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Micronutrient deficiencies following bariatric surgery: a comparative analysis between sleeve gastrectomy and Roux-en-Y gastric bypass.

Deficiências de micronutrientes após cirurgia bariátrica: análise comparativa entre gastrectomia vertical e derivação gástrica em Y de Roux.

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A B S T R A C T

Objective: to compare the prevalence of micronutrient deficiencies in patients submitted to sleeve gastrectomy (SG) and Roux- en-Y gastric bypass (RYGB). **Methods:** this is a comparative study of 576 patients submitted to bariatric surgery, 338 to SG and 238 to RYGB, and evaluated for hemoglobin, iron, ferritin, zinc and vitamin B12 serum levels. We performed these dosages in the preoperative period and at three, six, 12 and 24 months after surgery, for analysis and comparison of micronutrient deficiencies among the techniques. **Results:** the SG group consisted of 48 men and 290 women, with a mean BMI of 39.4±2.6kg/m^2, and a mean of age of 37.2±11 years; the group RYGB consisted of 77 men and 161 women, with mean BMI 42.7±5.9kg/m^2, and a mean age of 41.9±11.1 years. After 24 months, hemoglobin deficiency was present in 24.4% of the patients submitted to SG and in 40% of the RYGB individuals (p=0.054); iron deficiency was present in 6,6% of SG patients and in 15% of RYGB ones (p=0.127); ferritin deficiency occurred in 17.8% of the SG group and in 23.7% of RYGB one (p=0.399); the Zinc deficiency incidence was 6.6% in SG and 30% in RYGB (p=0.002); and B12 deficiency took place in 6.6% the SG patients and in 8.7% of RYGB ones (p=0.844). **Conclusion:** patients undergoing SG had serum levels of iron and zinc superior to the ones undergoing RYGB, the prevalence of the latter micronutrient deficit being significantly higher in the RYGB group.

Keywords: Obesity. Bariatric Surgery. Micronutrients. Nutritional Surveillance. Deficiency Diseases.

INTRODUCTION

In recent years, several studies have compared the loss of excess weight, the incretinic response and the resolution of comorbidities between patients submitted to sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB), showing statistical equivalence in the loss of excess weight and in the resolution rates of comorbidities in series with long-term follow-up[1,2].

Micronutrient deficiency is an important complication associated with both obesity and bariatric surgery, especially in the first year of postoperative follow-up, with an incidence of up to 50% of vitamin deficiency in these patients[3]. Nutritional deficiencies are observed both in patients submitted to SG and in those submitted to RYGB and, when uncorrected, may represent a significant threat to the health of these patients[4].

The mechanism by which a micronutrient deficiency ensues after bariatric surgery differs between SG and RYGB[5]. Nutritional changes related to SG are due to decreased food intake, increased gastric emptying velocity and duodenal-jejunal transit, and reduced secretion of hydrochloric acid and intrinsic factor[5,6]. In RYGB, nutritional deficiencies occur both by the restraining component, resulting in early satiety, and by the malabsorptive component, resulting from the exclusion of the duodenum and proximal jejunum[7,8].

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The objective of the present study was to compare the prevalence of micronutrient deficiencies in patients submitted to SG and RYGB, in order to determine the need for nutritional support in the former group.

METHODS

We conducted this study in the General Surgery Service of the Hospital das Clínicas of the Federal University of Pernambuco (UFPE) during the period from 2012 to 2017, through which we evaluated 576 patients submitted to surgical treatment for obesity, 338 of whom to SG, and 238, RYGB.

We included patients with indication for bariatric surgery according to the recommendations of the Brazilian Society of Bariatric and Metabolic Surgery, with ages between 18 and 65 years and absence of active use of alcohol and illicit drugs. We excluded from the research those carriers of prior digestive diseases able to compromise the nutritional status by intestinal malabsorption.

We divided the study participants into two groups (SG and RYGB) and submitted them to laboratory measurements of hemoglobin, iron, ferritin, zinc and vitamin B12 in the preoperative periods and at three, six, 12 and 24 months after surgery for analysis of micronutrient deficiencies. The cut-off values for nutritional deficit were: <12mg/dl for hemoglobin; <50µg/dl for iron; <20ng/ml for ferritin; <70mg/dl for zinc; and <200pg/ml for vitamin B12.

Due to the loss of follow-up, the number of patients in the postoperative evaluations was lower than in the preoperative period (SG=338 x RYGB=238); three months: SG=184 x RYGB=161; six months: SG=100 x RYGB=111; twelve months: SG=128 x RYGB=119; twenty-four months: SG=47 x RYGB=77.

All individuals involved in the research had orientation on vitamin and mineral supplementation from the immediate postoperative period onwards, as follows: Centrum® (substances: multivitamins and minerals) - one crushed tablet orally daily, in continuous use; Citoneurin® 5000IU (substances: Vitamin B1 - thiamine hydrochloride= 100mg; Vitamin B6 - pyridoxine hydrochloride= 100mg; Vitamin B12 - cyanocobalamin= 5000mcg) - one flask in deep intramuscular injection at the end of the first postoperative month; Neutrofer® (substance: Ferrochelate glycinate) - one 500mg tablet (equivalent to 100mg Fe^{3+}) orally daily for 90 days postoperatively.

The study was approved by the Ethics in Research Committee of the Health Sciences Center of the Federal University of Pernambuco (CEP/CCS/UFPE), according to Resolution nº 196/96 of the National Health Council, on December 17, 2012, under CAAE number 11258913.3.0000.5208.

We analyzed the data in the SPSS software. To describe the profile of the patients evaluated, we calculated the percentage frequencies and constructed the respective frequency distributions. For the quantitative variables, we calculated mean and standard deviation. We assessed normality of the quantitative variables with the Kolmogorov-Smirnov test. When the variable's normality was present, we used the Student's t-test to compare the measurements' means between the types of surgery to which the patients were submitted. In cases where normality was not present, we used the Mann-Whitney test.

RESULTS

The group subjected to SG comprised 338 patients (290 women and 48 men), with a mean BMI 39.4±2.6kg/m^2, and average age 37.2±11

years. Regarding comorbidities, systemic arterial hypertension (SAH) was present in 18%, type-2 diabetes (T2DM) in 15.1%, and dyslipidemia in 26%. The group submitted to RYGB consisted of 238 patients (77 men and 161 women), who had mean BMI 42.7±5.9kg/m^2 and a mean age of 41.9±11.1 years. SAH was present in 62.6%, T2DM in 42.4%, and dyslipidemia in 55.9% (Table 1).

The data in table 2 show that SG presented a significantly higher percentage of excess weight loss (%EWL) at three months (p<0.001) and six months (p=0.035) of postoperative follow-up. Two years after surgery, there was a reversal, with a trend of higher EWL% in the group submitted to RYGB, although without statistical significance (p=0.64).

Mean serum hemoglobin levels did not show significant difference between the groups at any of the moments of analysis. Serum iron levels, in turn, showed a statistically significant difference between the groups (higher values for SG) at all moments of evaluation, except at six postoperative months (p=0.158). Regarding ferritin, serum levels were higher in the group submitted to RYGB, with statistical significance up to six months postoperatively. Zinc presented higher values in the SG group at six, 12 and 24 postoperative months, with statistical significance. Analysis of vitamin B12 levels did not show a statistically significant difference between the groups at any of the moments of analysis (Table 3).

Table 1. *Characteristics of study participants in the preoperative period.*

Assessed factor	SG* (n=338)	RYGB** (n=238)	p-value
Men	48 (14.2%)	77 (32.4%)	<0.001[1]
Women	290 (85.8%)	161 (67.6%)	<0.001[1]
Mean age (years)	37.2±11	41.9±11.1	0.001[2]
Mean BMI (kg/m^2)	39.4±2.6	42.7±5.9	<0.001[2]
T2DM (%)	51 (15.1%)	101 (42.4%)	<0.001[1]
SAH (%)	61 (18%)	149 (62.6%)	<0.001[1]
Dyslipidemia (%)	88 (26%)	133 (55.9%)	<0.001[1]

** SG: sleeve gastrectomy; ** RYGB: Roux en Y gastric bypass; [1]Chi-square of Pearson for proportion comparison (if the p-value <0.05, the proportions differ significantly); [2]Student's t-test for independent samples (if the p-value <0.05, the means differ significantly).*

Table 2. *Analysis of the percentage of excess weight loss (%EWL) in the postoperative period (3, 6, 12 and 24 months after surgery) according to the type of surgery performed (SG x RYGB).*

Follow-up	%EWL*- SG**	%EWL*- RYGB***	p[1]
3 months	49.2%	43.7%	<0.001
6 months	68.1%	63.4%	0.035
12 months	84.6%	81%	0.126
24 months	81.1%	88.1%	0.064

** Percentage of excess weight loss; ** SG: sleeve gastrectomy; *** RYGB: Roux en Y gastric bypass; [1]Student's t-test.*

Table 3. *Analysis of serum micronutrient levels in the pre and postoperative periods (3, 6, 12 and 24 months after surgery).*

Micronutrient	Preop	3 Months	6 Months	12 Months	24 Months
	SG*	SG*	SG*	SG*	SG*
	RYGB**	RYGB**	RYGB**	RYGB**	RYGB**
	p-value	p-value	p-value	p-value	p-value
Hemoglobin (mg/dl)	13.5±1.1	12.8±1.4	13.0±1.0	12.7±1.1	12.6±1.1
	13.7±1.1	13.2±1.2	13.3±1.3	12.7±1.4	12.3±1.7
	0.059[2]	0.075[2]	0.174	0.897[1]	0.255[1]
Iron (µg/dl)	88.9±30.4	86.8±30.8	90.3±28.2	103.8±44.5	107.6±35.4
	82.7±28.9	72.1±25.8	85.0±24.6	87.9±30.4	84.0±33.5
	0.016[1]	<0.001[1]	0,158[1]	0.001[1]	0.001[1]
	146.3±153.6	143.3±143.0	146.6±128.4	123.3±120.0	115.6±114.0
	234.9±242.7	244.6±237.0	222.5±199.2	159.9±163.1	136.8±145.2
	<0.001[2]	<0.001[2]	0.022[2]	0,163[2]	0.977[2]
Zinc (mg/dl)	85.0±15.5	84.2±17.2	84.9±17.0	85.7±17.3	91.4±23.4
	92.8±77.8	87±19.7	79.5±24.1	80.9±20.2	77.4±16.2
	0.949[2]	0.357[2]	0.004[2]	0.050[1]	<0.001[1]
Vitamin B12 (pg/ml)	451.4±17	578.6±277.2	527.1±309.9	443.2±207.7	459.1±222.8
	482.7±320.9	647.2±349	476.0±214.1	437.7±202.4	422.9±194.1
	0.515[2]	0,124[2]	0.360[2]	0.948[2]	0.493[2]

** SG: sleeve gastrectomy; ** RYGB: Roux- en-Y gastric bypass; [1]Student's t-test; [2]Wilcoxon test for paired samples.*

Table 4 presents data on the prevalence of nutritional deficiencies. During the preoperative period, there was hemoglobin deficiency in 5.6% of the sample submitted to SG and 7.4% in those submitted to RYGB. The evolution of this deficit after the 12th (SG=37.2% x RYGB=30.5%) and 24th (SG=24.4% x RYGB=40.0%) postoperative months reached high values, although without a statistically significant difference between the two techniques.

Iron deficiency was present in 7.1% and 11.9% in the preoperative period of patients submitted to SG and RYGB (p=0.054), respectively. The prevalence of iron deficiency, at the end of 12 and 24 months of follow-up, reached values of 12.8% and 6.6% for SG, and 14.8% and 15% for RYGB, respectively, although without relevance (p=0.549 at 12 months and p=0.127 at 24 months).

In the preoperative period, serum ferritin deficiency was present in 3.5% and 2.9% of patients submitted to SG and RYGB (p=0.687), respectively. The development of this deficit after the 12th postoperative month reached rates of 20.4% (SG) and 16.4% (RYGB) and, later, at 24 months, 17.8% (SG) and 23.7% (RYGB). There was, however, no significant difference between the techniques in any of the evaluation moments.

Zinc deficiency did not present a significant difference between the techniques in the preoperative period and at 12 months postoperatively. However, at 24 months, the micronutrient deficiency was present in 30% of subjects submitted to RYGB and in only 6.6% of those in the SG group (p=0.002).

Table 4. *Prevalence of micronutrient deficit in the pre and postoperative periods (12 and 24 months after surgery).*

Micronutrients	Preop SG* RYGB** p-value[1]	12 Months SG* RYGB** p-value[1]	24 Months SG* RYGB** p-value[1]
Hemoglobin	19 (5.6%) 18 (7.4%) 0,349	29 (37.2%) 9 (30.5%) 0.230	11 (24.4%) 32 (40.0%) 0.054
Iron	24 (7.1%) 29 (11.9%) 0.054	10 (12.8%) 19 (14.8%) 0.549	3 (6.6%) 12 (15.0%) 0.127
Ferritin	12 (3.5%) 7 (2.9%) 0,687	16 (20.4%) 21 (16.4%) 0,479	8 (17.8%) 19 (23.7%) 0,399
Zinc	40 (11.8%) 34 (13.9%) 0,471	20 (25.6%) 34 (26.6%) 0.843	3 (6.6%) 24 (30.0%) 0.002
Vitamin B12	10 (2.9%) 9 (3.7%) 0.586	9 (11.5%) 8 (6.2%) 0.108	3 (6.6%) 7 (8.7%) 0.844

**SG: sleeve gastrectomy **RYGB: Roux-en-Y gastric bypass; [1]Chi square test for proportion comparison.*

As for vitamin B12, its deficit was present in 11.5% (SG) and 6.2% (RYGB) at 12 months, and in 6.6% (SG) and 8.7% (RYGB) two years after surgery. There was no statistically significant difference in any of the evaluation moments.

DISCUSSION

Nutritional deficiencies are common after bariatric surgery. Even with the introduction of nutritional supplementation, a large proportion of patients have deficiencies, mainly of micronutrients, in the postoperative period[9]. The prevalence of anemia in patients who are candidates for bariatric surgery in some cases is higher than in the general population, reaching levels of 10% to 15%, while the prevalence of iron deficiency as an independent factor can reach 30% to 40%[10]. In our sample, we had an increase in the prevalence of patients with anemia at 24 months, although there was no significant difference when comparing their prevalence between SG and RYGB. This result contrasts with the study by Kheniser *et al*., who found a significantly higher prevalence of individuals with hemoglobin deficiency anemia in the group submitted to SG (42%) compared with RYGB (21%) after two years of follow-up[11].

Probably, iron deficiency is the most common nutritional deficiency, and it is early developed by patients undergoing bariatric surgery, especially those undergoing techniques with disabortive components and duodenal deviations (RYGB and duodenal switch)[12]. In a study of micronutrient analysis after SG, Saif *et al*. reported no clinically relevant disturbance of iron and hemoglobin after five years of postoperative follow-up, despite findings of below-normal levels of these parameters in 28.6% and 25% of patients, respectively[13].

Haken *et al*. found a low incidence of anemia (1.6%) and iron deficiency (4.9%) in patients submitted to SG and followed for 12 months[14], while Capoccia *et al*. demonstrated, in an analysis of 138 patients submitted to SG, that in the first year the impact of bariatric surgery on serum iron levels was negligible with a daily oral supplementation of 5mg of this nutrient during the first six postoperative months[15].

Throughout the postoperative follow-up period, serum iron levels increased between each evaluation moment, and were significantly higher in the SG group than the levels presented by the RYGB group 12 and 24 months after surgery. The increased iron supplementation in the postoperative period, associated with maintenance of the duodenum and the proximal jejunum, may justify this increase in serum iron levels in patients submitted to SG in relation to preoperative levels and to the group submitted to RYGB at the end of the 24 months.

The knowledge of obesity as a chronic systemic inflammatory state through the action of adipose tissue, responsible for the production of cytokines, such as tumor necrosis factor alpha (TNF-a) and Interleukin 6 (IL-6), and the discovery of hepcidin and its relationship with serum iron, have brought new insights into the relationship between obesity, iron deficiency, ferritin levels, and chronic disease anemia in these patients[16].

Ferritin measurement was used in order to correlate it with iron deficiency, since in a relevant number of obese patients, ferritin may display high values as a result of the associated chronic inflammatory activity[11]. The lower prevalence of serum ferritin deficiency in relation to iron in the preoperative period, as well as the increase in the number of ferritin deficient patients at the end of postoperative follow-up, can be explained by the number of patients presenting above-normal ferritin levels due to the inflammatory effect of obesity, which leads to hyperferritinemia, since it behaves as an acute phase protein[11].

Obese individuals generally have decreased serum zinc levels in relation to the general population[17]. After bariatric surgery, given the metabolic changes induced by this procedure, the prevalence of deficiency of this micronutrient tends to increase[17]. A study by Madan *et al*. showed that the zinc deficit increased from 30% preoperatively to 36% one year after surgery[18]. In addition, zinc deficiency also negatively affects pancreatic secretion and peripheral insulin action, as well as the action of growth hormone (GH), causing greater damage to the metabolism of obese individuals[14].

A study conducted by Capoccia *et al*. showed that, in obese patients undergoing bariatric surgery, serum zinc deficiency may increase from 4% to 9% preoperatively to 20% to 24% in an 18-month follow-up[15]. Another study, comparing different surgical techniques, revealed zinc deficiency after 12 months of surgery in 40.7% of the patients submitted to RYGB and in 18.8% of the patients undergoing SG[17].

In the 24-month follow-up, the significant difference in the prevalence of zinc deficiency (SG=6.6% x RYGB=30.0% - $p<0.05$) may be related to the food transit deviation in patients submitted to RYGB, allied to the optimization of the time of gastric and proximal intestinal emptying in the patients submitted to the SG, allowing a greater contact of the nutrient with the brush border of the jejunum and proximal ileus enterocytes, as well as a possible difference of adhesion to vitamin supplementation between the groups. In our sample, patients submitted to RYGB had higher preoperative BMI, and this may be related to a psychological profile of greater resistance to dietary guidelines and vitamin supplementation.

In the literature, the relationship between the development of B12 deficiency over time in patients submitted to RYGB and the need for supplementation of this vitamin in the postoperative period of this procedure is already well-defined[9]. In a follow-up series of 12 to 24 months, the incidence of this deficiency ranges from 3.6% to 11%, varying according to the route of supplementation (oral x intramuscular), local socioeconomic conditions, and technical details of the surgical procedure[19,20].

Saif *et al,* in study that evaluated the nutritional behavior of 82 patients submitted to the SG one, three and five years postoperatively, found B12 deficit in 2.9% in the first year, without further identification of this alteration in three and five years[13]. In the same study, micronutrient replacement was used in 28.9% of the patients in the first year, 42.9% in the third year and 63.3% in the fifth year, highlighting the importance of supplementation in the prevention of B12 hypovitaminosis in such patients[13].

In the present study, the analysis of the values in the pre- and postoperative periods did not show a significant decrease in the serum levels of this vitamin during follow-up, nor did it show a significant difference between the two techniques. This result should be evaluated considering that the participants of this study used intramuscular cyanocobalamin in the first postoperative month, which is related to a correction of the B12 deficit in 91% of the cases according to the literature[21].

At the end a 24-month follow-up, we found that patients undergoing Sleeve Gastrectomy presented serum levels of iron and zinc superior to patients undergoing Roux-en-Y Gastric Bypass, and that the prevalence of the deficit of the latter micronutrient is significantly higher in the RYGB group. Thus, we can conclude that patients undergoing SG, though not needing the same nutritional support as those submitted to RYGB, do need some nutritional support.

R E S U M O

Objetivo: *comparar a prevalência das deficiências de micronutrientes nos pacientes submetidos à gastrectomia vertical (GV) e à derivação gástrica em Y de Roux (DGYR).* **Métodos:** *estudo comparativo de 576 pacientes submetidos à cirurgia bariátrica, 338 através de GV e 238 de DGYR e avaliados quanto às dosagens séricas de hemoglobina, ferro, ferritina, zinco e vitamina B12. Estas dosagens foram realizadas nos períodos pré-operatório e três, seis, 12 e 24 meses após a cirurgia, para análise e comparação das deficiências de micronutrientes entre as técnicas.* **Resultados:** *o grupo submetido à GV foi composto por 48 homens e 290 mulheres, com IMC médio de 39,4±2,6Kg/m² e média de idade de 37,2±11 anos; o grupo submetido à DGYR foi composto por 77 homens e 161 mulheres, com IMC médio de 42,7±5,9Kg/m² e média de idade de 41,9±11,1 anos. Após 24 meses, déficit de hemoglobina se fez presente em 24,4% dos pacientes submetidos à GV e 40% da DGYR (p=0,054); deficiência de ferro em 6,6% da GV e 15% da DGYR (p=0,127); déficit de ferritina em 17,8% da GV e 23,7% da DGYR (p=0,399); deficiência de zinco em 6,6% da GV e 30% da DGYR (p=0,002) e deficiência de B12 em 6,6% da GV e 8,7% da DGYR (p=0,844).* **Conclusão:** *pacientes submetidos à GV apresentaram níveis séricos de ferro e zinco superiores aos pacientes submetidos à DGYR, e a prevalência de déficit deste último micronutriente foi significativamente maior no grupo da DGYR.*

Descritores: *Obesidade. Cirurgia Bariátrica. Micronutrientes. Vigilância Nutricional. Deficiências Nutricionais.*

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