Effect of Guizhi Fuling Capsule on sex hormone level and tumor markers in patients with uterine fibroids

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ABSTRACT

Objective: To investigate the effect of Guizhi Fuling Capsule on sex hormones and tumor markers in patients with uterine fibroids, and observe its clinical efficacy. Methods: A total of 120 patients with uterine fibroids who were treated in our hospital from August 2016 to August 2017 were selected according to the order of treatment and divided into observation group and control group, 60 cases each. Mifepristone was administered to the control group and mifepristone combined with Guizhi Fuling Capsules was administered to the observation group. The levels of hemoglobin, vascular endothelial growth factor (VEGF), sex hormones, tumor markers, and inflammatory factors before and after treatment were compared between the two groups. Result: The levels of hemoglobin, vascular endothelial growth factor (VEGF), sex hormones, tumor markers, and inflammatory factors before and after treatment were compared between the two groups. After treatment, hemoglobin levels increased significantly in the two groups, VEGF, sex hormones FSH, LH and E2, tumor markers HE4, CA125, inflammatory cytokines TNF-α and IFN-γ levels decreased significantly. The hemoglobin level of the observation group was (117.09±11.51) g/L higher than that of the control group, and the level of VEGF was (0.69±0.06) pg/mL lower than that of the control group. The levels of sex hormone FSH, LH and E2 in the observation group were (15.87±1.56) U/L, (10.69±1.06) U/L and (4.95±0.51) pmol/L lower than those of the control group. The levels of HE4, CA125, TNF-α and IFN-γ in the observation group were (52.47±5.24) pmol/L, (40.41±4.05) and (16.72±1.62) pg/mL lower than those of the control group. Conclusion: Guizhi Fuling Capsule can significantly improve the level of sex hormones and tumor markers, relieve inflammatory stress and improve the therapeutic effect.

1. Introduction

Uterine fibroids is a common gynecologic disease in clinic. The latest statistics showed that the incidence is increasing year by year[1,2]. The main clinical manifestations of this disease are uterine bleeding, leukorrhagia, abdominal mass and anemia[3]. At present, the clinical treatments of uterine fibroids mainly include: drug treatment, surgical treatment and focused ultrasound treatment, etc[4,5]. Mifepristone is a common drug for uterine fibroids. It can competitive conjugation with progesterone receptor and change its structure, thereby reducing the level of progestin receptor and inhibiting the growth of benign tumor in the uterus[6]. Guizhi Fuling Capsule has the effect of activating blood and removing stasis, and can be used to treat dysmenorrhea, endometriosis, ovarian cysts, chronic pelvic inflammation and myoma of uterus, and so on[7]. This study aim to investigate the effects of Guizhi Fuling Capsule on sex hormones and tumor markers in patients with uterine fibroids, and observe its clinical efficacy.

2. Data and methods

2.1. Clinical data

A total of 120 cases of uterine fibroids patients in our hospital from August 2016 to August 2017 were selected for research...
control group according to the order of treatment, 60 cases in each group. The control group patients was 28-54 years old; the diameter of the myoma of patients was 2.81-10.27 cm, average (6.31 ± 0.62) cm; the course of disease was 2.52-8.46 months, average (3.54 ± 0.35) years, 35 cases of myoma, 14 subserous myoma and 11 submucous myoma. The age of the patients in the observation group was 27-55 years old; the diameter of the myoma was 2.90-10.32 cm, average (6.35 ± 0.63) cm; the course of disease was 2.59-8.52 months , average (3.60 ± 0.36) years, 34 cases of myoma, 15 subserous myoma and 11 submucous myoma. Exclusion criteria: 1) patients with severe heart, liver and kidney dysfunction; 2) patients with endometriosis, ovarian cysts, chronic pelvic inflammatory disease and malignant uterine tumors; 3) pregnant women and lactating women; 4) patients with mental illness. There was no statistical significance in the age, myoma volume, course of disease and disease type in all patients. The study was approved by medical ethics committee of our hospital.

2.2. Treatment methods

The control group was treated by mifepristone. The specific treatment: Mifepristone Tablets (Hubei Gedian fufu Pharmaceutical Co., Ltd., Chinese medicine quasi word: H20033551) was taken in the second days of menstruation, 1 tablets/times, 2 times/d, after meals. The observation group was treated with mifepristone plus Guizhi Fuling Capsule. Specific Treatment: Guizhi Fuling capsules (Jiangsu Kang Yuan medicine industry Limited by Share Ltd, Chinese medicine quasi word Z10950005) were taken on the second days of menstruation, 3 capsules/times, 3 times/d, after meals. The two groups were treated for 1 courses of 3 months.

2.3 Observation indexes

1) Hemoglobin determination: 2 mL fasting venous blood of patients with uterine fibroids was taken in the morning before and after treatment, and placed in EDTA anticoagulant tube. Hemoglobin was measured by automated hematology analyzer (purchased from MINDRAY Bio Medical Limited by Share Ltd, Shenzhen). 2) Detection of VEGF, sex hormone FSH, LH, E2 levels: 2 mL fasting venous blood of patients with uterine fibroids was taken in the morning before and after treatment, placed in an inert gel tube, and centrifuged to take the upper serum. The levels of vascular endothelial growth factor (VEGF), follicle generating hormone (FSH), luteinizing hormone (LH) and estradiol (E2) were measured by ELISA. 3) Detection of tumor markers and inflammatory factors: 2 mL fasting venous blood of patients with uterine fibroids was taken in the morning before and after treatment, placed in an inert gel tube, and centrifuged to take the upper serum. The levels of human epididymal protein 4 (HE4), cancer antigen 125 (CA125) and tumor necrosis factor-α (TNF-α) and interferon-γ (IFN-γ) were measured by ELISA. All the kits were purchased from Wenzhou Pu No company.

2.4 Statistical method

SPSS 21.0 software was used for statistical treatment. In the study, hemoglobin, VEGF and other indicators levels were verified to be in normal distribution and expressed by Mean ± SD. Independent t test was conducted to compare the levels of hemoglobin between groups, and the paired t test was used in the comparison within groups. Values of P<0.05 were considered to be statistically significant.

3. Results

3.1 Comparison of hemoglobin and VEGF levels in two groups of patients with uterine fibroids

Before treatment, there was no significant difference in serum hemoglobin and VEGF levels between the two groups (P>0.05). After treatment, the hemoglobin levels of the two groups increased significantly, and the level of VEGF decreased significantly. The hemoglobin level of the patients in the observation group was (117.09 ± 11.51) g/L higher than that of the control group (105.12 ± 11.63) g/L, and the level of VEGF was (0.69 ± 0.06) pg/mL, which was lower than that of the control group (1.22 ± 0.13) pg/mL (P<0.05), as shown in Table 1.

Table 1.
Comparison of hemoglobin and VEGF levels in two groups of patients with uterine fibroids.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>Hemoglobin (g/L)</th>
<th>VEGF (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before treatment</td>
<td>61.27±6.09</td>
<td>1.67±0.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>105.12±11.63</td>
<td>1.22±0.13</td>
</tr>
<tr>
<td>Observation group</td>
<td>60</td>
<td>Before treatment</td>
<td>61.31±6.13</td>
<td>1.61±0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>117.09±11.51</td>
<td>0.69±0.06</td>
</tr>
</tbody>
</table>

Comparison with the levels before treatment, *P<0.05; Comparison with the levels of control group after treatment, *P<0.05.

Table 2.
Comparison of FSH, LH and E2 levels in two groups of patients with uterine fibroids.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>FSH (U/L)</th>
<th>LH (U/L)</th>
<th>E2 (pmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before treatment</td>
<td>25.14±2.51</td>
<td>18.65±1.85</td>
<td>19.21±1.89</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>20.22±2.03</td>
<td>14.56±1.42</td>
<td>7.65±0.76</td>
</tr>
<tr>
<td>Observation group</td>
<td>60</td>
<td>Before treatment</td>
<td>25.21±2.54</td>
<td>18.61±1.81</td>
<td>19.17±1.90</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>15.87±1.56</td>
<td>10.69±1.06</td>
<td>4.95±0.51</td>
</tr>
</tbody>
</table>

Comparison with the levels before treatment, *P<0.05; Comparison with the levels of control group after treatment, *P<0.05.

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respectively, as shown in Table 4.

Comparison of TNF-α and IFN-γ levels in two groups of patients with uterine fibroids.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>TNF-α (pg/mL)</th>
<th>IFN-γ (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before treatment</td>
<td>81.23±8.12</td>
<td>20.51±2.06</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>48.96±4.91</td>
<td>18.22±0.13</td>
</tr>
<tr>
<td>Observation group</td>
<td>60</td>
<td>Before treatment</td>
<td>80.98±8.12</td>
<td>20.48±0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>40.41±4.05</td>
<td>16.72±1.62</td>
</tr>
</tbody>
</table>

Comparison with the levels before treatment, *P<0.05; Comparison with the levels of control group after treatment, †P<0.05.

Table 4.

Comparison of HE4 and CA125 levels in two groups of patients with uterine fibroids.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>HE4 (pmol/L)</th>
<th>CA125 (U/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before treatment</td>
<td>62.13±6.11</td>
<td>10.69±1.06</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>48.96±4.91</td>
<td>18.22±0.13</td>
</tr>
<tr>
<td>Observation group</td>
<td>60</td>
<td>Before treatment</td>
<td>80.98±8.12</td>
<td>20.48±0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>40.41±4.05</td>
<td>16.72±1.62</td>
</tr>
</tbody>
</table>

Comparison with the levels before treatment, *P<0.05; Comparison with the levels of control group after treatment, †P<0.05.

3.2 Comparison of FSH, LH and E2 levels in two groups of patients with uterine fibroids

Before treatment, there was no significant difference between the levels of serum FSH and other sex hormones in the two groups (P>0.05). After treatment, the levels of FSH, LH and E2 in the two groups were significantly reduced. The levels of FSH, LH and E2 in the observation group were (15.87 ± 1.56) U/L, (10.69 ± 1.06) U/L and (4.95 ± 0.51) pmol/L, respectively, which were lower than those of the control group (20.22 ± 2.03) U/L, (14.56 ± 1.42) U/L and (7.65 ± 0.76) pmol/L (P<0.05), as shown in Table 2.

3.3 Comparison of HE4 and CA125 levels in two groups of patients with uterine fibroids

Before treatment, there was no significant difference in the levels of HE4 and CA125 between the two groups (P>0.05). After treatment, the levels of HE4 and CA125 in the two groups were significantly reduced. The HE4 and CA125 levels of the patients in the observation group were (52.47 ± 5.24) pmol/L and (15.46 ± 1.53) U/mL, respectively, which were lower than those of the control group (62.13 ± 6.11) pmol/L and (19.12 ± 1.83) U/mL (P<0.05), respectively, as shown in Table 3.

3.4 Comparison of TNF-α and IFN-γ levels in two groups of patients with uterine fibroids

Before treatment, there was no significant difference in serum inflammatory factors TNF-α and IFN-γ levels between the two groups (P>0.05). After treatment, the levels of TNF-α and IFN-γ in the two groups decreased significantly. The levels of TNF-α and IFN-γ in the observation group were (40.41 ± 4.05) and (16.72 ± 1.62) pg/mL, respectively, which were lower than those of the control group (48.96 ± 4.91) and (18.22 ± 0.13) pg/mL (P<0.05), respectively, as shown in Table 4.

4. Discussion

Uterine fibroids is a common gynecologic disease of women of childbearing age, with the incidence of 20%–40%. The clinical manifestations of uterine fibroids are excessive menstruation, menstrual cycle extension, lower abdomen and lumbosacral pain and anemia[9,10]. Surgical treatment is the main way to treat such disease, however, postoperative complications always happen after operation, which may cause psychological impact on patients[11]. Mifepristone and Guizhi Fuling Capsule are commonly used drugs for treating this disease. Mifepristone is an anti-progestin drug that is competitive with progesterone receptor, which plays a role in anti-progestin, and could reduce progestrone and estrogen levels, so as to inhibit the growth of hysteromyoma[12]. Guizhi Fuling Capsule can inhibit effect the aggregation of platelet and the proliferation of tumor cell[13]. The effects of combination of the two drugs on sex hormones, tumor markers and inflammatory factors were systematically studied in this study.

This study found that uterine fibroids are hormone dependent diseases. Growth factors, such as VEGF, etc., play a key role in the formation of tumor[14]. Patients with uterine fibroids often suffer from anemia due to irregular bleeding[15]. The results showed that after treatment, the hemoglobin levels of the two groups increased significantly, and the levels of VEGF, sex hormones FSH, LH and E2 decreased significantly. The hemoglobin level of the observation group was (117.09 ± 11.51) g/L, which was higher than that of the control group (105.12 ± 11.63) g/L, and the level of VEGF was (0.69 ± 0.06) pg/mL, lower than that of the control group. The levels of sex hormones FSH, LH and E2 in the observation group were (15.87 ± 1.56) U/L, (10.69 ± 1.06) U/L and (4.95 ± 0.51) pmol/L, respectively lower than those in the control group. The results showed that Guizhi Fuling Capsule can significantly improve anemia, vascular endothelial function and sex hormone levels, consistent with previous studies[16,17]. The reason may be that Guizhi Fuling Capsule has the functions of resisting estrogen and regulating endocrine, inhibiting the proliferation of tumor cells, so as to exert the efficacy of drugs.

Traditional Chinese Medicine believes that qi stagnation and blood stasis are important causes of uterine fibroids[18]. The main
components of Guizhi Fuling capsules mainly include cinnamon twig, peach kernel, poria cocos, paeonia lactiflora pall, etc. Cinnamon twig is the monarch medicine, warm blood, replenishing qi; the peach kernel is the medicine for the minister, promoting blood circulation, removing blood stasis and relieving pain. Poria cocos is the adjuvant, the water is wet, the spleen is beneficial to the stomach. Paeonia lactiflora as adjuvant, bitter cold, has the effect of promoting blood circulation, dissipating blood stasis, cooling blood, removing blood stasis, and relieving. The combination use of these drugs plays the role of promoting blood circulation and removing blood stasis. TNF-α and IFN-γ have immunomodulatory effect, which can promote angiogenesis, and then promote the growth of uterine fibroids[19,20]. Related researches found that CA125 and HE4 have abnormal expressions in benign diseases such as uterine leiomyoma and endometriosis[21,22]. The results of this study showed that after treatment, the levels of tumor markers HE4, CA125, inflammatory factor TNF-α and IFN-γ decreased significantly in the two groups. The levels of HE4, CA125, TNF-α and IFN-γ in the observation group were (52.47 ± 5.24) pmol/L, (15.46 ± 1.53) U/mL, (40.41 ± 4.05) pg/mL and (16.72 ± 1.62) pg/mL, respectively, which were lower than those of the control group (P<0.05). The results showed that Guizhi Fuling Capsule could significantly improve the level of tumor markers and relieve inflammatory stress reaction. The possible reasons may be concluded as follows: 1) Guizhi Fuling Capsule can improve the immune function and anti-tumor effects of patients, thus improving the clinical symptoms of patients; 2) Guizhi Fuling Capsule can inhibit the medium of inflammation thus inhibit the synthesis of cytokines, playing anti-inflammatory effects.

To sum up, Guizhi Fuling Capsule can significantly improve the level of sex hormones and tumor markers, relieve inflammatory stress, and has significant curative effect, which is worthy for clinical application. There are still some inadequacies in this study: the number of cases is less, and all of them are from our hospital; there is no dynamic observation of serum hormone and inflammatory factors. Hence, there may be a deviation in the region and time. And it is necessary to expand the sample number for in-depth study.

References


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