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Changes in inflammatory factors, oxidative stress, glucose and lipid metabolism, and insulin resistance in patients with polycystic ovary syndrome

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a common disease in women, affecting women's menstruation and significantly impacting women's physical and mental health. Studies have shown that insulin resistance has an important relationship with polycystic ovary. It is of great significance to explore the changes of inflammatory factors, oxidative stress, glucose and lipid metabolism, and insulin resistance in patients with PCOS. In the study process, 642 polycystic ovary patients in the first half of 2019 were divided into insulin resistance (n=357) and non-insulin resistance (n=285) groups. Oxidative stress index, glucose, and lipid metabolism index, and inflammatory factors were detected during the study process. The results showed that the levels of hs-CRP, TNF- α, and IL-6 in the IR group were 5.9mg/L, 9.2μg/L, and 87.2ng /ml, while those in the non-IR group were 4.6mg/L, 6.3μg/L and 51.5ng/ml, respectively. Thus, IL-6 and insulin levels maintain a dynamic balance. Low levels of IL-6 can promote insulin secretion, while high levels can inhibit its secretion. The results of this study will provide a specific clinical reference value for the prevention and treatment of polycystic ovary syndrome.

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Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of childbearing age, with an incidence rate of 4%-12% (1). PCOS has a variety of clinical manifestations, such as delayed menstruation or even absence of menstruation, obesity, acne, hirsutism, acanthosis, infertility, etc (2). The biochemical changes, pathogenesis, and clinical manifestations of PCOS are very different, and the pathological reason is still unclear. Long-term complications include hypertension, hyperlipidemia, cardiovascular disease, diabetes, etc. (3).

The metabolic characteristics of polycystic ovary syndrome are abnormal glucose metabolism, abnormal lipid metabolism, obesity, cardiovascular diseases, and non-alcoholic fatty liver disease (4). Abnormal metabolism caused by polycystic ovary syndrome can affect women's life. Because of the persistent condition in Kaohsiung, the incidence rate of cardiovascular disease may continue to increase in postmenopausal women with polycystic ovary syndrome. Severe cases can even cause reproductive dysfunction, easy to cause endometrial cancer, great harm (5).

Because the pathogenesis of PCOS is still unclear, most of the treatment of PCOS is limited to symptomatic treatment (6). Clinically, Diane combined with metformin is usually used to improve Hyperandrogenemia (HA) and insulin resistance (IR). Metformin is an insulin sensitizer. It can increase the sensitivity of target tissues to insulin and reduce the stimulating effect of insulin on thecal cells and the level of luteinizing hormone (LH) (7). Recent studies have shown that metformin can regulate the activities of steroid hormone synthesizers (such as hsd382, capital) and mitochondrial respiratory chain complex to inhibit androgen production from improving HA. . In addition, metformin can improve IR and PCOS by inhibiting the internal reaction and reducing inflammatory factors. Of course, some studies have shown that metformin combined with Diane in the treatment of PCOS improves the ovulation rate and pregnancy rate rather than increasing the live birth

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rate based on correcting endocrine disorders (5). Thiazolidinediones, such as pioglitazone, are also used to treat insulin sensitivity. The improvement mechanism of pioglitazone is to combine with nuclear receptors after entering target cells and activate highly selective peroxisome proliferator-activated receptor-gamma nuclear transcription factor to improve IR in the human body (8). Pioglitazone can also directly inhibit enzyme activity from reducing ovarian and ovarian function; the basic androgen secretion of the adrenal gland is to achieve the purpose of lowering androgen levels (9). Therefore, thiazolidinedione is more effective than metformin in patients with severe IR.

Insulin resistance (IR) is an essential factor that leads to impaired glucose tolerance and diabetes mellitus. Impaired glucose tolerance (IGT) is a particular metabolic state between diabetes mellitus and average blood glucose, which is reversible and usually shows hyperglycemia after meals (9, 10). IGT usually has no clinical manifestations, and oral glucose tolerance (OGTT) is required for diagnosis and confirmation, so IGT is often ignored (11). IGT is also a pathological process of diabetes, from normal glucose metabolism to diabetes, which may last for several years or more (12). These studies have differences in the diagnosis of PCOS, mainly because of the differences in national background, dietary habits, and lifestyle, which may impact IGT and DM. Through reasonable lifestyle adjustment or drug treatment can effectively delay or even prevent IGT-induced diabetes (13, 14).

On the other hand, oxidative stress refers to the fact that when the human body is exposed to various harmful stimuli, the oxidation degree exceeds the removal rate of oxides, resulting in an imbalance between the oxidation system and the antioxidant system, leading to tissue damage (15, 16). IR refers to the biological effect of the body on the decrease of insulin sensitivity and the low activity of normal dose insulin secretion. Modern studies have confirmed that oxidative stress is a critical factor in the appearance and deterioration of IR. Abnormal oxidative stress can lead to excessive ROS production, decreased expression of SOD, GSH PX, and catalase, and cause islet dysfunction, which is one of the mechanisms of IR (17-19). In recent years, studies have shown that the levels of proinflammatory cytokines (TNF, CRP, IL-6, etc.) in peripheral blood of patients with PCOS are increased (20-22). Therefore, it is speculated that PCOS may be a low-grade chronic inflammatory disease, and these pro-inflammatory cytokines may be closely related to IR (23).

In the current study, we tried to investigate the changes in inflammatory factors, oxidative stress, glucose and lipid metabolism, insulin resistance in patients with polycystic ovary syndrome.

Materials and methods

Experimental Objects

In this study, we selected patients with polycystic ovary syndrome in the first half of 2019. We divided these patients into two groups: the insulin resistance group and the non-insulin resistance group. The number of patients in the insulin resistance group was 357 and that in the non-insulin resistance group was 285. In addition, our selection criteria were based on the data of the National Diabetes cooperative group survey (24), In other words, HOMA-IR $\geq$ 2.69 is defined as insulin resistance. On the other hand, because the number of people we choose is not consistent, so the experimental data in this study are based on the proportion of the number of people.

The related indexes of the insulin resistance group and non-insulin resistance group were detected, including fasting blood glucose, fasting insulin level, hormone and metabolic indexes, SOD, GSH Px, MDA, hs CRP, IL-6, TNF - α.

Detection of glucose and lipid metabolism indices

For glucose and lipid metabolism tests, patients were required to fast for 8-12h one night before the test. Venous blood was drawn on an empty stomach in the morning of the next day to determine the serum glucose level (glucose oxidase method) and insulin level of each group.

1. Who diagnostic criteria for diabetes: fasting blood glucose 3.9-6.0mmol/l is normal; 6.1-6.9mmol/l is impaired fasting blood glucose.

2. Impaired glucose tolerance: 2 hours after a glucose load test, 7.8 mmol / L $\leq$ fasting blood glucose$\leq$ 11.1 mmol / L.

3. Diabetes mellitus: fasting blood glucose $\geq$ 7.0mmol/l, and/or 2 hours after glucose load test blood glucose $\geq$ 11.1mmol/l.

Determination of hormone and metabolic index

Before the test, the patients were required to fast for 8-12h one night in advance. The venous blood was drawn on an empty stomach in the morning of the next day. The levels of estradiol (E2), luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), testosterone (T) and thyroid-stimulating hormone (TSH) were determined by immune chemiluminescence (Beckman). We used Hitachi 7600 automatic analyzer to analyze blood lipids, including total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), apolipoprotein B (apoB) and apoAI (apoAI).

Diagnostic criteria for dyslipidemia: according to the Chinese guidelines for the prevention and treatment of dyslipidemia in adults, one of the following four criteria is considered as defining dyslipidemia:

1. TC≥6.22mmol/L
2. LDL-C≥4.14mmol/L
3. TG≥2.27mmol/L
4. HDL-C<1.04mmol/L

Detection of oxidative stress index

The detection method in this study is as follows: firstly, 4 ml of elbow vein blood was extracted from patients, and then centrifuged for 10 minutes with the rotating speed of 3000 R / rain, and then the upper serum was taken for detection.

1.Serum SOD was determined by the xanthine oxidase method

2. Serum GSH PX activity was determined by 5', 5-dithiobis (2-nitrobenzoic acid) colorimetric method

3.Serum MDA level was determined by thiobarbituric acid fluorescence method

4.Insulin resistance index (HOMA-IR)

$$HOMA\text{-}IR=(FINS*FPG)/22.5 \quad (1)$$

Fins is fasting insulin level, FPG is fasting blood glucose

Detection of inflammatory factors

For this purpose, we first took 4 ml of venous blood from patients, then centrifuged with the instrument for 10 minutes, rotating speed of 3000 R / rain, and took the upper serum for detection.

1. Serum high sensitive reactive protein (hs CRP) was determined by immunoturbidimetry
2. IL-6 was measured by radioimmunoassay
3. TNF - α level was determined by ELISA

Data Processing

In order to make the data more convincing, the experimental data are processed in this paper. In this paper, spss19.0 statistical software is used in the data processing. In the process of data processing, the χ^2 test is used for counting, the standard deviation is used for measurement data, and t-test is conducted. Whether there is the difference in data is judged by $P < 0.05$. If $P < 0.05$, it means that the data has statistical significance.

Then the basic formula of X^2 is as follows:

$$x^2 = \sum \frac{(A-T)^2}{T} \quad (2)$$

Results and discussion

Relationship between Abnormal Glucose and Lipid Metabolism and Insulin Resistance in Patients with Polycystic Ovary Syndrome

According to the patients with insulin resistance or not, this study divided them into two groups for data statistics, compared the difference of the incidence rate of impaired glucose tolerance and dyslipidemia between the two groups, and analyzed the correlation between impaired glucose tolerance, dyslipidemia and insulin resistance. The specific analysis is shown in Figure 1.

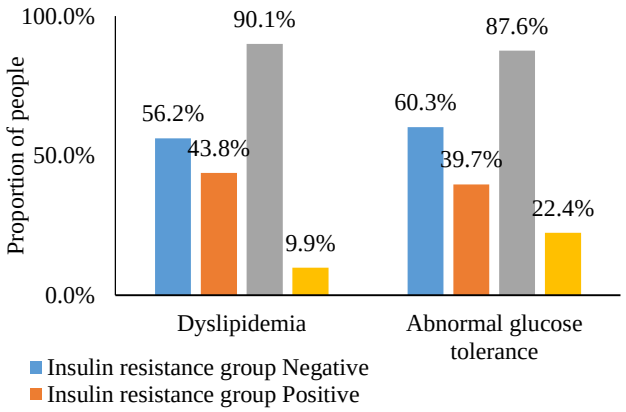

Figure 1. Analysis of abnormal glucose and lipid metabolism by insulin resistance or not

Relationship between Insulin Resistance and Oxidative Stress in Patients with Polycystic Ovary Syndrome

Patients with polycystic ovary syndrome were divided into IR groups and non-IR groups. Malondialdehyde, glutathione peroxidase and superoxide dismutase were detected respectively. The test results are shown in Figure 2.

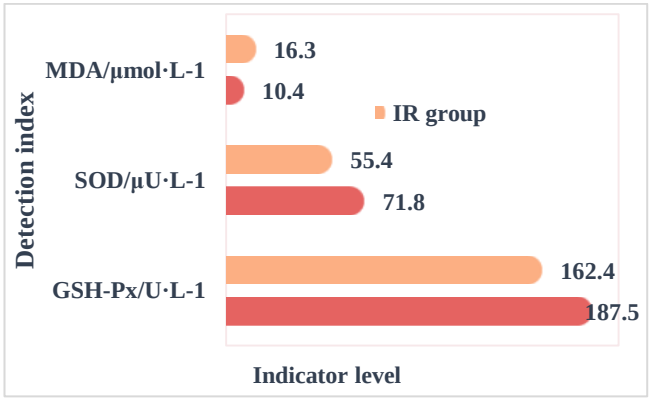

Figure 2. Analysis of SOD, GSH-Px and SOD levels between IR group and non-IR group

Analysis of Insulin Resistance and Inflammatory Factors in Polycystic Ovary Syndrome

In order to study the relationship between insulin resistance and inflammatory factors, patients with polycystic ovary syndrome were divided into IR group and non-IR group, and the levels of TNF, CRP and IL-6 were detected respectively. The detection results are shown in Figure 3.

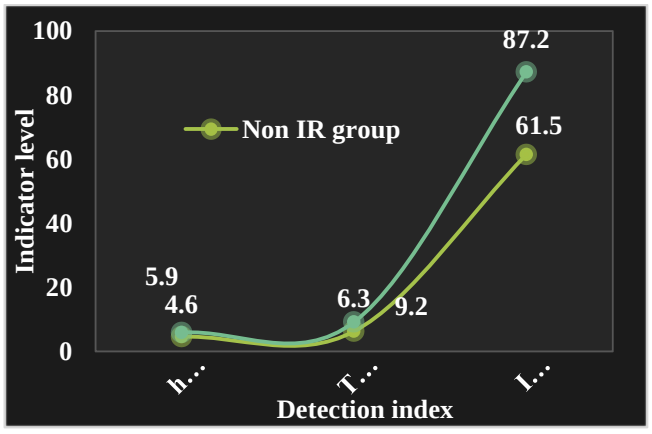

Figure 3. Insulin resistance, insulin resistance, non-insulin resistance and TNF, CRP, IL-6 levels in patients with polycystic ovary syndrome

Clinical Manifestations of Insulin Resistance in Patients with Polycystic Ovary Syndrome

In order to study the relationship between clinical manifestations of polycystic ovary syndrome and insulin resistance, the patients with polycystic ovary syndrome were divided into two groups for comparative analysis. The analysis results are shown in Figure 4.

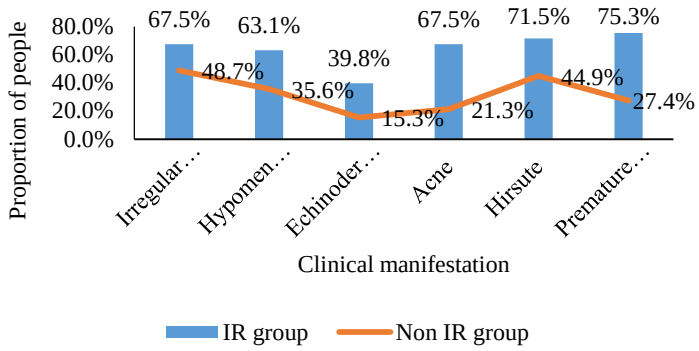

Figure 4. Comparison of clinical manifestations between insulin resistance group and non-insulin resistance group in patients with polycystic ovary syndrome

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None.

Interest conflict

The authors declare no conflict of interest.

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