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Clinical Efficacy of Dienogest Combined with Wenjing Tang in Adenomyosis

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Abstract: *Objective:* To investigate the clinical efficacy of Dienogest (DNG) combined with Wenjing Tang Formula in patients with uterine adenomyosis. *Methods:* 60 patients with adenomyosis were randomly divided into Group A and Group B. Group A patients received continuous oral treatment with DNG 2 mg/d for 3 months, while Group B patients were given Wenjing Tang Formula based on Group A treatment. The treatment effect, size of adenomyoma and incidence of adverse reactions were compared between the two groups. *Results:* The total effective rate of treatment in Group B was 96.67%, which was significantly higher than 73.33% in Group A ($P < 0.05$); the size of uterine adenomyoma in Group B was significantly smaller than that in Group A, with a significant difference ($P < 0.05$). In terms of the incidence of adverse reactions, group B was 6.67%, which was significantly lower than 26.67% in group A ($P < 0.05$). *Conclusion:* The treatment of adenomyosis of the uterus via dienogest combined with the addition and subtraction of Wenjing Tang showed higher therapeutic efficacy and significant tumor shrinkage, and at the same time, it could reduce the incidence of adverse reactions, which has a good prospect of clinical application, and it is recommended to be promoted for use in clinical practice.

Keywords: Dienogest; Wenjing Tang formula; Adenomyosis

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1. Introduction

Adenomyosis is a kind of endometriosis, which is characterized by the invasion of endometrial glands and mesenchyme into the myometrium, causing clinical symptoms such as uterine enlargement, dysmenorrhoea and menstrual abnormality, which seriously affects the quality of women's life and fertility. Its pathogenesis is complex and is currently believed to be closely related to the abnormal levels and effects of oestrogen. The main clinical manifestation of the disease is that endometrial tissue, including mesenchymal cells and glandular tissue that constitute its functional layer, abnormally appears in the myometrium and undergoes cyclic proliferation and bleeding at the ectopic site, which ultimately leads to changes in the structure of the uterus, with the phenomena of uniform uterine enlargement and hardening of the texture. Patients often suffer from progressive dysmenorrhoea, heavy menstruation and secondary infertility, which not only seriously affect their quality of life, but also harm their psychological health. As an important therapeutic means, conservative

drug treatment plays an active role in relieving symptoms, delaying disease progression, improving surgical treatment effects and assisting reproduction by regulating hormone levels and inhibiting inflammation, and is an indispensable part of the treatment of adenomyosis [1]. Dienogest (DNG) is a new type of drug that has attracted much attention in recent years and is mainly used in the treatment of endometriosis and adenomyosis. DNG has been proven to be effective in the treatment of endometriosis by regulating the hormone level, helping to alleviate the pain and discomfort caused by the disease, and improving the patient's quality of life [2]. In the theoretical system of Chinese medicine, adenomyosis is classified as a part of dysmenorrhoea and other related diseases, and many researchers believe that the underlying mechanism of its onset is mainly related to kidney deficiency and blood stasis, which is often due to a state of weakness caused by qi and blood deficiencies, coupled with the wind and cold evils that invade the meridians, ultimately leading to damage to the Chong Ren vein [3]. Western medical treatment is based on hormone therapy and surgery, but there are problems such as large side effects and high recurrence rates. Traditional Chinese medicine (TCM) has a long history of treating adenomyosis, with precise efficacy and has received more attention in recent years. As a classic formula for treating "blood deficiency and cold stagnation," Wenjing Tang has shown unique advantages in the treatment of adenomyosis. This study aims to investigate the clinical efficacy of dinoretin combined with Wenjing Tang in the treatment of adenomyosis and to provide new ideas and a basis for the effective treatment of adenomyosis by comparing the symptomatic improvement, adenomyoma size and the incidence of adverse effects before and after the treatment.

2. Information and methods

2.1. General information

Sixty patients with adenomyosis were collected and enrolled in the hospital and randomly divided into group A and group B. Each group consisted of 30 cases. The age range of patients in group A was 20–50 years old, with a mean age of (35.12 ± 4.31) years old and a mean duration of the disease (7.11 ± 1.21) months. The age range of patients in group B was 22–49 years old, with a mean age of (36.17 ± 4.63) years old and a mean duration of the disease (7.14 ± 1.23) months. The comparison of basic data was not statistically significant ($P > 0.05$). Inclusion criteria: (1) Confirmed diagnosis of adenomyosis, meeting the relevant diagnostic criteria [4]; (2) Age between 18 and 50 years old; (3) Patients were willing to participate in the study and signed the informed consent; (4) No serious comorbidities, able to tolerate the appropriate treatment plan; (5) Did not receive the relevant medication, surgery or other interventions for at least 3 months. Exclusion criteria: (1) Combined with other serious gynaecological diseases, such as uterine fibroids, ovarian tumors, etc.; (2) Pregnant or lactating women; (3) Allergic to the ingredients of dienogest or Wenjing Tang; (4) Patients with a bleeding tendency or coagulation dysfunction; (5) Patients who have received other hormone therapy or traditional Chinese medicine recently (within the past 3 months).

2.2. Methods

Patients in Group A received continuous uninterrupted oral treatment of dienogest 2 mg/d for 3 months. Patients in Group B were additionally given Wenjing Tang formula as compared to the treatment in Group A. One dose of water was decocted, which was later divided into two doses in the morning and evening for 3 months. Composition of Wenjing Tang: *Angelica sinensis* 10g, *Ligusticum striatum* 10g, *Paeonia lactiflora* 12g, *Rehmannia glutinosa* 12g, ginseng 6g, *Ramulus cinnamomi* 6g, *Glycyrrhiza uralensis* 6g, dried ginger 4g, *Pinellia ternata* 9g, donkey-hide gelatin 10g (melted), *Dwarf lilyturf* 15g, etc.

Notes on the customized formula:

(1) If obvious dysmenorrhea, add *Corydalis yanhusuo*, *Curcuma aromatica*;

(2) If low menstrual flow, add *Leonurus japonicus*, *Prunus persica*;
(3) If high menstrual flow, add *Typha angustifolia* L., Wulingzhi;
(4) High amount of leucorrhoea, add China root, Baizhu.

Wenjing Tang preparation method:

(1) All herbs are purchased from the hospital pharmacy, and identified by professionals.
(2) Add all herbs except melted donkey-hide gelatin to the appropriate amount of water and soak for 30 minutes.
(3) Boil on high heat, then turn to low heat and decoct for 40 minutes.
(4) Add donkey-hide gelatin, stir well and continue to decoct for 10 minutes.
(5) Pour out the decoction, add water to the dregs and decoct once more, combining the two medicinal liquids.
(6) Concentrate the combined medicinal liquid to the appropriate amount and take it twice in the morning and evening.

2.3. Observation indicators

2.3.1. Assessment of treatment effect

This study adopts the standards of the 15th edition of Gynaecology to systematically assess the treatment effect, specifically classifying the efficacy into three grades:

(1) Obvious effect means that the clinical symptoms and ultrasound results of the patients have significantly improved, and the degree of improvement of all biochemical indicators is more than 80%.
(2) Effective means that the patient's clinical symptoms and ultrasound results have improved, and the biochemical indicators have improved by more than 60%.
(3) Ineffective means that the patient fails to meet the criteria of obvious effect and there is no obvious change in symptoms.

2.3.2. Measurement of adenomyoma size

Before and after treatment, both groups of patients underwent colour Doppler ultrasonography to measure the changes in the size of the uterus. The specific test was arranged on the second day of the menstrual cycle to ensure the accuracy and comparability of the data.

2.3.3. Adverse reaction monitoring

During the treatment period, the adverse reactions of the two groups of patients were recorded and analyzed in detail, mainly including abnormalities in liver and kidney functions, irregular vaginal bleeding, insomnia, hot flashes, sweating, mood swings and breast discomfort.

2.4. Statistical methods

Statistical processing with SPSS 20.0, measurement data using mean ± standard deviation (SD), count data using [n (%)], t or ANOVA test, with $P < 0.05$ to indicate that the difference is statistically significant.

3. Results

3.1. Comparison of treatment effect between two groups of patients

The total effective rate of treatment in Group B reached 96.67%, which was significantly higher than the 73.33% in Group A. The difference was significant ($\chi^2 = 4.706$, $P = 0.030 < 0.05$). Please refer to **Table 1** for

specific data.

Table 1. Comparison of treatment effect between two groups of patients [*n* (%)]

Groups	*n*	Obvious	Effective	Ineffective	Overall effective rate
Group A	30	15 (50.00%)	7 (23.33%)	8 (26.67%)	22 (73.33%)
Group B	30	20 (66.67%)	9 (30.00%)	1 (3.33%)	29 (96.67%)
χ^2-value	-	-	-	-	4.706
P-value	-	-	-	-	0.030

3.2. Comparison of the degree of uterine reduction between the two groups of patients

In the comparison of the size of the uterus in the two groups of patients before treatment, the difference is not statistically significant ($P > 0.05$); after treatment, in the observation of the same period of menstruation, the size of adenomyoma in both groups of patients is reduced compared with that before treatment, and the size of adenomyoma in group B is significantly smaller than that in group A, the difference is statistically significant ($P < 0.05$). The specific data can be seen in **Table 2**.

Table 2. Comparison of adenomyoma size between the two groups before and after treatment (mean ± SD, cm)

Groups	*n*	Before treatment	After treatment	*t*-value	*P*-value
Group A	30	4.0 ± 0.5	3.6±0.5	3.098	0.003
Group B	30	4.0 ± 0.4	2.6±0.4	11.976	< 0.001

3.3. Comparison of the incidence of adverse reactions between the two groups

The total incidence of adverse reactions in Group B during the treatment period was 6.67%, which was significantly lower than the 26.67% in Group A. The difference was significant ($\chi^2 = 4.320$, $P = 0.038 < 0.05$). The specific data can be seen in **Table 3**.

Table 3. Comparison of the incidence rate of adverse reactions between the two groups [*n* (%)]

Groups	Irregular vaginal bleeding	Abnormalities in liver and kidney function	Insomnia and headache	Mood swings	Breast discomfort	Total
Group A ($n = 30$)	2 (6.67%)	2 (6.67%)	1 (3.33%)	1 (3.33%)	2 (6.67%)	8 (26.67%)
Group B ($n = 30$)	1 (3.33%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	2 (6.67%)
χ^2-value	-	-	-	-	-	4.320
P-value	-	-	-	-	-	0.038

4. Conclusion

Wenjing Tang is from "The Essentials of the Golden Chamber" by Zhang Zhongjing of the Han Dynasty. Its formula is rigorous and exquisite, reflecting the therapeutic principle of traditional Chinese medicine: 'Heat when it is cold, replenish when it is weak, and move when the blood is stagnant.' In the formula, *Tetradium ruticarpum* and *Ramulus cinnamomic* are the royal medicines, which are effective in warming menstruation, dispersing cold and facilitating blood circulation [5]. *Tetradium ruticarpum* is pungent and hot, which belongs to the liver, spleen, stomach and kidney meridians, dispersing cold and relieving pain, descending and stopping

vomiting and assisting Yang in stopping diarrhea. *Ramulus cinnamomic* is pungent, sweet and warm, which belongs to the heart, lungs and urinary bladder meridians, warming and clearing the blood vessels, assisting Yang in transforming the Qi and dispersing cold and relieving the surface. The combination of the two herbs complements each other, warming the meridians, dispersing cold and clearing the blood vessels [6]. The subject drugs *Angelica sinensis*, *Ligusticum striatum*, and peony bark, with the functions of tonifying, invigorating and cooling the blood, respectively, complete the formula. *Angelica sinensis* is sweet, pungent and warm, which goes to the liver, heart and spleen meridians, invigorates blood, dispels blood stasis, nourishes blood and regulates menstruation. *Ligusticum striatum* is pungent and warm, which goes to the liver, gallbladder and pericardium meridians, invigorates blood, dispels wind and relieves pain. Peony bark is bitter, pungent and cool, which goes to the heart, liver and kidney meridians, clears heat and cools blood, and invigorates blood to disperse stasis. The combination of the three drugs not only helps to warm the meridians and disperse cold, activate blood circulation and remove blood stasis but also prevents warmth and dryness from hurting Yin so that the whole formula is coordinated [7,8].

This study suggests that the total effective rate of treatment in Group B was significantly higher than that in Group A ($P < 0.05$), indicating that the treatment plan of Group B has obvious advantages in improving adenomyosis, which may be related to its nature of comprehensive treatment. In addition, the size of adenomyoma in patients in Group B was significantly smaller than that in Group A, and the difference was equally significant ($P < 0.05$). In terms of adverse reactions, the incidence rate of Group B was significantly lower than that of Group A. This result suggests that the treatment plan of Group B is more advantageous in terms of safety. The reason for this is that Wenjing Tang formula can play a role in the treatment of adenomyosis through multiple pathways and targets, which mainly include:

(1) Improve blood circulation and promote tissue repair

The pathogenesis of adenomyosis is closely related to the obstacle of local blood circulation in the uterus. Wenjing Tang formula in the *Tetradium ruticarpum*, *Ramulus cinnamomi*, *Ligusticum striatum* and other drugs have the effect of activating blood circulation and removing blood stasis, warming the menstruation and opening the collaterals, which can effectively improve the uterine local microcirculation, increase the blood flow, and promote the repair of tissues. The alkaloids in *Tetradium ruticarpum* can act on the uterus, diastole the uterine smooth muscle, improve the speed of uterine blood circulation, and ultimately increase uterine blood flow [9]. The two active ingredients of cinnamon aldehyde and sodium cinnamate contained in *Ramulus cinnamomi* can dilate the blood vessels of the organism to a certain extent, thus strengthening the ability of blood circulation [10]. As a blood-activating herb, *Ligusticum striatum* can improve the tension of the uterus by regulating blood rheology and effectively promoting the systolic-diastolic movement of the uterus, thus ultimately enhancing local blood flow irrigation [11].

(2) Regulating immune function and inhibiting inflammatory response

The development of adenomyosis is closely related to immune dysfunction and inflammatory response. Drugs such as *Angelica sinensis* and peony bark in Wenjing Tang have the functions of regulating immunity, anti-inflammatory and analgesic, which can inhibit the release of inflammatory factors and reduce the inflammatory reaction, thus relieving the pain and other symptoms associated with adenomyosis.

(3) Regulating hormone levels and inhibiting the growth of ectopic lesions

The occurrence of adenomyosis is related to estrogen dependence. Wenjing Tang can control the development of the disease by regulating the function of hypothalamic-pituitary-ovarian axis, lowering the level of estrogen and inhibiting the growth of ectopic endometrium.

In summary, norethindrone combined with the addition of Wenjing Tang provides a new and effective

option for the management of adenomyosis, which is worthy of further promotion and application in clinical practice. Future studies can further explore the mechanism of this comprehensive treatment option and its effects in larger samples, providing a more solid basis for clinical practice.

Disclosure statement

The author declares no conflict of interest.

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