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Research Paper

Evaluation of glucose metabolism in women with multiple ovarian follicles

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Abstract

Objective: To investigate glucose metabolism in women with multiple ovarian follicles (MOF) and explore the relationship between glucose metabolism, insulin resistance and body weight. **Methods:** We evaluated 46 women with MFO and 30 normal women as controls. All the subjects were given 75g of glucose orally in order to perform the oral glucose tolerance test (OGTT) and insulin releasing test (IRT), and they were also evaluated for insulin resistance using the insulin resistance index with homeostatic model assessment (HOMA). **Results:** The occurrence of impaired glucose tolerance in women with MOF was 10.87%, which was significantly higher than that in the control group (3.33%, $P < 0.05$). The rate of insulin resistance was 30.43% in the study group as compared to 10.00% in the control group. The results showed that there was significant difference between the two groups ($P < 0.05$). The levels of FSH, LH, PRL, E_2, T and P between the two groups had no significant difference ($P > 0.05$). BMI in women with impaired glucose tolerance was correlated positively to insulin resistance ($r = 0.567$, $P < 0.05$). **Conclusion:** Abnormal glucose metabolism was observed in women with unitary multiple ovarian follicles, and this could be attributed to obesity and insulin resistance. Women with MOF and associated obesity should be subjected to OGTT so that their glucose levels can be monitored as a preventive measure.

Keywords: multiple ovarian follicles, glucose metabolism, insulin resistance, impaired glucose tolerance

INTRODUCTION

Some women were detected with multiple ovarian follicles (MOF) but did not present with any clinical symptoms and/or any biochemical features of menstrual disorder and hyperandrogenism. Under type-B ultrasonic inspection, up to10 ovarian follicles with diameters from 0.2 to 0.8 cm can be detected in either unilateral or bilateral ovaries but without any mesenchymal diversity or augmentation in the volume of the ovaries. Although studies like ours are rarely conducted, we chose our focus, evaluating glucose metabolism in women with MOF, with the objective that such a study will assist in early detection and thus, treatment of such cases.

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MATERIALS AND METHODS

Subjects

This study included 46 women with MOF who attended the Reproductive Endocrinology Clinic at the First Hospital of Xi'an Jiaotong University between May 2004 and December 2005. Their age ranged from 17 to 33 (22.3 ± 3.6)years. The control group consisted of women with normal menstrual cycles who came for progestation consultation, aged 21-30 with an average age of 21.3 ± 4.1years. There was no statistical difference in age ($P > 0.05$).

Diagnostic criteria for MOF: Women with more than 10 ovarian follicles with diameters ranging from 0.2 to 0.8 cm, (detected by type-B ultrasonic inspection in either unilateral or bilateral ovaries). The levels of hormones, including follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin

(PRL), estradiol (E_2), progesterone (P), and testosterone (T) assayed during the 3rd to 5th day of menstrual cycle, were normal. These women did not have any menstrual problems nor did they present with hirsutism or acne. Endocrine disorders were not present in these women.

Standard of control group

Women with less than 8 ovarian follicles in each ovary, (detected as above). The levels of hormones, including follicle-stimulating hormone (FSH), lut enizing hormone (LH), prolactin (PRL), estradiol (E_2), progesterone (P), and testosterone (T) assayed during the 3rd to 5th day of menstrual cycle, were normal. These women also had normal menstrual cycles and did not have hirsutism or acne. Endocrine disorders were not present in these women either.

Methods

Measurement of body mass index (BMI) and waist-to-hip ratio (WHR): the body weight, body height, waist circumference and hip circumference of all the subjects for accurate calculation of their BMI and WHR were measured by the same technician.

Ferriman-Gallwey score: the Ferriman-Gallwey score was used to evaluate hirsutism[1].

Type-B ultrasonic inspection: all subjects were examined by Type-B ultrasonic inspection on the 3rd to 5th day of their menstrual cycles by the same technician. The unmarried women were examined using trans-abdominal ultrasound with a 3.5 MHz probe and the married women were examined using transvaginal ultrasound with a 7.5 MHz, Hitachi EUB 500.

Assay of sex hormones: 4 ml venous blood was collected from all the subjects on fast on the 3rd to 5th day of their menstrual cycles. The serum was separated and kept in a freezer below 60℃. Serum levels of FSH, LH, PRL, E_2, P and T were assayed using a radioimmunoassay (RIA) kits which were made by Depu Biotechnology Corporation in Tianjin.

Oral glucose tolerance test (OGTT) and synchronous insulin releasing test (IRT): after measuring the fasting blood glucose levels of the subjects, they were given 75g of glucose powder orally. Venous blood samples of these subjects were then taken after 30 min, 60 min, 120 min and 180 min, glucose levels were measured by the glucose oxidase method, and insulin levels were measured by radioimmunoassay.

Evaluation Criteria

Standard for impaired glucose tolerance (IGT): blood glucose ($7.8 \leqslant BG \leqslant 11.1$ mmol/L OGTT 120 min)[2]

Assessment of insulin resistance (IR): homeostasis model assessment of insulin resistance (HOMA IR)[3]. HOMA IR = fasting serum glucose (mmol/L) × fasting blood insulin (mIU/L)/22.5[4]. IR was judged if HOMA IR was greater than 2.69 which were calculated according to the prediction of the National Diabetes Prevention and Cure Group[5].

Diagnosis of diabetes: fasting blood glucose ≥ 7.0 mmol/L or blood glucose ≥ 11.1 mmol/L (OGTT 120 min)[2].

Statistical Analysis

SPSS 12.0 was applied to analyze data and the data was expressed as mean ± SD and analyzed with *t*-test. $P < 0.05$ was considered statistically significant.

RESULTS

Comparison of the general state

The BMI of the women in the study group was significantly higher than that of the women in the control group. This difference in their BMI was of statistical significance, but there was no significant difference in age, F-G score, and WHR of the two groups (***Tab 1***).

Tab 1 **Comparison of Age, BMI, F-G, and WHR between the two groups** ($\bar{x} \pm s$)

Group	*n*	Age (Year)	BMI (kg/m²)	F-G	WHR
MOF	46	22.300 ± 3.6	24.63 ± 5.12*	6.01 ± 1.8	0.62 ± 0.31
Control	30	22.323 ± 4.1	22.51 ± 3.72	5.81 ± 1.6	0.54 ± 0.26

*$P < 0.05$ *vs.* control

Comparison of glucose tolerance

There was significant difference for the glucose tolerance between the two groups. In the study group, 41 women had normal glucose tolerance. The incidence of IGT in the study group was 10.87% (5/46). In the control group, 29 women had normal glucose tolerance. The incidence of IGT in the control group was 3.33% (1/30). The two groups had a significant statistical difference ($P < 0.05$) in their glucose tolerance levels.

Comparison of sex hormones

There was no significant difference ($P > 0.05$) in the levels of FSH, LH, PRL, E_2, P and T between the two groups (***Tab 2***).

Comparison of fasting serum glucose (FSG), insulin (INS) and HOMA IR

There was a significant difference ($P < 0.05$) in

Tab 2 **Serum levels of FSH,LH,PRL,E_2,and T in the two groups of women** ($\bar{x} \pm s$)

Group	*n*	FSH (IU/L)	LH (IU/L)	PRL (Ug/L)	E_2 (pmol/L)	T (nmol/L)
MOF	46	7.81 ± 3.26	13.58 ± 8.69	16.64 ± 13.93	112.53 ± 37.83	2.08 ± 1.89
control	30	8.10 ± 3.98	9.20 ± 5.70	14.63 ± 8.12	176.58 ± 142.56	1.93 ± 0.87

insulin resistance among the women in the two groups. The incidence of insulin resistance in the study group was 30.43% (14/46) compared to 10.00% (3/30)in the control group. A significant statistical difference ($P < 0.05$)was also observed in the insulin levels and HOMA IR levels between the two groups. However, there was no significant statistical difference in the FSG levels between the two groups(***Tab 3***).

Relationship between BMI and IR in women with IGT in the study group: The HOMA IR had positive correlation with BMI($r = 0.577, P < 0.05$).

Tab 3 **Comparison of FSG,INS,and HOMA-IR in the two groups** ($\bar{x} \pm s$)

Group	*n*	FSG(mmol/L)	INS(mIU/L)	HOMA IR	IR
MOF	46	5.58 ± 0.17	18.46 ± 10.21*	4.80 ± 0.18*	30.43%(14/46)*
Control	30	4.08 ± 0.81	15.18 ± 10.34	2.98 ± 0.67	10.00%(3/30)

*$P < 0.05$ *vs*. control

DISCUSSION

Changes in Glucose Metabolism in Women with MOF

The results showed that 14 cases had insulin resistance in the MOF group. The incidence rate of IR was 30.43%, significantly higher than that of the control group (P <0.05), whereas the sex hormone (FSH,LH,PRL,E_2,Pand T) of the two groups had no significant difference($P > 0.05$). There have been many studies which have shown that insulin resistance is directly related to obesity[6-9]. Our study also shows that the BMI of the MOF group was significantly higher than that of the control group ($P < 0.05$), and the BMI had positive correlation with IR for women with impaired glucose tolerance($r = 0.577$, $P < 0.05$), which implied that higher body weight might be the reason for the higher incidence of IR in the MOF group. The insulin resistance may be the cause of multiple ovarian follicles in obese women. Some scholars point out that whatever the reason of polycystic ovarian syndrome(PCOS), the hyperinsulinemia will aggravate the hyperandrogenism which will cause feedback and ultimately make for a vicious cycle[10-12]. Some studies also indicate that MOF may be the protophase sign of typical PCOS or indicate different stage of disease development. If the insulin resistance of these women is not corrected in time, there may be appearance of clinical manifestations and biochemical changes of hyperandrogenemia, which will influence their reproductive functions. The impaired glucose tolerance, (the disorder of glucose metabolism between normal and the diabetics state), has a high risk of causing type-2 diabetes and cardiovascular disease [13-15]. In normal people, the damage due to glucose tolerance becomes more serious with age, and in patients with PCOS, 35% of them will have glucose tolerance or diabetes[16,17]. In our study, 5 cases of impaired glucose tolerance was noted in the MOF group with an incidence rate of 10.87%, which was significantly higher than that of the control group incidence rate 3.33%($P < 0.05$). Our study showed that the latent disorder of glucose metabolism could be related to insulin resistance and body weight in obese women with MOF, which indicated that emphasis should be put on the monitoring and tracing of glucose metabolism in these women, especially those who were overweight.

Significance and Evaluation method of Glucose Tolerance Monitoring in Women with MOF

There have been research reports that positive intervention in the early stages of patients with disorders of glucose metabolism could prevent the genesis of type 2 diabetes [18]. A typical case of PCOS and related disorders of glucose metabolism can be easily diagnosed in the clinics;however cases of women with MOF have usually been ignored both by the patients and the clinicians, largely due to the lack of typical clinical manifestation and definite diagnostic criteria for MOF. Tests for glucose metabolism were rarely considered in such cases. Therefore, it was difficult to properly detect glucose metabolism in women with MOF. Our study showed that although the incidence rate of the glucose metabolism disorder and IR in these women was lower than those women with PCOS(the incidence rate of IR for patients with

PCOS was 50% to 70%)[19], and compared to the control group, the difference had statistical significance($P < 0.05$). This implied that it is important to monitor the glucose metabolism of women with MOF, especially those who are overweight. Although the evaluation of IR still lacks a unified standard, the HOMA IR has already been widely used in clinical work [20]. For women with MOF, especially those who are overweight, regular tests of OGTT and IRT are necessary. Based on the result of HOMA IR, early diagnosis and thus proper intervention can be applied to prevent the development of PCOS.

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