

The Prevalence of Glucose Intolerance in Women with Polycystic Ovary Syndrome

Kürşad Ünlühızarıcı* Ramiz Çolak* Yılmaz Şahin** Fahri Bayram*
Fahrettin Keleştimur*

Erciyes University Medical School, Kayseri, Turkey

* Departments of Endocrinology

** Gynecology and Obstetrics

Polycystic ovary syndrome (PCOS) which is commonly associated with insulin resistance is one of the most common endocrine disorders in women. In order to determine the prevalence of glucose intolerance in women with PCOS in our region, we have performed OGTT in 46 women who were diagnosed as PCOS. Fifteen healthy women served as a control group. Glucose tolerance was abnormal in 10 (21.7%) women: 8 (17.4%) had impaired glucose tolerance (IGT) and 2 (4.3%) had type 2 diabetes mellitus. Women with PCOS had significantly higher basal and stimulated insulin levels. These results show that the prevalence of IGT and Type 2 diabetes mellitus was higher in women with PCOS than expected in general population. We think that women with PCOS should be evaluated not only with reference to the gynecological aspects but also the metabolic aspects of the disease.

Key words : Polycystic ovary syndrome and glucose intolerance

Introduction

Impaired glucose tolerance (IGT) is a prediabetic state characterized by mild elevations in blood glucose levels. It is usually asymptomatic and its diagnosis requires an oral glucose tolerance test (OGTT) (1). The prevalence of Type 2 diabetes mellitus (DM) varies among the different populations and since it is an important health problem, strategies to its prevention or at least the delay of its onset have recently received great attention (2). Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women and it is characterized by hirsutism, oligomenorrhea, obesity

and insulin resistance (3). Because of the insulin resistance, women with PCOS are candidates for impaired glucose tolerance or Type 2 DM besides the reproductive dysfunction. In the present study, we evaluated the PCOS women with a standard OGTT to determine the prevalence of glucose intolerance in our region.

Patients and Methods

This study was carried out in the Endocrinology outpatient clinic of Erciyes University Hospital among women with PCOS. The diagnosis of PCOS was made on the basis of three or more of the following criteria: polycystic ovaries on pelvic ultrasound examination, oligo/amenorrhea, hirsutism, hyperandrogenemia and serum luteinizing hormone (LH)/serum follicle stimulating hormone (FSH) > 2. All the patients had hirsutism (modified Ferriman-Gallwey score >8) (4) and hyperandrogenemia (serum free testosterone > 3.1 pg/ml, normal range 0.3-3.1) Women with other causes of hirsutism such as

Correspondence address:

Kürşad Ünlühızarıcı
Department of Endocrinology, Erciyes University
Kayseri, TURKEY
E-mail: kursad@erciyes.edu.tr
Tel : 0 352 437 49 38
Fax : 0 352 437 58 07

Cushing's syndrome, non-classic congenital adrenal hyperplasia and androgen secreting tumors were not included in the study and these patients were excluded by appropriate tests. Fifteen healthy women with regular menses, no hyperandrogenemia and no evidence of hirsutism were served as a control group. None of the subjects in the PCOS or control group had received any medication for at least one year before the study. Before the treatment of hirsutism all patients had OGTT. Blood samples were obtained at baseline and at 30 min intervals for 2 h measurement of glucose and insulin after ingestion of 75 g glucose. Glucose tolerance was evaluated using American Diabetes Association (ADA) criteria (5). The glucose and insulin responses to OGTT were also expressed as area under the curve (AUC) estimated by the trapezoidal rule. The results are expressed as mean \pm S.E.M. The results of the PCOS and control subjects were compared by using the Mann-Whitney U test. A p value of < 0.05 was regarded as statistically significant.

Results

OGTT was performed in 46 PCOS women. The mean age was 24.6 ± 1.1 (19-30) years. The mean body mass index (BMI) was 27.1 ± 1.2 kg/m². PCOS women and control subjects did not differ in mean age or BMI. Using the 2 h blood glucose level during OGTT, 2 (4.3%) women had DM whose basal glucose values were compatible with impaired fasting glucose (IFG; fasting blood glucose level higher than 110 mg/dl and lower than 126 mg/dl),

Table 1. Clinical and laboratory characteristics of the PCOS women and control subjects*.

	PCOS women	Control subjects	P value
Age (year)	24.6 \pm 1.1	27.1 \pm 1.2	NS
BMI (kg/m ²)	27.1 \pm 1.2	26.1 \pm 0.9	NS
Hirsutism score	16.1 \pm 2	4.1 \pm 0.2	< 0.0005
FPG (mg/dl)	80.2 \pm 2.8	72.9 \pm 1.4	NS
AUCglucose (mg/dlx120 min.)	14816.2 \pm 787.2	12358.9 \pm 484.1	NS
Fasting insulin (μ IU/ml)	23.5 \pm 3.4	6.1 \pm 1.7	< 0.005
AUCinsulin (μ IU/mlx120 min.)	12218.7 \pm 1224.8	2411.8 \pm 261.7	< 0.005

* Results are given after the exclusion of the two patients with diabetes mellitus.

these being 115 and 120 mg/dl respectively, and 8 (17.4%) had IGT while 36 (78.3%) had a normal glucose tolerance test result. Some of the clinical and laboratory characteristics of the patients are shown in Table 1. Fasting and AUC insulin values are significantly ($p < 0.005$) higher in women with PCOS than in control subjects. Although the fasting plasma glucose and AUC glucose values were higher in PCOS women than in control subjects, they did not reach a significant level.

Discussion

Type 2 DM is a global public health problem and its prevalence differs widely among the various populations. Pathogenesis of the disease involves a combination of impaired insulin secretion and insulin resistance and both genetic and environmental factors (6). Type 2 DM is the end of a long metabolic derangement and IGT is a prediabetic glucose intolerant stage characterized by insulin resistance (7). During the last few years a number of studies have shown that PCOS is associated with insulin resistance and hyperinsulinemia (8,9,10) and women with PCOS have a substantially higher prevalence of IGT and diabetes than in age and weight matched healthy women (11).

In the present study, 2 (4.3%) patients had DM who are not aware of their disease. Also 17.4% of the patients had IGT. This prevalence of IGT is notably higher than the prevalence of IGT and DM previously known to us. Recently, we showed that the prevalence of diabetes and IGT was 6.9% and 9% respectively, in subjects over 30 years old (12). Also this study (12) showed that in a relatively young population (age 30-39) in our region the prevalence of type 2 DM and IGT was 2.3% and 5.3%, respectively. These results indicate that women with PCOS have a higher glucose intolerance than expected in our region. Ehrmann et al (11) reported the prevalence of IGT and type 2 DM as 35% and 10% respectively, in women with PCOS. These results are notably higher than ours. We think that this may be due to an important difference in BMI of the participants in the two studies (33 vs 27). Although it has been shown that insulin resistance in women with PCOS is not solely dependent on obesity (13), obesity itself an important contributing factor to insulin resistance.

It has been suggested that macrovascular disease develops earlier than microvascular disease and these abnormalities occur before the onset of diabetes. Also it has been suggested that since IGT is a disease of the non-fasting state, metabolic derangements during the fasting period may be inadequate (14). Additionally, in women with PCOS, the conversion of IGT to Type 2 DM is accelerated as much as 5 to 10 fold (11). So, our study and the others show that women with PCOS should be closely monitored for the presence of glucose intolerance.

A number of therapies have been successfully used for the treatment of insulin resistance in PCOS, including metformin (8,15,16) and troglitazone (17), and improvement in insulin sensitivity resulted in the improvement of metabolic and gynecological parameters such as oligomenorrhea and facilitation of pregnancies. In most women with PCOS the most troublesome complaint of the patient is hirsutism and the physician sometimes does not give enough attention for the metabolic features of the disease. We think that IGT is a relatively asymptomatic stage and patients may survive without any symptom for a long time. But in women with PCOS manifestations of androgen excess usually bring the patients to clinical examinations and may lead to early detection of IGT. Additionally, in some studies, it has been shown that treatment of insulin resistance may also improve menstrual irregularities, ovarian function and follicular growth (16,17,18)

In conclusion, women with PCOS are at a high risk for the development of IGT and subsequently Type 2 DM. While managing the hirsutism and menstrual irregularities, metabolic evaluation of the patient should be done.

References

- Polonsky K, Sturis J, Bell G. Non-insulin dependent diabetes mellitus: genetically programmed failure of the beta cell to compensate for insulin resistance. *N Eng J Med* **334**: 777-783, 1996.
- Edelstein SL, Knowler WC, Brain RP, Andres R, Barnett-Concor EL, Dowse GK, Haffner SM, Pettitt DJ, Sorokin JD, Muller DC, Collins VR, Hamman RF. Predictors of progression from impaired glucose tolerance to NIDDM: an analysis of six prospective studies. *Diabetes* **46**: 701-710, 1997.
- Franks S. Polycystic ovary syndrome. *N Eng J Med* **333**: 853-861, 1995.
- Hatch R, Rosenfield RL, Kim MH, Tredway D. Hirsutism implications, etiology and management. *Am J Obstet Gynecol* **140**: 815-830, 1981.
- The expert committee on the diagnosis and classification of diabetes mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* **21** (Suppl 1): S5-S19, 1998.
- Gerich JE. Pathogenesis and treatment of type 2 (Non-insulin dependent diabetes mellitus) diabetes mellitus. *Horm Metab Res* **28**: 404-412, 1996.
- Nielsen HB, Groop LC. Metabolic and genetic characterization of prediabetic states. Sequence of events leading to Non-insulin dependent diabetes mellitus. *J Clin Invest* **94**: 1714-1721, 1994.
- Nestler JE, Jacubowicz DJ. Decreases in ovarian cytochrome P450c17a activity and serum free testosterone after reduction of insulin secretion in polycystic ovary syndrome. *N Eng J Med* **335**: 617-623, 1996.
- Kandarakis ED, Dunaif A. New perspectives in polycystic ovary syndrome. *Trends in Endocrinol Metab* **1**: 267-271, 1996.
- Şahin Y, Ayata D, Keleştimur F. Lack of relationship between 17-hydroxyprogesterone response to buserelin testing and hyperinsulinemia in polycystic ovary syndrome. *Eur J Endocrinol* **136**: 410-415, 1997.
- Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK, Imperial J. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. *Diabetes Care* **22**: 141-146, 1999.
- Keleştimur F, Çetin M, Paşaoğlu H, Çoksevrim B, Çetinkaya F, Ünlühızarcı K, Ünal Ş, Köker AH. The prevalence and identification of risk factors for type 2 diabetes mellitus and impaired glucose intolerance in Kayseri, Central Anatolia, Turkey. *Acta Diabetol* **36**: 85-91, 1999.
- Chang JR, Nakamura RM, Judd HL, Kaplan SA. Insulin resistance in nonobese patients with polycystic ovary syndrome. *J Clin Endocrinol Metab* **57**: 356-359, 1983.
- Perry RC, Baron AD. Impaired glucose tolerance. Why is it not a disease? *Diabetes Care* **22**: 883-885, 1999.
- Ünlühızarcı K, Keleştimur F, Bayram F, Şahin Y, Tutuş A. The effects of metformin on insulin resistance and ovarian steroidogenesis in women with polycystic ovary syndrome. *Clin Endocrinol* **51**: 231-236, 1999.
- Velazquez EM, Mendoza S, Hamer T, Sosa F, Glueck CJ. Metformin therapy in polycystic ovary syndrome reduces hyperinsulinemia, insulin resistance, hyperandrogenemia and systolic blood pressure while facilitating normal menses and pregnancy. *Metabolism* **43**: 647-654, 1994.
- Ehrmann DA, Schneider DJ, Sobel AE, Cavaghan MK, Imperial J, Rosenfield RL. Troglitazone improves defects in insulin action, insulin secretion, ovarian steroidogenesis and fibrinolysis in women with polycystic ovary syndrome. *J Clin Endocrinol Metab* **82**: 2108-2116, 1997.
- Pirwany IR, Yates RWS, Cameron IT, Fleming R. Effects of the insulin sensitizing drug metformin on ovarian function, follicular growth and ovulation rate in obese women with oligomenorrhoea. *Hum Reprod* **14**: 2963-2968, 1999.