Effect of bushen tiaopi recipe on sex hormones, immune function and oxidative stress in patients with climacteric syndrome

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Objective: To explore the effect of Bushen Tiaopi Recipe on sex hormones, immune function and oxidative stress in patients with climacteric syndrome and guide clinical medication.

Methods: A total of 140 cases of climacteric syndrome patients who were treated in our hospital from May 2016 to May 2017 were selected according to the lottery method, 70 cases in each group. Control group was given Li Fumin treatment, and the observation group was given Li Fumin combined with Bushen Tiaopi Recipe. The levels of sex hormones, T lymphocyte subsets, leptin, adiponectin and oxidative stress were measured before and after treatment in both groups.

Result: There was no significant difference in the levels of sex hormones, T lymphocyte subsets, leptin, adiponectin and oxidative stress before treatment between the two groups. After 12 weeks of drug treatment, the level of sex hormone P increased and the levels of LH and FSH decreased in both groups. The research group P was (21.89±2.29) nmol/L higher than the control group, and the LH and FSH were (4.28±0.43) IU/L and (4.91±0.50) IU/L were lower than the control group. The LP level was decreased and the APN level increased in both groups. Moreover LP level in the research group was (15.34±1.52) μg/L lower than that in the control group, and the APN level was (8.39±0.84) mg/L higher than that in the control group. The SOD level was increased and MDA level decreased in both groups. And SOD level in the research group was (33.27±3.29) U/L, which was higher than that in the control group, and the MDA level was (12.47±1.25) nmol/mL, which was lower than that in the control group. CD4+ and CD4+/CD8+ levels were significantly elevated in both groups, and CD8+ levels were significantly decreased. In the research group, CD4+ and CD4+/CD8+ were (28.87±2.69)% and (1.41±0.14), respectively, higher than the control group, and the number of CD8+ cells was (21.05±2.23)% lower than the control group.

Conclusion: Bushen Tiaopi can significantly improve sex hormone levels in climacteric syndrome patients, improve immune function, relieve oxidative stress, and improve treatment effects.

1. Introduction

Climacteric syndrome (CS), also known as peri-menopausal syndrome, is mainly caused by a decrease in ovarian function leading to a decrease in estrogen levels, resulting in a reproductive-endocrine-metabolic dysfunction. The clinical manifestations are mainly menstrual disorders, and chest tightness, palpitation, insomnia, dreams, and sweating[1-3]. At present, the main clinical treatment is hormone replacement therapy (HRT), which has significant curative effect but many adverse reactions meanwhile, and there are still differences in dosage, administration route, and compatibility medication[4,5]. In recent years, clinical studies have found that Chinese medicine has a better therapeutic effect and has received clinical attention[6,7]. The aim of this study was to investigate the effects of Bushen Tiaopi Recipe on sex hormones, immune function and oxidative stress in patients with climacteric syndrome in order to guide clinical medication.
2. Materials and methods

2.1 Clinical data

A total of 140 patients with CS admitted to our hospital from May 2016 to May 2017, diagnostic criteria: 1) All patients met the CS diagnostic criteria of the 8th edition of Obstetrics and Gynecology[8]; 2) Typical clinical manifestations of CS, such as chest tightness, palpitation, insomnia, and sweating, etc.; 3) endocrine and metabolic disorders. According to the lottery method, 140 CS patients were divided into research group and control group, 70 cases each group. The control group was 46-60 years old; the course of disease was 6 months to 4 years, with an average of (2.3 ± 0.2) years. The research group was 45-60 years old; the course of disease was 6 months to 4 years, with an average of (2.3 ± 0.2) years. Exclusion criteria: 1) combined with diabetes or other metabolic diseases; 2) took birth control pills or took sex hormones recently; 3) combined with breast cancer or cervical cancer; 4) patients with mental illness; 5) patients with serious cardiovascular disease or heart, liver, kidney and other organs with severe functional insufficiency. The age and disease course of all patients in this study were not statistically significant, it was comparable. The study was approved by the Medical Ethics Committee of the hospital.

2.2 Treatment method

The control group was treated with Li Fumin, the specific medication method: Li Fumin tablets (Germany Xiapu Natural Medicine Pharmaceutical Company, registration number Z20130001) 1 piece/time, 2 times/d. The research group was treated with Bushen Tiaopi Recipe on the basis of Lifmin treatment. The specific usage: Bushen Tiaopi Recipe (30 g of raw oyster, 30 g of raw keel, 20 g of scutellaria, 15 g of medlar, 15 g of white peony, 15 g of epimedium), 15 g of poria with hostwood, 15 g of Achyranthes, 15 g of Cistanche, 15 g of teasel, 15 g of Atractylodes, 20 g of Rehmannia glutinosa, 12 g of radix curcumae, 10 g of Hawthorn), each dose/d, 2 times/d. Patients in both groups were treated for 12 weeks.

2.3 Observation indicators

1) Detection of sex hormones FSH, LH and P In the morning, 1 mL of fasting peripheral blood were taken from CS patients in both groups before and after treatment, and serum was taken by centrifugation. The levels of progesterone (P), Luteinising Hormone (LH) and follicle-stimulating hormone (FSH) were determined by ELISA. 2) Detection of LP, LPN, SOD and MDA. In the morning, 1 mL of fasting peripheral blood were collected from CS patients in both groups before and after treatment, and serum was taken by centrifugation. Leptin (LP), adipose tissue (APN), malondialdehyde (MDA) and superoxide dismutase (SOD) levels were determined by ELISA method. All kits in this study were purchased from Wenzhou Gaodian Biological Co., Ltd. 3) Detection of T lymphocyte subsets In the morning, 5 mL of fasting peripheral blood were taken from CS patients in both groups before and after treatment. CD4+ and CD8+ levels were measured by flow cytometry (purchased from BD China Branch), and CD4+/CD8+ was calculated.

2.4 Statistical methods

The data of this study were analyzed by SPSS 21.0 statistical software. All the indicators in this study were verified to be in a normal distribution, expressed as mean ± standard deviation, and independent t test was used for the comparison of both groups. Paired t-test was used for intra-group comparison and $P<0.05$ indicated that the difference was statistically significant.

3. Results

3.1 Comparison of sex hormone levels between the two groups before and after treatment

The difference of P, LH and FSH levels between the two groups before treatment was not significant ($P>0.05$). After 12 weeks of drug treatment, P levels increased, LH and FSH levels decreased in the two groups, and P level in the research group was (21.89±2.29) nmol/L, which was higher than that in the control group, and LH and FSH level were (4.28±0.43) IU/L and (4.91±0.50) IU/L respectively, which were lower than the control group (both $P<0.05$), as shown in Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>P (nmol/L)</th>
<th>LH (IU/L)</th>
<th>FSH (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>70</td>
<td>Before treatment</td>
<td>12.87±1.32</td>
<td>8.32±0.83</td>
<td>11.94±1.21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>18.08±1.81</td>
<td>6.75±0.68</td>
<td>6.74±0.68</td>
</tr>
<tr>
<td>Research group</td>
<td>70</td>
<td>Before treatment</td>
<td>12.90±0.29</td>
<td>8.37±0.84</td>
<td>12.08±1.24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>21.89±2.29</td>
<td>4.28±0.43</td>
<td>4.91±0.50</td>
</tr>
</tbody>
</table>

Compared with before treatment, $^*P<0.05$; compared with the control group after treatment, $^{*'}P<0.05$. 

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Table 1. Comparison of sex hormone levels before and after treatment in both groups.

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4. Discussion

The results show that the levels of P, LH and FSH were significantly different before and after treatment in the two groups ($P<0.05$). The levels of P were reduced, LH and FSH were increased in both groups, indicating that the levels of sex hormones were significantly different before and after treatment in the two groups ($P<0.05$).

5. Conclusion

The results show that Li Fumin and Bushen Tiaopi Recipe can effectively regulate the levels of sex hormones and improve the clinical symptoms of CS patients, and the effects of Bushen Tiaopi Recipe are better than Li Fumin, which provides a new idea for the treatment of CS.
3.2 Comparison of LP and APN levels before and after treatment in the two groups

The difference in the levels of LP and APN before treatment between the two groups was not significant (P<0.05). After 12 weeks of drug treatment, the LP levels of the two groups were decreased, and the APN level was increased, and the LP level in the research group was (15.34±1.52) μg/L, which was lower than that of the control group, and the APN level (8.39±0.84) mg/L was higher than control group (both P<0.05), as shown in Table 2.

Table 2.

Comparison of LP and APN levels before and after treatment in both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>LP (μg/L)</th>
<th>APN (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>70</td>
<td>Before</td>
<td>23.31±2.32</td>
<td>6.12±0.62</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>18.75±1.88</td>
<td>7.35±0.74</td>
</tr>
<tr>
<td>Research group</td>
<td>70</td>
<td>Before</td>
<td>22.90±2.29</td>
<td>6.08±0.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>15.34±1.52</td>
<td>8.39±0.84</td>
</tr>
</tbody>
</table>

Compared with before treatment, *P<0.05; compared with the control group after treatment, †P<0.05.

3.3 Comparison of SOD and MDA levels before and after treatment in both groups

The difference of SOD and MDA levels between the two groups before treatment was not obvious (P<0.05). After 12 weeks of drug treatment, SOD levels were increased and MDA levels decreased in both groups, and SOD level in the research group was (33.27±3.29) U/L, which was higher than that of the control group, and the MDA level was (12.47±1.25) nmol/mL that was lower than the control group (both P<0.05), as shown in Table 3.

Table 3.

Comparison of SOD and MDA levels before and after treatment in both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>SOD (U/L)</th>
<th>MDA (nmol/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>70</td>
<td>Before</td>
<td>22.47±2.27</td>
<td>25.34±2.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>26.44±2.64</td>
<td>15.65±1.51†</td>
</tr>
<tr>
<td>Research group</td>
<td>70</td>
<td>Before</td>
<td>23.14±2.31</td>
<td>25.27±2.53†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>33.27±2.99</td>
<td>12.47±1.25†</td>
</tr>
</tbody>
</table>

Compared with before treatment, *P<0.05; compared with the control group after treatment, †P<0.05.

3.4 Comparison of T lymphocyte subsets before and after treatment in both groups

The difference of T lymphocyte subsets between the two groups before treatment was not dramatical (P<0.05). After 12 weeks of drug treatment, the levels of CD4+ and CD4+/CD8+ were significantly increased in both groups, and CD8+ level was significantly decreased, and the CD4+ and CD4+/CD8+ level in the research group were (28.87±2.69)% and (1.41±0.14)%, respectively. Which was higher than the control group, the number of CD8+ cells was (21.05±2.23)% lower than that of the control group (all P<0.05), as shown in Table 4.

Table 4.

Comparison of T lymphocyte subsets before and after treatment in both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>CD4+ (%)</th>
<th>CD8+ (%)</th>
<th>CD4+/CD8+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>70</td>
<td>Before</td>
<td>22.56±2.26</td>
<td>26.69±2.67</td>
<td>0.83±0.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>25.86±2.42</td>
<td>22.37±2.24</td>
<td>1.22±0.11†</td>
</tr>
<tr>
<td>Research group</td>
<td>70</td>
<td>Before</td>
<td>23.06±2.31</td>
<td>26.62±2.51</td>
<td>0.82±0.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>28.87±2.69†</td>
<td>21.05±2.23†</td>
<td>1.41±0.14†</td>
</tr>
</tbody>
</table>

Compared with before treatment, *P<0.05; compared with the control group after treatment, †P<0.05.

4. Discussion

According to the epidemiological survey report, the number of menopausal women in China has reached 130 million, of which the clinical manifestation is about 100 million CS%. The clinical manifestations of CS are diverse and the pathogenesis is still unclear. Therefore, it is particularly important to seek effective drugs to treat this disease. Li Fumin is a natural botanical that exerts a therapeutic effect by modulating serotonin receptor activity. The efficacy of traditional Chinese medicine in the treatment of CS patients is significant and has received clinical attention. Therefore, this study used Bushen Tiaopi Recipe combined with Li Fumin to treat CS, and explored its effects on sex hormones, leptin, adiponectin, oxidative stress and immune function.

The theory of traditional Chinese medicine attributes CS to "the syndromes before and after menopause", and it believes that kidney deficiency and stagnation are the main pathogenesis. Traditional Chinese medicine believes that women's diseases are closely related to liver, kidney and spleen. Kidney and spleen can regulate the secretion of sex hormones, women's irregular menstruation is mostly caused by spleen deficiency, kidney deficiency. The study found that more CS patients with chest tightness, insomnia, dreams, obesity and lack of energy and other symptoms of spleen Qi deficiency, the spleen and white peony can supplement the blood and solid essence, and the cistanche can smooth dry blood, and herba epimedii can nourish blood and regulate menstruation, radix curcumae can be able to relieve qi...
and expel stasis, and all kinds of medicines can be used together to supplement blood and nourish yin, strengthen spleen and solidify kidney, and replenish qi and promote blood circulation[15]. Therefore, the treatment of CS needs to adjust the yin and yang of liver and kidney, nourish spleen and Qi. This study found that there was no significant difference in the levels of P, LH and FSH between the two groups before treatment (P<0.05). After 12 weeks of drug treatment, P level increased, LH and FSH levels decreased in the two groups, and P in the research group was (21.89±2.29) nmol/L higher than that in the control group, and LH and FSH level were (4.28±0.43) IU/L and (4.91±0.50) IU/L respectively, which were lower than the control group (both P<0.05). The results showed that Bushen Tiaopi Recipe can regulate sex hormones level in the body and improve sexual hormone disorder. The possible reason might be that Bushen Tiaopi Recipe has the functions of nourishing blood and nourishing yin, strengthening spleen and solidifying kidney and replenishing qi and activating blood circulation, which can improve spleen and kidney function and regulate the secretion of sex hormones.

Studies have reported that the lack of estrogen and the increase of androgen can increase the risk of insulin resistance[16]. The reproductive-endocrine-metabolic dysfunction of CS patients leads to the occurrence of sex hormone disorders and insulin resistance. Leptin is a peptide hormone secreted by adipose tissue, which regulates reproductive function, promotes lipid metabolism and controls appetite[17]. Adiponectin is a protein secreted by adipocytes that increases insulin sensitivity and is inversely correlated with HOMA-IR levels[18]. Insulin resistance is closely related to oxidative stress, hyperglycemia and high free fatty acids promote the production of ROS in tissues and cells, leading to oxidative stress[19]. MDA is an important product of membrane lipid peroxidation and is negatively correlated with oxidative stress injury[20]. SOD is an antioxidant enzyme with anti-aging, regulating blood lipids, immune regulation and anti-tumor effects, and is positively correlated with oxidative stress injury[21]. The study found that the LP level of the two groups was decreased, and the APN level was increased, the LP of the research group was (15.34±1.52) μg/L lower than that of the control group, and the APN was (8.39±0.84) mg/L higher than the conventional group. All (P<0.05). The SOD level was increased and the MDA level was decreased in the two groups. The SOD of the research group was (33.27±3.29) U/L higher than that in the control group, and the MDA was (12.47±1.25) nmol/mL lower than the control group. The results showed that Bushen Tiaopi Recipe can up-regulate the expression of adiponectin and leptin and alleviate oxidative stress, which is consistent with previous studies[22,23].

Studies have shown that the immune system is associated with ovarian function and can affect ovarian function by participating in follicular development and atresia[24]. The interaction and mutual restraint between T cell subsets maintain a moderate immune response and remove foreign body antigens that invade the body without damaging the tissues. CD8+ T cells directly kill virus-infected cells. After the body is stimulated by antigen, CD4+ T cells can differentiate into different cells and perform diverse functions. The results showed that after 12 weeks of drug treatment, CD4+ and CD4+/CD8+ levels were significantly increased in both groups, and CD8+ levels were significantly decreased, and in the study group CD4+ and CD4+/CD8+ were (28.87±2.69)% and (1.41±0.14)% respectively, that was higher than the control group, and the number of CD8+ cells was (21.05±2.23)% lower than that in the control group (both P<0.05), indicating that Bushen Tiaopi Recipe can improve immune function and exert therapeutic effects. The reason may be that Bushen Tiaopi Recipe can benefit Qi and spleen, supplement the spleen and stomach, and then improve the immune function.

In summary, Bushen Tiaopi Recipe can significantly improve sex hormone levels in patients with climacteric syndrome, improve immune function, relieve oxidative stress, and improve treatment.

References


