

## Original Article

# Efficacy and adverse reactions of adjuvant traditional Chinese medicine enema and super light microwave irradiation added to western medicine anti-inflammatory therapy for chronic pelvic inflammatory disease

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**Abstract:** Objective: To observe the clinical efficacy, adverse reactions and relapse rate of anti-inflammatory therapy of western medicine with adjuvant therapy of traditional Chinese medicine enema and super light microwave irradiation in the treatment of chronic pelvic inflammatory disease. Methods: A total of 100 patients with chronic pelvic inflammatory disease eligible for the clinical criteria for diagnosis were randomly assigned to receive western medicine anti-inflammatory therapy alone (the control group, also referred to as Group A) or traditional Chinese medicine enema and super light microwave irradiation added to the western medicine anti-inflammatory therapy for 30 minutes (the treated group, also referred to as Group B). Each group treated for a course of 14 days. The clinical efficacy, laboratory examinations, adverse reactions, and relapse rates at 3-month follow-up were compared between the two groups of patients at the end of the treatment course. The efficacy assessment was based on the calculation of corresponding effective rates according to *The Guidance Principle of Clinical Study on Traditional Chinese Medicine*. Results: The treatment was effective in the patients of both groups (92% in Group B vs. 66% in Group A,  $P < 0.05$ ). Reduced concentrations of C-reactive protein, erythrocyte sedimentation and CA125 were observed in both groups in the course of treatment ( $P < 0.05$ ). The rate of adverse reactions was higher in Group B (18%) than in Group A (14%), but not significantly different ( $P > 0.05$ ). The relapse rate was notably lower in Group B (4%) than in Group A (26%) at the end of the treatment courses ( $P < 0.05$ ). Conclusion: With the law of treatment based on syndrome differentiation of Chinese medicine, the adjuvant therapy of traditional Chinese medicine enema and super light microwave irradiation added to the anti-inflammatory therapy of western medicine was evidently effective in chronic pelvic inflammatory disease and its relapse rate was low, so it was worthy of a extensively clinical application.

**Keywords:** Chronic pelvic inflammatory disease, traditional Chinese medicine enema, super light microwave

## Introduction

Chronic pelvic inflammatory disease (CPID) refers to the chronic inflammatory lesions that occur in internal genitalia and connective tissues around the pelvic cavity of women. CPID, one of the common gynecological diseases, is more common in delivery, abortion and after gynecological surgery. It is a chronic inflammation that occurs in internal genitalia and connective tissues around it and between the pel-

vic peritoneum in women. The major pathogens of CPID are Streptococcus and Staphylococcus [1]. The pathological changes are mostly proliferation of pelvic tissue with inflammatory exudation, inflammatory cell infiltration, tissue edema or fiber hyperplasia and harden and hardening [2-5]. The main clinical manifestations of patients are increased vaginal discharge, menstrual disorders and lumbar-abdominal pain, which could occur repeatedly, seriously affecting the patients' quality of life [6].

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To date, in the modern medicine world, no regimens are exactly effective for CPID and drug treatment is mainly aimed at relieving pain and eliminating inflammation, but the treatment courses are long and it is prone to recurrence [7]. In a large number of clinical practices, Chinese medicine administered in various ways, including oral medication, enema, acupuncture and moxibustion, shortwave infrared, is effective in the treatment for CPID. In this study, we selected a total of 100 outpatients with CPID to receive the standard Western medicine treatment or an integrated therapy of traditional Chinese and western medicine from August 2015 to July 2016, then investigated clinical effects, adverse reactions and the effects of relapse rate of these therapies on patients with CPID.

### Materials and methods

#### *Clinical data*

From August 2015 to July 2016, a total of 100 outpatients with chronic pelvic inflammatory disease enrolled in the Department of Obstetrics and Gynecology of our hospital were randomly assigned to receive conventional western medicine alone (the control group, hereafter referred to as Group A, n=50) or an integrated therapy of traditional Chinese medicine and western medicine (the treated group, hereafter referred to as Group B, n=50). Patients were aged from 22 to 45 and had courses of disease varying from five months to three years. Patients of the two groups were confirmed by relevant medical examinations and there were no significant differences in the data on age or course of disease between the two groups. All of them expressed no objection against our informed investigation which was approved by the Hospital Medical Ethics Committee.

*Inclusion criteria:* Patients confirmed as having CPID according to diagnostic criteria of western medicine; Women of 22 to 45 years; Those who are sane, articulate, and cooperative; Those who received the procedure as planned; Those who provided written informed consents.

*Exclusion criteria:* Patients who did not meet the diagnostic criteria; Patients who had associated diseases including gynecologic tumors, endometriosis (EMs) and adenomyosis (AM) according to gynecological examinations, B-

mode ultrasound and other examinations; Pregnant women; Those with such severe comorbidities of internal diseases, like hypertension, coronary heart disease or diabetes mellitus (DM).

*Rejection criteria:* Patients with severe adverse events impacting the planned procession of this trial; Those who presented severe comorbidities during the treatment; Those who did not receive the treatment at clinicians' discretion during the trial; Those who withdrew from the trial or lost to follow-up.

*Diagnostic criteria:* Diagnostic criteria were set according to Guidelines for the Diagnosis & Treatment of Pelvic Inflammatory Disease from the Centers for Disease Control. All eligible patients had chronic pelvic pain and uterine or adnexal tenderness on bimanual examination [8].

#### *Methods*

Antibiotics were administered to the controls (Group A) based on past experience. They received levofloxacin (0.3 g) and tinidazole (0.5 g) by intravenous drip once daily. Meanwhile, sensitive antibiotics were administered to them according to the results of bacteriological culture and drug sensitivity test for their vaginal discharge and cervical secretion for two seven-day cycles of treatment. In the treated group (Group B), the patients received Chinese medicine enema and super light microwave irradiation based on the antibiotic treatment. The ingredients of Chinese medicine enema include 15 g of fructus liquidambaris, 15 g of cortex phellodendri, 20 g of corydalis yanhusuo, 30 g of smilax glabra, 30 g of dandelion, 30 g of hedyotis diffusa, 30 g of patrinia and 30 g of caulis sargentodoxae. All the ingredients were decocted for decoction. Then 50 ml decoction was used for retention enema at bedtime. As for the procedures of enema, excrement and urine was emptied before enema. The patient was placed in the left lateral position with 15 cm-lifted buttock, as well as the bent right leg and the extended left leg. A 50 ml disposable syringe connected with a urinary catheter was inserted into the rectum of anus for about 20 cm deep after the disposable syringe was coated with paraffin. Then the prepared decoction was slowly injected into the body and kept for more than 2 h after injection. The procedures

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**Table 1.** Comparison of general information among the patients

| Clinical information          | Group A    | Group B     | t/ $\chi^2$ | P    |
|-------------------------------|------------|-------------|-------------|------|
| Age (x±s) (years)             | 34.5±6.68  | 34.76±6.54  | 0.18        | 0.86 |
| Disease course (x±s) (months) | 27.80±9.61 | 28.32±10.45 | 0.23        | 0.71 |
| Disease distribution          |            |             | 5.16        | 0.17 |
| Mild (n)                      | 10         | 8           |             |      |
| Moderate (n)                  | 24         | 28          |             |      |
| Severe (n)                    | 16         | 14          |             |      |

for super light microwave irradiation were as follows: the patient's hypogastrum was exposed to radiation with the use of a super light microwave therapeutic apparatus (power at 40 W) for two successive seven-day cycles (twice daily and 30 min every time). The probe was placed at 2-4 cm above the patient's pelvic cavity. The patients were observed before the treatment, at the end of the two cycles of treatment and at 3 months after treatment.

## *Efficacy criteria and indexes*

*Criteria for efficacy assessment:* After treatment, the patients were cured if their symptoms and signs like hypogastrum pain and lumbosacral swelling pain resolved completely and the results of gynecological and laboratory examinations were normal. The treatment was effective if the patients' clinical symptoms and signs were relieved and the results of gynecological and laboratory examinations were significantly improved. The treatment was excellent if the clinical symptoms and signs were better. And it was ineffective if there were no clinical symptoms and signs in the patients. Total effective rate = cure rate + significant effective rate + improvement rate [9].

*Comparison of indexes related to laboratory examinations:* C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are on the increase in most acute or chronic inflammations. Serum CA125 in patients' blood is usually on the rise [10], which is clinically regarded as one of the measures for inflammatory infiltration. Therefore, the relevant indexes in the patients' serum were detected before the treatment and at the end of the two cycles of the treatment, and the results were compared.

Adverse reaction refers to any reaction occurs in the medication process which is not in conformity with the medication purpose and brings

discomfort and pain to patients. According to the medication and treatment in this trial, the symptoms including nausea, vomiting, diarrhea, skin rash and ambustion are regarded as adverse reactions and statistically analyzed at the end of the two cycles of treatment.

## *Statistical analysis*

The data analysis in our clinical trial was performed using SPSS17.0 statistical analysis system. Enumeration data were expressed as percentage (%), and measured by the chi-square test. Quantitative data were expressed as means ± standard deviation, and detected by repeated-measures analysis of variance. The threshold of significance  $\alpha$  was equal to 0.05, and  $P < 0.05$  was considered statistically significant.

## **Results**

### *General information*

All of the 100 eligible subjects were outpatients with chronic pelvic inflammatory disease from the department of obstetrics and gynecology in our hospital between August 2015 and July 2016. They were randomly assigned to receive the conventional western medicine (Group A, n=50) or an integrated therapy of western and Chinese medicine (Group B, n=50). No patients were lost or excluded during the whole treatment. The general information concerning age and disease course of all the patients in both groups was as follows.

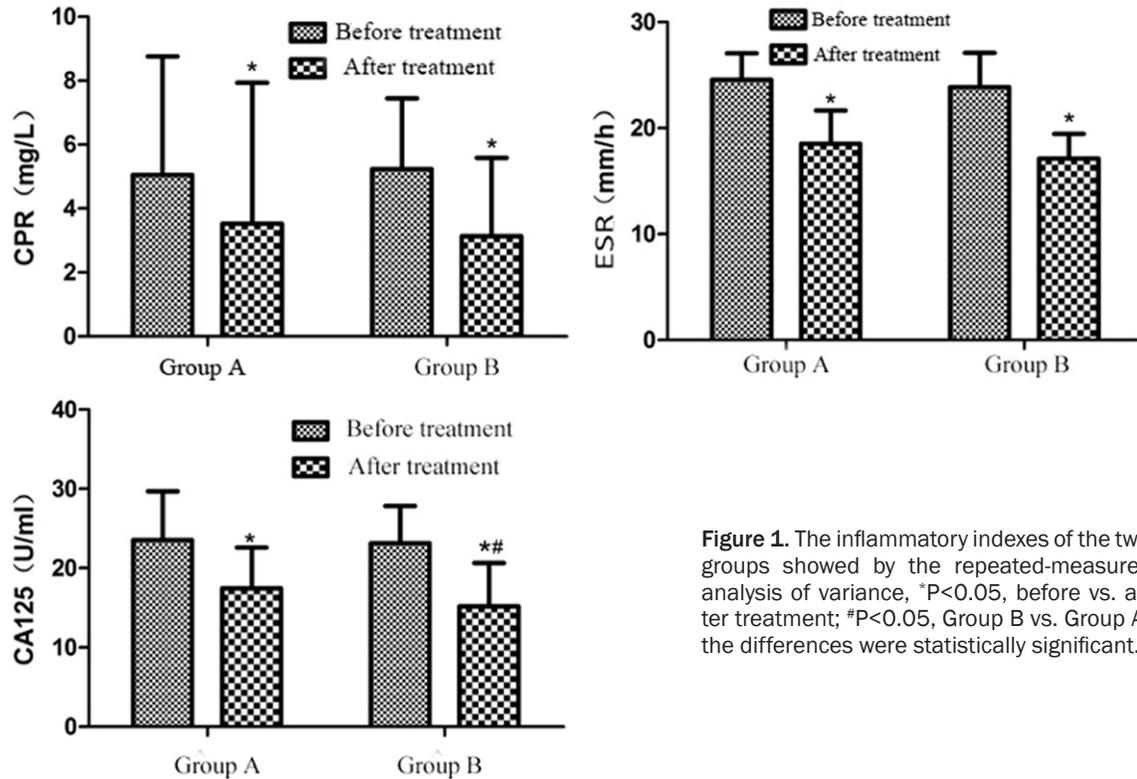
The patients in Group A had mean age of 34.5±6.68 years, and the mean disease course of 27.80±9.61 months while the patients in Group B had mean age of 34.76±6.54 years and mean disease course of 28.32±10.45 months. The differences between the two groups were not statistically significant but were comparable ( $P > 0.05$ ). According to the grading criteria from *Clinical Guidelines for the New Chinese Medicine for the Treatment of Chronic Pelvic Inflammatory Disease* (version 2002), 10 mild, 24 moderate and 16 severe cases were observed in Group A whereas 8 mild, 28 moderate and 14 severe cases were observed in Group B. With the results detected

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**Table 2.** Comparison of efficacy between the two groups

| Group | Total Cases | Recovery | Excellent | Effective | Ineffective | Total effective rate | $\chi^2$ | P     |
|-------|-------------|----------|-----------|-----------|-------------|----------------------|----------|-------|
| A     | 50          | 12       | 24        | 10        | 4           | 92%                  | 8.14     | 0.041 |
| B     | 50          | 8        | 17        | 18        | 17          | 66%                  |          |       |

Note: The  $\chi^2$  test,  $P < 0.05$ , showed the difference in efficacy between the two groups was statistically significant.



**Figure 1.** The inflammatory indexes of the two groups showed by the repeated-measures analysis of variance, \* $P < 0.05$ , before vs. after treatment; # $P < 0.05$ , Group B vs. Group A, the differences were statistically significant.

by the  $\chi^2$  test, the differences were not statistically significant ( $P > 0.05$ , **Table 1**).

### Efficacy assessments after treatment

The total effective rate was markedly higher in Group B (92%) than in Group A (66%), and the difference was statistically significant ( $P < 0.05$ , **Table 2**).

### Assessments on inflammatory markers after treatment

CRP, erythrocyte sedimentation rate (ESR) and CA125 were obviously decreased before the treatment than after the treatment among the patients in both groups, and the differences were statistically significant ( $P < 0.05$ ), indicating both regimens had the effects of inflammatory suppression. Meanwhile, as compared with Group A, CA125 was significantly declined

in Group B ( $P < 0.05$ ), showing that the integrated therapy had preferable efficacy for inflammatory infiltration (**Figure 1**).

### Comparison of adverse reaction and relapse rate

The rate of adverse reactions was 18% in Group B and 14% in Group A. No significant difference was found regarding adverse reactions between the two groups. During the follow-up period, 2 patients (4%) had a relapse in Group B and 13 (26%) in Group A. The differences in relapse between the two groups were statistically significant ( $\chi^2 = 19.397$ ,  $P = 0.012$ , **Table 3**).

### Discussion

In recent years, the incidence of chronic pelvic inflammatory disease is on the increase, seriously affecting the health of patients. The anti-

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**Table 3.** Comparison of adverse reactions between the two groups

|   | Cases | Nausea and vomiting | Diarrhea | Skin rash | Skin burn | Total incidence | $\chi^2$ | P    |
|---|-------|---------------------|----------|-----------|-----------|-----------------|----------|------|
| A | 50    | 2                   | 3        | 2         | 0         | 7               | 5.73     | 0.14 |
| B | 50    | 3                   | 4        | 1         | 1         | 9               |          |      |

Note: The  $\chi^2$  test showed,  $P>0.05$ , the difference in adverse reactions between the two groups was not statistically significant.

inflammatory drugs like levofloxacin and tinidazole can kill pathogens but they may cause drug resistance because of the long cycle of treatment. Thus they fail to achieve the expected efficacy. With the increasing development of traditional Chinese medicine, integrated therapies of traditional Chinese and western medicine have being explored to treat chronic pelvic inflammatory disease, for the purposes of improving the cure rate while reducing adverse reactions and relapse rate.

There is not a special name for chronic pelvic inflammatory disease in Chinese medicine, but according to its main symptoms, the disease can be covered in such diseases as leukorrheal diseases or female abdominal pain [11, 12]. In traditional Chinese medicine, it is believed that chronic pelvic inflammatory disease is mostly due to the fact that acute pelvic inflammatory disease has not been completely cured or the patient has a weak constitution, so the pathogenic heat and residual poison remain in the body and compete with Chong and Conception Channels. The pathogenic factors are persistent and cause damages to Qi and blood. In addition, overused bitter cold drugs or damaged yang qi results in insufficient healthy energy in the body, so the patient is incapable of beating pathogens. Blood stasis is the core mechanism of the disease [13-15]. Therefore, in the Chinese traditional treatment, attempts are mainly taken to clear heat, dissolve dampness and resolve phlegm. Most patients develop chronic pelvic inflammatory disease after menstruation or delivery, when their uterine vessels are weak and lack of healthy energy. Pathogenic factors like moist heat invade the body and combine with congestion, and then retain in the uterus. The Chinese regimen in our trial was prescribed to integrate the heat-clearing, detoxifying, anti-inflammatory, and immune-regulating effects. In addition, the ingredients activating blood and resolving sta-

sis in the regimen were able to improve the blood circulation, especially microcirculation, so as to promote the recovery of pathological changes.

The blood circulation in female reproductive organs is poor because of women's special anatomic structure, so drugs are difficult to reach the inflammatory sites by oral administration.

In addition, the venous plexus of female pelvic organs are dense, with abundant blood circulation and slow blood flow. With the use of Chinese herbal enema, the drugs can have an effect of dissipating adnexitis after they are absorbed in the mucosa of rectum. Due to the long duration of pelvic inflammatory disease, long-term oral medication may cause damages to the spleen and stomach. As compared with oral medication, Chinese herbal enema has higher compliance and the drugs can be absorbed by the rectum more rapidly. In this way, the first-pass effects in the liver can be avoided, so the burden on the liver is eased [16, 17]. Besides, it can make the drugs maintain the effective concentration for a long time, promote the local blood circulation, and is conducive to the absorption of inflammatory lesions. The findings in our trial show that the treatment was more effective in Group B than in Group A, and the B-mode ultrasonography showed more significant dissipated adnexitis, as well as reduced pelvic effusions and pelvic mass.

Physiotherapy can bring about improved local blood circulation, histotrophic nutrition, metabolism, effects of traditional Chinese medicine and inflammatory resolution. Lamina S performed the ultrashort wave therapy and found that this method was effective and noninvasive [18]. Clinicians also mainly use antibiotics plus ultrashort wave therapy to treat the disease [19, 20]. The trial also showed that the integrated therapy improved the absorption of inflammatory exudation and tissue restoration. The results also demonstrated the effectiveness of the integrated therapy. Erythrocyte sedimentation rate and CRP increased in inflammatory reaction, but the specificity was not strong. Serum CA125 is an antigen which is expressed on the surface of embryonic coelomic epithelium-derived cells and human fetal derived cells

[21]. It is mainly used in the diagnosis and curative observation of ovarian cancer [22]. CA125 was significantly increased in patients with pelvic inflammatory diseases, which was related to the severity of inflammation affecting peritoneum. It can be seen as a predictor for the treatment of pelvic inflammatory disease. Our trial showed that as compared with the conventional western medicine, the integrated therapy was more effective in preventing the inflammation from affecting peritoneum.

Due to the short time of our trial, the results could not fully reflect the advantages of the integrated therapy of traditional Chinese and western medicine. Long-term follow-ups are required investigating the recurrences of the patients.

In conclusion, our trial confirms that, as compared with traditional western medicine, in the treatment of chronic pelvic inflammatory disease, the integrated therapy of traditional Chinese and western medicine is effective in suppressing the inflammatory response and improving the functions of pelvic tissues, and it has low adverse reactions and relapse rate. Therefore, the therapy is worth extensive application.

### Disclosure of conflict of interest

None.

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