 DOI: 10.19600/j.cnki.issn2152 - 3924.2024.02.010

# Effects of Wuwei Xiaodu Decoction on Uterine Energy Metabolism and Serum Inflammatory Factors in Rats with Acute Pelvic Inflammatory Disease

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**Abstract** [**Objectives**] To observe the effects of Wuwei Xiaodu Decoction on uterine energy metabolism and serum inflammatory factors in the acute pelvic inflammatory disease (APID) model. [**Methods**] 75 Wistar rats (females) were randomly divided into control group, model group and Wuwei Xiaodu Decoction low, medium and high dose groups ($n=15$). Except for the control group, the rat APID model was established by right uterine inoculation. On the fifth day after inoculation, the low, medium and high dose groups of Wuwei Xiaodu Decoction were administered at 4, 8 and 16 g/kg, and the control group and model group received normal saline. Rats were killed 12 h after nondose administration, blood was collected from the abdominal aorta and measured by ELISA for serum interleukin-6 (interleukin-6, IL-6), IL-8, and C-reactive proteins (CRP); the right uterus of rats was tested for high-energy phosphate adenosine phosphate (AMP), adenosine diphosphate (ADP), adenosine triphosphate (ATP) and total adenine nucleotides (TAN) level to evaluate the uterine energy metabolism. [**Results**] AMP, ADP, ATP and TAN were significantly higher in the Wuwei Xiaodu Decoction of low, medium and high dose than the model group, while the serum IL-6, IL-8 and CRP were significantly lower than the model group, and the difference between the low, medium and high doses ($P<0.05$). [**Conclusions**] The Wuwei Xiaodu Decoction can dose-dependent promote uterine energy metabolism and inhibit inflammatory response in APID model rats.

**Key words** Wuwei Xiaodu Decoction, Acute pelvic inflammatory disease, Uterine energy metabolism, Inflammatory factors

## 1 Introduction

Acute pelvic inflammatory disease (APID) is the most common acute inflammatory reaction of gynecological reproductive organs, connective tissue around the uterus and pelvic peritoneum. It has the characteristics of acute disease, severe disease and rapid progress. If there is not timely treatment or complete treatment, it can develop into chronic pelvic inflammation[1]. APID is mostly caused by heat poison, so it is appropriate to promote blood circulation and remove blood stasis, clear heat and detoxify and cool blood for treatment[2]. In this study, the rat APID model was established by bilateral intrauterine inoculation with mixed bacterial solution, and the effects of different doses of Wuwei Xiaodu Decoction on uterine energy metabolism and serum inflammatory factors in APID model rats were observed.

## 2 Materials and methods

**2.1 Experimental animals and grouping** Animals and 75 grouped female Wistar rats, 7 to 8 weeks of age, body weight (210.0 to 215.0) g, and experimental animals followed the 3R principle. First, all rats were numbered in the random number table, and were divided into control group, model group, Wuwei Xiaodu Decoction low, medium and high dose groups according to the random principle ($n=15$). Animals drink water freely, with room humidity of 65% - 75%, temperature of 22 - 24 ℃, and natural light.

**2.2 Drug preparation** Wuwei Xiaodu Decoction (Taraxaci Herba 6 g, Chrysanthemi Indici Flos 6 g, Lonicerae Japonicae Flos 15 g, Muskroot-like Semiaquilegia Root 6 g, Violae Herba 6 g) provided by Ezhou Steel Hospital Pharmacy, by accurate weighing before being soaked in water for 1 h, 30 min after filtration, was prepared into three doses of the original medicine solution containing 4, 8, 16 g per mL.

**2.3 After APID model** Each group of rats fasted for 6 h but with water, and pentobarbital sodium (3%) was injected intraperitoneally. The rats were fixed in the small animal operating table. At 2 cm above the pubic combination, the median abdominal white line was cut downward, the rat bladder was exposed, and the fat, bladder and rat intestine were pushed up to fully expose the uterus. Except for the control group, all the other groups absorbed 0.2 mL of the mixture (including *E. coli* and *Staphylococcus aureus*) and injected the needle into the ovary at the bifurcation and entered the uterine cavity respectively. 0.1 mL of the mixture was injected, and the endometrial tissue was mechanically damaged. After injection, the abdomen was layered and sterilized[3]. The control group operated the same way but did not mechanically damaged endometrial tissue and was injected with an equal amount of saline control.

**2.4 Treatment** After 5 d of modeling, the Wuwei Xiaodu Decoction of low, medium and high dose groups were administered once daily for 3 weeks (4, 8, 16 g/kg), and the control group and model group were given saline control.

**2.5 Blood collection and testing** Rats were killed by cervical dislocation after completion of treatment. 3 mL of blood was collected from the abdominal aorta, and the rat serum levels of IL-6, IL-8 and CRP were determined by ELISA. The right uterus was

Received: January 4, 2024 Accepted: March 27, 2024
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taken, 5 mg was weighed accurately, and the levels of high energy phosphocompounds AMP, ADP, ATP, and TAN were detected by using Coomassie Blue Staining Kit (conventional method).

**2.6 Statistical processing** Experimental results were processed with SPSS 21.0 statistical analysis software, the resulting data are presented as ($\bar{x} \pm s$), paired data $t$-test, and $P < 0.05$ was statistically significant.

## 3 Results and analysis

**3.1 Effect of five disinfection drinks on serum inflammatory factors** From Table 1, it was found that the levels of IL-6, IL-8 and CRP in the low, medium and high dose groups of Wuwei Xiaodu Decoction were significantly lower compared with the model group ($P < 0.05$); and the difference between the low, medium and high dose groups was significant ($P < 0.05$).

**Table 1 Comparison of acute pelvic inflammatory disease** (μg/L, $n = 15$, $\bar{x} \pm s$)

| Group | IL-6 | IL-8 | CRP |
|---|---|---|---|
| Control | 2.91 ± 0.24 | 0.29 ± 0.08 | 0.58 ± 0.07 |
| Model set | 10.89 ± 0.55[a] | 1.24 ± 0.17[a] | 1.87 ± 0.19[a] |
| Wuwei Xiaodu Decoction Low Dose | 7.26 ± 0.47[b] | 1.09 ± 0.15[b] | 1.23 ± 0.12[b] |
| Wuwei Xiaodu Decoction Medium Dose | 5.81 ± 0.34[bc] | 0.80 ± 0.11[bc] | 0.79 ± 0.10[bc] |
| Wuwei Xiaodu Decoction High Dose | 3.27 ± 0.42[bcd] | 0. 37 ± 0.09[bcd] | 0.65 ± 0.07[bcd] |

**NOTE** [a]$P < 0.05$; [b]$P < 0.05$ compared with the model group; [c]$P < 0.05$ compared with the low dose group; [d]$P < 0.05$ compared with the medium dose group. The same below.

**3.2 Effects of Wuwei disinfection drinks on uterine energy metabolism** AMP, ADP, ATP, and TAN were significantly different from the model group ($P < 0.05$); and the difference between the low, medium, and high dose groups was statistically significant ($P < 0.05$). See Table 2.

**Table 2 Comparison of AMP, ADP, ATP, and TAN levels in the uterine tissues of each group** (nmol/L, $n = 15$, $\bar{x} \pm s$)

| Group | TAN | ADP | AMP | AATP |
|---|---|---|---|---|
| Control | 45.45 ± 2.94 | 12.80 ± 0.97 | 28.39 ± 1.52 | 21.71 ± 1.42 |
| Model set | 31.07 ± 1.46[a] | 6.15 ± 0.72[a] | 16.26 ± 1.23[a] | 13.29 ± 1.17a |
| Wuwei Xiaodu Decoction Low Dose | 34.86 ± 1.60[b] | 8.17 ± 1.09[b] | 20.81 ± 1.05[b] | 15.08 ± 1.22[b] |
| Wuwei Xiaodu Decoction Medium Dose | 39.04 ± 2.57[bc] | 10.45 ± 1.43[bc] | 23.09 ± 1.91[bc] | 17.27 ± 2.10[bc] |
| Wuwei Xiaodu Decoction High Dose | 44.94 ± 2.69[bcd] | 12.49 ± 1.27[bcd] | 27.70 ± 2.05[bcd] | 20.35 ± 1.92[bcd] |

## 4 Discussion

APID is a common gynecological acute abdominal disease[4]. Although APID can achieve good results with antibiotic treatment, it is accompanied by different degrees of adverse reactions, a large amount of inflammatory exudate caused by pelvic inflammation and drug resistance caused by antibiotics are also an important factor for APID to become chronic common pelvic inflammation, so APID is prone to lead to repeated disease and is not easy to cure. Traditional Chinese medicine has its unique features in treating infectious diseases. In this study, the classical prescription Wuwei Xiaodu Decoction with heat-clearing and detoxification was used to treat APID model rats to analyze the mechanism of action.

After treatment with Wuwei Xiaodu Decoction of low, medium and high doses, the levels of IL-6, IL-8 and CRP were significantly reduced compared with the model group, indicating that the inflammation was controlled. In addition, the levels of AMP, ADP, ATP and TAN were significantly improved after treatment compared with the model group, indicating that Wuwei disinfection drink may play the effects of clearing heat and detoxification, promoting blood circulation and removing blood stasis, and replenishing and strengthening qi[5]. The experimental results show that while inhibiting the inflammatory reaction, Wuwei disinfection drink can also correct the APID uterine energy metabolism disorder, improve tissue energy supply, promote energy metabolism, reduce the uterine damage and maintain the normal physiological function of the uterus. Moreover, this effect is also dose-dependent, which indicates that the prescription and dosage should be adjusted according to the specific condition in the clinical treatment of APID.

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