43	
After 6 months	0	0.03 ± 0.16	0.02 ± 0.14	< 0.0001
After 1 year	0	0	0	

*Kruskal-Wallis test for total values.

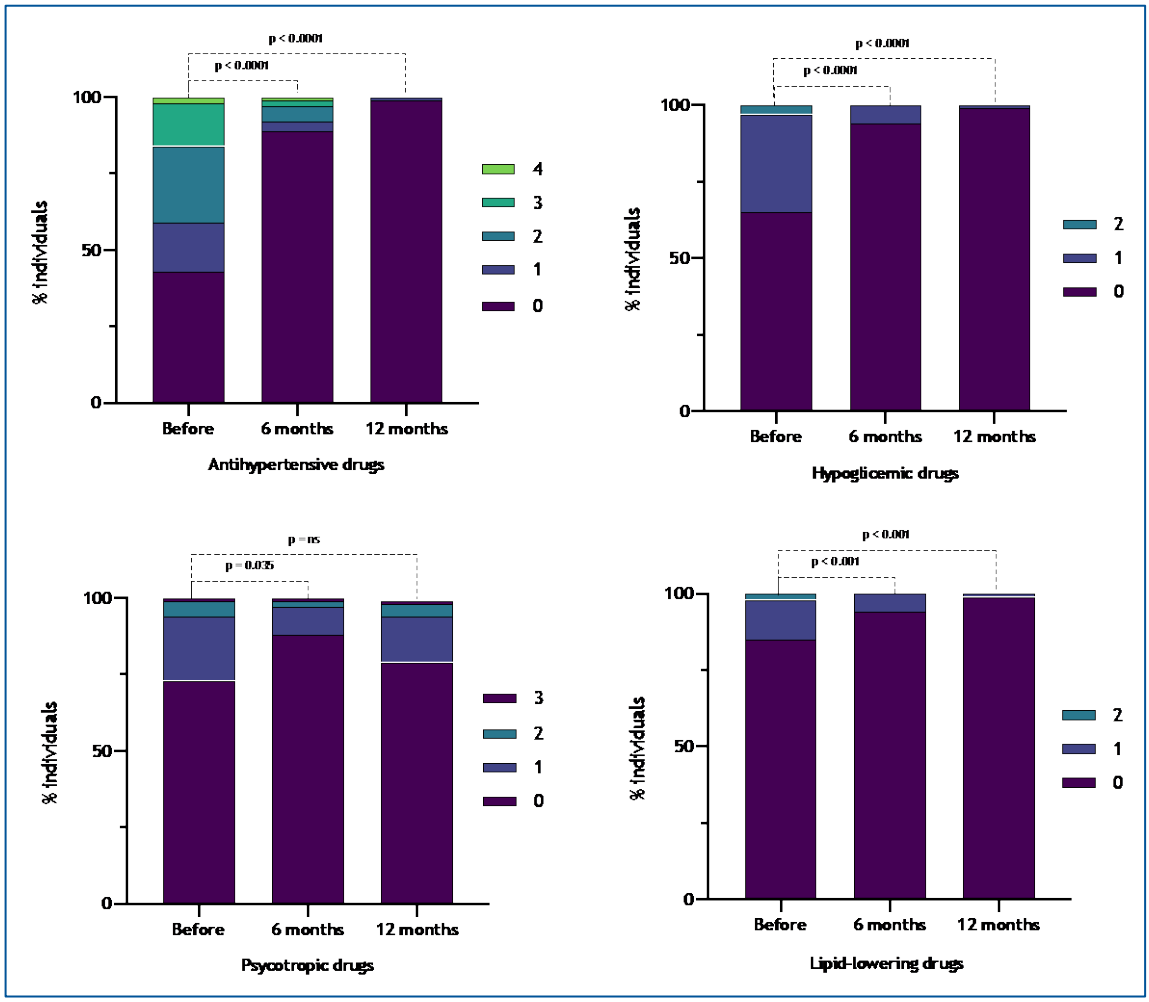

Figure 2 — Graphical representation of the number of different types of antihypertensive, hypoglycemic, psychotropic and lipid-lowering drugs used by individuals undergoing bariatric surgery, before surgery and after 6 and 12 months. P values correspond to Dunn's posthoc test at 6 and 12 months compared to before surgery (ns = non significative).

Table 5 —- Spearman correlation coefficient values (ρ) between the body mass index variation and the number of antihypertensive, hypoglycemic, psychotropic, and lipid-lowering drugs used by individuals undergoing bariatric surgery after 6 and 12 months.

Drug class	6 months (n = 86)		12 months (n = 61)	
	ρ	95% CI	ρ	95% CI
Antihypertensive	0.16	-0.13;0.43	-0.05	-0.38;0.30
Hypoglycemic	-0.12	-0.47;0.27	No variation	
Psychotropic	0.21	-0.23;0.58	0.51	-0.11;0.84
Lipid-lowering	0	-0.54;0.54	-0.22	-0.77;0.52

CI = confidence interval.

(food loop), and a loop draining the digestive enzymes (enzymatic loop). A small gastric pouch is formed with a vertical orientation using surgical staplers, with a volume of less than 50 cm^3. A small intestine section is made about 100 cm from the Treitz ligament. The divided intestine's distal end is then connected to the gastric pouch, creating an end-to-side gastrojejunal anastomosis. The proximal end of the divided intestine is anastomosed about 100 to 150 cm from the gastrojejunal anastomosis. After RYGB, the gastric pouch restricts the volume of eaten food to approximately 90%-95% of the stomach[17,18].

Evidence supports YRGB's capability to act in several ways to improve numerous aspects of metabolic control, thus constituting a metabolic intervention to reduce the process of primary disease in DM2 and its complications, including secondary kidney disease[19,20]. The effects of bariatric surgery result from endocrine and neural signals that regulate appetite and satiety, and complex interactions between malabsorption and gastric restriction. The exclusion of approximately 95% of the gastric chamber reduces ghrelin secretion (orexigenic hormone) and anti-incretins that decrease insulin release and increase insulin resistance. Theoretically, the rapid delivery of nutrients to the large intestine stimulates L cells, resulting in increased secretion of incretins (such as the anorexigenic peptide from YY hormones and glucagon-like peptide - GLP1), which in turn increase secretion and the action of insulin. Some hypotheses state that excluding nutrients from the duodenum and the proximal jejunum can inhibit the secretion of a signal that usually induces insulin resistance and DM2[21,22].

In addition to the direct effects of reducing hyperglycemia, bariatric surgery diminishes systemic arterial hypertension, cholesterol, and low-density lipoprotein (LDL) levels, reducing myocardial hypertrophy, use of drugs and cardiovascular risk parameters, as it is associated with a decrease of up to 50% in general and cardiovascular mortality in 10 years[3,9].

The average decrease in BMI observed in this study is comparable to others published. Monteforte et al. observed a mean reduction in BMI of around 15 kg/m^2 after one year in a systematic review with meta-analysis[23]. Similar results were observed concerning bodyweight reduction in a Brazilian study with 141 women, showing stabilization in the loss of excess weight after two years[24] and a Dutch series of 450 patients with an average BMI reduction of 13.5 kg/m2[25]. Although excess weight loss is still the most used parameter to measure the result of bariatric surgery, there is a tendency to adopt the percentage of absolute weight loss due to its more significant correlation with laboratory and clinical indicators[26].

The excessive use of drugs in morbidly obese patients has also been studied by Elliot et al.[11], who showed, in mainly white women, the average daily consumption of 4.4 drugs, most (28.2%) for the cardiovascular system. It was not possible to compare this finding with that of this study since few classes of drugs were studied, not including analgesics, thyroid therapy, bronchodilators, among others.

Other authors have also investigated the reduction in the number of drugs after bariatric surgery. In a literature review, Yska et al.[27] observed reductions of around 50% in the use of cardiovascular drugs and 40%-59% in statins after one year. The reduction in the use of medications for hypothyroidism was 43% after surgery. In another observational study, reductions in the use of hypoglycemic, cardiovascular, anti-inflammatory and anti-rheumatic, and drugs for respiratory failure were found in 71.3%, 34.5%, 45.5%, and 33.1%, respectively[25]. Segal et al.[12] observed reductions in medications for diabetes, hypertension, and hyperlipidemia in one year of 76%, 51%, and 59%, respectively. In this study, higher rates of decrease in the number of medications were observed, especially antihypertensive and hypoglycemic agents. This difference can be explained by the younger age of the sample, with fewer comorbidities and drugs in use in the preoperative phase. Besides, this study analyzed only patients operated using the RYGB technique, which is more suitable for those with less severity and need for disabsorptive techniques.

It was possible to observe a large usage of psychotropic drugs, including benzodiazepines, hypnotics, appetite regulators, anticonvulsants, and, mainly, antidepressants. This polypharmacy of psychotropics, however, was observed in a small portion of the sample. It turns out that there was no considerable reduction in the use of these drugs over a year after surgery, which leads us to believe that other factors unrelated to weight influence their use or that the reduction of excess weight only transiently reduces psychological problems. Dosage adjustment was not taken into account, which may underestimate the real reduction in the use of these classes of drugs. Similar

findings were observed by Cunningham et al.[28], who found an increase of 23% in the use of antidepressants after RYGB, maintenance in 40%, change of medication in 18%, and decrease or cessation in only 16% of the sample. Therefore, a careful assessment of these patient psychological status and mood disorders is necessary, even after years of surgery[29].

It was not possible to correlate the degree of weight loss with the reduction in the number of drugs. Possibly small and initial reductions in body fat in the first months are responsible for an immediate reduction in hypertension and hyperglycemia. Therefore, it is possible to infer that risk factors control does not occur in parallel with the weight reduction.

The reduction in drug use in this population is significant given its clinical, economic, and quality of life benefits. The socioeconomic impact of bariatric surgery can be seen in reducing medication costs[30], even though there is no increase in average labor income and its overall cost is still high[31]. Even after two and three years of surgery, the overall cost of health care for patients does not decrease[32]. Cost-benefit analysis, including quality of life and increased survival, is perhaps the best way to analyze the long-term impact of bariatric surgery instead of simple cost reduction calculations[33].

The study has limitations since it was retrospective, with significant sample loss due to incomplete medical record data, including little information after 12 months of surgery. From this, it was not possible to perform a paired and temporal analysis of each individual. Still, there was no note of the dosage of drugs and the calculation of the actual dose adjusted for the reduced weight, which could give more value to the reduction findings. There is a need to develop standardized medical records and collect routine laboratory tests that can measure blood glucose, dyslipidemia, and hypothyroidism controls in the long-term.

CONCLUSION

There was a significant reduction in the use of antihypertensive drugs, hypoglycemic and lipid-lowering agents after 6 and12 months in patients undergoing bariatric surgery, but there was no significant reduction in the use of psychotropic drugs after 12 months. The reduction in the use of drugs was not correlated with a reduction in BMI. The large amount of antihypertensive and psychotropic drugs observed in the sample is noteworthy.

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