



Original Article

Therapeutic Potential of Silodosin for Chronic Prostatitis: Efficacy and Safety Insights

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ABSTRACT

Chronic prostatitis is a common urological condition impacting men globally and poses a considerable clinical challenge due to its diverse symptoms and vague causes. The symptoms significantly affect patients' quality of life. **Objective:** To investigate the efficacy and safety of silodosin in men with chronic prostatitis who have not previously been treated with alpha-blockers for this condition. **Methods:** A quasi-experimental study was conducted from July 2022 to June 2023 at Niazi Welfare Foundation Teaching Hospital, Sargodha. Eighty-two patients with chronic prostatitis were treated with 4 mg of silodosin once daily and monitored for 12 weeks. Data collection commenced following IRB approval (NM&DC-IRB-43) and informed consent from all participants. Descriptive statistics were used to calculate the mean and standard deviation. Mean differences in NIH-CPSI score were computed through paired t-test at p -value < 0.05 , using SPSS version 25.0. **Results:** Results show noticeable improvement in CP and NIH-CPSI scores following treatment. The change in symptoms of CP and NIH-CPSI score before and after silodosin indication were statistically significant ($p < 0.05$). Additionally, the treatment was well-tolerated, with minimum adverse events reported. **Conclusions:** Silodosin, a novel selective inhibitor of the α 1A-adrenergic receptor, proved to be effective in treating chronic prostatitis without significant side effects.

INTRODUCTION

Chronic prostatitis (CP) is a prevalent issue of urology that contributes to 9% of the global disease burden [1]. This condition can affect men of all ages and ethnic backgrounds, but it is more prevalent among younger men, with an average onset age of 42 years [2]. Chronic prostatitis is characterized by pain, or discomfort in the pelvic area, accompanied by urinary symptoms and, or sexual dysfunction, persisting for > 3 months out of the past 6 months [3]. Chronic prostatitis consequences on the patient's quality of life (QoL) are significant [4]. It falls under Category IIIA and IIIB: Chronic Prostatitis/Chronic Pelvic

Pain Syndrome (CP/CPPS) of NIH-CPSI (NIH-Chronic Prostatitis Symptom Index) by the National Institutes of Health (NIH) [5]. CP/CPPS impacts 2-16% of adult men, making it one of the most prevalent urological conditions with an incidence of 5% in Pakistan [6]. The symptoms of CP/CPPS profoundly impact patients' quality of life (QoL), manifesting as pelvic pain, discomfort, lower urinary tract symptoms (LUTS), and sexual dysfunction. Lower urinary tract symptoms such as hesitancy, reduced flow, and frequent urination frequently accompany CP/CPPS. Approximately 10% of CP/CPPS cases may exhibit

urodynamic evidence of obstructive symptoms [7]. CP/CPPS could result from recurrent infections, inflammation of the prostate or surrounding nerves, or muscle spasms in the pelvic region [8]. The underlying mechanisms of CP/CPPS (NIH Category III) remain unclear. It is believed to involve abnormal immune responses triggered by previous bacterial infection, neural inflammation, and neurogenic damage following an adverse event [9]. Multiple theories suggest that numerous etiologies are accountable for chronic prostatitis and, therefore need a comprehensive approach to deal with the associated symptom complex because few therapies demonstrate significant efficacy in alleviating CP/CPPS-specific symptoms [10]. Management of CP/CPPS requires symptom-based intervention to deal with this debilitating illness [11]. Diagnosing CP/CPPS requires four key elements: a) symptoms that appear in the perineal and, or lower abdomen b) evidence of prostate infection and, or inflammation through lab results c) pain and discomfort associated with the prostate and lower UTI, and d) symptoms arising after a trigger with varying incubation periods. Each individual presents with a primary complaint and a combination of other symptoms, which typically fluctuate but persist for at least 3 months [12]. Despite its prevalence and clinical impact, effective treatment options remain limited, often necessitating a multimodal approach [12]. Medicinal treatment focuses on alleviating discomfort, pain, and urinary problems to enhance QOL [13]. The main medications prescribed include α -blockers, non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, and 5- α reductase inhibitors. But, prolonged use of these drugs can lead to adverse events like low blood pressure and gastrointestinal issues [14]. Additionally, because of the absence of optimal treatment approaches, medical treatment costs are high [15]. Studies have demonstrated that α -blockers can successfully combat the symptoms in patients, particularly in reducing suffering and enhancing QOL, with strong anti-inflammatory and analgesic effects [16]. Silodosin selectively blocks α 1A-adrenergic receptors in the lower urinary tract and central nervous system. This action reduces peripheral and central neuropathy, improves voiding function, and alleviates pain associated with CP/CPPS [17]. Understanding the precise mechanisms through which Silodosin exerts these effects will be crucial for optimizing its use in clinical practice [14]. Recently, there has been considerable advancement in the research of using α -blockers to treat chronic prostatitis. This study aimed to evaluate the efficacy and safety of Silodosin (4mg) for men with chronic prostatitis.

METHODS

A quasi-experimental study was performed from July 2022 to June 2023 at Niazi Welfare Foundation Teaching

Hospital, Sargodha with the following ethical clearance of research from IRB & Ethics Committee (NM&DC-IRB-43). Z2pq/d2 formula was employed to calculate sample size in open Epi software with a prevalence rate of 5% [6], and a margin of error = 0.05 at a confidence interval of 95%. The calculated size was 73. Considering a dropout rate of 10%, the adjusted sample size was 82 patients. A non-probability convenient sampling method was employed. The inclusion criteria for this study involved: (1) NIH-CPSI Category IIIA and IIIB CP/CPPS patients who have not previously received any treatment; (2) Patients aged 18 to 55 years; (3) Patients experienced chronic recurrent pelvic pain and discomfort with pain score of ≥ 4 points, from >3 month on NIH pain scale and had associated urinary symptoms and sexual problems. Exclusion criteria included patients with: (1) acute prostatitis; (2) those with other reproductive tract infectious diseases or serious liver and kidney diseases; (3) those who had used antibiotics or α -receptor blockers in the previous 2 weeks; (4) those with paratyphoid fever, seminal vesiculitis, varicocele, or tumors affecting the bladder, urethra, or prostate; (5) those who had undergone any prostate surgery; (6) those with cardiovascular, cerebrovascular or hematopoietic diseases. Written informed consents were obtained from all the study participants. Outcome variable of the study "efficacy" was the change in NIH-CPSI score on NIH-CPSI questionnaire [18] from baseline to week 12. The NIH-CPSI comprises 9 questions with a total possible score ranging from 0 to 43. It assesses three primary domains of the prostatitis experience: pain (ranging from 0 to 21), voiding disturbances (ranging from 0 to 10), and quality of life/impact (ranging from 0 to 12). Safety parameters were recorded on a specific predesigned performa that included blood pressure monitoring with mercury sphygmomanometer to detect hypotension, gastrointestinal evaluations to identify any discomfort or other gastrointestinal issues, general physical examinations to detect adverse reactions, and laboratory tests, including liver and kidney function tests, to monitor for any potential systemic effects at each follow-up visit. Blood samples were collected to estimate LFTs and RFTs. Demographic variables of participants (age and disease duration) were noted. The initial assessment involved completion of NIH-CPSI questionnaire and evaluation of safety parameters on specific performa. Patients were explained to take Silodosin at a dosage of 4 mg once daily with food at breakfast for a duration of 12 weeks. The medication was administered orally. Patients were advised for regular follow-ups at baseline week 0, week 4, week 8, and week 12. At week 4, first follow-up is done to monitor the initial response to treatment, any side effects, and treatment adjustment if required. At week 8, patients were assessed for ongoing efficacy, monitored for side effects, and ensured treatment adherence. Finally, 12th week follow-up was done to evaluate overall efficacy and safety

of the study's intervention. If patients experienced side effects or complications, they were provided with appropriate medical intervention. Mild to moderate side effects were managed with supportive care, while severe side effects necessitated discontinuation of the study medication and provision of alternative treatments. Treatment failure was lack of significant improvement in NIH-CPSI scores (less than a 30% reduction from baseline) by week 12, or the occurrence of severe side effects leading to discontinuation of the medication. The drop-out rate and reasons for drop-out were recorded. Any patient who missed two consecutive follow-up visits was considered lost to follow-up. Data were processed using SPSS 25.0 software. Categorical data was presented as frequency and percentage while continuous data were reported as mean and standard deviation (SD). Paired t-test was used to compare intra-group differences at significance level, $p < 0.05$.

RESULTS

The demographic information included 75 patients with ages ranging from 18 to 55 years, having an average age of (41.57 ± 6.54) years. The average disease duration was (2.34 ± 1.03) years. Following treatment, there was a significant reduction in pain and, discomfort scores, urinary symptom scores, and QOL scores among patients with chronic prostatitis (Table 1).

Table 1: Comparison of NIH-CPSI Score

NIH-CPSI Score	Before Treatment Mean \pm SD	After Treatment Mean \pm SD	p-value
Pain and Discomfort Domain	11.63 \pm 2.13	5.63 \pm 1.23	$p < 0.001$
Urinary Symptom Domain	8.04 \pm 0.45	4.36 \pm 1.23	$p < 0.0001$
Quality of Life Domain	9.65 \pm 3.65	5.27 \pm 1.27	$p < 0.001$
Total Score	29.32 \pm 2.20	15.26 \pm 1.80	$P < 0.001$

Regarding safety parameters, insignificant changes at baseline and week 12 ($p > 0.05$). Gastrointestinal evaluation revealed incidence of nausea and vomiting in 1 (1.2 %) participants. Incidence of headache and dizziness was found in 2 (2.4%), while skin itching in 1 (1.2 %). Lab values (LFT and RFT) show non-significant changes after 12 weeks of therapy ($p > 0.05$). No serious adverse effects or complications were noted during the 12-week period that required discontinuation of therapy (Table 2).

Table 2: Evaluation of Safety Parameter

Safety Parameter	Baseline Mean \pm SD	Week 12 Mean \pm SD	p-value
Blood Pressure (mm Hg)			
Systolic	120.4 \pm 7.2	120.8 \pm 6.9	0.432
Diastolic	80.6 \pm 5.5	80.3 \pm 5.2	0.508
Gastrointestinal Evaluations			
Nausea and Vomiting Incidence n (%)	0	1 (1.2%)	-
General Physical Examinations			
Headache and Dizziness Incidence n (%)	0	2 (2.4%)	-

Skin Itching Incidence n (%)	0	1 (1.2%)	-
Laboratory Tests			
Liver Function Tests (LFT)			
ALT (U/L)	25.3 \pm 7.5	25.6 \pm 7.2	0.687
AST (U/L)	22.8 \pm 6.4	23.1 \pm 6.1	0.582
Alkaline Phosphatase (ALP, U/L)	70 \pm 15	72 \pm 14	0.399
Gamma-Glutamyl Transferase (GGT, U/L)	25 \pm 8	26 \pm 7.7	0.416
Serum Bilirubin (mg/dL)	0.8 \pm 0.2	0.8 \pm 0.18	0.52
Prothrombin Time (PT, seconds)	12.5 \pm 1	12.6 \pm 0.9	0.520
International Normalized Ratio (INR)	1.0 \pm 0.1	0.98 \pm 0.08	0.178
Total Protein (g/dL)	7.0 \pm 0.5	6.9 \pm 0.6	0.269
Albumin (g/dL)	4.0 \pm 0.31	4.1 \pm 0.37	0.074
Kidney Function Tests (RFT)			
Creatinine (mg/dL)	0.88 \pm 0.16	0.89 \pm 0.15	0.735
BUN (mg/dL)	14.5 \pm 3.2	14.6 \pm 3.1	0.829
Glomerular Filtration Rate (GFR, mL/min/1.73 m ²)	90 \pm 10	91 \pm 10.1	0.543

In this study, there were 7 dropouts resulting in a dropout rate of 8.54%. The main reason for dropout was missing two consecutive visits. All the statistics were calculated after excluding dropouts.

DISCUSSION

This study aimed to evaluate the efficacy and safety of Silodosin (4 mg) in treating chronic prostatitis. Results showed a significant efficacy, indicating that the majority of patients experienced notable improvement in NIH-CPSI scores following the treatment. Silodosin proved a helpful regime in treating pain and discomfort caused due to CP. Results suggest significant differences in pain and discomfort scores ($p < 0.001$) that contribute to therapy. Along with pain score improvement, patients also experienced differences in urinary symptoms ($p < 0.0001$) and QOL score ($p < 0.001$). Significant differences gave fruitful information regarding the benefits of silodosin therapy. Silodosin accounts for the betterment of NIH-CPSI scores from baseline to week 12 periods, which is remarkable. These results are comparable with a study depicting the notion that silodosin provides a promising effect in combating CP-associated symptoms; its role in symptom score reduction is noteworthy. The therapeutic effects of silodosin on QOL offer evidence that it's a useful approach in clinical practice [19]. The finding of a study by Creta *et al.*, confirms the importance of silodosin in the treatment of CP/CPSPs particularly in alleviating the associated symptoms and improving patient well-being [20]. The significant effect of silodosin in NIH-CPSI improvement is consistent with studies evaluating α 1-adrenergic receptor antagonists' role in symptom alleviation in chronic prostatitis [21]. Moreover, the incidence of side effects with the use of 4 mg silodosin was 4.8% in our study viz. headache 2.4%, nausea and vomiting 1.2%, and skin itching 2.4% which were negotiable.

Minimum side effects provide key evidence regarding safety parameters linked with the clinical use of silodosin for achieving therapeutic outcomes. The efficacy and safety of silodosin revealed that treatment with α -blockers offers a safe option in clinical practice [21]. Similarly, studies showed that only a few side effects were reported with Alpha1-blockers. Alpha1 blockers offer a safe option for CP/CPSP patients with negligible side effects. Silodosin, a new selective α 1A-adrenergic receptor inhibitor, has demonstrated effectiveness in improving symptom scores and is free from significant side effects [22]. Our study provides valuable data on the therapeutic outcomes of silodosin in clinical areas. The limitations of the study were the small sample size and the short follow-up duration of only 12 weeks. These limitations emphasize the further need for experimental studies with a control group to elaborate on the extensive role of silodosin for therapeutic outcomes.

CONCLUSIONS

Silodosin (4mg), a selective inhibitor of the α 1A-adrenergic receptor, proved to be an effective approach that helps in improved symptom scores and is free of significant side effects. Silodosin could serve as a preferred choice in clinical practice for patients with CP/CPSP.

Authors Contribution

Conceptualization: ABN

Methodology: ABN, IA, SA

Formal analysis: MA, WA, SG

Writing-review and editing: SA, SG

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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