Short-term effect of gastric bypass in obese diabetic patients

O efeito em curto prazo do bypass *gástrico sobre pacientes obesos diabéticos*

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A B S T R A C T

Objective: To study the effect of gastric bypass on blood glucose levels and the use of antidiabetic medication in obese patients with diabetes. **Methods**: We carried out a retrospective cohort study with 44 obese patients with T2DM, from 469 patients undergoing gastric bypass from December 2001 to March 2009. The primary endpoints evaluated were fasting glucose and the need for antidiabetic medication. **Results**: The study population consisted of ten (22.7%) men and 34 (77.3%) women, with a mean age of 45.3 (±8.23) years and a body mass index of 40.9 (±5.03) kg/m□. The average time to progression of T2DM was 63.6 (±60.9) months. Of the 40 patients who used medication to control type 2 diabetes, 20 (50%) had their medication discontinued at discharge and 13 (32.5%), until nine months later. In one patient it was not possible to evaluate the use of medication, this being the only exception. Insulin was suspended in ten (100%) patients who used it, six (60%) at discharge. Fasting plasma glucose levels decreased throughout the study period ($p < 0.05$) when compared with preoperative values, and values below 100mg/dl were achieved within seven to nine months. **Conclusion**: Obese patients with T2DM undergoing gastric bypass showed improved glycemic control and reduced use of hypoglycemic agents in the short-term.

Key words: Patients. Obesity. Diabetes mellitus, type 2. Blood glucose. Gastric bypass.

INTRODUCTION

Diabetes mellitus (DM) is a chronic disorder characterized by impaired glucose metabolism, which results in hyperglycemia and its complications[1].

DM type 2 (T2DM) is the most common presentation of the disease, found in over 90% of the diabetic population. It typically develops after the age of 40 and it is mostly associated with obesity[2].

The prevalence of obesity and T2DM increased exponentially, constituting one of the largest problems of public health[3]. Beyond weight loss, surgical treatment of morbid obesity causes control of comorbidities and mainly T2DM[4].

Recent studies have questioned the mechanism by which morbidly obese patients have their T2DM controlled after bariatric surgery. Most of these patients are discharged from hospital after the operation without the need for T2DM medications, while still not losing weight. In fact, the weight loss is partly responsible for the reversal of T2DM. The intestinal derivation that is performed in these operations causes an immediate improvement effect and an increased insulin production due to the greater production of Glucagon-like peptide-1 (GLP-1) and the improved action of gastric inhibitory polypeptide(GIP), or glucose-dependent insulinotropic polypeptide, which contribute to the improvement of blood glucose levels and, consequently, T2DM[5-8].

The impact of bariatric surgery on the improvement of T2DM might resemble the discovery of insulin, and certainly we are experiencing a new moment in history of medicine. The aim of this study was to evaluate the effects of Roux-en-Y gastric bypass on blood glucose and on the use of hypoglycemic drugs in obese patients with T2DM.

METHODS

We conducted a retrospective cohort study with obese patients with T2DM undergoing Roux-en-Y gastric bypass, in the period from December 11th, 2001 to March 30th, 2009, in which the primary endpoints were evaluated: fasting plasma glucose and the use of antidiabetics. The

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study followed the recommendations of Resolution 196/96 of the National Health Council, was approved and registered under No 080 025 of the Ethics Committee of the Hans Dieter Schmidt Regional Hospital (Joinville, SC).

Inclusion criteria were: patients with T2DM and grade III (BMI> 40kg/m□) or grade II obesity (BMI 35 to 39.9 kg/m□), undergoing gastric bypass with a 50cm biliopancreatic loop and a 100cm Roux-en-Y alimentary loop.

The diagnosis of DM followed the criteria proposed by the American Diabetes Association (ADA)[1].

All data were collected from medical records: age, gender, time since diagnosis of diabetes, fasting plasma glucose, need for antidiabetic medications, weight, BMI (weight / height □) and the percentage of excess weight loss (EWL). We considered six intervals of evaluation: one month, two to three months, four to six months, seven to ten months and nine to 12 months after surgery.

The data collected were analyzed using descriptive statistics through means and standard deviation, and by the t test with paired samples for averages with a significance level of 5% and correlation test.

RESULTS

Roux-en-Y gastric bypasses totaled 469 in the period, without mortality,. Of these, 44 patients were diagnosed with T2DM. The study population (n = 44) was composed of ten (22.7%) men and 34 (77.3%) women, mean age 45.3 (±8.23) years and BMI of 40.9 (±5.03) kg / m□. The average time to progression of T2DM was 63.6 (±60.9) months.

Regarding the use of medications to control diabetes, 43 patients were analyzed, of whom 40 (93%) used medication and three (7%) controlled diabetes only with diet and physical activity. The control with only oral medication was done by 30 individuals (75%), insulin associated with oral medication by nine (22.5%) and with insulin only by one (2.5%). In one patient, it was not possible to evaluate the use of medication due to lack of data in the chart, that being the only exception.

The use of insulin was suspended in ten patients: six (60%) at discharge, two after one month and two after a period of two months. Of the 40 patients who used medication to control type 2 diabetes, 20 (50%) had discontinued their medication at discharge and 13 (32.5%) until nine months later. Thus, 33 (82.5%) individuals stopped using medication to control T2DM, and seven continued (Figure 1).

When compared to preoperative values, there was decreased fasting glucose at the first evaluation, one month postoperatively ($p < 0.05$). The result remained so at all times of the study period. Within seven to nine months, the mean fasting glucose values presented below 100mg/

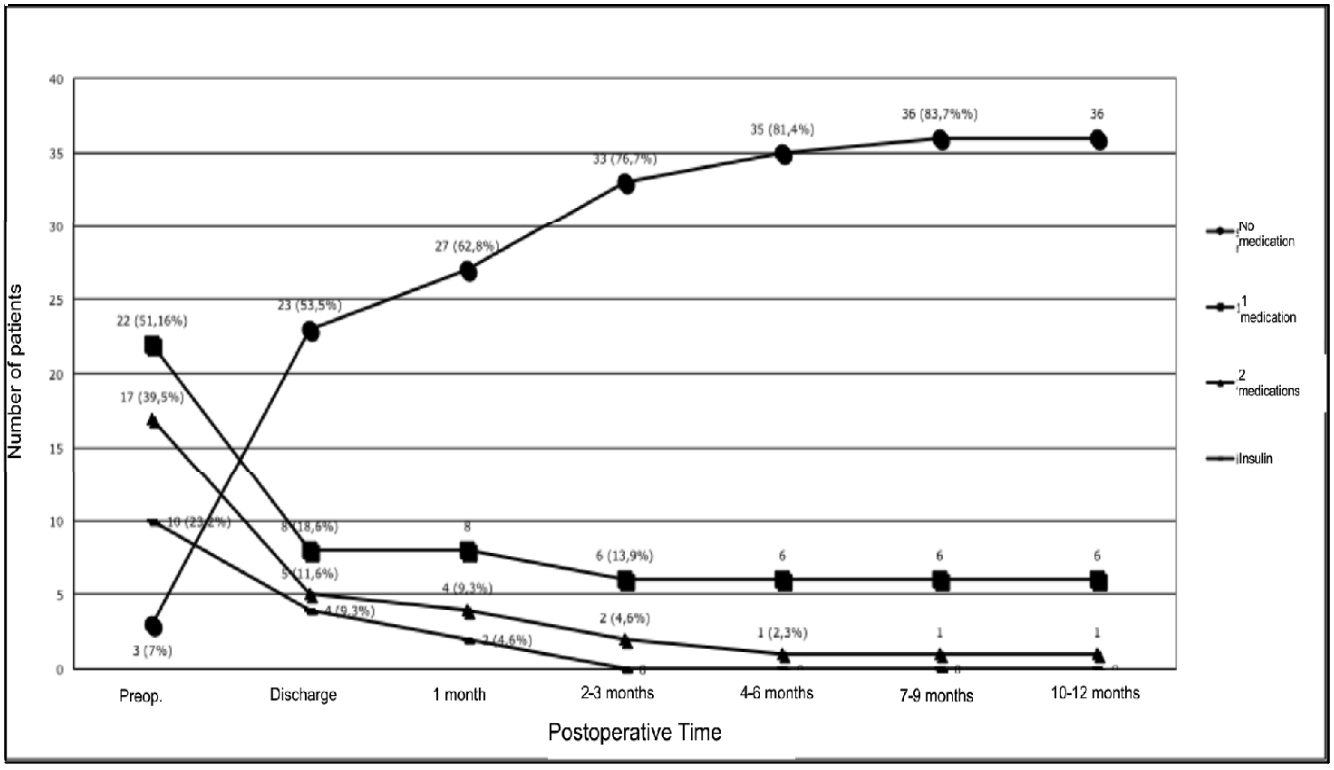

Figure 1 - *Use of medication to control diabetes in patients undergoing gastric bypass. Pre-op = preoperatively*

dl. After 12 months, there was a reduction of mean preoperative fasting glucose, from 151.85 ± 45.96 to 89.68 ± 18.13 (p <0.01 – Figure 2).

Regarding secondary outcomes, average weight were decreased (p <0.01) compared with the preoperative one (107.33 ± 17.32 kg) at all time points assessed (74 40 ± 14.40 kg). At 12 months there was reduction in mean BMI form 40.90 ± 5.03 kg/m□ to 29.01 ± 3.65 kg/m^2 (p <0.01). During this period, the percentage of excess weight loss (EWL) was 66.95% ± 17.47%. In the analysis of the curves, there was a positive correlation coefficient between fasting glucose and the following factors: weight (±0.98), BMI (±0.98), and medication use (±0.94). The correlation was negative between fasting glucose and EWL (Figure 3).

DISCUSSION

Type-2 Diabetes is a disorder associated with obesity in approximately 20% of patients[4]. In this study, 9.4% of obese patients undergoing gastric bypass had diabetes, approximately half of that in the literature. This is a retrospective study where patients analyzed were operated in the past ten years, with primary indication being morbid obesity (BMI> 40) and we included operations performed at the beginning of last decade, when the medical community had not raised interest in the effects of bariatric surgery on diabetes. Some tests, such as glycosylated hemoglobin, insulin and C-peptide were not part of the preoperative routine, the reason for which they were not evaluated. Pories *et al.*[9] published on this topic in 1995. However, it was from the work was published in 2004 by Rubino[10] that surgeons effectively turned their attentions to the effects of bariatric surgery on T2DM.

In this study, the average time to progression of T2DM was 63.6 (± 60.9) months. The shorter history of T2DM contributed to the high rates of improved glycemic control.

Patients with diabetes of short duration appear to have more complete or sustained resolution of the disease. One of the factors responsible for the failure in the surgical treatment of morbidly obese diabetics is the time history of the disease more than ten years (120 months)[11,12]. Gastric bypass is effective in weight loss, but its beneficial action on the T2DM decreases with longer duration of disease due to lower residual beta cell mass. These results are a good argument for proposing surgical treatment for obese patients with T2DM as soon as possible[13,14].

There is no accepted definition of what constitutes remission of T2DM after bariatric surgery[15]. The American Diabetes Association tried to establish a consensus definition of remission for T2DM in 2009 by publishing a summary of definitions and recommendations: partial remission: blood glucose levels between 100-125mg/dl; complete remission: normal glucose (value <100mg/dl) and one year without drug treatment; and prolonged remission: parameters are

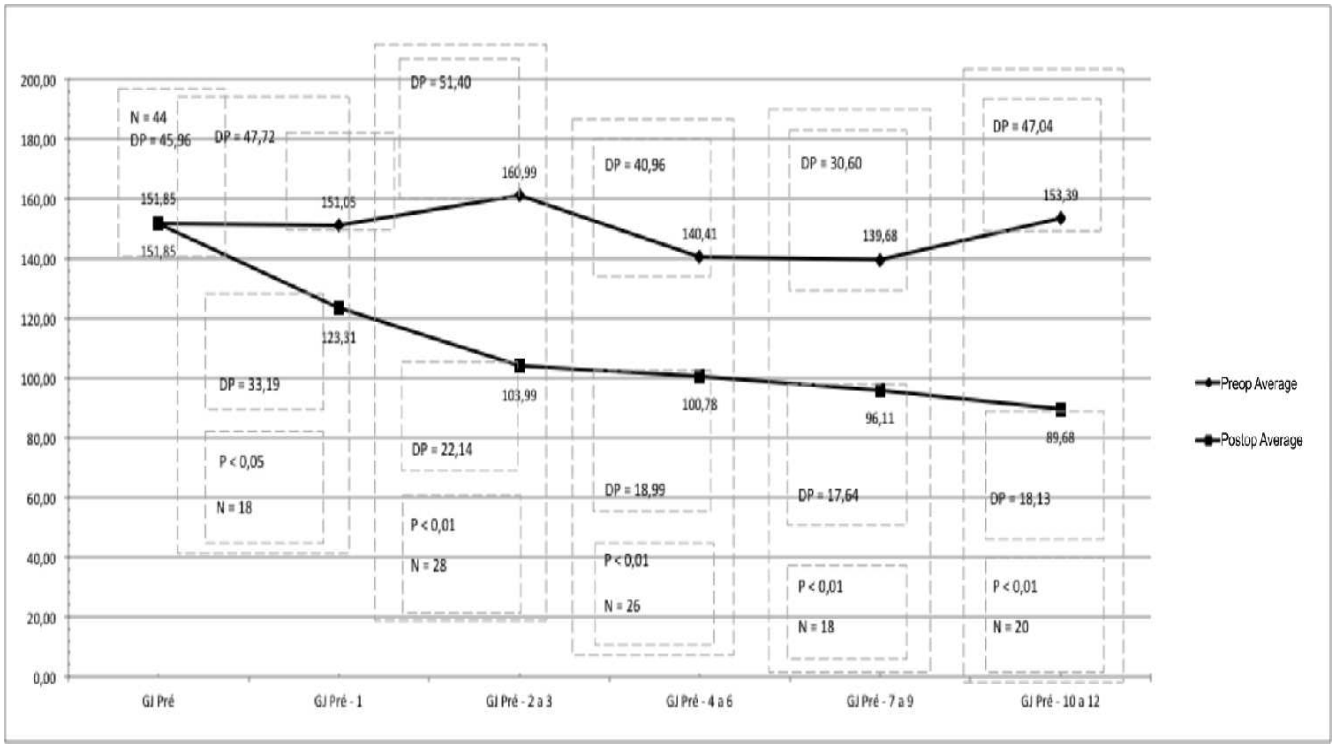

Figure 2 - *Comparison of fasting glucose values in the study period with the preoperative value.*
GJ Pré: preoperative; GJ Pré-1: 1 month postoperatively; GJ Pré-2 a 3: 2 to 3 months postoperatively; GJ Pré-4 a 6J: 4 to 6 months postoperatively; GJ Pré-7 a 9: 7 to 9 months postoperatively; GJ Pré-10 a 12: 10 to 12 months postoperatively .

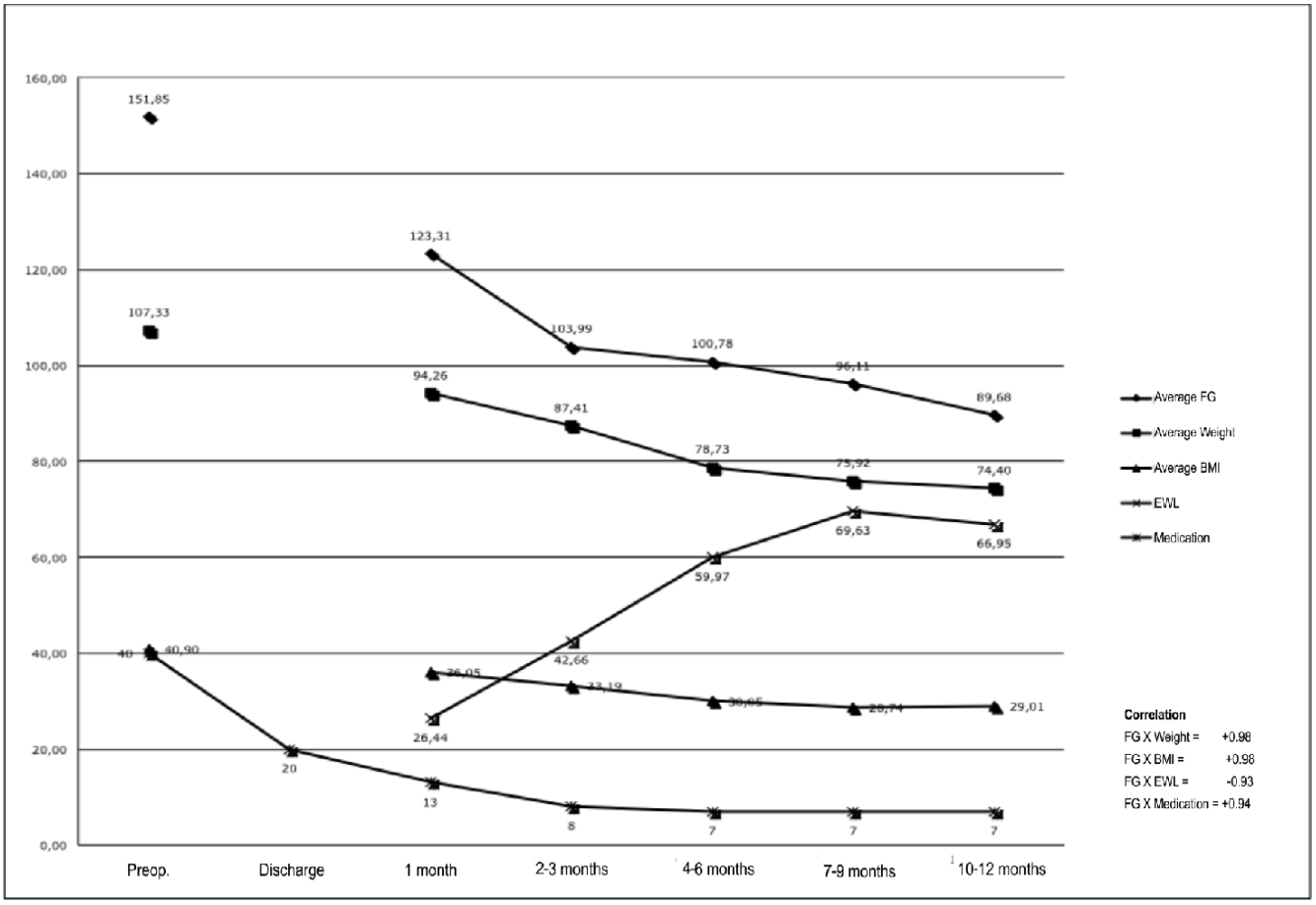

Figure 3 - *Correlation between fasting glucose, weight, BMI, EWL and medication.*
FG = fasting plasma glucose, BMI = body mass index; EWL = percentage of excess weight loss.

maintained for more than five years, with normal glycated hemoglobin (<6.5%) and no medication or procedure in progress[16]. Schauer *et al.*, in a four-year postoperative follow-up, observed that blood glucose returned to normal in 83% of cases and improved in 17%[12]. Other authors found significant reductions in blood glucose levels compatible with partial remission of T2DM in an average of 12 to 24 months post-operatively[4,17]. The adjustable gastric band procedures are associated with a lower average (50-60%) of clinical remission of T2DM[18].

The studies with gastric bypass were associated with the prevention of diabetes in patients with glucose intolerance in 99-100% of cases, and a clinical resolution of 80-90% for early diagnosed T2DM[18]. In a study conducted in France with 35 patients undergoing laparoscopic gastric bypass, in which all patients were treated with oral hypoglycemics or parenteral insulin before operation, T2DM was resolved in 60% of cases and reduction of drug therapy was observed in 31.42% one year after the procedure[19]. In several articles, both improvement and remission of diabetes are variable: remission ranging from 58 to 89% of cases and improvement from 42 to 86.6%[20-23]. Mottin *et al.* demonstrated control of T2DM in 97.6% of patients 18 months after gastric bypass[4]. We found that some authors use the term resolution, while others use control and others remission[24].

In this study, reduction in blood glucose occurred since discharge, and within seven to nine months the mean fasting glucose values presented below 100mg/dl. Half of the patients (50%) discontinued the medication for T2DM control at hospital discharge and 13 (32.5%) within nine months. We cannot evaluate remission with these data; it would require a time longer than one year of follow-up. However, we noticed improvement in diabetes, since at the end of 12 months, 36 (83.7%) patients no longer used medication and only seven (16.3%) required to continue with medication to control type 2 diabetes. We also observed that 100% of patients who used insulin had it discontinued within four months after the operation.

Weight loss plays an important role in long-term remission and durability of remission[15,25]. Bariatric surgery is currently the most efficient method to cause weight loss and to control comorbidities, and the Roux-en-Y gastric bypass is the most common technique[26].

Regarding secondary outcomes, the loss of excess weight was 66.95 (± 7.47%), higher than the 55.9% of the meta-analysis and systematic review of Buchwald, 2009[23]. Other authors found values similar to our findings (67%), in one year of follow-up[20]. We also found in the literature a reduction of BMI and weight loss similar to this study[19,27].

According to the Ministry of Health, the mortality of diabetes is increasing in Brazil. Deaths increased from 30 to 33 per 100,000 inhabitants in the analyzed period (1996 to 2007). Deaths caused by the disease rose by 10%. A decrease in deaths related to diabetes was reported by Laville *et al*.[14].

The reduction in mortality with surgical treatment occurs primarily due to a decrease in the number of cardiovascular deaths[28]. An observational study showed that patients undergoing gastric bypass had a 40% decrease in relative risk of death compared with the control group, and diabetes-related deaths were reduced by 92%[29].

Bariatric surgery is a treatment option for effective and safe weight loss, increases longevity and quality of life of the morbidly obese and has an acceptable rate of morbidity and mortality. The operative mortality rate described in the literature ranges from 0.1 to 2%, depending on the procedure and characteristics of the patients[23]. Our mortality in bariatric surgery, in a previous publication, was 1.21%[30]. In this study there was no mortality, though.

In this study's model, after gastric bypass in obese and diabetic patients, we observed a reduction in blood glucose levels to normal ones and a reduction in the need of use of hypoglycemic agents in the immediate postoperative period and throughout the period of one year.

R E S U M O

Objetivo: *estudar o efeito do* bypass *gástrico sobre a glicemia e o uso de medicação antidiabética em pacientes obesos portadores de diabetes.* ***Métodos:*** *estudo de coorte retrospectivo com 44 pacientes obesos portadores de DM2, provenientes de 469 pacientes submetidos ao* bypass *gástrico no período de dezembro de 2001 a março de 2009. Os desfechos primários avaliados foram: glicemia em jejum e a necessidade de medicação antidiabética.* ***Resultados:*** *a população foi composta de dez (22,7%) homens e 34 (77,3%) mulheres, com média de idade de 45,3 (+8,23) anos e índice de massa corporal de 40,9 (+5,03) kg/m□. O tempo médio de evolução do DM2 foi 63,6 (+60,9) meses. Dos 40 pacientes que utilizavam medicação para controle do DM2, 20 (50%) tiveram sua medicação suspensa na alta hospitalar e 13 (32,5%) até nove meses depois. Em uma paciente não foi possível avaliar o uso de medicação, sendo essa a única exclusão. A insulina foi suspensa nos dez (100%) pacientes que a utilizavam, sendo seis (60%) na alta hospitalar. Houve redução (P<0,05) da glicemia em jejum, em todo o período estudado, em comparação com o valor pré-operatório, e foram atingidos valores inferiores a 100mg/dl no período de sete a nove meses.* ***Conclusão:*** *Pacientes obesos portadores de DM2, submetidos ao* bypass *gástrico, apresentaram melhora do controle glicêmico e redução do uso de hipoglicemiantes em curto prazo.*

Descritores: *Pacientes. Obesidade. Diabetes mellitus tipo 2. Glicemia. Derivação Gástrica.*

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