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Impact of Bariatric Surgery in A Cohort of Patients with Type 2 Diabetes and Obesity

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1. Abstract

1.1. Aims: To evaluate the metabolic effects of Bariatric Surgery (BS) and bone mineral metabolism changes after BS in a population of obese diabetic patients.

1.2. Materials and Methods: 56 patients were evaluated before and after undergoing BS. Personal background, anthropometric measurements, blood pressure, body mass index (BMI), hemogram, liver panel, glycemia, 25-OH-Vitamin-D, lipid profile, HbA1c, renal function, and calcium, phosphorus, magnesium, creatinine, and ionogram in plasma and 24-hs urine were analyzed.

1.3. Results: BMI decreased between preoperative and postoperative periods (p<0,0001). There were no significant differences in blood pressure. Regarding metabolic parameters, significant differences were observed for glycemia, HbA1c, triglycerides (TG), TG/HDL, HDL, and uric acid. Hypoglycemia and anemia were found in 3, 5% and 14, 28% of patients post BS, respectively. There was a statistically significant reduction between pre and post BS levels for serum calcium, magnesium, sodium and creatinine, and a statistically significant increase between pre and post BS levels for 25-OH-Vitamin-D, serum and urinary phosphate, and urinary creatine.

1.4. Conclusions: As seen by other authors we found that BS produces improvements in terms of BMI, metabolic parameters, and the use of medications. There were no significant differences in blood pressure levels. The negative effects on bone mineral metabolism due to BS are multifactorial since the decrease in serum calcium, magnesemia, natremia, and urinary calcium might be explained by the lower intestinal absorption after BS. Less urinary volume in the post-surgery group may be attributed to less gastric volume. A better understanding of these consequences allows us to improve follow-up treatments.

2. Introduction

The prevalence of type 2 diabetes mellitus (DM2) has increased notably in the last decade. These data correlate with a rise in the prevalence of obesity. More than 90 % of patients with DM2 are overweight [1]. Thus, the management of obesity is essential in the treatment of DM2.

For patients with diabetes and obesity, it is difficult to achieve weight and metabolic control goals solely with changes in lifestyle and pharmacological treatment. Bariatric surgery (BS) has been shown to be effective in the control of obesity and diabetes. Its results are not only evidenced in terms of weight loss, but also in the resolution of comorbidities, life-quality improvement, and reduction of derived complications [2]. It is the most effective long-term therapeutic alternative for patients with severe obesity and related metabolic diseases [3]. Different guidelines recommend BS for the treatment of DM2 in patients with inadequate metabolic control and a body mass index (BMI) higher than 35 kg / m2. They also suggest that for certain carefully selected patients with BMI 30–35 kg / m2, BS should also be considered as a therapeutic option [4, 5].

Roux-en-Y Gastric Bypass (RYGB) is considered the gold standard. There are other types of BS such as the single anastomosis gastric bypass (SAGB), which is also an option for obese patients with DM2 [5, 6].

Despite the great benefits that BS provides, there are negative anatomical and metabolic implications that will require follow-up and even lifetime replacement of micronutrients [7].

This study aimed to evaluate the effect of BS on the cardio metabolic risk and the phosphocalcic metabolism in a cohort of obese patients with DM2.

3. Materials and Methods

We carried out a retrospective, observational, descriptive cohort study. We analyzed the medical records of 128 patients with DM2 who underwent BS between 2014 and 2019 at the Surgery Service of the Churruca Visca Hospital in Buenos Aires. Patients who had had sleeve surgery (n 49), gastric band (n 2), gastric balloon (n 5), and those who discontinued follow-up at our center (n 16) were excluded. Those who had RYGB and SAGB were analyzed (n 56). From these patients, personal data (comorbidities and medication), anthropometric measurements (weight and height), and blood pressure were collected. The body mass index (BMI) was calculated. We also collected, laboratory data such as hemogram, blood glucose, liver panel, lipid profile, albumin, and calcium, phosphorus, magnesium, sodium and potassium in plasma and 24-hour urine (colorimetric methods), HbA1c (HPLC) and vitamin D3 (chemiluminescent immunoassay).

The DiaRem Score [8], which considers age, HbA1c, insulin dependence, and usage of diabetes medication, was used for predicting diabetes remission.

3.1. Statistical Analysis: To establish the association between pre and post-surgery differences of measured variables and the time elapsed since the latter, we calculated Spearman's correlation coefficient. Independent samples t-test (parametric case) or Mann–Whitney test (nonparametric cases), as appropriate, were performed to confirm whether there is a statistically significant difference between the up-to-30-months group and the 31-or-more-months group. For those variables that did not show an association, we performed paired samples tests to confirm whether there is a significant difference between pre and post-surgery values (Student's test for paired samples for parametric case and Wilcoxon test for nonparametric case). To test the normal distribution assumption of analyzed variables, the Shapiro-Wilks test was used. We considered differences to be statistically significant when the p-value was lower than 0.05.

The study was approved by the institutional biomedical ethical committee of Churruca Visca Hospital.

4. Results

Data from 56 patients (35 women and 21 men) with DM2 who underwent BS, with an average age of 52 ± 9.6 were analyzed. Out of the 56 patients, 29 (52 %) underwent SAGB and 27 (48 %) underwent RYGB. Pre and post-surgery data were recorded, with a post-surgery time between 3 and 79 months, with an average time of 32 months. At the time of surgery, patients were on the following treatment: 77 % were on metformin, 52 % were receiving insulin, 23 % were on inhibitors of dipeptidyl peptidase 4 (IDPP-4), 69 % were on treatment for dyslipidemia and all of them were on antihypertensive treatment. After surgery, medicine intake decreased: 14 % continued on metformin, 7 % keep up receiving insulin, 11 % continued on IDPP-4, 31 % maintain treatment for dyslipidemia and 54 % persisted on anti-hypertensive. Table 1 shows patients' anthropometric variables. We found a significant decrease in weight and BMI after surgery. Patients who underwent SAGB presented a significantly greater reduction in BMI than those who underwent RYGB (p = 0.02). No differences were found in blood pressure. Table 2 shows patients' biochemical variables. Significant differences were found in the liver and lipid panels, blood glucose, HbA1c, and creatinine in favor of BS. Patients who underwent SAGB had a greater reduction in triglycerides and non-HDL (p 0.01 and 0.03, respectively) compared to patients who received RYGB. No significant differences were found in the variables of the liver panel. There was a significant correlation between the number of months elapsed after surgery and TG (r 0.27, p 0.04) and TG/HDL (r 0.34, p 0.01). Table 3 shows the variables associated with bone mineral metabolism. The mean post-surgery values decreased significantly for serum calcium, magnesium, sodium and creatinine, while increased significantly for vitamin D, serum phosphate, and urinary potassium and creatine. A negative correlation was found between the number of months elapsed after surgery and the urinary volume (r –0.35, p 0.05). Patients who underwent SAGB had less urinary calcium levels (p 0.03). A negative correlation was observed between BMI and magnesemia (r –0.39, p 0.03). There were no differences between men and women in the studied variables.

With regard to DM2 remission, 21 patients (38 %)—10 who had undergone RYGB and 11 who received SAGB — remained in remission throughout the study period. We analyzed the variables to evaluate the prognosis. There was no significant difference concerning age, but patients in remission had a lower HbA1c (p 0.001) and were only receiving metformin before surgery. As to long-term surgery complications, 3.5 and 14% of patients presented hypoglycemia and anemia, respectively. Only one patient developed kidney stones and no fragility fractures occurred during the studied period.

Table 1: Anthropometric variables and blood pressure

	Pre BS	Post BS	p
Weight (kg)	120.43 ± 27	80 ± 16	<0,0001
Height (m)	1,65 ± 0,09	1,65 ± 0,09	NS
BMI (kg/m^2)	43,87 ± 9,99	29,49 ± 5,82	<0,0001
Systolic blood pressure (mmHg)	128 ± 13	122 ± 21	NS
Diastolic blood pressure (mmHg)	80 ± 8	74 ± 14	NS

BS: bariatric surgery. BMI: body mass index. NS: non-significant. Variables are expressed as mean ± standard deviation

Table 2: Biochemical variables

	Pre BS	Post BS	p
Hemoglobin (g/dl)	14 ± 1.88	13 ± 1,3	0,002
White blood cells (10^{9}xL)	8.437 ± 2.158	7.300 ± 2.136	0,0002
Platelets (10^{9}xL)	250.347 ± 60.996	227.704 ± 58.145	0,014
Glycemia (mg/dl)	149.95 ± 58.19	101.16 ± 21.29	<0,0001
HbA1c (%)	8.14 ± 2.54	5.86 ± 1,03	<0,0001
Creatinine (mg/dl)	0.81 ± 0.23	0.77 ± 0.22	0,003
AST (UI/L)	33 ± 21	31 ± 17	NS
ALT (UI/L)	37 ± 22	50 ± 16	NS
ALP (UI/L)	82.55 ± 27	81.16 ± 23	NS
Total bilirubin (mg/dl)	0.64 ± 0.35	0.64 ± 0.33	NS
Total cholesterol (mg/dl)	184 ± 38	174 ± 43	NS
LDL (mg/dl)	109 ± 35	101 ± 36	NS
HDL (mg/dl)	41 ± 10	53 ± 13	<0,0001
TG (mg/dl)	159 ± 69	106 ± 60	<0,0001
TG/HDL	4,11 ± 2,08	2,14 ± 1,45	<0,0001
No HDL cholesterol (mg/dl)	140 ± 39	122 ± 37	0,007
Uric acid (mg/dl)	5,44 ± 2,47	4,74 ± 1,04	0,0004

NS: non-significant. Variables are expressed as mean ± standard deviation

Table 3: Mineral bone metabolism variables.

	Pre BS	Post BS	*p*
Serum calcium (mg/dl)	9,36 ± 0,42	9,12 ± 0,47	0,026
Urinary calcium (mg/24 hs)	139 ± 98	112 ± 61	NS
Serum phosphate (mg/dl)	3,66 ± 0,63	4,02 ± 0,57	0,002
Urinary phosphate (mg/24 hs)	867 ± 379	786 ± 334	NS
Serum magnesium (mg/dl)	1,92 ± 0,18	1,96 ± 0,18	0,033
Urinary magnesium (mg/24 hs)	91 ± 37	100 ± 45	NS
Serum sodium (mEq/l)	138 ± 2.99	139 ± 2.62	0,028
Urinary sodium (mEq/24hs)	180 ± 84	152 ± 81	NS
Serum potassium (mEq/l)	4.19 ± 0.44	4.12 ± 0.4	NS
Urinary potassium (mEq/24 hs)	70 ± 30	48 ± 28	0,003
Serum creatinine (mg/dl)	0.81 ± 0.23	0.77 ± 0.22	0,030
Urinary creatinine (mg/24 hs)	1.458 ± 473	1.251 ± 422	0,034
Albumin (g/dl)	4.04 ± 0.33	3.98 ± 0.43	NS
Vitamin D (ng/dl)	23.24 ± 8.80	29.07 ± 11.22	0,014
Urinary volume (ml/24 hs)	2.366 ± 929	1.925 ± 1.194	NS

NS: non-significant. Variables are expressed as mean ± standard deviation.

5. Discussion

We have observed a significant drop in weight, improvement in glycemic control, and insulin sensitivity as measured by the TG/HDL index. BSs are effective for weight reduction due to several mechanisms: malabsorptive procedures limit the absorption of nutrients at the intestinal level, thus reducing caloric consumption and, on the other hand, gastric restriction causes early satiety. In turn, different hormonal alterations have been described: the decrease in ghrelin levels and the increase in the gastrointestinal level of GLP-1, GIP, peptide YY and leptin, which lead, among other things, to the decrease in appetite. In this way, weight loss, together with the hormonal changes described above, leads to an improvement in insulin sensitivity, a critical component in the pathogenesis of diabetes [9].

Such an improvement implies a decrease in the use of oral antidiabetic and insulin, as was also demonstrated by other authors [10, 11]. Although we did not find a significant decrease in blood pressure, the decrease in the use of antihypertensive drugs allows us to infer a remission of hypertension (blood pressure <140/90 mmHg without medication) as observed by Puzziferri et al. and Yang et al. their meta-analysis [12, 13]. Concerning the lipid profile, as mentioned above and in relation to the improvement in insulin sensitivity, we found an increase in HDL and a decrease in triglycerides and non-HDL cholesterol, the latter also associated with high cardiovascular risk. These changes are similar to those found by different authors [10, 13, 14]. We also observed a decrease in creatinine levels in the postoperative period, which could be due to the changes in muscle mass that accompany the massive weight loss, as well as due to a decrease in hyper filtration, present in obese patients. Likewise, we found a decrease in uricemia after BS. This coincides with the already known relationship of DM2 and obesity with elevated serum uric acid levels, and the influence of BMI on hyperuricemia [15-17]. It is worth noting the statistically significant decrease in the values of hemoglobin, white blood cells and platelets in the postoperative period, yet without clinical consequences in most cases. The low rate of anemia in our study could be because most of the patients were receiving prophylactic vitamin supplements to cover potential micronutrient deficiencies of iron, vitamin B12 and copper, as described in the literature [18, 19]. A decrease in leukocytes and platelets after surgery, although within a normal range, has also been described by other authors. The cause has not been clarified yet, but could be due to the complex interrelation between micronutrient deficiencies and inflammatory, immunological, infectious or drug-related factors. Some reviews suggest a role for adipokines and other hormonal changes in the development of hematopoietic abnormalities [18, 20].

Remission of DM2 is defined by normal fasting blood glucose levels and/or normal HbA1c after at least a year off any antidiabetic medication [9]. In our study, we observed a rate of DM2 remission somewhat lower than that reported by other authors [7, 21, 22]. Regarding the predictive markers related to remission of diabetes, we found statistically significant differences only in those patients with lower baseline values of HbA1c and the pre-surgical use of metformin alone, but we did not find a relationship with other factors mentioned by other studies, such as age, BMI and duration of diabetes [23-26].

It has been widely described that BS is associated with abnormalities of bone mineral metabolism, such as accelerated remodeling, increased turnover and bone loss, and decreased bone mineral density [27, 28]. The deleterious effect on bone is multifactorial and depends on the type of procedure, the degree of weight loss, micronutrient deficiencies and hormonal changes [27-29]. Regarding the changes that we describe in the postsurgical phosphocalcic laboratory, although most studies report that the vitamin D deficit worsens after BS due to its malabsorption [27, 28, 30], we found a significant increase in Vitamin D levels after BS. One review mentions an initial increase in Vitamin D levels two years after BS, which then drops after five years of follow-up [31]. Likewise, most of the literature agrees that Vitamin D deficiency is usually more severe after BS 32 and our patients were accordingly supplemented. Concerning the other determinations, we found non-statistically significant decreasing trends in 24-hour urinary calcium and urinary volume—as indicated in other studies [29, 33]—consequence of the lower intestinal calcium absorption and the lower gastric volume after BS. During the post-surgery follow-up, we did not detect cases of fractures. Studies published up to date have very heterogeneous and conflicting results due, in part, to the fact that most of them are observational and, therefore, difficult to interpret. Despite this, it is sensible to expect a higher risk of fracture after BS, although most studies were unable to demonstrate a significant increase [34, 35]. In contrast, the drop in bone mineral density after BS has been widely described [36]. The etiology is multifactorial: lower calcium intake, lower intestinal absorption of calcium (due to lower gastric acidity and the bypass of the proximal intestine) and lower mechanical load [27]. Bone resorption markers increase to a greater extent than those of formation, leading to a net loss of bone; yet, the clinical relevance of this fact is unknown [29, 36]. Another complication of mineral metabolism is the presence of kidney stones. In our study, only one patient presented kidney stones in the postoperative period. Some studies reported an increase in the incidence of de novo renal lithiasis after gastric bypass in between 3.1 and 7.7% of cases, associated with a decreased urinary volume, hyperoxaluria and hypocitraturia seen after BS [33, 37, 38].

Regarding other complications—besides those related to anemia, which were already described above—we found two cases of symptomatic hypoglycemia, which represents 3.5% of cases. Some authors found 38% self-reported symptomatic hypoglycemia, 12% of which needed assistance. However, accurate estimation is difficult given the different diagnostic criteria used in studies and the low awareness of this complication both by patients and health care providers [39, 40].

Like every work, ours has strengths and limitations. One of its strengths is that the cohort of patients we have worked with had a clinical and metabolic follow-up of almost six years with an average of almost three years. On the other hand, a limitation is the small number of patients. Future studies with longer clinical follow-up are necessary to confirm the results presented here and thus highlight the possible differences between each surgical procedure and their beneficial effects.

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