Prevalence of Abnormalities of Glucose Metabolism in Patients With Polycystic Ovary Syndrome

ABSTRACT

Patients with polycystic ovary syndrome (PCOS) present a higher risk for abnormalities of glucose metabolism (AGM). For to study this in our population, we submitted 85 patients, with body mass index (BMI) of 28.5 ± 6.6 kg/m^2 and aged 25.5 ± 5.4 years old, to an oral glucose tolerance test (OGTT), and assessed the impact of BMI on the prevalence of impaired glucose tolerance (IGT) and of diabetes mellitus (DM). The states of glucose tolerance were classified considering fasting plasma glucose (FPG) according to the American Diabetes Association (ADA) criterion and plasma glucose at 120 minutes according to the Word Health Organization (WHO) criterion. According to the ADA criteria, 83.5% classified as normal and 16.5% as with AGM, with 15.3% presenting impaired fasting glucose and 1.2% DM, while according to the WHO criteria, 68.2% were classified as normal and 31.8% as with AGM, with 27.0% of them presenting IGT and 4.8% DM. Seventy-three percent of PCOS patients with IGT by WHO criterion had normal FPG by ADA criterion. The prevalence of AGM for both criteria increased with the body mass index. In conclusion, we found a higher prevalence of AGM in PCOS patients than that found in the general population, being the highest in obese patients. Glycemia at 120 minutes on the OGTT identified more patients with AGM than fasting glycemia. We recommended that the assessment of AGM must be done by the OGTT in all patients with PCOS. **(Arq Bras Endocrinol Metab 2007;51/4:601-605)**

Keywords: Polycystic ovary syndrome; Impaired glucose tolerance; Diabetes mellitus

RESUMO

Prevalência de Anormalidades do Metabolismo de Glicose em Pacientes com a Síndrome dos Ovários Policísticos.
Pacientes com a síndrome dos ovários policísticos (SOP) têm um risco maior para desenvolver anormalidades do metabolismo da glicose (AMG). Para avaliarmos a prevalência dessas anormalidades na nossa população, submetemos 85 pacientes, com índice de massa corporal (IMC) de 28,5 ± 6,6 kg/m^2 e média etária de 25,5 ± 5,4 anos, a teste de tolerância oral à glicose (TTOG). Os estados de tolerância à glicose foram classificados considerando a glicemia de jejum (GJ; *American Diabetes Association* – ADA) e glicemia aos 120 minutos (G120; Organização Mundial de Saúde – OMS). De acordo com a ADA, 83,5% das pacientes foram normais e 16,5% com AMG, com 15,3% apresentando glicemia de jejum imprópria e 1,2% diabetes mellitus (DM). De acordo com a OMS, 68,2% foram normais e 31,8% com AMG, com 27,0% apresentando intolerância à glicose (IG) e 4,8% DM. Observamos que 73% das pacientes com IG pelos critérios da OMS apresentavam GJ normal pelos critérios da ADA. A prevalência de AMG para ambos os critérios foi maior entre as pacientes com IMC mais elevado. Conclusão: encontramos maior prevalência de AMG nas pacientes com a SOP do que na população geral, sendo mais elevada entre as pacientes obesas. Além disso, a G120 no TTOG identificou maior número de pacientes com AMG do que a GJ. Assim, recomendamos avaliação de AMG através do TTOG para todas as pacientes portadoras da SOP. **(Arq Bras Endocrinol Metab 2007;51/4:601-605)**

Descritores: Síndrome dos ovários policísticos; Intolerância à glicose; Diabetes mellitus

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Polycystic ovary syndrome (PCOS) is a heterogeneous disorder, characterized by chronic anovulation and hyperandrogenism, affecting between 6 to 10% of women of reproductive age (1). It is currently considered a complex metabolic disorder and a risk factor for diabetes mellitus (DM), cardiovascular disease and endometrial cancer (2-4). It is believed that insulin resistance might be a link between carbohydrate intolerance and the increase in cardiovascular risk and PCOS (5).

In 1992, Dalghren et al. (6) reported that the prevalence of DM in menopause women with PCOS was 15%. Recent reports on North American Caucasian and African-American origin patients established the prevalence of IGT as being 31.1–35% and DM as 7.5–10% in PCOS patients (2,7,8).

The aim of this study is to assess the prevalence of abnormalities of glucose metabolism (AGM) in PCOS patients from the city of São Paulo and to evaluate the usefulness of the recommendation of the American Diabetes Association (9) versus the Word Health Organization (WHO) (10) on diagnosis of carbohydrate tolerance states.

PATIENTS AND METHODS

All patients registered as having PCOS at the Outpatient Hirsutism Clinic of the Endocrine Unit of Hospital das Clínicas de São Paulo from 2000 to 2004 were studied retrospectively. The patients were referred to the clinic for hirsutism evaluation. The PCOS diagnosis was based on the presence of hirsutism and menstrual dysfunction, after exclusion of Cushing's syndrome, late-onset 21-hydroxylase deficiencies, thyroid dysfunction, hyperprolactinemia, or androgen-secreting tumor by appropriated tests. None of the subjects had other diseases or were taking any medication for at least 6 months prior to the study.

Oral glucose tolerance test (OGTT) was performed between 7:30 and 8:30 A.M. After an overnight fast, blood samples were obtained through an IV catheter placed in the forearm for the determination of fasting blood glucose. A 75 g of glucose load was given, and blood collected after 30, 60, 90 and 120 minutes thereafter, for determination of glucose.

Plasma glucose concentration was determined by the glucose oxidase method using a glucose analyzer (Beckman Instruments, Palo Alto, CA).

The states of glucose tolerance were classified considering fasting plasma glucose (FPG) according to the ADA criteria from 2003 (impaired fasting plasma glucose – IFG: plasma glucose > 99 mg/dL and < 126 mg/dL; DM: plasma glucose ≥ 126 mg/dL) (9) and plasma glucose at 120 minutes according to the WHO criterion from 1999 (IGT: plasma glucose ≥ 140 mg/dL and < 200 mg/dL; DM: plasma glucose ≥ 200 mg/dL) (10).

Statistical analyses

Unpaired and nonparametric Student's t-test was used to compare plasma glucose between the groups. Results are expressed as the means ± standard deviation (SD). A two-tailed p-value less than 0.05 was considered as statistically significant for all analyses.

RESULTS

Eighty-five patients with body mass index (BMI) of 28.5 ± 6.6 kg/m² and aged 25.5 ± 5.4 years old, met the adopted criteria of PCOS. All of them presented menstrual abnormalities. According to the BMI, 34.1% were normal, 31.8% were overweight and 34.1% of them were obese, while 7% were morbidly obese.

Regarding the prevalence of AGM, according to the WHO criteria, 68.2% were classified as normal and 31.8% as with AGM, been 27.0% with IGT and 4.8% with DM. According to the ADA criteria, 83.5% classified as normal and 16.5% as with AGM, with 15.3% presenting IFG and 1.2% DM.

Seventy-three percent of the PCOS patients with IGT by WHO criterion had normal fasting glucose levels by ADA criterion. Of the four patients with diabetes by the WHO criterion, one had fasting plasma glucose (FPG) > 126 mg/dL, one had FPG between 99 and 126 mg/dL and two had FPG < 100 mg/dL.

According to the BMI, the FPG was 86.4 ± 7.7 mg/dL, 90.9 ± 10.6 mg/dL and 95.3 ± 11.9 mg/dL in normal, overweight and obese patients, respectively, with a significant difference between normal and overweight (p= 0.04) and between normal and obese (p≤ 0.001) patients. The plasma glucose at 120 minutes of the GTTO was 115.6 ± 46.2 mg/dL, 115.7 ± 33.4 mg/dL and 133.3 ± 58.6 mg/dL in normal, overweight and obese patients, respectively, without significant differences among the groups. The prevalence of AGM by the BMI is shown in figure 1. There was an increased prevalence of AGM according to the increase in BMI. The plasma glucose at 120 minutes of OGTT identified AGM 6.76, 2.16 and 1.27 times more than FPG in the normal, overweight and obese patients, respectively.

According to the age range, the glycemia at 120 minutes of the OGTT was 110.3 ± 22.2 mg/dL for those < 20 yr (n= 12), 121.2 ± 56.8 mg/dL for 20 to 24 yr (n= 25), 118.9 ± 35.2 mg/dL for 25 to 29 yr (n= 33), 132.6 ± 83.2 mg/dL for 30 to 34 yr (n= 9) and 145.2 ± 36.4 mg/dL to ≥ 35 yr (n= 6), with significant difference only between the youngest and the oldest groups (p= 0.03). As can be seen in figure 2, there was a higher prevalence of AGM in the age group > 35 yr.
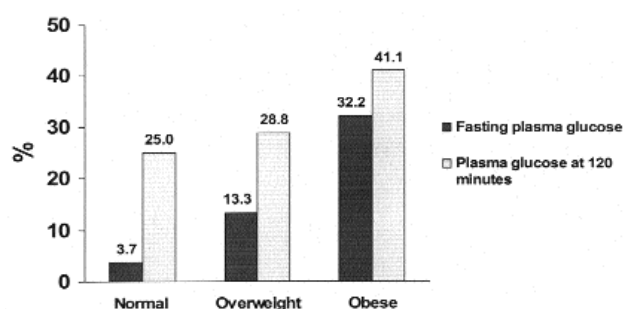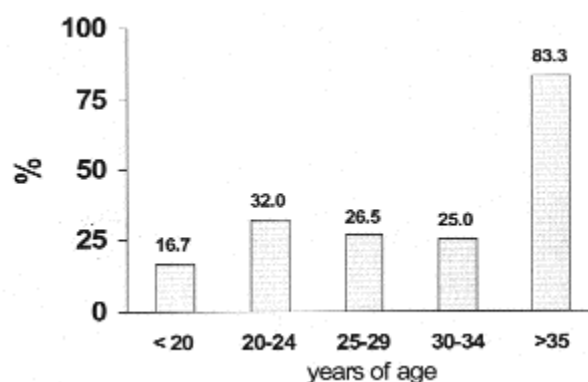
Figure 1. Prevalence of abnormalities of glucose metabolism according to the ADA criteria (fasting plasma glucose) and the WHO criteria (plasma glucose at 120 minutes of the oral glucose tolerance test) in patients with polycystic ovary syndrome according to body mass index.

Figure 2. Prevalence of abnormalities of glucose metabolism (plasma glucose at 120 minutes on the oral glucose tolerance test) in patients with polycystic ovary syndrome according to age.

DISCUSSION

In this study, the prevalence of AGM in patients with PCOS was 31.8% according to the WHO criteria, and 16.5% according to the ADA criteria. This prevalence was well above those reported among normal Brazilian women of similar ages. In a two-stage, multicenter, cross-sectional survey in a random sample of 21,847 individuals aged 30–69 yr from nine large cities, according to WHO recommendations, the overall rates were 7.6 and 7.8% for diabetes and IGT, respectively, with similar rates being found among whites (7.8%) and nonwhites (7.3%) (11). For the aged 30–39 yr, the prevalences were 2.7 and 5.9% for diabetes and IGT, respectively. In another study, in a two-stage, cross-sectional home survey in the city of Ribeirão Preto, SP, with an urban random sample of 1,473 individuals aged 30–69 years, the prevalences of IGT and DM based on WHO criteria were 12.1 and 7.7%, respectively (12). Differences in the diabetes rates for whites (11.6%) and nonwhites (13.3%) were not significant, while IGT was more prevalent among whites.

The prevalence rates of AGM in PCOS change according to the population study and the criterion used for the diagnosis of glucose intolerance. As one of the aims of this study was to compare the prevalence rate of AGM according to the WHO versus ADA criteria, we will discuss mainly the studies that also done this comparison. In the United States, according to the WHO criteria, the prevalence rates were 31.1% for impaired glucose tolerance and 1.5% for diabetes (2), while the ADA diagnostic criteria failed to detect a significant number of PCOS women with diabetes by post challenge glucose values (3.2% for glucose intolerance and 4.7% for diabetes). Considering the WHO

criterion, this prevalence was substantially higher than those found in a major-normal population-based study carried out in Second National Health and Nutrition Study with patients of similar ages (IGT: 7.8%; DM: 1.0%) (13) and also above those reported among United States normal Hispanic and African-American women of similar ages (14). These prevalence rates of IGT and DM did not differ in two groups of PCOS patients studied, one from an urban, ethnically-mixed group and one from a rural, ethnically-homogeneous group (2). A report by Ehrmann et al. (8) found similar prevalence rates in an ethnically-mixed PCOS population from the Chicago area, which could imply that PCOS is a more important risk factor for glucose intolerance in young patients than age and ethnicity (2,8).

A higher prevalence of glucose intolerance in PCOS patients according to the WHO criteria was also seen in a group of 79 patients from Thailand (IGT: 20.3%; DM: 9.5%) (15). However, when the fasting blood glucose was assessed according to the ADA criteria, the prevalence of IFG decreased to 3.8% and the prevalence of DM decreased to 6.3%.

Fasting glucose levels were poor predictors of AGM in this study, as well as in the study of Legro et al. in the United States (2) and in that of Weerakiet et al. in Thailand (15), since the ADA criteria failed to detect a significant number of PCOS patients with AGM. Considering the ADA criteria, 16.5% of our patients had AGM. On the other hand, considering the post challenge glucose value, the prevalence of these disturbances abnormalities increased to 31.84%. This means that, if we considered only the fasting plasma glucose value as a diagnostic criterion for AGM, one in two patients according to the ADA criteria would be missed. Similarly, one patient with diabetes according to the post-challenge glucose value

would be considered as having normal glucose tolerance by the fasting glucose value, according to the ADA criteria. This is especially true for patients with normal BMI, as glucose at 120 minutes of the OGTT detects 6.76 times more cases of AGM than fasting plasma glucose, and while in obese patients glucose at 120 minutes of the OGTT detects only 1.27 more cases of AGM than FPG.

In this study, only 34.1% of the patients were obese, with 7% of them being morbidly obese. In the study by Legro et al., 73% had a BMI ≥ 27 kg/m² (2), while in Thailand, only 26.6% of the study subjects were obese, in the same age range (15). As we observed, for FPG, a higher prevalence of AGM was attained using the WHO criteria. According to this criterion, the BMI impact on the prevalence of AGM was observed only for a BMI ≥ 30 kg/m², while according to the ADA criteria, there was a progressive impact of BMI on the prevalence rates of glucose intolerance, increasing from 3.7% in the range of < 25 kg/m² to 32.2% in the range of ≥ 30 kg/m². It is interesting to note that, although the prevalence of obesity in our population was greater than that observed in the study from Thailand (34.1% vs. 26.6%), the prevalence of the AGM, mainly which of diabetes, for both criteria, was much higher in Thailand. This way, risk factors others than BMI must be considered, as the genetic background, a positive family history of type 2 diabetes and the degree of hyperandrogenism.

We observed that the prevalence of AGM, by the WHO criteria, occurred before the one that is commonly seen by age in normal women. Similar results were observed by Legro et al., by the WHO criteria, although in a more advanced age range (> 40 yr). In the study of Weerakiet et al., from Thailand (15), the smaller prevalence of AGM according to WHO criteria was seen for patients less than 20 years of age (2.5%) and increased up to 11.4% in the other age ranges, without a clear influence for each age range. An important bias regarding these data is the lower number of patients in more advanced age range. Nevertheless, in the present study, obesity was not more prevalent in patients ≥ 35 yr than those in the other age ranges. It's possible that this increase in prevalence in the fourth decade of life can reflect the natural history of AGM in patients with PCOS. In fact, AGM, as categorized by WHO criteria, tends to worsen over time in women with PCOS, with a non-significant nearly 2-fold increase in the rates of conversion for subjects with PCOS and baseline normal glucose tolerance, without a concomitant change in BMI (16).

In conclusion, the risk of AGM among PCOS patients seems to be at least 2-fold higher, increasing with the BMI, and occurring at an earlier age than in the normal population. Glycemia at 120 minutes on the OGTT (the WHO criteria) identified more patients than fasting glycemia (ADA criteria), mainly in patients with normal BMI. We recommended that the assessment of AGM must be done in all patients with PCOS, been in those patients with normal BMI by the OGTT, and repeated over time, mainly after the 5th decade of life.

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