



# Influence of promoting blood circulation to remove blood stasis combined with laparoscopy on serum MCP-1, RANTES, oxidative stress and hormones in infertile patients with endometriosis

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## ABSTRACT

**Objective:** To observe the influence of promoting blood circulation to remove blood stasis combined with laparoscopy on serum MCP-1, RANTES, oxidative stress and hormones in infertile patients with endometriosis. **Methods:** A total of 60 infertile patients with endometriosis were randomly divided into observation group (30 cases) and control group (30 cases). Observation group: promoting blood circulation to remove blood stasis combined with laparoscopy; control group: patients were treated only by laparoscopy. Recording and comparing the levels of MCP-1, RANTES, oxidative stress and hormones before and after treatment. **Results:** (1) Before treatment, there was no statistically significant difference in the serum MCP-1, RANTES, AOPP, MDA, SOD, levels between the two groups. After treatment, compared with the same group before treatment, the serum RANTES, AOPP, MDA levels of the two groups were significantly lower, the serum SOD level of the two groups were significantly higher, and those levels of observation group were significantly better than the control group, there was significant difference between the two groups. (2) Before treatment, there was no statistically significant difference in the serum FSH, LH, E2, P, PRL levels between the two groups. After treatment, compared with the same group before treatment, the serum FSH, LH, P, PRL levels of the two groups were significantly higher, the serum E2 level of the two groups were significantly lower, and those levels of observation group were significantly better than the control group, there was significant difference between the two groups. **Conclusion:** Promoting blood circulation to remove blood stasis combined with laparoscopy for infertile patients with endometriosis can reduce the levels of serum MCP-1, RANTES, oxidative stress, hormones and be beneficial to protect their uterine function.

## 1. Introduction

Endometriosis (EM) means that the endometrial tissue grows beyond the normal range is one of the common diseases in women of childbearing age, and about 30%-40% of patients with infertility[1]. At present, the pathogenesis of this disease is not clear, and laparoscopic surgery is the main clinical treatment[2]. Traditional Chinese medicine theory holds that the basic pathogenesis of endometriosis is blood stasis syndrome, so the treatment of promoting blood circulation to remove stasis can improve the

curative effect[3]. Therefore, the purpose of this study is to observe the influence of promoting blood circulation to remove blood stasis combined with laparoscopy on serum MCP-1, RANTES, oxidative stress and hormones in infertile patients with endometriosis, so as to provide a theoretical basis for the clinical treatment of endometriosis infertility.

## 2. Information and methods

### 2.1. General information

A total of 60 cases were selected from August 2014 to August 2016 in our hospital for the diagnosis and treatment of endometriosis infertility patients, and were randomly divided into control group

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and observation group, 30 cases each. The average age of the patients in the observation group was (33±3) years, and the course of disease was (4±2) years; The mean age of the patients in the control group was (33±4) years, and the course of disease was (4±3) years. There was no significant difference in age, clinical stage and other general data between this two groups ( $P>0.05$ ). The inclusion criteria included: (1) Laparoscopic diagnosis of endometriosis patients[4]; (2) Consistent with the diagnostic criteria for infertility, that is, normal sexual life, but without contraception for 1 years without pregnancy[5]; (3) The patient was informed of the treatment and signed the informed consent form; (4) Excluding those with serious diseases such as heart and lung.

## 2.2 Therapeutic method<sup>[6]</sup>

(1) All patients underwent laparoscopic surgery at 3-7 d after the last menstrual period, and antibiotics were used to prevent infection after operation. (2) after the end of surgery, the observation group was treated with Chinese herbal medicine therapy, before ovulation using alchemy Xiaoyi prescription (prescription: 15 g Salvia miltiorrhiza, 10 g Triangular, 10 g Excrementum pteropi, 10 g Pollen Typhae, 10 g curcuma zedoary, 15 g Caulis Spatholobi, 10 g seaweed, 10 g Pollen Typhae, 10 g Fritillaria thunbergii Miq, 15 g Motherwort, 10 g Rhizoma Cyperi ) water decoction, 1 dose daily, 2 times/d; ovulation after taking Zishenyutai pill, 5 g/time, 3 times/d. The treatment cycle was 3 menstrual cycles, and the pregnant women stopped taking the medicine immediately. The control group only received laparoscopic surgery without additional drug treatment.

## 2.3 Observation indexes

(1) monocyte chemoattractant protein-1 (MCP-1) and activated regulatory factor (RANTES): serum MCP-1 and RANTES levels were detected and compared before and after treatment in all subjects; (2) Oxidative stress levels: before and after treatment, 4 mL fasting venous blood was taken for centrifugation and modified witko-sarsat method was used to detect advanced protein oxidation products (AOPP), the levels of superoxide dismutase (SOD) and malondialdehyde (MDA) were detected by thiobarbituric acid spectrophotometry and colorimetric method. (3) Sex hormone levels: 5 serum levels of routine sex hormones were detected before

and after treatment, including follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), progesterone (P), and prolactin (PRL).

## 2.4 Data processing

We Used SPSS 20.0 software package to process the test result data, the statistical data of age, oxidative stress and other measurement data were statistically described by mean ± standard deviation, the use of t test was to compare the difference between groups, The data of clinical stages were counted by frequency, and  $\chi^2$  test was used to compare and analyze the differences between the two groups.  $P<0.05$  is considered to have a statistically significant difference.

## 3. Results

### 3.1 Comparison of serum MCP-1 and RANTES levels between two groups

Before treatment, there was no significant difference in the levels of MCP-1 and RANTES between the two groups ( $P>0.05$ ); After treatment, compared with the same group before treatment, the two groups' MCP-1 and RANTES levels were significantly decreased ( $P<0.05$ ), The levels of MCP-1 and RANTES in the control group were respectively (176.20±50.94) ng/L, (452.71±116.48) µg/L, that in observation group were (140.32±49.13) ng/L, (240.95±92.36) µg/L, were significantly lower than the control group, the difference between the two groups was statistically significant ( $P<0.05$ ), see Table 1.

### 3.2 Comparison of oxidative stress levels between two groups of subjects

Before treatment, there was no significant difference in the levels of AOPP, MDA and SOD between the two groups ( $P>0.05$ ); After treatment, compared with the same group before treatment, the two groups' AOPP, MDA levels were significantly lower, SOD levels were significantly increased ( $P<0.05$ ). The levels of AOPP and MDA in the control group were respectively (59.55±14.88) µmol/L, (6.10±1.71) µmol/L, that in the observation group were

Table 1.

Comparison of MCP-1 and RANTES levels between the observation group and the control group ( $n=30$ ).

Group	Time	MCP-1 (ng/L)	RANTES (µg/L)
Observation group	Before treatment	210.69±56.78	736.48±132.64
	After treatment	140.32±49.13 <sup>#</sup>	240.95±92.36 <sup>#</sup>
Control group	Before treatment	208.45±57.77	740.33±140.59
	After treatment	176.20±50.94 <sup>*</sup>	452.71±116.48 <sup>*</sup>

Note: Compared before and after treatment <sup>\*</sup> $P<0.05$ ; Comparison between observation group and control group <sup>#</sup> $P<0.05$ .

Table 2.

Comparison of oxidative stress levels between the observation group and the control group ( $n=30$ )

Group	Time	AOPP ( $\mu\text{mol/L}$ )	MDA ( $\mu\text{mol/L}$ )	SOD (nU/L)
observation group	Before treatment	73.65±20.63	8.56±2.55	77.85±21.67
	After treatment	39.42±12.35 <sup>#</sup>	4.37±1.43 <sup>#</sup>	122.32±16.45 <sup>#</sup>
control group	Before treatment	75.36±18.29	8.51±2.67	78.03±21.98
	After treatment	59.55±14.88 <sup>*</sup>	6.10±1.71 <sup>*</sup>	108.4±22.24 <sup>*</sup>

Note: <sup>\*</sup>compared before and after treatment  $P<0.05$ ; <sup>#</sup>said comparison between observation group and control group  $P<0.05$ .

Table 3.

Comparison of sex hormone levels between the observation group and the control group ( $n=30$ ).

Group	Time	FSH (IU/L)	LH (IU/L)	E2 (pmol/L)	P ( $\mu\text{g/L}$ )	PRL ( $\mu\text{g/L}$ )
Observation group	Before treatment	4.12±1.08	5.32±1.58	325.91±50.16	21.67±9.56	28.12±2.74
	After treatment	6.04±1.87 <sup>#</sup>	8.56±1.47 <sup>#</sup>	200.34±34.12 <sup>#</sup>	31.32±5.83 <sup>#</sup>	45.97±2.01 <sup>#</sup>
Control group	Before treatment	4.51±1.33	5.04±1.03	327.25±51.67	22.01±8.93	27.89±4.08
	After treatment	6.72±1.96 <sup>*</sup>	9.22±1.87 <sup>*</sup>	158.51±42.23 <sup>*</sup>	36.42±6.25 <sup>*</sup>	50.02±5.18 <sup>*</sup>

Note: compared before and after treatment <sup>\*</sup> $P<0.05$ ; said comparison between observation group and control group <sup>#</sup> $P<0.05$ .

(39.42±12.35)  $\mu\text{mol/L}$ , (4.37±1.43)  $\mu\text{mol/L}$ , were significantly lower than the control group, the level of SOD in the observation group was (122.32±16.45) nU/L, which was significantly higher than that of the control group (108.4±22.24) nU/L, and the difference between the two groups was statistically significant ( $P<0.05$ ). see Table 2.

### 3.3 Comparison of sex hormone levels between the two groups

Before treatment, there was no significant difference in the levels of FSH, LH, E2, P and PRL between the two groups ( $P>0.05$ ); After treatment, compared with the same group before treatment, the two groups' FSH, LH, P, PRL levels were significantly increased The level of E2 decreased significantly ( $P<0.05$ ). The levels of FSH, LH, P and PRL in the control group were respectively (6.72±1.96) IU/L, (9.22±1.87) IU/L, (36.42±6.25)  $\mu\text{g/L}$ , (50.02±5.18)  $\mu\text{g/L}$ , that in the observation group were (6.04±1.87) IU/L, (8.56±1.47) IU/L, (31.32±5.83)  $\mu\text{g/L}$ , (45.97±2.01)  $\mu\text{g/L}$ , were significantly lower than the control group, the level of E2 in the observation group was (200.34±34.12) pmol/L, which was significantly higher than that of the control group (158.51±42.23) pmol/L, and the difference between the two groups was statistically significant ( $P<0.05$ ). see Table 3.

## 4. Discussion

The main clinical manifestations of endometriosis are chronic pelvic pain, dysmenorrhea and infertility, and the incidence is increasing in recent years[7,8]. Through laparoscopic surgery can remove lesions, decomposition of adhesions, therefore the laparoscopic surgery is the preferred method of treatment of endometriosis, but it may also exist in cyst rupture, intra-abdominal adhesions or deep lesions such as omission of malpractice[9,10]. Chinese medicine believes that the pathogenesis of EM is mainly the "blood stasis" in the

treatment of Promoting blood circulation and removing blood stasis principle, so with the development of Chinese medicine, Chinese herbal medicine has been paid more and more attention in the treatment of infertile patients with endometriosis. Chinese herbs for activating blood circulation to dissipate blood stasis can effectively improve hemodynamics, improve microcirculation disorders and hemorheology. It has the effects of dilating blood vessels, regulating blood flow velocity, improving blood viscosity and viscosity[11,12].

Studies have shown that increased levels of chemokines in endometriosis patients can cause disorders of the pelvic and abdominal neuroendocrine nervous system, leading to a vicious circle of disease[13]. Monocyte chemoattractant protein -1 (MCP-1), activation of regulatory factors (RANTES) are two important chemokines, leukocyte chemotactic activation is involved in immune, inflammatory reaction, and play an important role in endometriosis in the planting process[14]. AOPP is a protein marker of oxidative stress and a sensitive indicator of the degree of protein oxidation[15]. MDA is a metabolite of lipid peroxidation and an index reflecting the extent of cell damage. Superoxide dismutase (SOD) is a metal enzyme antioxidant. It can scavenge oxygen free radicals and protect cells. A number of studies have confirmed that oxidative stress may cause oxidative damage to DNA, and may also be an important cause of endometriosis associated infertility[16,17]. In addition, the ectopic endometrium is also regulated by ovarian sex hormones, and increases or shrinks with the level of E2 in the blood. Endometriosis and its surrounding tissues contain aromatase, which can promote androgen into estradiol, E2 hypersecretion, and promote the growth of endometrium. Increased levels of sex hormones, can also promote the generation of nitric oxide (NO), and NO of follicular development, oocyte toxicity, and affect the function of the fallopian tube, become one of the causes of patients with endometriosis and infertility[18-20]. In this study, the use of Promoting Blood Circulation to Remove Blood Stasis combined with laparoscopic surgery in the treatment of endometriosis infertility patients showed:

The levels of serum MCP-1, RANTES and oxidative stress in the observation group were better than those in the control group, indicating that the traditional Chinese medicine for activating blood circulation to remove blood stasis not only has the effect of reducing chemokines and resisting inflammation, also can reduce the level of oxidative stress, antioxidant effect[21]. After treatment, the levels of FSH, LH, P and PRL in the two groups were significantly increased, while the level of E2 was significantly decreased, this may be related to the high temperature induced by electrocoagulation during laparoscopic surgery, which may affect the secretion of hormones[22]. But the increase of FSH, LH, P, PRL level and the decrease of E2 level in the observation group were significantly lower than those in the control group, it shows that the combination of activating blood circulation and removing stasis herbs can effectively improve the level of sex hormone after operation.

In summary, Promoting blood circulation to remove blood stasis combined with laparoscopy for infertile patients with endometriosis can reduce the levels of serum MCP-1, RANTES, oxidative stress, hormones and be beneficial to protect their uterine function.

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