

EFFECTS OF POLLEN EXTRACT PREPARATION PROSTAT/POLTIT ON LOWER URINARY TRACT SYMPTOMS IN PATIENTS WITH CHRONIC NONBACTERIAL PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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ABSTRACT

Objectives. To assess the efficacy and safety of the pollen extract preparation Prostat/Poltit in the treatment of patients with chronic nonbacterial prostatitis/chronic pelvic pain syndrome.

Methods. In a double-blind study, 60 patients between 20 and 55 years old with chronic nonbacterial prostatitis/chronic pelvic pain syndrome were randomized to receive Prostat/Poltit or placebo for 6 months. The patients had been symptomatic for more than 6 months without response to any given therapy. The patients were evaluated at the start of the treatment and after 6 months of treatment with the help of a symptom questionnaire covering the symptoms in seven pain locations, five voiding symptoms, three storage symptoms, and four sex-related symptoms.

Results. The overall clinical evaluation of the treatment result showed that after treatment for 6 months more patients taking Prostat/Poltit were cured or improved than patients taking placebo. No adverse reactions to the treatment were found.

Conclusions. Prostat/Poltit is superior to placebo in providing symptomatic relief in men with chronic nonbacterial prostatitis/chronic pelvic pain syndrome. UROLOGY 67: 60–63, 2006. © 2006 Elsevier Inc.

Chronic nonbacterial prostatitis/chronic pelvic pain syndrome (CNBP/CPPS) is a common health problem among men.^{1,2} The clinical presentation is highly variable but always includes genitourinary and pelvic pain³ and a variety of lower urinary tract symptoms.^{4,5} Sexual function is often disturbed.⁶ CNBP/CPPS can be physically and psychologically devastating, significantly hampering the quality of life of many patients.⁷

The treatment of CNBP/CPPS can be a frustrating challenge to the physician and patient.^{8,9} The optimal treatment for CNBP/CPPS remains unestablished, and new methods should be tried. Earlier studies have shown pollen extract preparations to give a durable and marked symptom reduction

in men with CNBP/CPPS,^{10,11} with improvement in semen quality¹² and a significant reduction in the National Institutes of Health-Chronic Prostatitis Symptom Index (CPSI) score.¹³ However, these trials were all open, uncontrolled studies. Therefore, an obvious need exists to investigate the clinical efficacy of pollen extract preparations in a randomized, double-blind, placebo-controlled study of adequate duration. The present report is an account of such a study in which men with CNBP/CPPS were treated with the pollen extract preparation Prostat/Poltit or with placebo for 6 months. The clinical efficacy suggested by the results from the earlier, uncontrolled studies of pollen extract was confirmed by the results of this study.

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MATERIAL AND METHODS

STUDY POPULATION

Patients previously diagnosed with CNBP or CPPS were screened for inclusion in the study. All patients had been symptomatic for more than six months and had had at least one 3-month course of antimicrobial drugs or other medica-

TABLE I. Symptom score (modified University of Washington symptom score)

Symptom Domain	Start of Treatment		After 6 mo Treatment		Score Reduction	
	Prostat/Poltit	Placebo	Prostat/Poltit	Placebo	Prostat/Poltit	Placebo
Pain	9.5 ± 2.9	6.6 ± 3.2	2.8 ± 3.3	4.9 ± 3.8	6.7 ± 4.5	1.7 ± 3.2
LUTS						
Voiding symptoms	5.2 ± 2.7	4.4 ± 2.7	1.4 ± 2.1	2.8 ± 2.8	3.8 ± 3.6	1.6 ± 2.7
Storage symptoms	2.5 ± 1.5	2.5 ± 1.5	0.9 ± 1.3	1.9 ± 1.8	1.6 ± 2.0	0.7 ± 1.3

Key: LUTS = lower urinary tract symptoms.

Data presented as mean ± SD.

tion for their condition. The screening included digital rectal examination, urodynamics, bacterial culture of semen or expressed prostatic secretions and of urine, cystoscopy, ultrasound investigation of the prostate, and prostate-specific antigen determination. Of the 163 screened patients, 60 met the defined criteria for inclusion. The remaining 103 patients were excluded after examination because they were found to have bacterial prostatitis (25 patients), bladder neck contraction (17 patients), benign prostatic hyperplasia (15 patients), abnormal ultrasound findings (12 patients), urethral stricture (10 patients), abnormal urinalysis (9 patients), acute prostatitis (8 patients), abnormal uroflowmetry findings (4 patients), or a prostate-specific antigen level greater than 4 ng/mL (3 patients).

The study population had a mean age of 35 years (range 20 to 55). The 60 patients were drawn from a mixture of ethnic groups and consisted of whites (36 patients), Asians (5 patients), African Americans (6 patients), Hispanics (3 patients), and Middle Eastern (10 patients). The patients in the study had had their symptoms for periods ranging from 6 months to 6.5 years. All 60 patients were extensively informed about the study and offered participation. All patients participated voluntarily and gave their informed consent.

STUDY INCLUSION AND EXCLUSION CRITERIA

The patients entered into the study had to have had lower urinary tract symptoms indicative of CNBP or CPPS (National Institutes of Health category IIIa and IIIb), with symptoms persisting for at least 6 consecutive months without response to any given therapy. No bacteria were to be detected in the semen and/or prostatic fluid culture or in urine voided before and after expression of prostatic secretions. Their age had to be between 20 and 60 years. No abnormalities were allowed on cystoscopy or ultrasonography. The cystometrography findings had to be normal. Finally, the serum prostate-specific antigen level had to be less than 4 ng/mL.

Patients were excluded if they were also diagnosed with benign prostatic hyperplasia with the American Urological Association Symptom Index score exceeding 15, or if they had complicating factors such as bladder neck constriction or urethral stricture, or abnormal uroflowmetry results. Patients were also excluded if more than 3 to 5 erythrocytes or leukocytes per high power field were found in the urine sample.

STUDY DESIGN

The patients in the study were randomized in a double-blinded way to treatment with either placebo (30 patients) or Prostat/Poltit (30 patients). Randomization was performed by a computer software program (Microsoft Excel, version 7.0, Random Number Generation analysis tool). The double-blind protocol consisted of labeling bottles "A" or "B" for the active tablets and the placebo tablets, respectively, and assigning the bottles randomly to the patients in the two equal groups of the

study, and then secreting the information from the investigating physician until after the study was completed.

Before starting the medication, each patient gave his subjective ratings of his symptoms using a questionnaire routinely used in the clinic. This questionnaire, similar to the one devised by Krieger *et al.*,³ covers the symptoms in seven pain locations (pain in the lower back, lower abdomen, rectal area, testes, and penis and at urination and ejaculation), five voiding symptoms (incomplete bladder emptying, dribbling, interrupted urination, straining, and weak urinary stream), three storage symptoms (frequency, nocturia, and urgency), and four sex-related symptoms (decreased libido, erectile dysfunction, premature ejaculation, and delayed ejaculation). For each question on pain and voiding and storage symptoms, the patient assigned a score from 0 to 3, with 0 being no symptoms or problems and 3 being marked symptoms or problems. For the sex-related symptoms, the patient noted "yes" or "no," without additional stratification. The patients then began their medication, either Prostat/Poltit or placebo. The dose was three tablets daily. The tablets with Prostat/Poltit contained 74 mg highly defined extract of pollen from selected Graminae species. The placebo tablets were identical in appearance to the active tablets but contained no pollen extract. The study medication was produced by Allergon AB, a Pharmacia company located in Angelholm, Sweden.

Treatment continued for 6 months, at which point the patients were seen again and examined and asked again for their symptoms using the same questionnaire as at the beginning of the study. The investigating physician also made his own overall clinical evaluation of the treatment result, not knowing whether the patient had taken active drug or placebo. The patients were seen also briefly 2 weeks after the start of the treatment and again 3 months after the start of the treatment. On those occasions, the patients could report adverse events and collect study medication for the next period. The patients were instructed not to take any other medication or any other treatment for their urinary problems, except the study medication, during the length of the study. They were also instructed not to take any other phytotherapeutic agents or dietary supplements or to make any changes in their diet or lifestyle for the duration of the study.

STATISTICAL ANALYSIS

The data were entered into a computer spreadsheet program and a statistical package was used for analysis. The differences between groups were analyzed by *t* test (double sided) or chi-square analysis using a computer program (Microsoft Office Excel 2003, Data Analysis Tools), with *P* < 0.05 considered statistically significant.

RESULTS

Of the 60 patients who entered this study, 58 completed it. Two patients, both randomized to

TABLE II. Sexual dysfunction

Symptom	Dysfunction at Start of Treatment		Dysfunction After 6 mo	
	Prostat/Poltit	Placebo	Prostat/Poltit	Placebo
Sexual dysfunction				
No.	36	44	7	36
Mean \pm SD	1.2 \pm 0.9	1.6 \pm 0.9	0.2 \pm 0.5	1.3 \pm 1.1
Decreased libido (n)	4	8	1	7
Erectile dysfunction (n)	10	14	3	13
Premature ejaculation (n)	14	18	3	13
Delayed ejaculation (n)	8	4	0	3

TABLE III. Overall clinical response

Treatment	Total	Free of Symptoms, Cured	Clinically Improved	Unimproved
Prostat/Poltit (n)	30	6	16	8
Placebo (n)	28	0	10	18

treatment with placebo, did not come to the evaluation at 6 months and were lost to follow-up. At baseline, the patient characteristics in the two groups were similar, except for the pain score, for which the patients randomized to Prostat/Poltit turned out to be significantly more symptomatic than the patients in the placebo group (Table I).

The patients who received Prostat/Poltit had a significantly lower pain score, less voiding symptoms, and less storage symptoms at the end of the 6-month treatment period than the patients who had received placebo (Table I).

Sexual dysfunction is common in patients with CNBP/CPPS. In this study, no difference was found at the start of the treatment between the two groups regarding the frequency of decreased libido, erectile dysfunction, premature ejaculation, or delayed ejaculation (Table II). After 6 months of treatment, sexual function was significantly better in the patients taking Prostat/Poltit than in the patients taking placebo.

The patients were subjectively, but blindly, evaluated for their overall clinical response by the study investigator after treatment for 6 months with Prostat/Poltit or placebo. Of the 30 patients taking Prostat/Poltit, 22 were considered clinically improved or cured, whereas only 10 of the 28 evaluated patients taking placebo were considered improved (Table III). The difference between the treatment groups was statistically significant.

No adverse effects were reported by the patients taking Prostat/Poltit or those taking placebo. Both treatments were well tolerated.

COMMENT

Few clinical conditions encountered by the urologist cause more patient and physician frustration

than CNBP/CPPS. Traditional medical therapy is often unsuccessful and fails to improve the symptoms of most patients with CNBP/CPPS.^{1,9} However, with the pollen extract preparation used in this study, pain and lower urinary tract symptoms were significantly more reduced than after placebo, sexual dysfunction significantly more improved, and the overall clinical response significantly better, with 6 of 30 patients clinically cured. This positive effect is in concordance with several earlier investigations of the effect of pollen extract preparation in this group of patients.¹⁰⁻¹³ However, all these earlier investigations lacked a placebo control.

Allergon, the producer of Prostat/Poltit, earlier produced the pollen for Cernilton, another pollen extract preparation. Since the mid-1990s, Allergon has produced its own pollen extract preparation, Prostat/Poltit, with similar active ingredients and composition as Cernilton had until then. Therefore, it can be considered justified to regard the documentation for Cernilton—when based on the Allergon-produced pollen (until the mid-1990s)—as applicable also to Prostat/Poltit. The source and composition of the pollen presently used in Cernilton is not known to Allergon.

The results of the present study were based on the patients' own evaluation of their symptoms with the help of a questionnaire routinely used in the clinic. This questionnaire, similar to the one devised by Krieger *et al.*,³ covers the symptoms in seven pain locations, five voiding symptoms, three storage symptoms, and four sex-related symptoms. It has been shown to be a reliable and useful tool in the diagnosis and follow-up of patients with CNBP/CPPS over many years of use by the investigator. Therefore, it is likely that very similar results

would have been obtained if another symptom questionnaire (eg, the CPSI or Giessen prostatitis symptom score^{14,15}) had been used in the present study. A high efficacy for Prostat/Poltit when analyzed by the reduction in the CPSI score has been demonstrated in the results of a study by Li *et al.*¹³ In their study, 106 patients with CNBP/CPPS were treated with Prostat/Poltit for 8 weeks. The treatment led to a reduction of the mean CPSI score from 24.1 to 12.2 ($P < 0.0001$). Similar results were obtained by Monden *et al.*¹⁶ who found that the CPSI score was significantly reduced in 34 patients with CNBP/CPPS by treatment for 4 to 6 weeks with a pollen extract preparation very similar to Prostat/Poltit.

The results of the present study render more than a glimmer of hope that patients with CNBP/CPPS can be treated successfully. Additional studies of Prostat/Poltit in this difficult group of patients comparing its efficacy with more conventional therapies are warranted to elucidate fully its role in the treatment of this condition.

CONCLUSIONS

In this study, the pollen extract preparation Prostat/Poltit administered for 6 months was shown to ameliorate the symptoms associated with CNBP/CPPS effectively. The efficacy was significantly greater than that of placebo. The preparation was very well tolerated. Additional comparative studies of Prostat/Poltit in patients with CNBP/CPPS are warranted to elucidate fully its role in the treatment of this condition.

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