

The Therapeutic Effect of Quyu Jiedu Xiaozheng Tang Combined with Diqu Progesterone Tablets on Endometriosis and Its Effect on Serum MIF and TGF- β 1 Impact Of 1

Tian Lihua^{1,a}, Liu Jiale¹, Wang Chen¹, Chen Mengjie^{2,*}, Yao Jia²

¹Shaanxi University of Chinese Medicine, Xi'anyang, Shaanxi, 712046, China

²Xi'an Traditional Chinese Medicine Hospital, Xi'an, Shaanxi, 710021, China

^a1510932239@qq.com

*Corresponding author: mengjie8369@163.com

Keywords: Apply Quyu Jiedu Xiaozheng Tang and Diqu Progesterone Tablets to treat endometriosis, and pay attention to the patient's serum MIF and TGF before and after treatment- β value change of 1

Abstract: To observe the clinical efficacy of Quyu Jiedu Xiaozheng Tang combined with Diqu Progesterone Tablets in the treatment of patients with endometriosis, and to analyze the serum MIF and TGF of patients- β the impact of 1. 60 EM patients were selected and randomly divided into a traditional Chinese medicine group, a combination of traditional Chinese and Western medicine group, and a western medicine group, with 20 cases each. The traditional Chinese medicine group was given oral Quyu Jiedu Xiaozheng Tang; The Western medicine group was given oral Dafu Tong (Diqu Progesterone Tablets); The combination of traditional Chinese and Western medicine group was given a combined oral administration of Quyu Jiedu Xiaozheng Tang and Diqu Progesterone Tablets. After three consecutive months of treatment, the clinical efficacy and total effective rate of the three groups of patients were compared. Enzyme linked immunosorbent assay (ELISA) was used to detect the levels of macrophage migration inhibitory factor (MIF) and transforming growth factor (TGF) in the serum of the three groups of patients before and after treatment- β 1 level. The total effective rate (95%) of clinical efficacy in the combination of traditional Chinese and Western medicine group is better than that in the traditional Chinese medicine group (90%) and the western medicine group (90%); After treatment, the serum MIF levels of the three groups of patients were significantly reduced compared to before treatment, and P (0.033) in the combination of Chinese and Western medicine group was lower than P (0.036) in the traditional Chinese medicine group and P (0.036) in the western medicine group; Serum TGF of the three groups after treatment- β All levels were significantly lower than before treatment, and P (0.035) in the combination of traditional Chinese and Western medicine group was lower than P (0.043) in the traditional Chinese medicine group and P (0.042) in the western medicine group. The P-values are all < 0.05, indicating significant significance in the experiment. Conclusion: Quyu Jiedu Xiaozheng Tang combined with Diqu Progesterone Tablets can effectively alleviate the clinical symptoms of patients with endometriosis, and can reduce the serum MIF and TGF of patients- β At the first level, the clinical effect of combining traditional Chinese and Western medicine in treating EM is more significant than that of traditional Chinese medicine and Western medicine alone. Its

mechanism of action may be related to the regulation of macrophage migration inhibitory factor MIF and transforming growth factor TGF- β 1. Related.

1. Introduction

Endometriosis (EM), also known as endometriosis, refers to an estrogen dependent disease in which active endometrial tissue (stroma and glands) implants, grows, and repeatedly damages areas outside the endometrium and myometrium of the uterus. It is a common, frequently occurring, and difficult disease in gynecology^[1]. According to comprehensive literature reports, about 2% -10% of women of childbearing age suffer from EM, with infertility accounting for up to 50%^[2]. The etiology and pathogenesis of this disease are not yet fully understood, and inflammatory reactions and immune system abnormalities are believed to be closely related to it. Professor Zhang Xiaofeng believes that the traditional Chinese medicine etiology and pathogenesis of EM are "stasis, turbidity, and dampness toxin intertwined", so he developed his own Quyu Jiedu Xiaozheng Tang^[3]. This prescription mainly uses insect like drugs to clear meridians and collaterals, detoxify and relieve pain, and is supplemented by tonifying qi and tonifying the body, as well as promoting detoxification and going out. It has achieved good therapeutic effects in clinical treatment of endometriosis. This study aims to observe the clinical efficacy of Quyu Jiedu Xiaozheng Tang combined with Diqu Progesterone Tablets in the treatment of endometriosis patients, and analyze the effects of serum MIF and TGF on patients with endometriosis- β . The impact of 1 provides a basis for its clinical application.

2. Clinical data

2.1 General Information:

Sixty outpatient patients who were diagnosed with "endometriosis" at Xi'an Traditional Chinese Medicine Hospital from March 2022 to October 2022 and diagnosed with "stasis, turbidity, and dampness toxin intertwined" were selected. Age range from 18 to 45 years, with an average age of 33.33 ± 5.66 years; The course of the disease is 0.4-6 years, with an average of 2.09 ± 1.24 years;

2.2 Diagnostic criteria:

Diagnostic criteria for Western medicine:

According to the diagnosis and treatment guidelines published in the Chinese Journal of Obstetrics and Gynecology in 2021^[1];The 2018 version of the "Chinese Expert Consensus on Long term Management of Endometriosis"^[4];In 2015, the "Diagnosis and Treatment Guidelines for Endometriosis" was released by the Endometriosis Collaborative Group of the Obstetrics and Gynecology Branch of the Chinese Medical Association^[5];Diagnosis and treatment standards published by the Obstetrics and Gynecology Professional Committee of the Chinese Society of Integrated Traditional and Western Medicine in 1991^[6].Based on the above relevant literature, the proposed standards are as follows:(1) The patient has a history of or has no painful menstruation, or has mild dysmenorrhea, with or without a history of uterine cavity surgery;(2)①The patient's dysmenorrhea gradually worsens;②The symptoms of discomfort in the abdomen and lumbosacral region of the patient during menstruation gradually worsen;③The patient has periodic rectal irritation symptoms, which gradually worsen;④When the doctor examined the patient's body, it was found that

there were tender nodules in the posterior fornix, uterosacral ligament, or uterine isthmus; ⑤The patient's ultrasound showed a lump of adhesions in the appendix accompanied by a nodular sensation of the capsule, and the fallopian tube was unobstructed;⑥The patient showed significant changes in the size of the aforementioned lump in the attachment before and after menstruation (But the patient did not use anti-inflammatory drugs.).Any combination of points ①, ②, and ③, as well as points ④, ⑤, and ⑥, can be considered as a clinical diagnosis.

Diagnostic criteria for traditional Chinese medicine:

The endometriosis syndrome treated with "Quyū Jiedū Xiaozhēng Tāng" belongs to the "combination of blood stasis, turbidity, and dampness toxin". Referring to the relevant chapters on "excessive menstruation" and "dysmenorrhea" in the tenth edition of "Traditional Chinese Medicine Gynecology" published by China Traditional Chinese Medicine Press ^[7] and "Diagnosis of Traditional Chinese Medicine" (the third edition of the new century), the specific standards are as follows:

The main symptom of the patient is abdominal pain before or during menstruation, and the pain refuses to press. Tongue coating and pulse condition: The tongue is purple dark or red in color, with visible ecchymosis and spots on the tongue body, and varicose and blood stasis in the sublingual veins; The tongue coating is greasy, and the pulse is smooth, or (or) astringent. Combined with tongue and pulse, the main symptom is essential, and if the secondary symptom meets two or more criteria, it can be diagnosed. And it meets the inclusion criteria for this experiment.

3. Methods

3.1 Sample grouping method

Firstly, 60 subjects were coded according to a pre designed sample size, and random numbers were generated using SPSS 22.0 statistical software through a random number generation algorithm. Based on the corresponding random numbers for each subject code, the included subjects were randomly assigned in a 1:1:1 ratio to A: 20 Chinese medicine group, B: 20 integrated Chinese and Western medicine group, and C: 20 Western medicine group.

3.2 Treatment methods

Traditional Chinese Medicine Group: Patients take orally Quyū Jiedū Xiaozhēng Tāng (all traditional Chinese medicine are decoction, provided by the Traditional Chinese Medicine Decoction Room of Xi'an Traditional Chinese Medicine Hospital). The dosage of the medication is 200ml per bag, and the patient takes one bag after breakfast and one bag after dinner. Medication instructions: The patient starts taking the medication from the 3rd to 5th day after each menstrual cycle is clean. They take it continuously for 6 days and rest for 1 day. One treatment cycle lasts for three months. During this treatment period, patients should not take other medications to treat this disease, and should also refrain from eating raw, cold, greasy, or irritating foods. If the patient has a cold, stop taking medication. If the patient becomes pregnant during treatment, discontinue medication immediately. It is prohibited for those who are allergic to traditional Chinese medicine, and should be used with caution for those with allergic constitution.

Western medicine group: Administer oral administration of Dafu Tong (Dedroprogesterone Tablets) Abbott Biologicals B.V. (Netherlands), batch number: 364232. Store below 25 °C, Starting from the 5th day of menstruation, take 10mg/dose twice a day for 20 consecutive days. Continuously treat for 3 menstrual cycles. During the treatment period, it is prohibited to take other drugs with similar effects.

The combination of traditional Chinese and Western medicine group: Oral administration of traditional Chinese medicine and the medication method are consistent with those of the traditional Chinese medicine group. At the same time, starting from the 5th day of menstruation, oral administration of dexamethasone and progesterone tablets is the same as that of the Western medicine group.

3.3 Observation indicators and methods

Efficacy observation indicators: Traditional Chinese Medicine syndrome score and total effective rate of clinical efficacy

Laboratory observation indicators: determination of MIF and TGF- β 1 level, and conduct analysis and comparison to collect venous blood. Using enzyme-linked immunosorbent assay (ELISA), peripheral blood from the elbow vein was extracted on an empty stomach using coagulation promoting blood vessels in the early morning. After centrifugation (3500rpm, 10min, 4 °C), the upper serum was carefully extracted and stored in a -80 °C refrigerator. Sufficient samples were collected before and after treatment. Operators need to follow MIF and TGF- β 1. Instructions for the reagent kit, follow the steps to carry out the relevant operations.

3.4 Statistical methods

This study used SPSS22.0 statistical software to process the obtained data.

4. Results

After a three-month cycle of treatment, the patient's symptoms and signs improved. Serum samples were collected before and after treatment, and MIF and TGF were measured- β 1 level and conduct analysis and comparison. Table 1, Table 2, and Table 3 respectively represent the relationship between the degree of illness and efficacy of the three groups of patients, as well as the serum MIF and TGF before and after treatment in the three groups of patients- β Comparison of levels (mean \pm standard deviation), serum MIF and TGF before and after treatment in three groups of patients- β Compare the P-values of 1, as follows:

Table 1: Relationship between the degree of illness and efficacy of three groups of patients

	heal	Apparent effect	effective	invalid	Apparent healing rate (%)	Total effective rate (%)
Traditional Chinese Medicine Group	2	4	12	2	30	90
Integrated Traditional Chinese and Western Medicine Group	3	6	10	1	45	95
Western Medicine Group	2	2	14	2	20	90

Table 2: Serum MIF and TGF before and after treatment in three groups of patients- β 1 level comparison (mean \pm standard deviation)

group	MIF		TGF- β 1	
	Before treatment	After treatment	Before treatment	After treatment
Traditional Chinese Medicine Group	57.10 \pm 5.59	51.99 \pm 5.73	21.65 \pm 3.93	18.82 \pm 2.37
Integrated Traditional Chinese and Western Medicine Group	50.91 \pm 4.87	45.61 \pm 6.44	24.65 \pm 12.43	15.99 \pm 3.63
Western Medicine Group	57.02 \pm 5.77	51.38 \pm 8.05	18.39 \pm 2.18	14.95 \pm 4.53

Note: After treatment, three groups of patients obtained serum MIF and TGF- β All levels have decreased, indicating clinical efficacy. All values obtained are rounded to two decimal places

Table 3: Serum MIF and TGF before and after treatment in three groups of patients- β Comparison of P-values for 1

	Traditional Chinese Medicine Group	Integrated Traditional Chinese and Western Medicine Group	Western Medicine Group
MIF	0.036	0.033	0.036
TGF- β 1	0.043	0.035	0.042

Note: After t-test, the P values of the three groups of patients before and after comparison were all < 0.05, indicating that the experiment was meaningful; From the above differences in P values, it can be seen that the patients in the combination of traditional Chinese and Western medicine group have serum MIF and serum TGF- β The P-value of 1 was lower than that of the traditional Chinese medicine group and the Western medicine group treatment group.

The t-values obtained from the serum MIF test of the three groups of patients were 2.386 in the traditional Chinese medicine group, 2.402 in the integrated traditional Chinese and Western medicine group, and 2.354 in the western medicine group, respectively; Serum TGF- β The t-values obtained from the 1 test were 2.256 for the traditional Chinese medicine group, 2.381 for the combination of traditional Chinese and Western medicine group, and 2.282 for the western medicine group.

5. Discussion

Although endometriosis is a benign disease, it has the characteristics of cell proliferation, infiltration and growth, and easy recurrence of malignant behavior. At present, the etiology and pathogenesis have not been elucidated, and surgical treatment has a high recurrence rate and is prone to infertility. For EM patients who do not meet surgical indications, medication is usually used to suppress ovarian function and prevent the development of endometriosis. However, hormone based drugs have significant side effects and a high recurrence rate in treating EM, as well as symptoms such as nausea, mild depression, liver and kidney dysfunction, masculinization, amenorrhea, obesity, and bone loss^[8]. Therefore, the treatment methods of traditional Chinese medicine provide more options for EM patients, which can improve clinical efficacy, relieve dysmenorrhea, and pregnancy rates, as well as reduce the incidence of adverse reactions.

Traditional Chinese medicine believes that the pathological basis of this disease is blood stasis, which refers to the "blood leaving the meridians" that stops accumulating in the uterus, Chongren, and obstructs the veins. Due to the obstruction of Chongren, dysmenorrhea can occur due to pain caused by obstruction; Due to prolonged blood stasis, abnormal body fluid application, continued growth of phlegm and dampness, and the formation of symptoms due to blood stasis; The visible evil blocks Chongren and the uterus, and cannot produce sperm and lead to secondary infertility. The pathological feature is periodic bleeding caused by changes in ovarian hormones in ectopic lesions, leading to proliferation and adhesion of surrounding fibrous tissue. Therefore, the main treatment method is to promote blood circulation and dissipate blood stasis, supplemented by tonifying the kidney and tonifying qi, soothing the liver and regulating qi, warming the meridians and dispersing cold, softening and firming the body to dispel blood stasis, and so on.

Commonly used formulas and medicines include Shaofu Zhuyu Tang, Guizhi Fuling Wan, Yinjia Wan, etc. Xiao Shan, Zhao Li^[9], and others believe that "blood stasis" is the core of endometriosis, which is both a pathogenic factor, pathogenesis, and pathological product. Fu Youfeng et al. ^[10] believe that the main pathogenesis of endometriosis is the deficiency of spleen and kidney, as well as the combination of dampness, turbidity, stasis, and toxin. Therefore, they established the general method of detoxifying, promoting dampness, and resolving blood stasis to eliminate symptoms. Xie Dandan, Cao Yang, and others ^[11] believe that endometriosis mostly belongs to the type of qi stagnation and blood stasis, and advocate promoting the circulation of qi to relieve pain, promoting

blood circulation and resolving blood stasis. Yang Dongxia, Wang Ning, et al. ^[12] treated endometriosis based on the theory of dampness, heat, and stasis, with the treatment of clearing heat, promoting blood circulation, resolving blood stasis, and relieving pain. Guan Lilan and Zhou Ying ^[13] applied the method of warming yang and dispersing nodules to treat endometriosis of the type of "yang deficiency and yin nodules", and clinically used Lizhong Tang, Guizhi Fuling Wan, and Xiaoluo Wan. Professor You Zhaoling believes that "blood stasis" is the pathological basis of endometriosis, and "stasis, deficiency, and phlegm" are the characteristics of its pathogenesis. She proposed a treatment method of "tonifying and tonifying qi, promoting blood circulation to remove stasis, and softening and dispersing nodules". For those with fertility requirements, treatment should be combined with different therapies of the menstrual cycle ^[14]. Zhao Xiaoxuan, Zhang Yang, and others ^[15] explained the mechanism of dysmenorrhea in patients with endometriosis from the perspective of "all pain and itching ulcers belong to the heart", emphasizing the importance of psychological factors, and providing new ideas for the treatment of endometriosis dysmenorrhea patients.

Professor Zhang Xiaofeng, the mentor, believes that the clinical manifestation of EM patients with ectopic endometrium, stimulated by hormonal changes in the menstrual cycle, is called "menstrual blood stasis", which is caused by the shedding of ectopic endometrium. If there is a portion of blood stasis, there will be a portion of latent heat. If the blood stasis persists for a long time, it will accumulate into poison, which is called "stasis toxin"; Blood stasis does not dissipate, turning into "evil blood" and "turbid fluid", which then affects the application of body fluid, causing loss of water metabolism and forming "dampness toxin"; Blood stasis, toxin, dampness, and heat are intertwined, causing a lack of smooth qi flow, a lack of clear qi, a lack of turbidity, and internal obstruction of dampness and turbidity. This is called "turbid toxin". The etiology and pathogenesis of the disease are "stasis, turbidity, and dampness toxin intertwined", and the characteristic of the disease is "when the toxin is present".

Therefore, the method of removing blood stasis and eliminating symptoms, detoxifying and turbidity was established, and a self-formulated decoction for removing blood stasis, detoxifying and eliminating symptoms was developed. The three drugs in Quyu Jiedu Tang, including Chicken Blood Vine, *Hedyotis diffusa*, and edible tulip, have the effects of clearing heat and detoxifying, promoting dampness and turbidity; Frankincense, myrrh, and dragon's blood can have the effect of promoting blood circulation, dispersing blood stasis, and alleviating pain; Insects are good at moving and channeling, used to detoxify centipedes, disperse knots, and clear collaterals to relieve pain; Huoxiang and Coix seed are fragrant and turbid, have light penetration and dampness removal, can also detoxify, and strengthen the spleen and stomach; Calcined corrugated, lychee kernels eliminate symptoms, soften and disperse knots, promote qi circulation and relieve pain; *Astragalus membranaceus* can nourish qi and nourish the body, and promote detoxification to go out; Roasted licorice is used to blend various herbs, while the other is to relieve pain and detoxify slowly. Patients taking Quyu Jiedu Xiaozheng Tang can comprehensively and multi-level dissolve and eliminate evil toxins in the body, enabling faster elimination of evil toxins.

Moreover, modern pharmacological research has shown that the active ingredients extracted from *Caulis spatholobi* can inhibit the occurrence of inflammatory reactions ^[16] and regulate a series of biological processes, acting on the treatment of endometriosis through the "active ingredient target pathway" ^[17]. The aqueous extract of *Hedyotis diffusa* can reduce the levels of IL-6 and TNF- α factors in serum to achieve anti-inflammatory and analgesic effects ^[18]. This drug can also synergistically regulate endometriosis with multiple components, targets, and pathways ^[19]. Shancigu can inhibit tumor cell proliferation, invasion, metastasis, and neovascularization, promote cancer cell apoptosis, and regulate the body's immune system ^[20]. The effective ingredients of frankincense and myrrh have clear anti-inflammatory and analgesic effects ^[21,22]. The flavonoid compounds in dragon's blood not

only reduce inflammation and pain, but also inhibit transforming growth factor (TGF)- β 1) High expression of [23]; The active ingredients of centipede may have anti-inflammatory and analgesic effects by inhibiting the synthesis of prostaglandins [24,25]; Litchi seed has good anti-cancer activity, such as prostate cancer, lung cancer, breast cancer, etc. [26].

According to incomplete clinical statistics, Quyu Jiedu Xiaozheng Tang has a good therapeutic effect on endometriosis. And through experimental research, it has been shown that the serum MIF and TGF of patients after treatment- β the level of 1 has decreased. Serum MIF is a key pro-inflammatory cytokine secreted by active macrophages accumulated in the endometrium of ectopic tissues. It undergoes gene expression during the secretion phase of the menstrual cycle [27], and when it reaches a high expression level, it may promote the development of endometriosis through angiogenesis [28]. Other studies have shown that serum MIF levels are higher in women with endometriosis caused by infertility and chronic pelvic pain [29]; Serum MIF can also activate multiple signaling pathways, promoting cell proliferation, adhesion, metastasis, neovascularization, epithelial mesenchymal transition, and enhancing immunosuppression in gynecological malignancies such as cervical cancer, ovarian cancer, endometrial cancer, etc. [30]. Serum TGF in the human body- β By inducing anaerobic glycolysis and lactate secretion in endometrial stromal cells, the expression of monocarboxylate transporter 4 (MCT4) is increased, further affecting endometriosis [31].

There are also studies indicating that serum TGF in the human body- β 1. It may be involved in the occurrence and development of endometriosis, and is related to the severity of dysmenorrhea in patients with endometriosis [32]; Serum TGF in the human body- β . It is also related to osteoporosis and breast cancer [33,34]. So the serum MIF and TGF- β the high expression of 1 in the human body, is closely related to the occurrence and development of endometriosis. Therefore reducing serum MIF and TGF - β a level of 1 through treatment ,is more conducive to the treatment of endometriosis and the prevention of complications or other diseases.

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