

## Research Article

## Short course of dutasteride in treatment of a refractory category IIIB chronic prostatitis (A placebo-controlled study)



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## ABSTRACT

**Objective:** To evaluate the short-term efficacy of Dutasteride in the management of chronic prostatitis (CP)/chronic pelvic pain syndrome.

**Materials and methods:** A randomized placebo-controlled double-blind study was conducted that including 50 patients diagnosed with CP based on the presence of pelvic pain for  $\geq 3$  months of the preceding 6 months. Patients were randomized into 2 equal groups to evaluate Dutasteride of 0.5 mg once daily that was given for 3 months compared to a placebo.

**Results:** Forty-nine patients were evaluated after the follow-up period with no statistically significant difference in the perioperative demographic data. The mean age of the Dutasteride group was 48.3 (range 41–62) compared to a mean age of 46.5 (range 44–60) in the placebo group. There was a highly statistically significant improvement in the Dutasteride group compared to its preoperative parameters and the placebo compared group in the terms of pain, urinary scores, and total National Institutes of Health CP symptom score. Moderate and marked improvement in patients' symptomatology was seen in 56% of the dutasteride group, while only 8% in the dutasteride group failed to show an improvement with no significant side effects noted in our study.

**Conclusion:** The short-term outcome of dutasteride therapy showed an improvement in the National Institutes of Health-CP symptom score compared to a placebo in the treatment of category IIIB CP.

**The trial was registered in the clinical trial.gov registry with a registration number:** NCT04756206.

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## 1. Introduction

Nonbacterial prostatitis refers to a condition that affects patients who present with the symptoms of prostatitis without a positive culture for urine or expressed prostate secretions (EPSs). With time, our understanding of prostatitis evolved to include a different clinical phenotype with a variety of voiding presentations and symptomatology rather than just inflammation and infection. The two main clinical presentations of prostatitis include pelvic pain and lower urinary tract symptoms.<sup>1–3</sup>

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The US National Institutes of Health and the National Institute of Diabetes and Digestive and Kidney Diseases (NIH-NIDDK) proposed the first classification of prostatitis into 4 categories in 1995 that was later published in 1998. Bacterial prostatitis represented categories I and II while nonbacterial prostatitis including chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) was categorized as category III. This was further subdivided into class IIIa (inflammatory CPPS) and IIIb (non-inflammatory CPPS). Category IV encompasses asymptomatic inflammatory prostatitis usually discovered on histopathological examination of prostatic tissue.<sup>4,5</sup>

CP/CPPS could not be attributed to a single cause. However, it is mostly of a multifactorial origin. Shoskes et al mentioned that inflammation and increased cytokines release in the prostate secondary to an inflammatory process led to the presenting symptoms in such a condition.<sup>6</sup> Some even reported a cross-relation between disease severity and the microbiome in urine or gastrointestinal tract.<sup>7</sup>

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The recently introduced UPOINT phenotype categorization of CP/CPPS (urinary, psychosocial, organ-specific, infection, neurological/systemic, tenderness of the skeletal muscle) shows up to 60% of men have at least prostate-organ-associated symptoms.<sup>1,3</sup>

Different medications were tried in the management of CP such as antibiotic therapy, anti-inflammatory drugs, alpha-blockers, phytotherapy, or 5 alpha-reductase inhibitors (5ARIs). Others tried non-drug therapy like prostatic massage, lifestyle changes, or supportive therapy.<sup>8–10</sup>

The prostate lies under the hormonal control of dihydrotestosterone; thus, 5ARIs might be beneficial in the treatment of prostatitis.<sup>11</sup> Dutasteride is a 5 $\alpha$ -reductase inhibitor, and hence is a type of anti-androgen. It works by decreasing the production of DHT in certain parts of the body like the prostate gland.<sup>12,13</sup>

5ARIs have been previously evaluated on a narrow scale in the management of prostatitis with the promising results of safety and efficacy.<sup>3,14–16</sup> Due to the paucity of information supporting the monotherapy of 5ARIs in the management of CP/CPPS, especially in those who are not responding to the antibiotic and alpha-blocker therapy, we constructed a placebo-controlled study to evaluate the efficacy of Dutasteride in the management of CP/CPPS.

## 2. Materials and methods

This was a randomized placebo-controlled double-blind study that was conducted in two tertiary Urological centers from January 2020 to May 2021 that included 50 patients aged between 30 and 50 years old, diagnosed with CP based on the presence of pelvic or perineal pain for  $\geq 3$  months of the preceding 6 months with no other identifiable cause detected. Patients included were mostly complaining as well as other storage or voiding urinary symptoms or ejaculatory pain and not responding to the alpha-blocker and antibiotic therapy. Urine culture and the two- or four-glass Meares–Stamey test were used to diagnose CPPS and exclude any bacterial prostatitis in our study patients. Patients with bacterial prostatitis, documented site of infection along the urinary tract, benign prostatic hyperplasia-related symptoms, urinary bladder tumors, prostate cancer, previous history of pelvic radiation, or chemotherapy were excluded from our study.

After the approval of the ethical review committee in our institute, written consent was obtained from every patient. Patients were randomized into 2 equal groups with a 1:1 ratio using a computer-based system. Monotherapy of Dutasteride of 0.5 mg once daily or a similar starch-filled capsule (placebo) was given to every patient for 3 months. Patients, the data collector, and the statistician were all blinded to the type of intervention.

All patients were assessed by proper history taking, symptom scoring by the NIH CP symptom index,<sup>17</sup> clinical examination and investigation using urine analysis and culture, PSA level, pelvic ultrasound, and four-glass Meares–Stamey test. Clinical evaluation and symptom scoring were performed twice for each patient: first before starting treatment and then after 3 months of treatment.

Our primary outcome measure was the improvement in NIH CP symptom index. Patient improvement was graded as no improvement, mild ( $\leq 25\%$ ) improvement, moderate (26–50%) improvement, or marked improvement if  $>76\%$ . Our secondary outcome measures included the side effects related to the medication including loss of libido and erectile dysfunction.

## 3. Ethical consideration

The study gained the approval of the Research ethical committee of the faculty of medicine, Ain Shams University. The trial was registered at [ClinicalTrials.gov](https://www.clinicaltrials.gov) with trial registration number: NCT04756206.

## 4. Statistical analysis

Data were analyzed using the statistical package for social science (IBM SPSS) version 23. Data were expressed as Mean  $\pm$  SD for quantitative parametric measures in addition to both number and percentage for categorized data. Chi-square test ( $\chi^2$ ) was used for comparison and association between two qualitative variables; Fisher exact test was used instead when the expected count in any cell was less than 5. An independent t-test was used with quantitative data and parametric distribution. Paired t-test was used in the comparison between two paired groups with quantitative data and parametric distribution. *P*-value  $< 0.05$  was considered statistically significant and less than 0.01 was considered highly significant.

## 5. Results

Out of 50 patients included in our study, 49 patients were evaluated after the follow-up period as shown in the consort flow chart in [Fig. 1](#). There was no statistically significant difference in the age, duration of symptoms, or the proportion of sexual dysfunctions ([Table 1](#)).

A comparative evaluation based on the NIH CP symptom score was done before and after treatment in both groups as shown in [Table 2](#). There was a statistically highly significant improvement in symptoms following Dutasteride treatment compared to the pre-operative evaluation and the placebo group. In the Dutasteride group, the total NIH score has dropped from  $26.5 \pm 4.4$  to  $15.6 \pm 2.6$  (*P*-value  $< 0.001$ ) with improvement in all parameters including NIH-pain score from  $7.8 \pm 1.1$  to  $4.2 \pm 1.83$ , NIH-urination score from  $9.4 \pm 1.8$  to  $7.1 \pm 1.73$ , and NIH-QoL from  $9.3 \pm 1.5$  to  $4.3 \pm 0.5$ . On the other hand, no statistically significant change in symptoms or NIH CP symptom score following treatment with placebo was noted.

Further analysis of the results revealed that 92% of patients treated with Dutasteride had a noticeable improvement in their symptoms after treatment (56% had moderate to marked improvement), while only 16.7% of placebo-treated patients had mild improvement in their symptoms after treatment ([Table 3](#)).

In our study population, only 3 patients (12%) complained of loss or decrease in libido with dutasteride treatment, while this was not reported in any of the placebo-treated patients. However, no treatment-related erectile dysfunction was observed in this study.

## 6. Discussion

Category III CP/CPPS is characterized by chronic pelvic pain symptoms and voiding symptoms in the absence of UTI. Those patients usually present with pelvic pain or discomfort which may be associated with urinary symptoms and/or sexual dysfunction, lasting for at least 3 of the previous 6 months. This category is further not only divided into IIIA, inflammatory, and IIIB, non-inflammatory. CP/CPPS does not present with physical symptoms but also with a psychological affection that seriously affects the patient's quality of life.<sup>14,18</sup>

There is no clear consensus on the optimal management of chronic nonbacterial prostatitis. Medications, such as antibiotics, phytotherapy, anti-inflammatory agents, alpha-blockers, supportive therapies, including behavioral and psychotherapy, biofeedback, electrical stimulation, acupuncture, and even surgery in severe cases, have been proposed for the treatment of such conditions.<sup>8,9</sup>

Clinical data suggested that 5ARI therapy may be effective as a treatment for some men with CP/CPPS. Evidence from animal studies suggests that hormonal imbalances in the prostate can

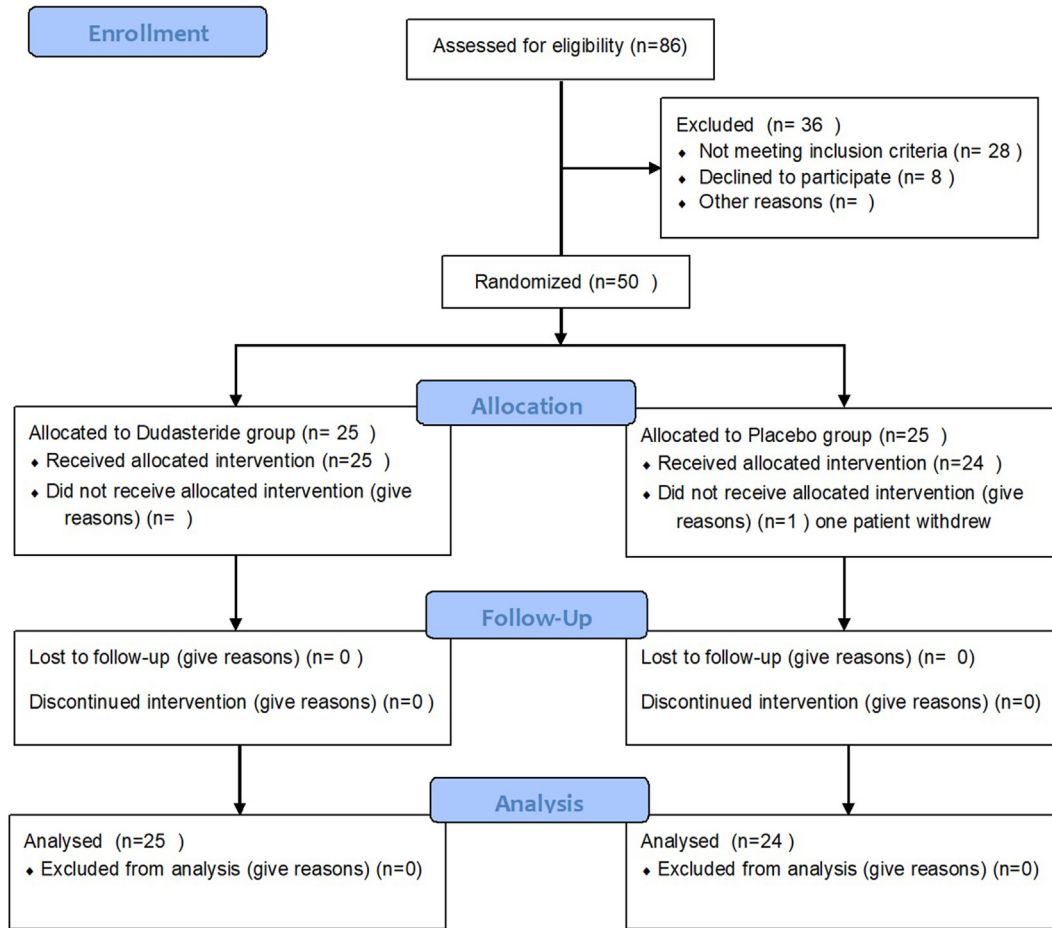


Fig. 1. Consort flow chart.

influence the development, persistence, and severity of nonbacterial prostatitis.<sup>19</sup>

In our study, dutasteride was shown to reduce the symptoms of CP/CPPS. These changes were prominent in reducing the pain, urinary, and QoL scores according to the NIH-CP symptom score with a highly significant statistical difference in comparison to the premedication parameters. This true explanation of this improvement is not clear yet. However, some explanations suggested that 5ARIs may decrease prostatic edema and pressure sensation that may reduce the symptoms of prostatitis. In addition to the effect of 5ARIs in the reduction of the prostatic glandular elements leading to a decrease in the prostatic pressure and inflammation and eventually symptoms reduction.<sup>14</sup>

In the REDUCE trial, the role of 5ARIs in CP/CPPS was suggested. The decrease of dihydrotestosterone may affect the size and the inflammation in the prostate. So these anatomical changes may influence 2 of the theoretical causes of CP/CPPS which are prostatic reflux and dysfunctional voiding.<sup>20,21</sup> This anatomical remodeling

and reduction in the transitional zone size improve the voiding symptoms. On the other hand, the decrease in tissue pressure improves the pain-related symptoms.<sup>3,22</sup>

The rate of improvement in our study was shown in Table 3. In the dutasteride group, mild, moderate, and marked improvements were 36%, 36%, and 20% respectively where only 8% showed no improvement. Nickel et al 2004, evaluated finasteride in CPPS through a multicenter RCT over 64 patients. Mild improvement in the finasteride group was 54%, while moderate and marked improvements were 44% and 27% respectively. They concluded from their study that finasteride could be beneficial for category IIIA CPPS but not as a monotherapy.<sup>19</sup>

The REDUCE trial was designed to evaluate the effect of dutasteride on reducing prostate cancer diagnosis. A correlation between dutasteride usage and prostatitis could be figured out from this study as they included patients with prostatitis and the CPSI score was evaluated at the baseline and all through the study. A significant reduction of 31% in the risk of prostatitis was reported in the study compared to placebo and reducing in the CPSI total and subscores after 48 months of therapy.<sup>3</sup>

Other small studies suggested that 5ARIs could be considered for men with CP/CPPS. Leskinen et al study on 41 patients, reported a clinically significant benefit in favor of finasteride compared to placebo after 12 months of therapy.<sup>14</sup> A randomized comparative trial done by Kaplan et al for one year showed a significant improvement in men with CP/CPPS treated with finasteride compared with those treated with the herbal treatment saw palmetto.<sup>9</sup>

Table 1  
Patients demographic data

	Dutasteride group (n = 25)	Placebo group (n = 24)	P
Age in years Mean ± SD	41.3 ± 6.3	40.5 ± 7.4	0.451
Duration of the complaint in years Mean ± SD	4.3 ± 2.4	3.9 ± 2.1	0.663
Erectile dysfunction	1	2	0.721
Ejaculatory dysfunction	0	0	-

**Table 2**  
(change in NIH chronic prostatitis score in both groups)

NIH-chronic prostatitis symptom score		Before treatment Mean $\pm$ SD	After treatment Mean $\pm$ SD	P
NIH-pain score	Dutasteride	7.8 $\pm$ 1.1	4.2 $\pm$ 1.83	<0.001
	Placebo	6.9 $\pm$ 2.1	6.5 $\pm$ 1.2	0.995
	P-value	0.941	0.002	
NIH-Urination score	Dutasteride	9.4 $\pm$ 1.8	7.1 $\pm$ 1.73	<0.001
	Placebo	9.5 $\pm$ 1.6	9.2 $\pm$ 1.4	0.783
	P-value	0.873	0.04	
NIH-QoL	Dutasteride	9.3 $\pm$ 1.5	4.3 $\pm$ 0.5	<0.001
	Placebo	9.6 $\pm$ 1.7	9.6 $\pm$ 1.8	0.564
	P-value	0.542	<0.001	
Total score	Dutasteride	26.5 $\pm$ 4.4	15.6 $\pm$ 2.6	<0.001
	Placebo	26.8 $\pm$ 5.4	25.4 $\pm$ 0.6	0.881
	P-value	0.922	<0.001	

P-value was evaluated between both groups in each follow-up period in a vertical manner, also P-value was evaluated in the same group after 3 months of therapy.

**Table 3**  
The results of improvement in Dutasteride versus placebo groups in men diagnosed with Category IIIB CP/CPPS.

	Dutasteride group (n = 25)	Placebo group (n = 24)	P
No improvement	2 (8%)	20 (83.3%)	<0.001
Mild improvement (0–25%)	9 (36%)	4 (16.7%)	0.023
Moderate improvement (26–50%)	9 (36%)	0	<0.001
Marked improvement (>51%)	5 (20%)	0	<0.001
Treatment-related side effects	Libido affection	3 (12%)	0
	Erectile dysfunction	0	0

Franco et al conducted a Cochrane systematic review in 2020 regarding the pharmacological therapy for treating CP/CPPS. Based on 2 studies with 177 participants, 5ARIs (finasteride) may reduce prostatitis symptoms compared to placebo without an increase in the side effects.<sup>23</sup>

In the reported previous studies, no serious side effects were reported. In the study by Leskinen et al, only 3 patients in the finasteride group experienced partial impotence.<sup>14</sup> In a study by Nikel et al, 5 patients in the finasteride group showed an adverse effects including a decrease in libido, mood changes, fatigue, and gastrointestinal discomfort compared to 7 patients in the placebo group with side effects including decreased libido, decreased ejaculatory volume, rash, dry mouth, throat constriction, increase in acne and weight gain.<sup>19</sup> In our study, only 3 patients (12%) complained of low libido with dutasteride treatment. No erectile dysfunction was noted in our patients and no observed side effects with placebo treatment.

Our study disclosed a significant value of dutasteride in the treatment of symptoms of CP/CPPS. The main limitations of the study are the small number of patients, the short duration of treatment, and follow-up as it was a big concern of the treatment-related side effects, especially in the ejaculatory function in sexually active men is why we preferred the short course of medication. Thus, we recommend performing further larger studies with longer treatment duration and follow-up to assess the long-term efficacy as well the degree and duration of side effects related to the use of dutasteride in the management of CP/CPPS.

## 7. Conclusion

The results of our study revealed that a short course of dutasteride was effective for symptom improvement in CP/CPPS over a placebo.

## Funding

We received no fund in our study.

## Submission declaration

Our manuscript has not been published previously or under consideration for publication elsewhere, and its publication is approved by all authors in the current form, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder.

## Conflicts of interest

No competing interests to declare.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pnml.2022.06.002>.

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