Effects of Danzhi Xiaoyao pill combined with metformin on related factors in patients with polycystic ovary syndrome

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ABSTRACT

Objective: To study the clinical efficacy and effects of danzhi xiaoyao pill combined with metformin on related factors in patients with polycystic ovary syndrome (PCOS). Methods: A total of 80 patients with PCOS in our hospital from January 2014 to December 2017 were enrolled in this study. The subjects were divided into the control group (n=40) and the experimental group (n=40) randomly. The control group were treated with metformin, the experimental group were treated with danzhi xiaoyao pill combined with metformin, and the two groups were treated for 3 menstrual cycles. The serum CRP, IGF-1, TNF-α, FSH, LH, E2, T, FINS, FPG, VF, LEP, APN and HOMA-IR of the two groups before and after treatment were compared.

Results: There were no significantly differences of the serum CRP, IGF-1, TNF-α, FSH, LH, E2, T, FINS, FPG, VF, LEP, APN and HOMA-IR of the two groups before treatment. After treatment, the serum CRP, IGF-1, TNF-α, LH, E2, T, FINS, FPG, VF, LEP and HOMA-IR of the two groups were significantly lower than before treatment, the serum APN of the two groups were significantly higher than before treatment, and that of the experimental group after treatment were significantly better than the control group.

Conclusion: Danzhi xiaoyao pill combined with metformin on patients with PCOS has a good efficacy. It can reduce the inflammatory cytokines and sex hormones, and improve the insulin resistance and sugar, lipid metabolic disorders. Therefore, it is worthy of clinical application.

1. Introduction

Polycystic ovary syndrome (PCOS) is a reproductive disorder and metabolic disorder characterized by systemic neuroendocrine metabolic disorders and persistent anovulation. The clinical manifestations are ovarian polycystic changes, scanty menstruation, amenorrhea, infertility, obesity, hairy and dysfunctional uterine bleeding[1]. In recent years, with the acceleration of people’s pace of life and the increase of working pressure, the incidence of PCOS has been increasing, which accounts for about 2/5 of gynecological endocrine diseases[2]. At present, the clinical treatment of PCOS mainly uses anti estrogen, gonadotropin, surgical treatment and other measures, but the clinical effect is not obvious[3]. Metformin is an insulin synergist, which can reduce liver gluconeogenesis and reduce insulin resistance, decrease the stimulating effect of insulin on luteotrophic hormone (LH) and lessen the level of LH, thus helping to improve the body’s hormone levels, promote follicle development and discharge[4]. Danzhi Xiaoyao Pill is a Chinese patent medicine prepared from Xiaoyao Pill plus Cortex Moutan and Gardenia jasminoides Ellis. It has the functions of nourishing blood, strengthening spleen, soothing liver and clearing heat, and helps to regulate qi and blood[5]. The aim of this study was to investigate the effect of the combination of Danzhi Xiaoyao Pill and metformin on the clinical efficacy and related factors in patients with PCOS.
2. General information and research methods

2.1 General case information

A total of 80 patients with PCOS in our hospital from January 2014 to December 2017 were enrolled in this study. Criteria for case inclusion: (1) in line with the diagnostic criteria of PCOS proposed by the American Society for Reproductive Medicine (ESHRE/ASRM) and European Society of Human Reproduction and Embryology (ESHRE); (2) aged 18-40 years; (3) informed and signed informed consent. Case exclusion criteria: (1) patients with serious heart and liver kidney diseases; (2) combined with other patients with Kaohsiung hormone disease; (3) patients with ovulatory disorders; (4) patients who had taken glucocorticoids in the last 3 months.

The subjects were divided into the control group (n=40) and the experimental group (n=40) randomly. In the control group, the age was 20-38 years old, the average age was (31±5) years, the course of disease was 1-5 years, the average age was (3±1) years, the body mass was 48-62 kg, the average body mass (54±4) kg; In the experimental group, the age was 20-40 years old, the average age was (32±6) years, the course of disease was 1-5 years, the average course was (2±2) years, the body mass was 48-64 kg, and the average body mass (55.11± 6.34) kg. The general data of the two groups are comparable. The study was approved by the Medical Ethics Committee of our hospital.

2.2 Research methods

2.2.1 Treatment methods

The patients in the control group were treated with metformin (purchased from Taiyuan Pharmaceutical Co., Ltd., 0.5 g/piece, H20080411), oral administration, 0.5 g/time with 2 times/d. On the basis of the control group, the patients in the experimental group were treated with Danzhi Xiaoyao Pill (purchased from Laiyang Yongkang Pharmaceutical Co., Ltd., specification 6 g/piece, Chinese medicine quasi word Z37020916), oral administration, 6 g/time with 2 times/d; On the last 3 months. The two groups were treated for 21 d for 3 consecutive menstrual cycles.

2.2.2 Detection index

Before and after treatment, 5 mL venous blood of two groups was collected and centrifuged at a speed of 3 000 r/min for 15 min. The serum was separated and stored in refrigerator at -80 ℃.

The SPSS 19.0 software package was used to process the test result data, and the counting data were expressed by the percentage (%) and tested by Chi square test; The measurement data were expressed by mean ± standard deviation by t test and P<0.05 showed that the difference was statistically significant.

2.3 Data processing

The inflammatory factor index, including C reactive protein (C-reactive protein, CRP), tumor necrosis factor - alpha (tumor necrosis factor- alpha, TNF- α), were all selected by the double anti sandwich enzyme linked immunosorbent assay kit produced by Shanghai bio technology Co., Ltd. Test; (2) sex hormone related indicators, including follicle-stimulating hormone (FSH), luteinizing hormone (luteotropichormone, LH), estradiol (estradiol, E2), testosterone (testosterone, T), They were all detected by chemiluminescence. The full automatic chemiluminescence analyzer was DX1800, purchased from Backman Kurt; (3) Islet function related indicators, including insulin like growth factor (insulin like growth factor-1, IGF-1), fasting serum insulin (fasting serum lisulin, FINS), fasting blood glucose (fasting plasma glucose). The test of IGF-1 was detected by ELISA test kit. The kit was purchased from Shanghai Jianglai Biotechnology Co., Ltd., FINS was detected by chemiluminescence, FPG was detected by glucose oxidase method, and the testing instrument was Hitachi 7600-020 automatic biochemical analyzer, and the insulin resistance index (HOMA-IR) was calculated by steady state model. The calculation formula was HOMA-IR=FPG x FINS/22.5. (4) Fat related factors, including visfatin (VF), leptin (LEP) and adiponectin (adiponectin, APN), were detected by radioimmunnoassay, and the detection kit was bought from Shenzhen Jing Mei bio company.

3. Results

3.1 Comparison of serum levels of CRP, IGF-1 and TNF- α in two groups before and after treatment

Before treatment, there was no significant difference in the levels of CRP, IGF-1, TNF- α between the control group and experimental group (P>0.05). After treatment, the levels of serum CRP, IGF-1 and TNF- alpha in the control group and experimental group were lower than those before treatment, and the levels of serum CRP, IGF-1 and TNF- alpha in the experimental group were better than those in the control group (P<0.05), as shown in Table 1.

### Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>CRP (mg/L)</th>
<th>IGF-1 (ng/L)</th>
<th>TNF- α (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>40</td>
<td>Before treatment</td>
<td>4.25±1.18</td>
<td>0.49±0.09</td>
<td>109.25±18.34</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>3.76±0.83</td>
<td>0.34±0.06</td>
<td>82.62±10.72</td>
</tr>
<tr>
<td>Experimental</td>
<td>40</td>
<td>Before treatment</td>
<td>4.21±1.20</td>
<td>0.47±0.10</td>
<td>110.51±15.40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>3.01±0.61</td>
<td>0.21±0.04</td>
<td>39.38±6.54</td>
</tr>
</tbody>
</table>

Note: compared with the same group before treatment, *P<0.05; compared with the same period in control group, *P<0.05.
Comparison of the serum VF, LEP and APN levels before and after treatment in the two groups.

Table 4.

Comparison of islet function related indexes in two groups before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>FINS (mIU/L)</th>
<th>FPG (mmol/L)</th>
<th>HOMA-IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>40</td>
<td>Before treatment</td>
<td>26.0±6.51</td>
<td>5.6±0.31</td>
<td>5.5±0.20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>13.1±4.02</td>
<td>4.9±0.15</td>
<td>3.3±0.14</td>
</tr>
<tr>
<td>Experimental group</td>
<td>40</td>
<td>Before treatment</td>
<td>25.7±5.89</td>
<td>5.5±0.29</td>
<td>5.4±0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>8.0±3.12</td>
<td>4.0±0.10</td>
<td>2.3±0.11</td>
</tr>
</tbody>
</table>

Note: compared with the same group before treatment, *P*<0.05; compared with the same period in control group, #P*<0.05.

Table 3.

Comparison of islet function related indexes in two groups before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>VF (ug/L)</th>
<th>LEP (ug/L)</th>
<th>APN (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>40</td>
<td>Before treatment</td>
<td>79.0±14.14</td>
<td>44.1±7.24</td>
<td>4.0±0.86</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>52.4±10.05</td>
<td>31.9±5.02</td>
<td>7.1±1.48</td>
</tr>
<tr>
<td>Experimental group</td>
<td>40</td>
<td>Before treatment</td>
<td>78.8±13.39</td>
<td>45.0±7.62</td>
<td>4.1±1.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>40.8±8.45</td>
<td>25.1±3.89</td>
<td>10.5±2.12</td>
</tr>
</tbody>
</table>

Note: compared with the same group before treatment, *P*<0.05; compared with the same period in control group, #P*<0.05.

3.2 Comparison of sex hormone related indexes in two groups before and after treatment

Before treatment, there was no significant difference in the levels of FSH, LH, E2, T between the two groups (P>0.05). After treatment, there was no significant difference in serum FSH level between the two groups (P>0.05). The levels of LH, E2 and T in the two groups were lower than those before treatment (P<0.05), and the changes of LH, E2 and T in the experimental group were all better than those of the control group (P<0.05), as shown in Table 4.

3.3 Comparison of islet function related indexes in two groups before and after treatment

Before treatment, there was no significant difference in the levels of FINS, FPG, HOMA-IR between the two groups (P>0.05). After treatment, the levels of FINS, FPG and HOMA-IR of the two groups were lower than those before treatment (P<0.05), and the changes of FINS, FPG and HOMA-IR in the experimental group were better than those in the control group (P<0.05), as shown in Table 3.

3.4 Comparison of the serum VF, LEP and APN levels before and after treatment in the two groups

Before treatment, there was no significant difference in the levels of serum VF, LEP and APN between the two groups (P>0.05). After treatment, the levels of serum VF and LEP in the two groups were lower than those before treatment, and the level of serum APN was higher than that before treatment, and the levels of serum VF, LEP and APN after treatment in the experimental group were all better than those of the control group (P<0.05), as shown in Table 4.

4. Discussion

At present, the pathogenesis of PCOS is still not clear. It is generally believed that the comprehensive effect of environmental and genetic factors is related to many factors such as neuroendocrine, protein metabolism, sugar metabolism, fat metabolism, and local regulation of the ovary. So the treatment of PCOS is still in the exploration[8,9]. Metformin is a clinically commonly used hypoglycemic drug. It is believed that it can prevent PCOS endocrine vicious cycle through multiple angles, improve the inhibitory effect of sex hormone and high insulin on ovulation in Kaoshung, and improve ovulation function of the ovary. However, it can cause a series of gastrointestinal adverse reactions and limit the clinical effect. Extensive application[10]. According to TCM, PCOS belongs to the category of “late menstrual cycle”, “amenorrhea”, “scanty menstruation”, “infertility”, “symptom” and so on. This disease is mainly due to qi stagnation fire, yin and blood burning, blood sea emptiness, thus the imbalance of yin and yang, so that the menstruation is not adjusted and infertility, at the same time, the liver qi stagnation and abnormal catharsis lead to the loss of qi and blood stasis and stagnation of blood stasis, and the removal of infertility. Therefore, the treatment should be suitable for clearing heat and liver, strengthening the spleen and nourishing blood, and regulating qi and blood[11,12].

Danzi Xiaoyao Pill has the effect of dispersing the liver, clearing
liver and fire, filling the liver and regulating qi and blood. The traditional Chinese medicine, such as Atractylodes, Poria cocos, Gardenia jasminoides and peony skin, can reduce the blood sugar, improve the follicle microenvironment and the local insulin resistance, promote the development of follicle, improve the metabolism of sugar and fat, and facilitate the functional recovery of the ovary[13,14]. The aim of this study was to explore the effect of Danzhi Xiaoyao Pill combined with metformin on the clinical efficacy and related factors in patients with PCOS, in order to provide ideas for clinical treatment of PCOS.

The results of this study showed that the serum levels of CRP, IGF-1, TNF-, LH, E2, T, FINS, FPG, VF, LEP and HOMA-IR were lower than those before the treatment, and the level of serum APN was higher than that before the treatment. The change was better than that of the control group (P<0.05). This suggests that the combination of Danzhi Xiaoyao Pill with metformin can significantly reduce the levels of inflammatory factors and sex hormones in PCOS patients, improve insulin resistance and disorder of glucose and lipid metabolism. The study suggests that chronic inflammation mediated insulin resistance is closely related to the occurrence and development of PCOS. Inflammatory factors such as CRP and TNF-a can interfere with the signal transduction of insulin. Hyperinsulinemia stimulates the secretion of follicle stimulating hormone, causes follicular cell proliferation and free androgen levels, increases the atresia follicle, and leads to ovulatory disorders and endocrine disturbances, which ultimately results in insulin resistance, promote the development of follicle, improve the insulin sensitivity, and reduce the levels of inflammatory factors and sex hormones.

In summary, the clinical efficacy of Danzhi Xiaoyao Pill combined with metformin in the treatment of PCOS is significant. It can obviously reduce the level of inflammatory factors, sex hormone levels, and improve insulin resistance and disorder of glucose and lipid metabolism. It is worthy of clinical application.

References


