

Original Article

A clinical observation of the combined treatment of Yishen decoction with antibacterial drugs for chronic prostatitis

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Abstract: Objective: To explore the clinical effect of the combined treatment of Yishen decoction with antibacterial drugs for chronic prostatitis (CP). Methods: A total of 210 patients with chronic prostatitis were randomized into the control group (105 cases) and the treatment group (105 cases). The control group was treated with levofloxacin hydrochloride capsules and terazosin hydrochloride tablets, while the patients in the treatment group were treated with self-made Yishen decoction on the basis of the administration of the control group. The National Institutes of Health chronic prostatitis symptom index (NIH-CPSI) was used for the treatment group and the control group before the treatment and one month after the treatment. Expressed prostatic secretions (EPS) related indexes, including white blood cells (WBC), red blood cells (RBC), and lecithin small body (LSB) in the prostate fluid, were examined by microscopy. Hematological inflammatory factors, including IL-8, TNF- α , and IFN- γ were measured by ELISA. At the same time, the Meares localization method was used for the bacterial detection. The treatment effect and satisfaction rate were evaluated, and the results were statistically analyzed. Results: In the treatment group, 42 cases were cured and 62 cases were improved, with an effective rate of 99.05%, and in the control group, 38 cases were cured and 60 cases were improved, with an effective rate of 93.33%, with statistically significant differences ($P < 0.05$). Before treatment, there were no statistically significant differences between the two groups in their NIH-CPSI scores, EPS related indicators, or hematology inflammatory factors, but after treatment, the mentioned indexes in the treatment group were all lower than they were in the control group, with significant differences (all $P < 0.05$). The satisfaction rates of treatment in the treatment group and the control group were 98.10% and 91.43%, respectively, with statistically significant differences ($P < 0.05$). Conclusion: Yishen decoction can effectively treat chronic prostatitis by relieving pain and discomfort and improving the CP patients' quality of life.

Keywords: Chronic prostatitis, Yishen decoction, clinical curative effect treatment

Introduction

Chronic prostatitis (CP) is a kind of urinary system disease which often occurs in young and middle-aged men, with an incidence rate of 6%-15% [1, 2]. According to relevant statistical data, as many as 35% to 50% of adult males are affected by prostatitis at some point in their lives, and about 25% of all urological visits are due to the onset of prostatitis, which has increased progressively year by year [3, 4]. CP is characterized by the typical different degrees of urinary problems, such as frequent micturition, urgency of micturition, odynuria, and urinary tenesmus, accompanied by discomfort in the perineum and pelvic floor [5]; and in severe

cases, chronic prostatitis may cause infertility or sexual dysfunction and affect the patients' physical and mental health [6, 7]. Epidemiological data shows a positive correlation between the incidence of prostate cancer and prostatitis, and the former disease ranks as the second most common male malignant tumor in terms of mortality [8, 9]. Therefore, it is of great importance to prevent and treat chronic prostatitis, which is difficult to treat due to its complicated causes and protracted course.

Relevant studies have shown that the effects of antibacterial treatment with antibiotics are unclear, because only a few antibiotics, such as quinolones and sulfonamides can penetrate

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the capsule of the prostate and be effective, but the majority of drugs can play a limited role [10, 11]. Chronic prostatitis is defined as “Jingzhuo” and “Linzhuo” in traditional Chinese medicine (TCM), and its pathogeneses are mostly kidney-Yang deficiency, bladder dampness-heat, and blood stasis, etc. And the symptoms can be improved by TCM treatment, which has obvious advantages in the treatment of CP and improves its clinical cure rate [12]. In a previous study, Luo proved that Yishen decoction had the effects of clearing heat and removing dampness, improving vital energy and blood and enhancing the body's immunity [13]. On this basis, the therapeutic effect of Yishen decoction on chronic prostatitis was evaluated in this study, which had a good guiding significance for clinical use.

A total of 210 patients with chronic prostatitis were recruited from Lianyungang TCM Hospital Affiliated to Nanjing University of Chinese Medicine between March 2017 and March 2018 to discuss the curative effect of Yishen decoction on chronic prostatitis.

Materials and methods

General materials

This study was approved by the Ethics Committee of Lianyungang TCM Hospital Affiliated to Nanjing University of Chinese Medicine, and all the patients agreed to and signed the informed consent. A total of 210 patients with chronic prostatitis in Lianyungang TCM Hospital Affiliated to Nanjing University of Chinese Medicine from March 2017 to March 2018 were selected as study objects and divided into two groups, with 105 cases in the treatment group and 105 cases in the control group according to the random number table method. The subjects' general information included age, course of the disease, frequency of sexual activity, and treatment history, etc.

Inclusion criteria: (1) According to the CP diagnostic criteria in the *Chinese Guidelines for the Diagnosis and Treatment of Urological Diseases* [14]: (a) If the patient had the following symptoms: frequent micturition, urgency of micturition, odynuria, and urinary tenesmus, and swelling and pain in the perineum, lower abdomen and the pelvic floor; (b) If the patient had tenderness and harder nodules in the prostate

according to a digital rectal examination (DRE); (c) CP could be confirmed if any of the following two results were evident in the expressed prostatic secretion (EPS) examination: the bacterial culture was positive, or the bacterial culture was negative but the white blood cell count in the prostatic secretion was equal to or greater than 10/HP and (or) with a reduction or the absence of lecithin bodies.

Exclusion criteria: (1) Patients with oliguria or anuria caused by acute prostatitis, benign prostatic hyperplasia, urinary tract stenosis, and renal failure, and patients with an abnormal congenital urinary system structure; (2) Patients who also had a urinary system infection; (3) Patients who also had urinary calculus; (4) Patients with neurogenic bladders, posterior urethral sclerosis, and urological malignancies; (5) Patients with an allergic constitution or an allergic reaction to a variety of drugs; (6) Patients with serious dysfunction of the heart, brain, liver, or kidney; (7) Patients with mental nervous system diseases; (8) Patients who were unable to cooperate with the treatment; (9) Patients with prostate-related treatment within the past two weeks; (10) Patients with diabetes, hypertension, or immune diseases; (11) Patients complicated by prostatic varicose veins.

Treatment methods

The patients in the control group orally took levofloxacin hydrochloride capsules (Zhejiang Jingxin Pharmaceutical Co., Ltd., SFDA approval), 0.2 g every time, twice daily, and terazosin hydrochloride tablets (Shanghai Abbott Laboratories Co., Ltd., SFDA approval), 1.0 mg every time, once daily. The patients in the treatment group were treated with Yishen decoction on the basis of the relevant drug treatment in the control group. Yishen decoction included *Dioscorea hypoglauca Palibin* (15.0 g), *Polygonum cuspidatum* (15.0 g), longhairy antenoron herb (10.0 g), plantain herb (10.0 g), *Patrinia* (10.0 g), Cortex Moutan (15.0 g), radix paeoniae rubra (15.0 g), *Eucommia ulmoides* (15.0 g), *Cuscuta chinensis* (15.0 g), and licorice 10.0 g (Bozhou Anhuaitang Pharmaceutical Co., LTD). The medicines were boiled with water to a decoction of about 900.0 mL every day, and the decoction, 300.0 mL at each time, was taken orally before breakfast, lunch, and dinner, respectively. The treatment duration was one

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month. While they were taking the medication, the patients were forbidden from eating raw and cold, and spicy and pungent food and were prohibited from drinking.

Outcome measures

(1) National Institutes of Health chronic prostatitis symptom index (NIH-CPSI) [15]: The patients completed the NIH-CPSI questionnaire both before and after the treatment. The questionnaire included questions about pain and discomfort symptoms (0-21 points), micturition symptom scores (0-10 points), the influences of the symptoms (0-6 points), the life and treatment scores (0-6 points) and a total score, and the scores were proportional to the severity of the symptoms; (2) EPS-related index detection: after micturition, the patients were in an erect bending position or in a chest-knee position. The doctor placed his right index finger, which was covered by lubricant-covered finger gloves, into the anus of the patient, pressed both sides of the prostate from the upper lateral side to the lower medial side 2-3 times, then he pressed from the right upper central sulcus to the anal orifice for 2-3 times, and extruded the perineal urethra. The white prostate secretion that flowed out was collected with sterile tubes for analysis. Two groups of patients were compared for the conditions of the white blood cells (WBC), red blood cells (RBC) and lecithin small body (LSB) in the prostatic secretions before and after treatment. An EPS microscopic examination score was used for the evaluation, with the detection microscopy (Olympus CX23, Shanghai Fulai Optical Technology Co., Ltd.): $+-<WBC \leq ++++$, denoted as 0-4 points; $+-<RBC \leq ++++$, denoted as 0-4 points; $+-<LSB \leq ++++$, denoted as 0-4 points; (3) Meares localization: Before the detection, the patient drank 300.0 mL of water, and the vulva and the interior foreskin were cleaned. First, 10.0 mL of primary urine was collected, and then 200.0 mL of urine was excluded; after that, 10.0 mL of intermediate urine was collected and the patient was asked to stop urination. The prostate was massaged, and 3-5 drops of prostatic fluid was collected as EPS. Then the patient was asked to urinate again, and 10.0 mL of urine was collected for the third time. If the prostatic fluid was not collected, the urine was observed whether it was turbid or not. If the urine was turbid, the prostatic component may be considered. And a microbial culture was carried out on

each of the above specimens. (4) Inflammatory factors in serology: Venous blood was collected before and after treatment in both groups, and IL-8, TNF- α , and IFN- γ were measured using an ELISA according to the kit's instruction (all the kits were from Shang-hai Xinfan Biotechnology Co., Ltd., China, XF130618; the detection equipment was a SpectraMax iD5 spectrometer, Germany); (5) Curative effect evaluation criteria: (a) Cured: after treatment, the patients' clinical symptoms related to the discomfort in urination had completely disappeared, the prostate examination results were negative, and there was no discomfort in the perineum or on pelvic floor. The routine examination of prostatic fluid showed no WBC or RBC, and the LSB in the prostatic fluid recovered to more than 65% gradually after 2 weeks without treatment. (b) Improved: after treatment, if the patient occasionally had clinical symptoms related to discomfort in urination, and occasionally showed mild tenderness in the prostate examination, and slight discomfort in the perineum and pelvic floor; EPS inspection found WBC > 10/HP, RBC > 5/HP, and the number of lecithin bodies was gradually increased but did not recover to more than 65%. (c) Invalid: after treatment, there was no improvement in the previous clinical symptoms, or the disease got worse. Efficiency = (cured cases + improved cases)/total cases * 100%; (6) Satisfaction rate evaluation: the post-treatment satisfaction was investigated with the self-designed satisfaction questionnaire, which included questions on: the frequency of sexual activity, adverse reactions and physical recovery, etc. The total score of the questionnaire was 100 points, with 81-100 points indicating that the patient was very satisfied with the treatment, 61-80 points indicating satisfied, and less than 60 points indicating unsatisfied. Patients' satisfaction = (very satisfied cases + satisfied cases)/total cases * 100%.

Statistical analysis

SPSS 22.0 was used for to analyze the related data. The mean \pm standard deviation ($\bar{x} \pm SD$) were used to present the data, and two independent samples t-tests were used to calculate the differences between the two groups in the measurement data with a normal distribution. The enumeration data was represented by the number/rate (n/%), and the chi-square method was used for the differences between groups.

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Table 1. Comparison of the two groups of patients in terms of their general information

	Treatment group (n=105)	Control group (n=105)	t/ χ^2	P
Age (y)	39.29±6.72	38.38±5.86	1.046	0.297
Course of disease (y)	1.44±0.63	1.45±0.81	-0.099	0.921
Frequency of sexual activity (times/week)	3.52±1.11	3.47±1.06	0.334	0.739
The history of treatment			0.491	0.484
Yes	64	59		
No	41	46		
Meares localization method			0.865	0.834
Staphylococcus aureus	6	5		
Streptococcus faecalis	3	3		
Escherichia coli	3	2		
Molds	1	2		

P<0.05 was considered as a statistically significant difference.

Results

General information about the patients in the two groups

The patients in the treatment group were from 21 to 58 years old, with an average age of 39.29±6.72 years; the course of disease was from 3 months to 2 years, with an average of 1.44±0.63 years; the frequency of sexual activity was 3.52±1.11 times/week. Sixty-four cases accepted treatment, but 41 cases did not. Meares localization test results showed that 13 patients had pathogenic bacteria growth (*Staphylococcus aureus* in 6 cases, *Streptococcus faecalis* in 3 cases, *Escherichia coli* in 3 cases, and molds in 1 case), and the remaining 92 cases did not have bacterial growth. The patients in the control group were aged from 22 to 59 years old, with an average age of 38.38±5.86 years; the course of disease was from 3 months to 1.9 years, with an average of 1.45±0.81 years; the frequency of sexual activity was 3.47±1.06 times/week. Fifty-nine cases accepted treatment, but 46 cases did not. Meares localization test results showed that 12 patients had pathogenic bacteria growth (*Staphylococcus aureus* in 5 cases, *Streptococcus faecalis* in 3 cases, *Escherichia coli* in 2 cases, and molds in 2 cases), and the remaining 93 cases did not have bacterial growth. There were no statistically significant differences between the two groups of patients in terms of general information, including age, course of disease, frequency of sexual activity, the histo-

ry of treatment, and the bacteriological detection (all P > 0.05) (**Table 1**).

Comparison in the chronic prostatitis index before and after treatment

Before treatment, there were no statistically significant differences between the two groups in their NIH-CPSI scores (pain, discomfort, urination, symptom effect, quality of life) and the overall scores (all P > 0.05). After treatment, each symptom score of the NIH-CPSI and total scores in the treatment group were significantly lower than those in the control group, with statistically significant differences (all P<0.05) (**Table 2**).

Comparison in EPS related indexes and inflammatory factors

Before treatment, the WBC, RBC, and LSB scores were 4.21±1.01 points, 4.38±0.95 points and 4.29±0.77 points in the treatment group, but they were 4.35±1.03 points, 4.26±0.92 points and 4.13±0.81 points in the control group, without significant differences (all P > 0.05). After treatment, the WBC, RBC, and LSB scores of both groups were decreased, 0.53±0.27 points, 0.89±0.38 points and 0.31±0.12 points in the treatment group, and 1.37±0.57 points, 1.43±0.51 points and 1.48±0.32 points in the control group, with statistically significant differences (all P<0.05, **Figure 1**). Before treatment, the relevant inflammatory markers IL-8, TNF- α and IFN- γ were 19.72±1.25 mg/L, 41.87±2.34 mg/L and 86.67±3.79 mg/L in the treatment group, but they were 19.63±1.19 mg/L, 42.08±1.99 mg/L and 85.96±3.68 mg/L in the control

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Table 2. Comparison of the NIH-CPSI scores before and after treatment

	Pain and discomfort		Urination		Symptom effect		Quality of life		Total scores	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Treatment group	12.13±2.19	5.09±1.76	3.45±0.92	1.46±0.87	3.42±1.39	1.38±1.04	3.34±0.96	1.95±1.15	22.38±5.14	10.15±4.17
Control group	12.14±2.17	6.98±2.34	3.44±0.95	1.82±0.76	3.43±1.41	1.93±1.21	3.32±0.95	2.25±0.89	22.36±5.12	12.75±4.38
t	-0.033	-6.614	0.077	-3.193	-0.052	-3.532	0.152	-2.114	0.039	-4.081
P	0.974	0.000	0.938	0.001	0.959	0.000	0.879	0.036	0.969	0.000

Note: NIH-CPSI: chronic prostatitis index score.

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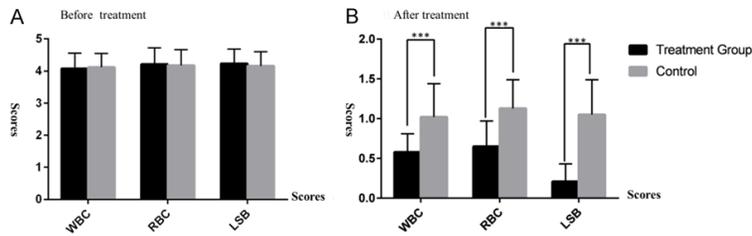


Figure 1. Comparison of the two groups in EPS-related indexes before and after treatment. A. Before treatment, there were no statistically significant differences between the treatment group and the control group in the relevant indicators in the prostatic fluid; B. After treatment, there were statistically significant differences between the treatment group and the control group in the relevant indicators in the prostatic fluid; *** $P < 0.001$. EPS, expressed prostatic secretion; WBC, white blood cells; RBC, red blood cells; LSB, lecithin small body.

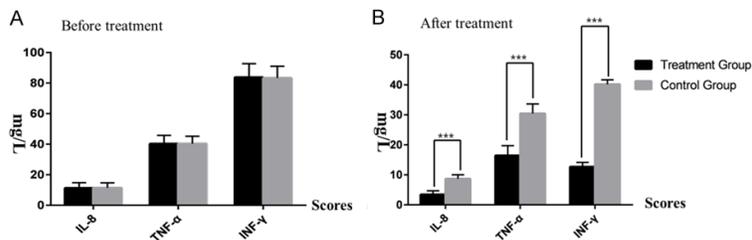


Figure 2. Comparison of the two groups in inflammatory indexes before and after treatment. A. Before treatment, there were no statistically significant differences between the treatment group and the control group in the relevant serological inflammatory indicators; B. After treatment, there were statistically significant differences between the treatment group and the control group in the relevant serological inflammatory indicators, *** $P < 0.001$. IL-8, interleukin -8; TNF- α , tumor necrosis factor - α ; IFN- γ , interferon - γ .

group, without significant differences (all $P > 0.05$). After treatment, the inflammatory markers were 3.22 ± 0.98 mg/L, 19.34 ± 2.35 mg/L and 13.24 ± 1.88 mg/L in the treatment group, but they were 9.86 ± 1.05 mg/L, 29.58 ± 2.76 mg/L and 41.85 ± 1.94 mg/L in the control group. The markers in the treatment group were significantly lower than those in the control group, with statistically significant differences (all $P < 0.05$) (Figure 2; Tables 3, 4).

Comparison of two groups of patients in the curative effects

In the treatment group, 42 patients were cured, 62 were improved, and 1 case was invalid, with an effective rate of 99.05%; and in the control group, 38 patients were cured, 60 were improved, and 7 cases were invalid, with an effective rate of 93.33%; and the difference of the effective rate was statistically significant ($P = 0.031$) (Table 5).

Comparison of two groups of patients in the satisfaction rate

The satisfaction rates of treatment in the treatment group and the control group were 98.10% and 91.43%, respectively. The satisfaction rate of the treatment in the treatment group was significantly higher than it was in the control group ($P < 0.05$) (Table 6).

Discussion

The main pathogenesis and mechanisms of chronic prostatitis are still unclear, but they may be related to autoimmune disorder and bacterial or mycoplasma or chlamydia infection [16]. Antibacterial drugs are often used in the treatment of chronic prostatitis, but the treatment effect of just a single antibacterial drug is poor, and the symptoms cannot be well relieved; and drug resistance may be generated during the long-term application of antibacterial drugs, causing repeated attacks and delayed

healing [17]. Traditional Chinese medicine believes that chronic prostatitis is caused by the interaction of dampness-heat, stasis and kidney-deficiency, which results in delayed healing, so it is difficult to treat [18]. Therefore, on the basis of antibiotic treatment, Yishen decoction can achieve a comprehensive treatment effect.

In this study, it was found that the effective rate of treatment in the treatment group was 99.05%, higher than it was in the control group, and the NIH-CPSI score was lower than it was in the control group after treatment, indicating that the combined treatment of antimicrobial agents and Yishen decoction could better relieve the clinical symptoms. This is because different components in Yishen decoction play different roles. *Dioscorea hypoglauca* Palibin and longhairy antenoron herb have the effect of clearing heat and detoxification, and *Patrinia*, cortex moutan, and radix paeoniae rubra have

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Table 3. EPS, WBC, RBC, and LSB scores in the two groups of patients

	WBC scores		RBC scores		LSB scores	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Treatment group	4.21±1.01	0.53±0.27***	4.38±0.95	0.89±0.38***	4.29±0.77	0.31±0.12***
Control group	4.35±1.03	1.37±0.57	4.26±0.92	1.43±0.51	4.13±0.81	1.48±0.32
t	-1.28	-13.647	0.955	-8.700	1.467	-35.080
P	0.199	0.000	0.340	0.000	0.143	0.000

Note: EPS, expressed prostatic secretion; WBC, white blood cells; RBC, red blood cells; LSB, lecithin small body; ***represented for P<0.001.

Table 4. Patients' peripheral blood inflammatory factors

	IL-8 (mg/L)		TNF-α (mg/L)		IFN-γ (mg/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Treatment group	19.72±1.25	3.22±0.98***	41.87±2.34	19.34±2.35***	86.67±3.79	13.24±1.88***
Control group	19.63±1.19	9.86±1.05	42.08±1.99	29.58±2.76	85.96±3.68	41.85±1.94
t	0.534	-47.372	-0.634	-28.946	1.377	-108.52
P	0.593	0.000	0.527	0.000	0.169	0.000

Note: IL-8, interleukin -8; TNF-α, tumor necrosis factor -α; IFN-γ, interferon -γ, ***represented P<0.001.

Table 5. Evaluation on curative effects of two groups of patients

	Cured	Improved	Invalid	Effective rate
Treatment group	42	62	1	99.05%
Control group	38	60	7	93.33%
χ ²				4.678
P				0.031

Table 6. Total satisfaction rates of two groups

	Very satisfied	Satisfied	Unsatisfied	Overall satisfaction rate
Treatment group	98	5	2	98.10%
Control group	74	22	9	91.43%
t/χ ²				4.701
P				0.030

the effect of promoting blood circulation and removing blood stasis, clearing heat in the blood and relieving pain [19, 20]. *Eucommia ulmoides* and *Cuscuta chinensis* have the effects of tonifying the kidney, curing the pain of lumbar spine, relieving urine dribble, and strengthening essence, etc. [21]. Licorice can relieve pain and harmonize medicinal nature [22]. Using the combination of the above drugs, both the symptoms of discomfort in CP patients and also their quality of life were greatly improved.

No statistically significant differences were found in this study between the treatment group and the control group in EPS, WBC, RBC, or LSB before treatment, but the WBC and RBC in the treatment group were significantly less than they were in the control group, and LSB was significantly lower than it was in the control group after treatment. This is due to the effect of *Polygonum cuspidatum* combined with licorice on the body, which is similar to the effect of the adrenocortical hormone [23]. The combination of *Patrinia*, cortex moutan, and radix paeoniae rubra can resist inflammation, relieve local pain and delay platelet aggregation [24]. WBC has

a phagocytic effect in the human body; as the inflammatory response was improved, the number of WBC was decreased, while the number of LSB was gradually increased, the activity was restored [25]. Meanwhile, the levels of IL-8, TNF-α, and IFN-γ in the serological tests after treatment in the treatment group were all lower than they were in the control group, and the results were similar to those of Yaodong et al. [26]. Modern pharmacology has also proved that the *Eucommia ulmoides*, *Cuscuta chinensis*, and licorice in Yishen decoction can en-

hance the function of the immune system while fighting against fibrosis, and they have the effect of activating blood circulation and removing stasis in patients with chronic prostatitis [27].

Chronic prostatitis patients are affected by urinary system symptoms for a long time, which decreases the couples' satisfaction in terms of sexual activity, and symptoms such as impotence and premature ejaculation may also occur, which result in a great threat to the physical and mental health of the patients [28]. Compared with previous studies, this study added an evaluation of the patients' satisfaction with the treatment, from the patients' lives to their psychology. The results of the study showed that the 98.10% of the patients in the treatment group were satisfied with the treatment, which was significantly higher than the satisfaction rate of the control group. This further suggests that the combined treatment of TCM and western medicine can achieve better curative effects in patients with chronic prostatitis. The relatively short follow-up time and small sample size of this study may lead to bias in the results, so longer prospective trials with a larger sample size may be conducted in the future, to widely promote the treatment mode of Yishen decoction combined with antibacterial drugs in clinical practice.

In conclusion, Yishen decoction combined with antibacterial drugs was adopted in this study for patients with chronic prostatitis, and relevant laboratory indexes were evaluated, and the patients' satisfaction was investigated; in this study we found that the mental changes during the progression of the diseases are more focused. And it was found that the combination method can improve the treatment effect and raise the patients' satisfaction.

Disclosure of conflict of interest

None.

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