Glycemic and lipid metabolic disorders in diabetic and non-diabetic patients bmi < 35 or > 35 before gastric bypass

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Abstract

Introduction: Obesity and diabetes are diseases with high prevalence worldwide. There is currently no effective medical treatment for combat the weight gain. It is precursor of diseases such as diabetes or metabolic syndrome. It is necessary to know if weight gain has cumulative effects on the glycemic and lipid metabolism as precursors of complications or comorbidities.

Patients and methods: We studied 131 patients (78 non-diabetic and 53 diabetic), 37 BMI ≤35 (3 BMI < 25, 18 BMI 25-29.9, 16 BMI 30-34.9) and 94 BMI ≥35 (81 BMI 35-49.9 and 13 BMI ≥50). We analyzed BMI, gender, diabetes and the time of evolution. Lipid profile, glucose, HbA1c and C-peptide evaluated after 12-hour fasting.

Results: Diabetic and diabese patients showed high triglycerides. Non-diabetics have impaired glucose (58% BMI < 35 and 36% BMI > 35). The 20% of non-diabetics BMI < 35 had high C-peptide, and 19% of BMI > 35 had high levels. The 5% of diabetics BMI < 35 had low C-peptide and 36% of BMI > 35 had high levels. HbA1c was higher in 40% of non-diabetic patients BMI < 35 compared to 13% BMI > 35.

Conclusions: Glucose and triglycerides increase with age and years of development of T2DM. Age of 51 and more, and men are more affected. The weight increase has cumulative effect by altering the metabolism favoring the onset of diabetes and comorbidities. Despite having intensive control treatment of diabetes, it continues its deleterious effects on patients through the years.

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Key words: Obesity. Diabetes mellitus. Diabetes. BMI. Metabolism.

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TRASTORNOS DEL METABOLISMO GLICÉMICO Y LIPÍDICO EN PACIENTES DIABÉTICOS Y NO DIABÉTICOS CON IMC < 35 Ó > 35 ANTES DE BYPASS GASTRICO

Resumen

Introducción: La obesidad y la diabetes son enfermedades de alta prevalencia a nivel mundial. Actualmente no existe un tratamiento médico eficaz para combatir el aumento de peso. La obesidad es precursora de enfermedades tales como la diabetes o el síndrome metabólico. Es necesario saber si el aumento de peso tiene efectos acumulativos sobre el metabolismo de la glucemia y los lípidos como precursores de complicaciones o comorbididades.

Pacientes y métodos: Se estudiaron 131 pacientes (78 no diabéticos y 53 diabéticos), 37 IMC ≤ 35 (3 IMC < 25, 18 IMC 25-29.9, 16 IMC 30-34.9) y 94 IMC ≥ 35 (81 IMC 35-49.9 y 13 de IMC ≥ 50). Se analizó BMI, género, diabetes y el tiempo de evolución. Lipid profile, glucosa, HbA1c y el péptido C fueron evaluados después de un ayuno de 12 horas.

Resultados: Los pacientes diabéticos y diabesos mostraron niveles altos de triglicéridos. Los pacientes no diabéticos tienen alteración de la glucosa (58% IMC <35 y 36% IMC > 35). El 20% de los no diabéticos IMC < 35 tenían péptido C alto, y un 19% de IMC > 35 tenían niveles altos. El 5% de los diabéticos IMC < 35 tenía bajos niveles de péptido C y 36% de IMC > 35 tenían niveles altos. HbA1c fue mayor en 40% de pacientes no diabéticos IMC < 35 frente al 13% de IMC > 35.

Conclusiones: La glucosa y los triglicéridos aumentan con la edad y los años de evolución de la DMT2. La edad de ≥51 años y los hombres son los más afectados. El aumento de peso tiene efecto acumulativo alterando el metabolismo favoreciendo la aparición de la diabetes y sus comorbididades. A pesar de tener un tratamiento de control intensivo de la diabetes, esta continúa con sus efectos nocivos sobre los pacientes a través de los años.

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Introduction

There is a growing epidemic of chronic diseases related to dietary changes and lifestyle. Over-weight and obesity are result of excess of energy intake. Fat intake in meals exceeds at least 10% of the daily recommendations. This can lead to abdominal obesity and insulin resistance, factors that increase 5 times the risk of developing diabetes.

Obesity is proposed as an inflammatory disease that may develop insulin resistance and type 2 diabetes mellitus (T2DM) as consequence. Obesity has unexpected connections to the risk of develop of cancer, lung diseases, and others diseases. There are a close relationship between excess of nutrients and energy consumption with the alterations in the innate immune response and the cellular and molecular mediators of immunity, where the delicate balance between the immune response and metabolism becomes a pathological relationship.

World Health Organization (WHO) mention that T2DM is a condition with permanent hyperglycemia that increase the risk of micro and macro vascular damage, which is associated with lower quality of life and reduced life expectancy. On the other hand, for the American Diabetes Association (ADA), T2DM is a metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion and/or action associated with damage, dysfunction, and long-term failure of several organs.

Worldwide, 4.8 million of deaths per year were attributed to T2DM. The people with diabetes in 2012 was 371 million and will increase to 552 million in 2030, or one adult in ten.

In America, the highest prevalence of T2DM is found in the United States of America (USA) and Mexico. The Centers for Disease Control and Prevention (CDC) of USA has estimated that 11.3% to 26.9% of U.S. citizens were diabetic in 2011.

The Mexican Diabetes Federation A.A. and the National Institute for Health and Clinical Excellence recommends physical activity; lose weight in order to get healthy BMI, eat diet rich in fiber, fruit and vegetables, and reducing fat of the diet. ADA and the European Association for the Study of Diabetes (EASD) recommend individualize each treatment according to the patient state for which there are several drugs.

Metabolic surgery is now considered as definitive treatment of diabetes, because of the immediate effect that is achieved with the improvement or resolution of T2DM after surgery, where the patient is discharged without antidiabetic treatment. The immediate resolution of T2DM depends on mechanisms due to the change of the gastrointestinal transit.

The obesity prevalence in USA for 2009 was 35.5% for women, and 32.2% for men. The Behavioral Risk Factor Surveillance System (BRFSS) and the CDC showed progressive increase of 1.1% of national prevalence of obesity in previous years, so some researchers suggest that by the year 2050, where perhaps 100% of U.S. citizens will have over-weight.

The National Institute of Public Health of Mexico for 2012 estimated that over-weight and obesity prevalence is 38.8% and 32.4% respectively.

In Europe, the obesity prevalence is higher in Italy, Portugal, Poland, Czech Republic, Romania and Albania. Eastern Europe and the Mediterranean countries have higher obesity prevalence than Western and Northern Europe. The consensus SEEDO 2007 of Spain estimated the obesity prevalence as 15.5%.

The increase in obesity is due to the presence of an obesogenic environment produced by the sedentary lifestyle and dietetic global changes. Besides, the cognitive aspects of reward and emotional factors play important roles in food intake that may override the homeostatic systems.

On the other hand, adipose tissue is an active endocrine organ that releases hormones and inflammatory mediators that regulate adipose tissue expansion, control of food intake, energy balance, and others. These effects are involved in the regulation of insulin signaling and lipid metabolism in peripheral tissues that can produce insulin resistance, T2DM or metabolic syndrome. When the adipose tissue becomes dysfunctional, insulin resistant and dysfunctional lipid storage begins as a sentinel event in the progression of obesity metabolic imbalance. Each increase of 5 kg of BMI over 25 kg/m² are associated with 29% increased of total mortality, 41% of mortality associated to vas-
cular disease and 21% of mortality associated with T2DM.

Treatments for obesity are limited due to the complexity of the disease. Diet and physical activity are effective but adherence is needed. Behavioral therapy, physical activity, stress management, stimulus control, problem solving, cognitive restructuring, contingency management, and social support are effective too. Specific drugs for obesity are limited and have not been approved for use indefinitely, despite the chronic nature of obesity.

When treatment fails, weight recovery begins. The safest option for long-term weight loss is through bariatric surgery that provides too resolution of comorbidities and could protect against the development of T2DM. Diabetic lean or obese patients, have improvement or remission of their diseases after surgery, secondary to the modification of the gastrointestinal transit.

**Patients and methods**

**Patients**

We evaluated 131 patients (78 non-diabetic patients and 53 diabetic). 37 patients BMI ≤ 35 (3 BMI < 25, 18 BMI 25-29.9, 16 BMI 30-34.9) and 94 patients BMI ≥ 35 (81 BMI 35-49.9 and 13 BMI ≥ 50). We analyzed BMI, gender, presence of diabetes and its time of evolution. The laboratory studies were evaluated after at least 12-hour fasting (lipid profile, blood glucose, HbA1c and C-peptide).

BMI was classified as showed in table I. Age was clustered in ranges 15-20, 21-30, 31-40, 41-50, and 51 years of age and older. The duration of T2DM was clustered into 1-5, 6-10, 11-15, 16-20, 21-30 and 31-40 years.

Patients attended medical consultation in order to be undergoing to tailored One Anastomosis Gastric Bypass (BAGUA) for their current state of diabetes, obesity or both conditions.

**Surgical procedure**

Before surgery, all patients eat only liquid diet during 5 (BMI 23-34) to 7 days (BMI 35-50) depending of preoperative BMI, received antibiotic and antithrombotic prophylaxis. Tailored BAGUA consisted in the construction of a gastric pouch from the gastroesophageal junction to the end of the minor gastric curvature at the lower level of the cisura angularis. The stapler line of the gastric pouch was fixed approximately 12 cm to the intestinal loop (first layer of the anti-reflux mechanism of BAGUA), and it was anastomosed in a laterolateral position to the mesenteric border of a small bowel loop 100 cm (BMI 23-29), 120 cm (BMI 30-32), 150 cm (BMI 33-34), 200 cm (BMI 35-40), 250 cm (BMI 40-45), and 280 cm distal (BMI 45-50) to the treitz ligament. The anti-reflux mechanism is completed fixing the afferent loop to the gastric remnant and the efferent loop to the antrum.

The size of the gastric pouch depends on the BMI of the patient. In BMI 23-32 we performed a floppy 36 French bougie pouch, while in BMI > 33 a narrow 36 French bougie one is performed. We left systematically a drainage during the 48 h of hospital stay. After surgery, they eat liquid diet in the 1st week, semifluids in 2nd week, purée in 3-4th weeks and normal diet after one month of surgery. The patient were reviewed at 10 days, 1, 3, 6 and 12 months.

**Blood sample processing**

Laboratory personnel of the Analysis Unit Clinical Laboratory of University Associated Hospital Parque San Antonio performed the extraction of blood samples from patients with at least 8 hours fasting. The laboratory samples analyzed were total cholesterol, HDL cholesterol, triglycerides and glucose by ultraviolet-visible spectroscopy. LDL-cholesterol was calculated by Friedman formula. C-peptide by chemiluminescent, and glycated hemoglobin by high performance liquid chromatography (HPLC)/UV-visible detector.

Normal levels of our laboratory are total cholesterol 130-220 mg/dL, HDL cholesterol > 35 mg/dL, LDL cholesterol < 150 mg/dL, triglycerides 40-160 mg/dL and glucose 65-105 mg/dL.

**Statistical analysis**

Descriptive statistics was used for comparisons. Differences among groups were analyzed by ANOVA when appropriate, and measures of central tendency according to study variables. Besides, we use percentages on gender, age, BMI, presence or absence of diabetes and its evolution time. For quantitative variables were used mean and standard deviation. To determine the association among explanatory and dependents variables was performed linear regression analysis.

We use SPSS (version 20 for Windows, SPSS, Chicago IL) and Excel 2010 programs.
Results

The 60% were non-diabetic and 40% were diabetic patients. By gender, 51% were women and 49% were men. The predominant age group was ≥ 51 years old (32% of patients). The mean age was 44 ± 13 years. The morbid obesity was predominant. The mean of evolution of T2DM was 13 ± 8 years.

Non-diabetic patients presented triglycerides 161 ± 144 mg/dl, total cholesterol 208 ± 45 mg/dl, HDL cholesterol 48 ± 13 mg/dl, LDL cholesterol 134 ± 44 mg/dl, glucose 97 ± 22 mg/dl, C-peptide 3 ± 1 ng/mL and HbA1c 5 ± 0%.

Diabetic patients presented triglycerides 165 ± 99 mg/dl, total cholesterol 188 ± 40 mg/dl, HDL cholesterol 45 ± 14 mg/dl, LDL cholesterol 112 ± 33 mg/dl, glucose 188 ± 68 mg/dl, C-peptide 2 ± 1 ng/mL and HbA1c 8 ± 1%.

Lipid metabolism

Patients with diabesity were most affected in certain laboratory studies as follow: Triglycerides were higher in diabetic patients (35% of BMI < 35, and 63% of BMI > 35) compared to non-diabetic patients (40% of BMI < 35, and 31% of BMI > 35). The 10% and 34% of non-diabetic patients BMI < 35 and > 35 respectively, had higher total cholesterol compared to 20% and 30% of diabetic patients BMI < 35 and > 35 respectively. Patients with the lowest levels of HDL cholesterol were 12% of non-diabetic compared to 42% of BMI > 35. Once again, the presence of diabetes increases the percentage of patients with LDL cholesterol abnormalities. LDL cholesterol is altered without a tendency to weight gain or adding T2DM.

Lipid profile is altered if the weight or BMI increases as show in figure 1.

As shown in the figure 1, there is a tendency to altered laboratory results with the increment of body weight. This upward trend of lipid profile may explain the vascular complications that may cause higher mortality in these patients.

Glycemic metabolism

There are high percentage of non-diabetic patients with altered serum glucose (58% of BMI < 35 compared to 36% of BMI > 35). C-peptide were found higher just in non-diabetic patients (20% of BMI < 35, and 19% of BMI > 35). The 32% of diabetics BMI < 35 had low C-peptide, and 8% had high levels. The 5% of diabetics BMI > 35 had low C-peptide and 36% had high levels.

![Fig. 1.—Altered metabolism of lipid with increased BMI.](image-url)
Glycosylated hemoglobin was found higher in non-diabetic patients BMI < 35 (40%) compared to BMI > 35 (13%), but diabetic patients had higher levels (100% of BMI < 35, and 84% of BMI > 35).

The data obtained showed how the weight gain is closely linked to the onset of metabolic diseases like diabetes.

Table II, show in detail the percentage of glucose alteration according to the level of BMI and the presence or absence of diabetes.

We found a high percentage of non-diabetic patients with hyperglycemia and still no diagnosis of diabetes, therefore it is important that all patients considered as non-diabetics performed serum glucose test in order to prevent the onset of diabetes.

We too found a high percentage of patients with poorly controlled diabetes. Figure 2 shows the mean trend of glycosylated hemoglobin and C-peptide as BMI increases.

By linear regression analysis, we obtained the following results (table III).

The increment of weigh increases the C-peptide, BMI increases total cholesterol, LDL cholesterol and C-peptide. Age increases triglycerides, LDL cholesterol, glucose, C-peptide and glycated hemoglobin. The evolution of T2DM increases the triglycerides and glucose. These data strongly suggest that the addition of factors mentioned in the table III may cause worsening of diabetes.

Discussion

Diabetes and obesity are diseases with high prevalence worldwide. Diabetes can lead to micro and macro vascular complications with significant impact on the patient and society. The impact of obesity on T2DM,
metabolic syndrome and several diseases are important, since they have both physical and psychological effect\(^{11,12,22}\). Worst of all is that there is no medical treatment to eliminate the progression of these diseases.

Both diseases have different effect on the metabolic state if one adds to the other\(^1\). It is important to know the functioning of the human body in its different types of metabolism for understanding the health damage, as occur if there is a sustained increase in weight that can impair health\(^11\).

There are a variety of treatments for both diseases, but just bariatric surgery offers long-term changes improving both disease and its comorbidities\(^{11,12,22}\). The importance of this study is because there is no information about the cumulative effect of the weight on the metabolism of lipids and glycemic with the addition of diabetes.

We evaluated 131 patients attending medical consultation in order to undergo to tailored One Anastomosis Gastric Bypass (BAGUA) because of their obesity and/or T2DM state. The presence of obesity and/or diabetes in these patients caused comorbidities as previously described\(^8\).

Subjects underwent a series of laboratory studies and were interpreted and analyzed statistically. These data indicate that increased BMI produces alterations in laboratory studies analyzed. The changes are prominent in patients with BMI > 35 where several comorbidities commonly are associated according to WHO\(^5\). Suzuki et al\(^24\) associate obesity with cardiovascular risk factors and T2DM. The Ontario Health Quality Study in 2005\(^27\) mention that obesity is associated with higher mortality independent of factors such as smoking. Patients with BMI < 30 are 50% more likely to die than non-obese people are, and the risk is twice from IMC > 35.

We agree with Diabetes Strategy National Health System of Spain 2012 National\(^3\), because they mention that obesity increases with age, and men are more affected than women are. As they said, our patients have altered laboratory studies especially in the age range of 51 years and predominantly in male patients. Diabesity patients have higher percentage of involvement.

The percentage of diabetic patients with abnormal lip profile is higher. From 31% to 63% of patients have hypertriglyceridemia, being most frequent in diabetic and obese patients. The 10% to 60% of patients had higher total cholesterol. From 12% to 45% have higher HDL cholesterol (predominantly in diabesity), and 57% to 100% had lower HDL cholesterol. This data shows higher cardiovascular risk with the increment of BMI as described by Savill\(^1\). These patients usually have insulin resistance due to hyperlipidemia as evidenced by Hu\(^16\). The CDC (8) mentions that higher BMI produces greater elevation of lipids associated with cardiovascular complications. Bille et al\(^34\) found that central obesity is related to higher levels of insulin and triglycerides circulating due to inflammatory role of adipose tissue that causes insulin resistance, ectopic lipid storage and release of dysfunctional inflammatory mediators affecting pancreatic islets, liver, muscle and hypothalamus, causing metabolic dysfunction as evidenced by other studies\(^{23,24}\).

The 32% of non-diabetic patients have hyperglycemia, 19% have higher C-peptide and 15% have elevated HbA1c. This shows undiagnosed diabetes as mentioned by Centers for Disease Control and Prevention\(^7\).

In general, the percentage of patients with high levels of C-peptide is higher if BMI increases, probably due to greater body mass that can lead to depletion of insulin production by excessive use of \(\beta\)-pancreatic cell in time, as demonstrated by studies ADA and EASD\(^4\).

Almost all diabetic patients have decreased C-peptide and elevated HbA1c. This highlights the higher risk of micro and macro vascular complications on this type of patients as mentioned by the United Nations\(^7\).

We found that diabetic patients have a greater increase in triglycerides and serum glucose with decreased C-peptide in relation to non-diabetics. These data confirm that dysfunctional adipose tissue causes

### Table III

<table>
<thead>
<tr>
<th>Levels of studies of laboratory</th>
<th>kg</th>
<th>BMI</th>
<th>P</th>
<th>Year of evolution T2DM</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides</td>
<td>0.06</td>
<td>0.017(^*)</td>
<td>0.012</td>
<td>0.000(^*)</td>
<td>0.16</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>0.0</td>
<td>0.000(^*)</td>
<td>0.008</td>
<td>0.000(^*)</td>
<td>0.06</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.0</td>
<td>0.000(^*)</td>
<td>0.21</td>
<td>0.000(^*)</td>
<td>0.7</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>0.0</td>
<td>0.000(^*)</td>
<td>0.0</td>
<td>0.000(^*)</td>
<td>0.085</td>
</tr>
<tr>
<td>Glucose</td>
<td>0.03</td>
<td>0.000(^*)</td>
<td>0.24</td>
<td>0.000(^*)</td>
<td>0.44</td>
</tr>
<tr>
<td>C-peptide</td>
<td>4.0</td>
<td>0.000(^*)</td>
<td>0.034</td>
<td>0.000(^*)</td>
<td>0.19</td>
</tr>
<tr>
<td>HbA1c</td>
<td>5.0</td>
<td>0.014(^*)</td>
<td>1.0</td>
<td>0.000(^*)</td>
<td>3.0</td>
</tr>
</tbody>
</table>

The data show that with increasing weight per kg and BMI in units, age in years, and every year since onset of T2DM, some laboratory studies were altered and may have deleterious effects on the human body. *Statistically significant \((p<0.05)\).
hypertriglyceridemia, insulin resistance, hyperglycemia and decrease of β-pancreatic cell function because of depletion (reduced C-peptide)\textsuperscript{17}. If all these data come together, the human body deteriorate with the development of the known complications. Diabetic patients despite having hypoglycemic treatment, continue with the progression of diabetes, as mentioned by the ADA and EASD\textsuperscript{16}.

Previous data confirmed that weight gain leads to increase of lipid metabolism alteration\textsuperscript{16}.

Patients who achieved morbid obesity were more affected than other kind of obesity, possibly because of the imbalance of adipose tissue expandability as described by Lumeng et al\textsuperscript{4} capable of triggering the comorbidities known by several mechanisms\textsuperscript{31}. It is impossible to identify obese patients who will have this imbalance, making it better preventing obesity and thereby directly influence the onset of diabetes\textsuperscript{12-14}.

Although the number of our patients is the main limitation of the study, the findings are very interesting and important, and should encourage further research into metabolic pathways, study larger amounts of patients long-term in order to prevent the development of several metabolic diseases.

Physicians are encouraged to advise bariatric or metabolic surgery in a timely manner to eliminate obesity and improvement or resolution of the whole complex of conditions including T2DM actions that can not only extend life, but also improve the quality of life\textsuperscript{17,18,27,30}.

Conclusions

The increment of weight produces metabolic disorders. Diabesity is well known that has serious and deleterious effects on the body. Diabesity and an increased duration of T2DM, generate higher percentages of patients with metabolic disorders compared to non-diabetics. The increment of age in years, the increment of weight, presence of diabetes and its time of evolution, produce cumulative alterations in specific metabolisms. There are high percentage of patients without diagnosed diabetes who have hyperglycemia. Although patients have a treatment for diabetes, advancing age and the years of evolution of diabetes, the glucose is rising along with triglycerides, which can influence the deleterious effects of complications on human body. The patients studied, due to its metabolic condition, took the best decision to undergo bariatric surgery for improvement or resolution of their diseases including diabetes mellitus, so it is important to inform the general population the benefits achieved today.

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