Effect of pioglitazone combined with cyproterone acetate on the reproductive hormone level and insulin resistance of patients with polycystic ovary syndrome

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Abstract

Objective: To analyze the effect of Pioglitazone combined with cyproterone acetate on the reproductive hormone level and insulin resistance of patients with polycystic ovary syndrome.

Methods: 96 patients with the polycystic ovary syndrome in our hospital were randomly divided into observation group and control group two groups, each of 48 cases. The control group was treated with the treatment of cyproterone acetate, observation group was treated with pioglitazone combined with cyproterone acetate treatment. The clinical efficacy of two groups were compared. The serum follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), testosterone (T) and fasting plasma glucose (FBG), fasting insulin (FINS) level before and after treatment and calculate the insulin resistance index (IR) were observed.

Results: After treatment, serum FSH, LH and T levels of two groups were significantly lower than that before treatment ($P<0.05$), and the observation group was significantly lower than the control group ($P<0.05$). The $E_2$ level of the two groups before and after treatment had no significant difference ($P>0.05$). FBG, FINS and IR of the patients in the observation group were significantly lower than the control group ($P<0.05$). Conclusion: pioglitazone combined with cyproterone acetate has significant therapeutic effect on polycystic ovary syndrome, can effectively improve the patients with insulin resistance and reproductive hormone disorder.

1. Introduction

Polycystic ovarian syndrome (PCOS) is an endocrine and metabolism disorder that is characterized by chronic anovulation, hyperandrogenaemia and insulin resistance. It often occurs in puberty girls and also the leading cause of infertility in women of childbearing age. In recent years, the incidence rate of PCOS is showing a rising trend and it has become one of the common diseases do serious harm to women's physical and mental health. Therefore, it’s essential to seek safe and effective drugs for the clinical treatment of PCOS[1-3]. Our study used Pioglitazone combined with cyproterone acetate in the treatment of patients with PCOS in our hospital from Apr. 2013 to Oct. 2014 and obtained satisfactory results, reports as follows.

2. Materials and methods

2.1. Clinical information

Study was undertaken of 96 cases of patients with polycystic ovarian syndrome in our hospital from Apr. 2013 to Oct. 2014. All patients diagnosed by the 2003 Rotterdam PCOS consensus criteria, patients age from 21 to 38 years old, weight from 46 to 75 kg, infertility duration from 0.6 to 10 years; with menstrual disorder 42 cases, amenorrhea 31 cases, hirsute 9 cases and acne 14 cases. Exclude patients with serious heart, liver, lung, kidney or other important organs dysfunction; diseases that cause hyperandrogenaemia, such as Cushing syndrome, congenital adrenal hyperplasia or androgen secreting tumor; other endocrine diseases,
such as thyroid diseases, hyperprolactinemia or diabetes; used hormone or drugs that affect insulin secretion among 3 months; drug contraindications or previous history of allergy patients; Pregnant or lactating women. Our study conforms to the requirements of Hospital Ethical Committee; all patients were voluntary and signed the protocol of treatment. According to the order of treatment, the patients were randomly divided into two groups, the observation group and the control group, each 48 cases. In the observation group, patients age ranged from 24 to 38 years old, with a mean age of (27.89±3.25); weight from 46 to 72 kg, with an average weight of (58.36±7.44) kg; Infertility duration from 0.6 to 9 years, with an average of (4.52±1.27) years; With menstrual disorder 20 cases, amenorrhea 16 cases, hirsute 5 cases and acne 7 cases. In the control group, patients age ranged from 21 to 36 years old, with a mean age of (27.89±3.25); weight from 46 to 72 kg, with an average weight of (58.36±7.44) kg; Infertility duration from 0.6 to 9 years, with an average of (4.52±1.27) years; With menstrual disorder 20 cases, amenorrhea 16 cases, hirsute 5 cases and acne 7 cases. Two groups had no significant difference in general clinical and other conditions (P>0.05).

2.2. Treatment method

The control group patients began to take cyproterone acetate tablets from the fifth day of menstrual cycle, 1 tablet/time, orally before bedtime for 21 d, starts the next cycle treatment from the fifth day of next time menstruation for 3 cycles. The observation group patients were given pioglitazone hydrochloride on the basis of the control group, take 15 mg/times, orally before breakfast for 3 months. Advice patients to control diet and proper exercise during the course of medication, stop medication immediately if appear ovulation.

2.3. The observation indexes

Patients’ Venous blood was collected in the morning in the fifth day of the menstrual cycle before and after treatment, separate serum through centrifuge. Serum follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2) and testosterone (T) levels were detected by Electrochemiluminescence immunoassay; Fasting blood glucose (FBG) level was measured by glucose oxidase method; Fasting insulin (FINS) level was detected by Radioimmunoassay; Insulin resistance index (HOMA-IR) was assessed by the homeostasis model with the formula HOMA-IR=FINS FBG/22.5.

2.4. Statistical analysis

Dates were analyzed by statistical software SPSS16.0, each index showed by (mean±SD), the groups were compared using t test, P<0.05 considered for the difference had statistical significance.

3. Results

3.1. Comparison reproductive hormone level of the two groups before and after treatment

Before treatment, the reproductive hormone level of the two groups showed no significant difference (P>0.05). After treatment, serum FSH, LH and T levels of the two groups were significantly lower than that before treatment (P<0.05), and those in the observation group were significantly lower than in the control group (P<0.05). The E2 level of the two groups had no significant difference before and after treatment (P>0.05). Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>FSH (IU/L)</th>
<th>LH (IU/L)</th>
<th>T (nmol/L)</th>
<th>E2 (pmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>48</td>
<td>Before</td>
<td>6.70±1.26</td>
<td>13.98±2.41</td>
<td>2.48±0.56</td>
<td>126.38±15.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>5.49±1.35</td>
<td>8.72±2.20</td>
<td>1.66±0.37</td>
<td>124.62±16.23</td>
</tr>
<tr>
<td>Observation</td>
<td>48</td>
<td>Before</td>
<td>6.83±1.32</td>
<td>14.03±2.62</td>
<td>2.52±0.58</td>
<td>129.15±17.31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>4.24±0.98</td>
<td>5.18±1.73</td>
<td>1.43±0.21</td>
<td>121.74±13.82</td>
</tr>
</tbody>
</table>

P<0.05 compared with the control group at the same time, †P<0.05; compared with the same group before treatment, ‡P<0.05.

3.2. Comparison FBG, FINS and IR of the two groups before and after treatment

Before treatment, FBG, FINS and IR of the two groups showed no significant difference (P>0.05). After treatment, FBG, FINS and IR of the patients in the observation group were significantly lower than in the control group (P<0.05). Table 2.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>FBG (mmol/L)</th>
<th>FINS (mIU/L)</th>
<th>IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>48</td>
<td>Before</td>
<td>6.4±0.83</td>
<td>23.7±9.62</td>
<td>4.8±1.76</td>
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<td></td>
<td></td>
<td>After</td>
<td>5.39±0.67</td>
<td>21.9±5.26</td>
<td>4.97±1.81</td>
</tr>
<tr>
<td>Observation</td>
<td>48</td>
<td>Before</td>
<td>5.72±0.81</td>
<td>24.1±6.48</td>
<td>4.85±1.92</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>3.58±0.54</td>
<td>13.28±4.21</td>
<td>3.26±1.34</td>
</tr>
</tbody>
</table>

P<0.05 compared with the control group at the same time, †P<0.05; compared with the same group before treatment, ‡P<0.05.

4. Discussion

Polycystic ovarian syndrome (PCOS) is a clinical common gynecological disease caused by endocrine and metabolism disorder which is characterized by chronic anovulation, hyperandrogenaemia and insulin resistance. The incidence rate is high and accounts for 5%~10% among the childbearing age women. If lacking timely and effective treatment, it will increase risk of type 2 diabetes, cardiovascular disease, breast cancer, endometrial cancer and other long-term complications, serious impact the physical and mental health, life quality and even endanger life safety of the patients[6-8].
The pathogenesis of PCOS is complex, studies found that[9] insulin resistance (IR) and compensatory hyperinsulinemia play an important role in the occurrence and development of PCOS, while the two influence each other and are reciprocal causation, result in the increasing condition of the patients[10-12]. On the one hand, high levels of insulin directly affect the ovarian theca cells, causing excess expression of functional androgen though the insulin receptor. On the other hand, IR and high levels of insulin can disrupt the normal function of the hypothalamic pituitary ovary axis, causing the rapidly secretion of hypothalamic gonadotropin-releasing hormone, the pituitary gland to secrete excess LH, the inhibition produce of sex secretion of hypothalamic gonadotropin-releasing hormone, the function of the hypothalamic pituitary ovary axis, causing the rapidly increase of LH and reducing the content of androgen in the blood. It can excessive secretion of androgens through inhibiting the synthesis androgenbinding globulin by liver, and over-produce of androgen by ovarian theca cells, to appear hyperandrogenaemia, leading to follicular dysplasia and infertility. In addition, hyperandrogenaemia will cause the abnormal glucose metabolism directly or indirectly, further increasing insulin resistance and forming a vicious spiral[13,14]. Studies found that most patients have different degree of insulin resistance and androgen level had positive correlation with insulin level. Therefore, reducing androgen levels and insulin resistance is the key to the treatment of PCOS.

Our study showed that after treated by pioglitazone combined with cyproterone acetate, FSH, LH, T, FBG, FINS and IR of the observation group were significantly lower than that of the control group, which indicated that pioglitazone combined with cyproterone acetate treatment has better effect in reducing the reproductive hormone level and improving insulin resistance than the single cyproterone acetate treatment. Cyproterone acetate is an oral contraceptive with strong progesterone activity, it can improve hyperandrogenism symptoms such as hirsute and acne due to the excessive secretion of androgens through inhibiting the synthesis of LH and reducing the content of androgen in the blood. It can further aggravate the disorder of glucose metabolism and increase the patient's IR status, so the drug’s clinical application is restricted. Pioglitazone is a new type of thiazolidinedione drugs, belonging to the insulin sensitizing agents. By stimulating the peroxisome proliferator activated receptor gamma (PPARγ), it can increase the sensitivity of peripheral tissues to insulin, improve insulin resistance, and then correct the LS secretion and hyperandrogenaemia, finally increase the ovulation and pregnancy rate of the patients[15,16]. Pioglitazone combined with cyproterone acetate treatment can lower androgen and LH levels, increase insulin sensitivity, block the vicious spiral of endocrine disorders and promote the recovery of menstrual cycle. It also fills up the deficiency of single cyproterone acetate treatment and has better clinical efficacy.

In summary, pioglitazone combined with cyproterone acetate treatment can effectively relieve insulin resistance, correct the reproductive hormone disorders of patients with PCOS, and worth the clinical promotion and application.

References