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Relationship between changes in hemoglobin glycosilated and improvement of body composition in patients with morbid obesity after tubular laparoscopic gastrectomy☆

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ABSTRACT

Background and objective: The objective of our study is to analyze the possible relationship between changes in glycemic profile and body composition parameters in morbid obesity patients after tubular laparoscopic gastrectomy.
Material and methods: A prospective observational cohort study with 69 patients was performed. The variables analyzed were body weight, blood glucose, haemoglobin, glycosylated, high density lipoprotein, low density lipoprotein, triglycerides, and waist and hip circumference. An analysis of variance of repeated measurements (ANOVA) and a correlation analysis through the Pearson test were carried out.
Results: A significant reduction in weight ($p < 0.001$ after surgery) and in glycosylated haemoglobin ($p < 0.036$) and waist hip ($p < 0.001$) were found at 6 months after surgery. There was no significant difference in the rest of the variables studied. In correlation analysis, a significant positive correlation was found between the change in concentration of haemoglobin glycosylated and hip circumference ($p = 0.047$; $r = 0.237$), the smaller the hip circumference, the lower the concentration of glycosylated haemoglobin.
Conclusions: Tubular laparoscopic gastrectomy is an effective technique for the treatment of morbidly obese patients with type 2 diabetes mellitus. The reduction in the perimeter of hip is related to glycosylated haemoglobin reduction 6 months after intervention.

Relación entre cambios en hemoglobina glucosilada y mejora de la composición corporal en pacientes con obesidad mórbida tras gastrectomía tubular laparoscópica

Palabras clave:
Diabetes mellitus
Gastrectomía tubular laparoscópica
Obesidad mórbida

RESUMEN

Introducción y objetivo: El objetivo de nuestro estudio es analizar la posible relación entre los cambios en el perfil glucémico y los parámetros de composición corporal en pacientes con obesidad mórbida tras gastrectomía tubular laparoscópica.
Material y métodos: Se realiza un estudio observacional prospectivo de cohortes donde el tamaño muestral es de 69 pacientes. Las variables analizadas son peso corporal, glucemia, hemoglobina glucosilada, *lipoprotein high density*, *lipoprotein low density*, triglicéridos y circunferencia cintura y cadera. Para llevar a cabo el objetivo de este estudio se ha utilizado un análisis de la variancia de medidas repetidas (ANOVA) y un posterior análisis de correlación a través del test de Pearson.

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Resultados: Tras el análisis estadístico se han encontrado una reducción significativa del peso tras la cirugía $p < 0,001$, una reducción significativa de la hemoglobina glucosilada entre los valores preintervención y a los 6 meses de la cirugía ($p < 0,036$) y un descenso significativo de los perímetros de cintura y cadera ($p < 0,001$). No existieron diferencias significativas en el resto de variables estudiadas. En el análisis de correlación, se encontró una correlación positiva significativa entre el cambio en concentración de hemoglobina glucosilada y perímetro de cadera ($p = 0,047$; $r = 0,237$), a menor diámetro de cadera, menor concentración de hemoglobina glucosilada.

Conclusiones: La gastrectomía tubular laparoscópica se muestra como una técnica efectiva para el tratamiento de pacientes obesos mórbidos con diabetes mellitus tipo 2. La reducción en el perímetro de cadera está relacionada con la reducción de hemoglobina glucosilada a los 6 meses de la intervención.

Introduction

Morbid obesity is a chronic and multifactorial disease characterized by an excess of body fat that causes a pathological weight gain (body mass index [BMI]) > 40 kg/m^2, or patients whose weight exceeds the ideal weight by 75 kg.[1]

Spain has experienced an increase of more than 200% in recent decades.[2] Most patients with morbid obesity have diabetes mellitus type 2 (DM2), the basis of its pathogenesis is the occurrence of insulin resistance linked to abdominal obesity, being the main risk factor for this condition.[3] DM2, arterial hypertension and dyslipidaemia are conditions that share insulin resistance and are part of the metabolic syndrome, which is a predictor of cardiovascular disease.[4] Non-invasive treatments for morbid obesity, diet, drugs, exercise, produce discrete results with a low long-term maintenance rate.[5] This fact is especially significant in the control of DM2 and the decrease in glycosylated haemoglobin (HbA1c). Decreasing blood pressure, improving the lipid profile and reducing glycosylated haemoglobin in morbidly obese patients is very difficult without surgery.[6] Bariatric surgery is extremely useful for morbidly obese patients with DM2, not only in terms of decreasing body weight, but also improving glycaemic control.[7] We do not currently have data that directly relate changes in biologic markers of glucose control with changes induced by bariatric surgery in the body composition of patients.

Patients undergoing bariatric surgery improve the lipid profile, blood pressure and obstructive sleep apnoea syndrome, among other complications associated with obesity.[8] One of the main bariatric surgery techniques is laparoscopic sleeve gastrectomy (LSG). This surgical technique, according to some studies, allows a weight loss of 57.6% per year and 70.1% after 3 years of its completion,[9] in addition to its simplicity as a surgical procedure, the maintenance of gastrointestinal continuity does not affect the quality of life of the patient, as occurs with other malabsorptive techniques. It is a procedure with few postoperative complications; that produces an improvement of cardiovascular risk factors: DM2, dyslipidaemia, high blood pressure, obstructive sleep apnoea syndrome.[10] The weight loss caused by surgery is associated with an improvement in DM2, which may or may not be related to the magnitude of weight loss.[9] Currently there are two mechanisms that could be involved in the improvement of hyperglycaemia from LSG: the hormonal response to meals and the improvement of fasting glycaemic control.[11] Morbid obesity is associated with the insulin resistance syndrome frequently observed with excess fat tissue, especially when there is an abdominothoracic or visceral distribution.[12] At present, there are no studies that evaluate at what point of the early follow-up there is an improvement in glycosylated haemoglobin and if this improvement coincides with the hip fat weight loss.

Morbid obesity is associated with hypertriglyceridemia, with a slight increase in total cholesterol, but with a significant decrease in HDL cholesterol (and therefore an increase in the total cholesterol/HDL cholesterol ratio).[13,14] On the other hand, something similar occurs with LDL, which receive triglycerides, these are partially metabolized by hepatic lipase and transformed into small and dense LDL, with a greater atherogenic potential.[15] Bariatric surgery improves hypercholesterolemia by 70% in malabsorptive techniques and by 45% in non-malabsorptive techniques.[16] Information currently available on the changes triggered during hypertriglyceridemia in early follow-up is reduced.

The aim of this study was to analyze the improvement in DM2 based on the decrease in HbA1c in patients with morbid obesity undergoing laparoscopic sleeve gastrectomy, and the possible relationship between changes in the glycaemic profile and the parameters of body composition occurred 6 months after the intervention.

Methodology

We used a prospective observational cohort study design with a 6-month follow-up period. To this end, 69 patients previously diagnosed with morbid obesity were invited to participate and underwent laparoscopic sleeve gastrectomy in the General Surgery and Gastroenterology Department of the San Cecilio Hospital in Granada, Spain. The study was carried out between the month of March 2011 and the month of June 2015. The inclusion criteria to participate in the study were the following: (1) patients >18 years of age, with severe obesity that met the criteria for surgical indication (BMI >35 with comorbidities or BMI >40 mg/kg^2). (2) Having signed the informed consent. Exclusion criteria: (1) general anaesthesia contraindication, (2) pregnancy, (3) previous abdominal surgery, (4) non-controllable medical conditions incompatible with the study's objective, (5) uncontrollable psychiatric conditions, (6) presence of ventral or hiatal hernia, (7) age ≥65 years. All patients who met the criteria accepted inclusion. Once informed, they signed the informed consent in accordance with the regulations of the Declaration of Helsinki. The data of the patients related to their demographic and clinical characteristics were obtained through a questionnaire prepared for this purpose, as well as through the patients' clinical history. The study was approved by the Clinical Research Ethics Committee of the Province of Granada. Participants were admitted to hospital 24 h before surgery. Two hours after hospital admission, the baseline parameters of the study were determined: questionnaires, laboratory and physical parameters. Surgery was always performed by the same surgical team using general anaesthesia, laparoscopy and 5 trocars (4 of 5 mm and 1 of 12 mm). Subsequently, two more determinations of all the parameters were analyzed 1-month and 6-months after surgery.

Study variables

Weight

Its determination was made by the research staff after 8 h of fast and barefoot, using a previously calibrated scale (DETECTO, model 2392, year 2009).

Glycemia and glycosylated haemoglobin in peripheral blood

Complete remission of DM2 is considered when the decrease in fasting plasma glucose concentrations is less than 100 mg/dL and HbAc1 below 6% (*Report of the Expert*). The biochemical determinations were carried out after 8 h of fast. Each patient underwent a blood venipuncture (2 ml). *High performance liquid chromatography*, with Beckman coulter, Olympus kit analysers, were used for the determination of HbA1c.

Cholesterol and triglycerides in peripheral blood

The blood obtained from the patient is placed in a siliconized biochemical tube. The blood volume is 3 ml. The laboratory determinations were carried out after 8 h of fast. Its study was performed by enzymatic method, elimination of catalase, difference equation and by glycerol phosphate oxidase assay. The analysis was carried out using a Beckman coulter, Olympus analyser kit.

Waist and hip circumference

They were measured according to a previously established methodology[17] for which an inextensible 0.5 cm wide × 2 m long flexible tape was used with an accuracy of 0.1 cm. The examiner measured the patient's waist in standing position by placing the tape measure at the midpoint between the last rib and the anterior superior iliac spine. The measurement always took place at the end of the exhalation. To measure the hip circumference the patient remained in standing position and the examiner placed the tape measure at the midpoint between both trochanters to the level of maximal protrusion of the gluteal muscles and the pubic symphysis.

Statistic analysis

The descriptive data of the sample are presented as mean ± standard deviation for the continuous variables and as absolute frequencies for the categorical ones.

Subsequently, a Kolmogorov–Smirnov test was used to verify the normal distribution of the variables studied. An analysis of variance (ANOVA) was performed using time as intrasubject variable (preintervention, one month and 6 months) and the Bonferroni test was used for the post hoc analysis. To answer the main objective of the study, a Pearson correlation analysis was performed using the variables of change between the baseline of the study and the value of these variables at 6 months of follow-up. The statistical analysis was carried out at a 95% confidence level and a p-value of less than 0.05 was considered statistically significant. Said analysis was carried out using the statistical package SPSS, version 22.0 (SPSS Inc., Chicago, IL, USA).

Results

The clinical and sociodemographic data of the sample are shown in Table 1.

Table 1
Sociodemographic data.

	Years	n	%
Age	45.82 ± 9.08		
Sample size		69	
Sex			
Male		24	34.8
Female		45	65.2
Civil status			
Married		16	23.2
Single		42	60.9
Divorced		4	5.8
Widower		7	10.1
Smoking			
Smoker		20	29
Non-smoker		48	69.6
Former smoker		1	1.4
Alcohol			
No alcohol		53	76.8
Monthly alcohol consumption		6	8.7
Weekly alcohol consumption		7	10.1
Daily alcohol consumption		3	4.3
Race			
Caucasian race		67	97.1
Black race		2	2.9
Education			
No studies		1	1.4
Basic studies		36	52.2
Intermediate studies		19	27.5
Higher education		13	18.8
Comorbidities			
Insulin-dependent diabetes		14	20.2
Insulin-independent diabetes		50	72.4
Hypertension		66	95.6
Obstructive sleep apnoea		56	81.1

It is important to highlight that patients were able to discontinue the oral antidiabetic medication in 100% of cases after 6 months of study follow-up.

Weight

The ANOVA results showed a statistically significant effect of the LSG-type surgery on weight reduction (F = 53.08; p < 0.001). The patients studied showed a reduction of 17.8 kg (95% CI 108.18–117.17) one month after surgery and 34.12 kg on average (95% CI 92.45–100.26) at 6 months.

Subsequently, the post hoc analysis showed that the weight reduction occurred between the pre-surgery values and the values at 1-month of LSG (p < 0.001), the value at 1-month and at 6-months of follow-up (p < 0.001) and between the pre-surgery values and those 6-months after LSG (p < 0.001) (Table 2).

Glycosylated haemoglobin

The ANOVA results showed a statistically significant effect for LSG-type surgery on the reduction of glycosylated haemoglobin levels (F = 3.23; p = 0.041). The post hoc analysis showed that the differences were found between pre-intervention values and 6 months post-surgery (p = 0.036), however, there were no differences between the pre-intervention values and those obtained one month after surgery (p = 0.833) (Table 2).

Waist and hip circumference

The ANOVA results showed a statistically significant effect for LSG-type surgery on waist (F = 55.05; p < 0.001) and hip (F = 24.29;

Table 2
Results of determinations expressed as mean (m) ± standard deviation (e).

	Baseline	1 month	6 months	p Value
Weight (kg)	130.47 ± 21.45 (125.32–135.63)	112.67 ± 18.98 (108.18–117.17)	96.35 ± 15.51 (92.45–100.26)	<0.001**
HBAc1 (%)	6.29 ± 1.38 (5.96–6.63)	6.07 ± 1.21 (5.78–6.36)	5.78 ± 0.99 (5.54–6.01)	0.041*
Glycemia (mg/dl)	76.31 ± 17.73 (72.05–80.57)	75.22 ± 16.47 (71.32–79.12)	73.08 ± 14.71 (69.60–76.56)	0.492
Triglycerides (mg/dl)	74.33 ± 48.59 (62.66–86.00)	75.57 ± 45.39 (64.83–86.32)	67.64 ± 37.11 (58.86–76.43)	0.514
HDL (mg/dl)	31.89 ± 15.77 (28.10–35.68)	32.12 ± 13.07 (29.03–35.22)	33.15 ± 15.82 (29.40–36.90)	0.868
LDL (mg/dl)	67.60 ± 47.27 (56.25–78.96)	69.18 ± 43.96 (58.78–79.59)	58.98 ± 36.20 (50.41–67.55)	0.312
Waist c. (cm)	132.39 ± 14.64 (128.87– 135.90)	121.54 ± 14.27 (118.16–124.92)	106.14 ± 14.24 (102.56–109.73)	<0.001*
Hip c. (cm)	139.44 ± 20.55 (134.51–144.38)	129.78 ± 13.57 (126.56–132.99)	119.45 ± 14.76 (115.79–123.11)	<0.001**

* $p < 0.05$.
** $p < 0.001$.

and $p < 0.001$) circumference. The results of the post hoc analysis also showed that changes had occurred between the three study intervals (pre-intervention, at one month and at six months post-intervention follow-up) ($p < 0.001$).

The ANOVA results did not show statistically significant differences regarding LSG-type surgery on blood glucose ($F = 0.71$; $p < 0.492$), triglycerides ($F = 0.66$; $p = 0.514$), blood HDL cholesterol ($F = 0.14$; $p < 0.868$) or LDL cholesterol ($F = 1.17$; $p < 0.312$) (Table 2).

Relationship between glycosylated haemoglobin and body composition parameters

A significant positive relationship was found between the reduction in glycosylated haemoglobin levels and the reduction in hip circumference 6 months after LSG surgery ($r = 0.27$; $p = 0.04$). The other body composition parameters did not show significant relationships with glycosylated haemoglobin levels.

Discussion

The aim of the present study was to analyze the changes in the cardiometabolic profile of morbidly obese patients undergoing LSG surgery. There was a significant improvement in HBA1c, weight and waist and hip circumference values.

The World Health Organization predicts that by the year 2030, around the world, almost 366 million people will have DM2.[18] The strongest association for the onset of this disease is an increase in body weight.[19] The published literature on bariatric surgery is full of articles that show an improvement in glycaemic parameters in patients with DM2 who undergo bariatric surgery.[4,5,7–18,20]

One of the essential novelties of the present study is the short-term determination of the changes that lead to this improvement, which is established by a window period of 6 months. Some studies like that of Mingorance et al.[21] and Schaucher et al.,[22] describe a decrease of 24.5 and 37% in DM2 remission rate, respectively, a year after surgery. In our study, this rate is around 10% at six months. Given the close relationship between obesity and DM2, weight loss has been suspected as the primary mechanism responsible for diabetes resolution after surgery.[20–23]

Weight loss in the present study is close to 30%, which coincides chronologically with the reduction of glycosylated haemoglobin. This chronological coincidence could be the result of different physiological mechanisms such as a reduction of fatty acids in the liver, associated with a reduction in insulin resistance, an increase in insulin secretion due to the incretin effect[24] or the increase in adiponectin levels that accompany the decrease of adipose tissue, especially in liver and muscle.[25–29]

Undoubtedly, the most interesting finding of this study is the relationship found between the decrease in glycosylated haemoglobin and hip circumference. The reduction of intra-abdominal fat due to the decrease in food intake caused by surgery explains the decrease in body circumferences.[26] This anorexia associated with lipolysis caused by changes in hormone levels that control appetite and an improvement in energy metabolism, associated with the patient's behavioural changes allow us to explain these improvements in the patient's body composition.

In women, the gynoid distribution of fat allows a lower volume of intra-abdominal fat, losing fat deposits in the hip after surgery, which in turn contributes to the improvement of glycosylated haemoglobin levels by the previously explained mechanisms.[27] Given that there were 50% more female patients than male patients in our study sample, such gender-differentiated distribution of body fat may have contributed to the greater correlation found between hip circumference and HBA1c levels at 6 months of follow-up.

Having used a prospective design with cohort follow-up, we can suspect a possible cause-effect relationship between the variation of the glycaemic metabolism and the hip circumference. The importance of clinical hip circumference monitoring during the follow-up of patients undergoing LSG is highlighted by these results.

In our study, with a follow-up of 6 months, we have not found an improvement in our patients' lipid profiles. Although previous studies have shown that LSG allows the correction of dyslipidaemia after follow-ups of 1-year,[28–30] a period of 6 months may be insufficient to produce these changes in the lipid profile.

The present study shows a series of limitations, first, the design used does not allow knowing if the changes produced are exclusively due to the LSG or if there are other determining factors that could have affected the results. The study does not have a control group because LSG is the most popular technique carried out in the unit from which the study is proposed, which makes comparison between groups difficult. Walking is the only exercise recommended to our patients until the second postoperative month, after that, they can engage in more intense physical activity. Potential mediating variables regarding the relationship between glycosylated haemoglobin and body composition should be part of future studies.

In addition, as the study has been conducted in a single hospital, it is possible that the results are dependent on the team of surgeons involved.

Conclusion

LSG is shown as an effective technique for the treatment of morbidly obese patients with a history of DM2. Both, a significant decrease in body composition and glycaemic control (HbA1) have been observed.

The decrease in HbC1 is related to the decrease in hip circumference.

Authorship/collaborators

Tania Gallart-Aragón: took part in the design of the article, acquisition and collection of data, analysis and interpretation of results and writing of the article.

Carolina Fernández-Lao: took part in the design of the article and its writing.

Antonio Cózar-Ibañez: took part in the design of the article and its writing.

Irene Cantarero-Villanueva: took part in the design of the article and its writing.

Jacobo Cambil-Martín: took part in the acquisition and collection of data and analysis and interpretation of the results.

José Antonio Jiménez Ríos: took part in the design of the study, critical review and approval of the final version.

Manuel Arroyo-Morales: took part in the design of the study, critical review and approval of the final version.

Conflict of interests

The authors declare no conflict of interest.

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