



Effect of Modified and accumulated decoction on serum ER, PR, sex hormone, IGF-I and IGF-I in patients with uterine fibroids

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ABSTRACT

Objective: To study the effect of Modified and accumulated Decoction on serum ER, PR, sex hormone, IGF-I and IGF-I in patients with uterine fibroids. **Method:** A total of 90 patients with uterine fibroids in our hospital from January 2015 to January 2017 were enrolled in this study. The subjects were divided into the control group ($n=45$) and the treatment group ($n=45$) randomly. The control group was treated with mifepristone, the treatment group was treated with Modified and accumulated Decoction combined with mifepristone, and both the two groups were treated for 3 months. The uterine fibroid volume and uterine volume of the two groups before and after treatment were compared. The serum ER, PR, P, E₂, LH, FSH, IGF-I and IGF-IR of the two groups before and after treatment were compared. **Result:** There were no significantly differences of the uterine fibroid volume and uterine volume of the two groups before treatment. The uterine fibroid volume and uterine volume of the two groups after treatment were significantly less than before treatment, and that of the treatment group after treatment were significantly less than the control group. There were no significantly differences among the serum ER, PR, P, E₂, LH, FSH, IGF-I and IGF-IR of the two groups before treatment. The serum ER, PR, P, E₂, LH, FSH, IGF-I and IGF-IR of the two groups after treatment were significantly lower than before treatment, and that of the treatment group after treatment were significantly lower than the control group. **Conclusion:** Modified and accumulated Decoction combined with mifepristone can significantly reduce the uterine fibroid volume, improve the serum ER, PR, sex hormone, IGF-I and IGF-I levels of the patients with uterine fibroids, and it was worthy clinical application.

1. Introduction

Uterine leiomyoma is a common benign tumor in the female reproductive system, which occurs in women aged 30-50 years, with an incidence of 20%-30%. It has the characteristics of high morbidity and easy recurrence. It can cause lower abdominal pain, abnormal menstrual volume, menstrual cycle disorder and so on, which seriously affect the daily life and normal work of the patients[1,2]. There is no obvious clinical symptom in the early

stage of hysteroscopy, When the volume of fibroids increases to a certain extent, it can cause abnormal vaginal bleeding and other abnormal manifestations, and severe cases can lead to anemia, bleeding and so on[3]. Uterine leiomyoma is a hormone dependent tumor. The levels of progesterone, estradiol and other hormones in patients with uterine fibroids are significantly higher than normal levels[4]. It is believed that the occurrence and development of uterine leiomyoma are closely related to estrogen, progesterone and other related growth factors[5]. At present, Clinical treatment of uterine fibroids mainly uses surgical measures, but the recurrence rate is as high as 30%, and the side effects caused by the operation is large, so looking for a safe and effective method for the treatment of uterine fibroids has important clinical significance[6]. Mifepristone is a progesterone antagonist commonly used in the treatment of

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uterine fibroids. Long term use of large doses may cause a variety of adverse reactions, which limits its wide clinical application[7]. This study was aimed to investigate the effects of Modified and accumulated Decoction combined with mifepristone on estrogen receptor, progesterone receptor, sex hormone, insulin growth factor - I and its receptor levels in patients with uterine fibroids. The results are as follows.

2. Information and methods

2.1. General information

This study selected 90 cases of uterine fibroids patients from January 2015 to January 2017 in our hospital. Case inclusion criteria: (1) Diagnostic criteria for uterine fibroids in accordance with obstetrics and gynecology (Sixth Edition)[8]; (2) Diagnosis of hysteromyoma by color Doppler ultrasonography; (3) The patients were 20-50 years old without menopause; (4) Informed consent of the study content and signed informed consent patients. Case exclusion criteria: (1) patients who has a single tumor size more than 5 cm; (2) Patients with malignant tendency; (3) The number of tumor was more than 3; (4) Patients with other malignant tumors; (5) Patients with adenomyosis and endometriosis; (6) Patients with liver and renal dysfunction; (7) Patients who do not cooperate with treatment.

All the patients were randomly divided into control group and treatment group according to random number table. There were 45 cases in each group. The patients in the control group were 30-50 years old, with an average age of (38.41 ± 5.15) years; the course of disease was 6-19 months, the average course of disease was (10.40 ± 2.18) months; the types of myoma were 25 cases of intramural myoma and 20 cases of submucous myoma. The patients in the treatment group were 28-50 years old, with an average age of (37.10 ± 6.24) years; the course of disease was 6-21 months, the average course of disease was (11.41 ± 3.11) months; the types of myoma were 24 cases of intramural myoma and 21 cases of submucous myoma. The general data of the two groups were comparable. This study was approved by the medical ethics committee of our hospital.

2.2 Treatment method

The control group was treated with mifepristone (purchased from Beijing Zizhu Pharmaceutical Co. Ltd., specifications 25 mg/time, Zhunzi H10950003) treatment, oral, 12.5 mg/time, started medication from the first day of menstruation medication, once/d, continuous treatment for 3 months. Patients in the treatment group

were treated with the addition and subtraction of flat accumulate Decoction on the basis of the treatment in the control group, whose prescription contains 20 g honeysuckle, 20 g Zedoary turmeric, 15 g Self-heal, 10 g rhizoma sparganii, 10 g radices trichosanthis, 10 g peach kernel, 10 g Rhizoma Pinellinae Praeparata, 10 g Gleditsia sinensis, 10 g endothelium corneum gigeriae galli, 6 g Leech, 6 g Licorice, 2 pieces of big centipedes, decocted with water, 200 mL/agent, 2 doses/d, take 1 times in the morning and evening, stop taking during the menstrual period, continuous treatment for 3 months.

2.3 Detection indicators

Color Doppler ultrasound measurements were used to calculate and compare the size of myoma of uterus and uterine volume in the two groups before and after treatment.

5 mL venous blood of the two groups before and after treatment in the morning fasting state was collected, and the supernatant was centrifuged as the serum and stored in the freezer at -70 centigrade. The levels of serum estrogen receptor (ER), progesterone receptor (PR), progesterone (P), E₂, luteinizing hormone (LH), follicle-stimulating hormone (FSH), insulin-like growth factor-I (IGF-I), insulin-like growth factor-I receptor (IGF-IR) were detected and compared between the two groups before and after treatment. The levels of serum P, E₂, LH and FSH were detected by radioimmunoassay, and the levels of serum IGF-I and IGF-IR were detected by double sandwich enzyme-linked immunosorbent assay (ELISA).

2.4 Data processing

We Used SPSS 19.0 software package to process the test result data, The general form of enumeration data was rate (%), and chi square 2 test was used; The measurement data is expressed as mean \pm standard deviation (Mean \pm SD), the use of t test was to compare the difference between groups, $P < 0.05$ is considered to have a statistically significant difference.

3. Results

3.1 Comparison of uterine fibroids volume and uterine volume before and after treatment in two groups

Before treatment, the volume of uterine fibroids and the volume of uterus in the control group were respectively (60.48 ± 13.41) cm³, (145.20 ± 18.67) cm³, that in treatment group were (61.03 ± 14.26) cm³, (144.97 ± 17.52) cm³, there was no significant difference

between the two groups ($P>0.05$); After treatment, the volume of uterine fibroids and the volume of uterus in the control group were respectively $(45.32\pm 11.10) \text{ cm}^3$, $(119.52\pm 14.07) \text{ cm}^3$, that in treatment group were $(32.58\pm 7.21) \text{ cm}^3$, $(101.32\pm 9.28) \text{ cm}^3$. The volume of uterine fibroids and uterine volume of the two groups after treatment were smaller than before treatment, and the volume of uterine fibroids and uterine volume after treatment in the treatment group were significantly less than those in the control group ($P<0.05$). See Table 1.

Table 1.

Comparison of uterine fibroids volume and uterine volume before and after treatment in two groups (cm^3).

Group	n	Time	Volume of uterine fibroids	Uterine volume
Control group	45	Before treatment	60.48±13.41	145.20±18.67
		After treatment	45.32±11.10 [*]	119.52±14.07 [*]
Treatment group	45	Before treatment	61.03±14.26	144.97±17.52
		After treatment	32.58±7.21 ^{*#}	101.32±9.28 ^{*#}

Note: compared with before treatment, ^{*} $P<0.05$; compared with the control group, [#] $P<0.05$.

3.2 Comparison of serum ER and PR levels before and after treatment in two groups

Before treatment, the levels of serum ER and PR in the control group were respectively $(1.59\pm 0.19) \text{ ng/mL}$, $(2.00\pm 0.17) \text{ ng/mL}$, that in treatment group were $(1.60\pm 0.21) \text{ ng/mL}$, $(1.98\pm 0.19) \text{ ng/mL}$, there was no significant difference between the two groups ($P>0.05$); After treatment, the levels of serum ER and PR in the control group were $(1.28\pm 0.14) \text{ ng/mL}$, $(1.46\pm 0.14) \text{ ng/mL}$, that in treatment group were $(0.65\pm 0.11) \text{ ng/mL}$, $(0.66\pm 0.10) \text{ ng/mL}$, The serum ER and PR levels of the two groups after treatment were smaller than before treatment, and the serum ER and PR levels in the treatment group were significantly lower than those in the control group ($P<0.05$). See Table 2.

Table 2.

Comparison of serum ER and PR levels before and after treatment in two groups (ng/mL).

Group	n	Time	ER	PR
Control group	45	Before treatment	1.59±0.19	2.00±0.17
		After treatment	1.28±0.14 [*]	1.46±0.14 [*]
Treatment group	45	Before treatment	1.60±0.21	1.98±0.19
		After treatment	0.65±0.11 ^{*#}	0.66±0.10 ^{*#}

Note: compared with before treatment, ^{*} $P<0.05$; compared with the control group, [#] $P<0.05$.

Table 3.

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

Group	n	Time	P ($\mu\text{g/L}$)	E ₂ (pmol/L)	LH (U/L)	FSH (U/L)
Control group	45	Before treatment	30.89±5.12	353.13±27.26	19.05±5.18	17.76±4.12
		After treatment	15.67±3.60 [*]	201.55±19.47 [*]	13.14±2.07 [*]	12.20±1.24 [*]
Treatment group	45	Before treatment	31.02±5.48	351.91±28.03	18.75±6.05	17.15±4.63
		After treatment	10.14±2.88 ^{*#}	143.35±16.14 ^{*#}	9.02±1.54 ^{*#}	8.63±1.05 ^{*#}

Note: compared with before treatment, ^{*} $P<0.05$; compared with the control group, [#] $P<0.05$.

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

Before treatment, the levels of serum P, E₂, LH, FSH in the control group were $(30.89\pm 5.12) \mu\text{g/L}$, $(353.13\pm 27.26) \text{ pmol/L}$, $(19.05\pm 5.18) \text{ U/L}$, $(17.76\pm 4.12) \text{ U/L}$, that in treatment group were $(31.02\pm 5.48) \mu\text{g/L}$, $(351.91\pm 28.03) \text{ pmol/L}$, $(18.75\pm 6.05) \text{ U/L}$, $(17.15\pm 4.63) \text{ U/L}$, there was no significant difference between the two groups ($P>0.05$); After treatment, the levels of serum P, E₂, LH, FSH in the control group were $15.67\pm 3.60) \mu\text{g/L}$, $(201.55\pm 19.47) \text{ pmol/L}$, $(13.14\pm 2.07) \text{ U/L}$, $(12.20\pm 1.24) \text{ U/L}$, that in treatment group were $(10.14\pm 2.88) \mu\text{g/L}$, $(143.35\pm 16.14) \text{ pmol/L}$, $(9.02\pm 1.54) \text{ U/L}$, $(8.63\pm 1.05) \text{ U/L}$, The levels of serum P, E₂, LH and FSH in the two groups after treatment were smaller than before treatment, and the levels of serum P, E₂, LH and FSH in the treatment group were significantly lower than those in the control group ($P<0.05$). See table 3.

3.4 Comparison of serum IGF-I and its receptor levels between the two groups before and after treatment

Before treatment, the levels of serum IGF-I and its receptor in the control group were $(1381.47\pm 106.33) \text{ ng/mL}$, $(2.17\pm 0.41) \text{ ng/mL}$, that in treatment group were $(1380.27\pm 110.15) \text{ ng/mL}$, $(2.16\pm 0.39) \text{ ng/mL}$, there was no significant difference between the two groups ($P>0.05$); After treatment, the levels of serum IGF-I and its receptor in the control group were $(788.50\pm 51.10) \text{ ng/mL}$, $(1.40\pm 0.27) \text{ ng/mL}$, that in treatment group were $(421.34\pm 42.26) \text{ ng/mL}$, $(0.69\pm 0.20) \text{ ng/mL}$, the serum IGF-I and IGF-IR levels of the two groups after treatment were smaller than before treatment, and the serum IGF-I and IGF-IR levels in the treatment group were significantly lower than those in the control group ($P<0.05$). See table 4.

Table 4.

Comparison of serum IGF-I and its receptor levels between the two groups before and after treatment (ng/mL).

Group	n	Time	IGF-I	IGF-IR
Control group	45	Before treatment	1381.47±106.33	2.17±0.41
		After treatment	788.50±51.10 [*]	1.40±0.27 [*]
Treatment group	45	Before treatment	1380.27±110.15	2.16±0.39
		After treatment	421.34±42.26 ^{*#}	0.69±0.23 ^{*#}

Note: compared with before treatment, ^{*} $P<0.05$; compared with the control group, [#] $P<0.05$.

4. Discussion

The malignant probability of uterine fibroids is very low, therefore, the clinical treatment of small volume of tumor is generally not given medicine, For larger volume tumors, conventional surgical resection is performed[9]. However, surgical treatment of uterine fibroids can rapidly relieve the clinical symptoms of the patients in a short period of time, but the recurrence rate is very high, Easily lead to persistent illness, repeated and difficult to completely treat, and can also cause damage to the reproductive function of patients, so most patients will choose conservative drug treatment measures[10]. Mifepristone can reduce the size of uterine fibroids by blocking the level of progesterone in patients with uterine fibroids, which has certain curative effect, but the effect of simple treatment is not significant[11]. Traditional Chinese medicine holds that Uterine leiomyoma belongs to the range of "mass" and "rock mass", "Chang Qing", "accumulation" etc., which is mainly caused by stagnation of blood stasis, blood feud, it should be treated with Xiaozheng Sanjie, blood stasis, heat clearing and detoxifying[12]. Modified and accumulated Decoction contains honeysuckle, rhizoma curcumae, Rhizoma sparganii, Prunella vulgaris, trichosanthes root, peach kernel, pinellia, Gleditsia sinensis, Gallus gallus, leech, licorice, centipede and other ingredients, among them, honeysuckle is monarch medicine, which has the function of dispersing wind heat and clearing away heat and toxic materials; Zedoary rhizome and rhizome have the effect of clearing away pain, breaking blood and promoting qi; Prunella vulgaris has the effect of clearing eyesight and detumescence and clearing liver and Dispersing Stasis; Trichosanthin has swelling and pus, thirst, clearing away heat and purging fire; Peach kernel has the effect of relieving cough, relieving asthma and promoting blood circulation to remove blood stasis; Pinellia has Xiaopi Sanjie, Jiangni antiemetic efficacy, the phlegm dampness; Gleditsia sinensis has the functions of dispelling wind pus and detumescence detoxification effect; ventriculi galli mucosa has the functions of invigorating the spleen and stomach, promote digestion; Leech has the effect of eliminating blood stasis and eliminating blood stasis and dysmenorrhea; Licorice has the effect of Clearing away heat and toxic substances, eliminating phlegm and relieving cough, invigorating spleen and Supplementing Qi, The centipede has the effect of Sanjie poison, Tongluozhitong, Xifeng spasm. All drugs are combined to play the role of eliminating symptoms, dispersing stasis, activating blood circulation to dissipate blood stasis and clearing away heat and toxic substances[13-15]. This study was aimed to investigate the effects of Modified and accumulated Decoction combined with mifepristone on estrogen receptor, progesterone receptor, sex hormone, insulin growth factor -I and its receptor levels in patients with uterine fibroids, so as to provide some inspiration for

the effective treatment of uterine fibroids.

The results of this study show that the volume of uterine fibroids and the volume of uterus after treatment were smaller than those before treatment in two groups, and the volume of uterine fibroids and the volume of uterus after treatment in the treatment group were significantly less than those in the control group, the differences were statistically significant ($P < 0.05$). This shows that the modified decoction combined with mifepristone can significantly reduce the tumor in patients with uterine fibroids. Mifepristone can inhibit the secretion of progesterone through the combination with PR, thereby reducing the expression of epidermal growth factor receptor in tumor tissue, slowing the enlargement of tumor body, and playing the role of reducing the volume of uterine fibroids[16]. It is suggested that the decoction can inhibit the hyperplasia of fibrous tissue, inhibit the formation of cardiovascular and inhibit the enlargement of tumor[17]. the combination of Modified Decoction and mifepristone in the treatment of mifepristone may have synergistic effect, and the treatment effect is better[18]. In addition, the results of this study show that The serum levels of ER, PR, P, E₂, LH, FSH, IGF-I and IGF-IR in the two groups were lower than those before treatment, and that in the treatment were lower than control group, the differences were statistically significant ($P < 0.05$). This suggests that the modified decoction combined with mifepristone can significantly improve the levels of estrogen receptor, progesterone receptor, sex hormone, insulin growth factor -I and its receptor in patients with uterine fibroids. Uterine fibroids are sex hormone dependent tumors. ER, PR, P, E₂, LH and FSH are highly expressed in the patients, and they are closely related to the occurrence and development of tumors[19]. It has been reported in the literature[20] that the growth of uterine leiomyoma is positively correlated with the increase of IGF-I and its receptor. Modified and accumulated Decoction combined with mifepristone can inhibit the proliferation of uterine leiomyoma cells, block tumor growth, play a therapeutic effect through the regulation of estrogen and progesterone receptors in patients with the expression level, reducing levels of growth factor receptor insulin-like growth factor -I receptor related cells.

In summary, Modified and accumulated Decoction combined with mifepristone can significantly reduce the uterine fibroid volume, improve the serum ER, PR, sex hormone, IGF-I and IGF-I levels of the patients with uterine fibroids, and it was worthy clinical application.

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