Efficacy of Prostant on chronic prostatitis in 119 patients

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ABSTRACT

AIM: To evaluate the efficacy and safety of Prostant in the treatment of chronic prostatitis. **METHODS:** One hundred and nineteen cases of patients who had been diagnosed of chronic prostatitis were treated by Prostant. The efficacy was evaluated by WBC in EPS and NIH Chronic Prostatitis Symptom Index after a one-month follow-up. **RESULTS**: After the one-month follow-up, the total improvement rate is 65.5 %, the WBC in the prostatic fluid were reduced from (21±20) to (12±13)/High-power field (HPF); the symptom index score changed from 12±4 to 7±5. The pain and voiding score of the symptom index were lowered from 8±3 to 5±3 and 3.9±2.7 to 2.3±2.3 respectively. All of above showed great statistic differences (P<0.05). Only 2 cases (1.7 %) reported serious diarrhea. **CONCLUSION:** The Prostant is effective and safe in the treatment of chronic prostatitis, especially on those cases whose symptom and inflammation in prostatic fluid are not too serious.

INTRODUCTION

Prostatitis is truly a major male health care problem. Patients with chronic prostatitis experience a negative impact on their quality of life similar to patients with unstable angina, a recent myocardial infarct, or active Crohn's disease[1].

It is considered by Chinese traditional medicine that prostatitis is mainly caused by the pathogenic dampness and heat and blood stagnation which blocked lower-energizer. So prostatitis is treated through clearing away the dampness and heat and promoting blood circulation to get rid of blood stagnation.

Prostant (Lizhu Pharmaceutical Factory, Shenzhen, China) is a suppository made up of several kinds of Chinese herds including Cortex Phellodendri, Fructus Gardeniae, Rhizoma Polygoni Cuspidati, Herba Lycopi and Radixet Rhizoma Rhei etc**.** These herbs have the functions of clearing away the dampness and heat, promoting blood circulation to get rid of blood stagnation, and dissolving mass. The quality-control ingredient is berberine no less than 15 mg per suppository. According to modern pharmacological research on Chinese herds, the main effective ingredients including berberine, emodin, chrysophanol, rhein, gardenoside, and so on, which could inhibit many kinds of bacteria[2-4], fungi, and viruses[5].

This study was to evaluate the efficacy and safety of Prostant in treatment of chronic prostatitis.

MATERIALS AND METHODS

The observation was carried out during 2001 Jul to 2002 Mar, in 119 patients who had been diagnosed of chronic prostatitis. None of the patients had any of the following situations: any acute diseases, prostate cancer, benign prostatic hyperplasia, psychoses, chronic diarrhea, urethral stricture, and any other severe diseases.

The 119 patients' age ranged from 20 to 68 a,

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36±10 (mean±SD), and the course of disease ranged from 1 month to 60 months (16±15).

Each patient took one Prostant suppository every night. The expressed prostatic secretion (EPS) was examined and the severity of symptom was evaluated by the NIH Chronic Prostatitis Symptom Index just before treatment and after the one-month follow-up. No other therapies had been taken during this period of time.

The efficacy of the therapy was divided into four levels: cure, the symptom index score is reduced over 90 %, and the number of WBC in the EPS is less than 10/High-power field (HPF); effective, the symptom index score is reduced by 60 %-89 % and the number of WBC in the EPS is lowered over 50 % or less than 15/HPF; improved, the symptom index score is reduced by 30 %-59 % and the number of WBC in the EPS is lowered over 25 %; no effect, the symptom index score is reduced less than 30 % or the number of WBC in the EPS is lowered no more than 25 %.

All the data were analyzed by SAS 6.12 software.

RESULTS

After follow-up, 8 cases (6.7 %) were cured and remarkable effectiveness could be seen in 25 cases (21.0 %), also 45 cases (37.8 %) showed improvement and the rest 41 cases (34.5 %) appeared to have no effect. The total improvement rate is 65.5 %. The average number of WBC in EPS reduced from (21±20) to (12±13)/HPF (P<0.05).

The average symptom score of 119 patients was 12±4 before treatment and 7±5 after follow-up (P<0.01), among which the pain score reduced from 8±3 to 5±3 (P<0.01) and the voiding score changed from 3.9±2.7 to 2.3±2.3 (P<0.01).

The effect of Prostant on some symptoms was shown in Tab 1.

Seventy cases (63.0 %) reported that the pain or discomfort appeared less often than before, and 94 patients (79.0 %) felt that the severity of pain or discomfort decreased more or less.

According to the course of disease (Tab 2), those who had shorter course showed better effect (P<0.05).

Tab 2. Efficacy related to course of disease.

Course of disease	No effect (%)	Improved (%)	Effective/ Cured (%)
1-6 months	12 (26.1 %)	16 (34.8 %)	18 (39.1 %)
6 months-2 years	19 (33.3 %)	25 (43.9 %)	13 (22.8 %)
More than 2 years	10 (62.5 %)	4 (25 %)	2 (12.5 %)

All of the patients were divided by the severity of symptom (Tab 3), which is evaluated by the NIH Chronic Prostatitis Symptom Index, into three groups: mild (whose symptom score is ≤9), moderate (the symptom score ranged from 10 to 18), and severe (the symptom score is ≤19). The patients whose symptoms were less severe appeared to have better results after the treatment (P<0.05).

Those patients with noninflammatory prostatitis responded better than other patients did (Tab 4), and along with the number of WBC in EPS rose, the effect

Tab 1. Effect of Prostant on some symptoms.

	Incidence rate/%	Effect
Pain or discomfort in perineum	58.8 % (70)[1)]	Cured rate 38.6 %
Pain or discomfort in testicles	31.1 % (37)	Cured rate 56.8 %
Pain or discomfort in the tip of penis	40.3 % (48)	Cured rate 54.2 %
Pain or discomfort in pubic or bladder area	63.9 % (76)	Cured rate 42.1 %
Pain or burning during urination	33.6 % (40)	Cured rate 40.0 %
Pain or burning during or after ejaculation	16.0 % (19)	Cured rate 68.4 %
Sensation of not emptying bladder after voiding	74.8 % (89)	Improved rate 62.9 %
Voiding too often	69.7 % (83)	Improved rate 61.5 %

[1)] Number of cases was in parenthesis.

Tab 3. Efficacy related to severity of symptom.

Severity of symptoms	No effect (%)	Improved (%)	Effective/ Cured (%)
Mild	11 (31.4 %)	7 (20.0 %)	17 (48.6 %)
Moderate	28 (36.4 %)	33 (42.9 %)	16 (20.8 %)
Severe	2 (28.6 %)	5 (71.4 %)	0 (0 %)

Tab 4. Efficacy related to WBC in EPS.

WBC in EPS	No effect (%)	Improved (%)	Effective/ Cured (%)
WBC 0-9/HP	7 (18.4 %)	22 (57.9 %)	9 (23.7 %)
WBC 10-30/HP	20 (37.1 %)	16 (29.6 %)	18 (33.3 %)
WBC 30-/HP	14 (51.9 %)	7 (25.9 %)	6 (22.2 %)

of treatment fell down (P<0.05).

Thirty seven patients (31.1%) were diagnosed of chronic prostatitis for the first time and had never been treated before; 74 cases (62.2 %) had taken medicine therapy before this observation and the rest 8 (6.7 %) had had intraprostatic drug injection (Tab 5). The improvement rate for those who had never been treated before was the greatest and the patients who had had intraprostatic injection showed worse effect compared with other two groups (P<0.01). The mean number of WBC in EPS (Fig 1) of this group was also significantly higher than the other two groups [(35±7) *vs* (22.1±2.4) and (14.9±2.4)/HPF, P<0.05].

Tab 5. Efficacy related to therapeutic history.

Therapy taken before	No effect (%)	Improved (%)	Effective/ Cured (%)
None	7 (18.9 %)	13 (35.2 %)	17 (45.9 %)
Drugs	27 (36.5 %)	31 (41.9 %)	16 (21.6 %)
Intraprostatic injection	7 (87.5 %)	1 (12.5 %)	0 (0 %)

Forty nine (41.2 %) patients reported adverse effects-discomfort in anus (28 cases; 23.5 %), stool washiness (17 cases; 14.3 %), and both (4 cases; 3.4 %). Five of twenty-one patients who reported stool washiness had diarrhea, but only 2 patients had serious symptoms. Most effects were mild to moderate and were tolerable to most patients. Twenty-nine cases reported that the AEs disappeared one or two weeks after the treatment began. No other AEs were found during the period of observation.

DISCUSSION

Berberine, an anti-microbial from plant[2,4], is the main component of Prostant which can intercalate DNA, inhibit DNA synthesis and reverse transcriptase to inhibit the multiplication of bacteria, fungi, and viruse[5]. It also can inhibit cyclooxygenase-2 transcriptional activity[6] and block the α-receptor[7], therefore reduce inflammation and relieve the tension of urethra. Moreover, a dose-dependent analgesic activity was determined, which was assessed by using the model based on the inhibition of acetic acid-induced writhing reflexes, as well as antipyretic activity on Freund' s complete adjuvant -induced increased body temperature[4].

Few drugs can penetrate into the prostatic fluid due to the special structure and environment in the prostate. Naber *et al*[8] studied five fluoroquinolones and finally found that none of which had higher concentration in prostatic fluid than in plasma. Shafik[9] discovered that there were 2-6 unidirectional communicating veins which transmitted the blood from rectal to the genitourinary plexus but not in the reverse direction. Lin *et al*[10] used [^{3}H]-berberine as the tracer isotope and found that it could be detected in the prostate tissue and serum only 5 min after drug was taken by rectum, and the concentration in prostate is much higher than in serum and other organs (except rectum, liver and kidney) during the next 24 h.

The total improvement rate was 65.5 % after follow-up, which is consistent with the previous double-blind, placebo-controlled trial[11]. But greater effect could only be seen in those patients whose symptoms were not too serious, so some other medicines such as α-blockers or analgesics should be applied to treat those patients with severe symptoms.

Prostant was found to had better effect on the patients with mild to moderate inflammation in EPS, especially on those cases whose number of WBC in EPS were less than 10/HP before treatment. The total improvement rate for those patients reached 81.6 %. Although berberine, the main component of Prostant,

is an antibiotic compound derived from coptis, it is not as potent as other antibiotics such as fluoroquinolones and trimethoprim. Therefore some antibiotics should be added when treating patients with chronic bacterial or inflammatory prostatitis (category II or IIIA).

Although it is estimated to be eight times more frequent than bacterial prostatitis[12], nonbacterial prostatitis remains in a condition of uncertain etiology and is rarely associated with any other infection in the urinary tract. Except for some possible organisms infection such as *Ureaplasma* and *Chlamydia*[13], many hypothesized causes of chronic nonbacterial prostatitis have been suggested, such as an unidentified noninfectious inflammatory agent[14], chemical prostatitis resulting from intraprostatic urinary reflux[15], an organism remnant acting as an antigen[16], a yet unidentified infections agent[14], an autoimmune response[17], a viral etiology[18], and increased tension in the muscles of bladder neck and prostatic urethra or myalgia of the pelvic floor[19]. Psychologic factors may also have an etiologic role[20]. The complex and uncertain etiology of prostatitis make it a real challenge for the proper management of chronic prostatitis, therefore, definite treatment is difficult. The result suggested that Prostant had better effect on the patients with disease-course less than 2 years. Due to no improvement after longtime treatment, some patients with long course of disease may even develop psychological problems such as depression or somatization that might aggravate the symptoms, and the abuse of antibiotics will also increase the chances of drug-resistance of bacteria.

Among the patients that reported AEs, only 2 patients had serious diarrhea, owing to the suppository itself and the water-absorbing effect[11], which disappeared right after the treatment stopped.

After the observation of 119 patients, it is concluded that the Prostant is effective and safe in the treatment of chronic prostatitis, especially on those cases whose symptom and inflammation in prostatic fluid are not too serious.

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