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Efficacy of Urovaxom for Improving Chronic Pelvic Pain Syndrome Symptoms in Prostate Cancer Patients Who Underwent Radical Prostatectomy: A Multicenter, Prospective Cohort Study

Jun-Koo Kang[1], Yun-Sok Ha[1], Sungchan Park[2], Tae Gyun Kwon[1], Tae-Hwan Kim[1]

[1]Department of Urology, Kyungpook National University Hospital, School of Medicine, Kyungpook National University, Daegu, Korea
[2]Department of Urology, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Korea

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Corresponding author:
Tae-Hwan Kim
Department of Urology, Kyungpook National University Hospital, School of Medicine, Kyungpook National University, 807 Hoguk-ro, Buk-gu, Daegu 41404, Korea
Email: doctork@knu.ac.kr
https://orcid.org/0000-0003-4924-4826

Purpose: Chronic pelvic pain syndrome (CPPS) is a multifactorial condition that can significantly diminish quality of life. Although some patients have reported persistent pelvic pain after radical prostatectomy (RP), the prevalence and direct causal relationship between CPPS and RP remain unclear. This multicenter prospective study aimed to evaluate the efficacy of Urovaxom for improving CPPS symptoms.

Materials and Methods: A total of 52 prostate cancer patients who underwent RP were enrolled and administered Urovaxom (60 mg/day) for 12 weeks. Changes in National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), overactive bladder symptom score (OABSS), International Prostate Symptom Score (IPSS), and inflammation markers (white blood cell [WBC], C-reactive protein [CRP]) were analyzed using the Wilcoxon signed-rank test.

Results: After 12 weeks of treatment, the NIH-CPSI total score significantly decreased from 19 (interquartile range [IQR], 16–23) to 12.5 (IQR, 8.0–16.8) ($p<0.001$). The OABSS total score decreased from 8 (IQR, 4–11) to 5 (IQR, 3.0–7.8), and the IPSS total score decreased from 13.5 (IQR, 10.0–22.8) to 10.5 (IQR, 5.0–17.0) ($p<0.001$). WBC levels showed a slight increase ($p=0.028$), but the clinical relevance of this change is uncertain and warrants further investigation. CRP changes were not statistically significant ($p=0.274$).

Conclusions: Urovaxom demonstrated significant efficacy in improving CPPS symptoms, particularly pain and reduced quality of life, in patients following RP. These findings suggest Urovaxom as a potential therapeutic option for CPPS after management using RP.

Keywords: Chronic pelvic pain syndrome, Urovaxom, Prostatectomy, Quality of life, National Institutes of Health Chronic Prostatitis Symptom Index

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• **Research Ethics:** Approval for the study was obtained from the Institutional Review Boards (IRBs) of all participating centers. The present trial was approved by the Institutional Review Board of Kyungpook National University Chilgok Hospital, Daegu, Republic of Korea (IRB No. KNUCH2022-04-019). The study was carried out in accordance with the guidelines of the Declaration of Helsinki. All patients provided written informed consent after a thorough explanation of the treatment.
• **Conflict of Interest:** The authors have nothing to disclose.

HIGHLIGHTS

In a prospective study of 52 patients with chronic pelvic pain syndrome symptoms after radical prostatectomy (RP), 12 weeks of Urovaxom treatment significantly improved National Institutes of Health Chronic Prostatitis Symptom Index, overactive bladder symptom score, and International Prostate Symptom Score. This study suggests Urovaxom as a potential therapeutic option for post-RP chronic pelvic pain syndrome.

INTRODUCTION

Chronic pelvic pain syndrome (CPPS) is one of the most common conditions associated with the prostate, with a lifetime prevalence of 2.0%–26.6% worldwide [1]. Despite its prevalence, the exact etiology remains unclear, and effective treatments are limited. CPPS is characterized by persistent perineal and lower abdominal pain, which can significantly affect patients' quality of life (QoL) [2,3]. Radical prostatectomy (RP), a standard treatment for localized prostate cancer, has been proven to improve survival rates. However, postsurgical complications, such as incontinence, sexual dysfunction, and chronic pelvic pain (CPP), frequently diminish patients' overall QoL [4-6]. While considerable efforts have been made to address incontinence and sexual dysfunction, CPPS symptoms following RP have remained underexplored, highlighting the need for targeted therapeutic approaches.

Urovaxom, a lyophilized bacterial lysate derived from *Escherichia coli*, has been widely used to prevent recurrent urinary tract infections and chronic prostatitis. Previous studies have suggested its potential role in reducing inflammation and alleviating symptoms associated with CPP [7,8]. Despite multiple studies focusing on urinary and sexual dysfunction, targeted therapeutic approaches for CPPS remain limited. This study aims to evaluate the efficacy of Urovaxom in improving CPPS symptoms in prostate cancer patients who have undergone RP. By assessing changes in National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) scores, as well as secondary outcomes such as urinary symptoms and QoL, this research seeks to establish Urovaxom as a potential therapeutic option and contribute to the development of evidence-based guidelines for managing CPPS.

MATERIALS AND METHODS

1. Study Design, Setting, and Study Population

This multicenter, prospective study was conducted at three medical institutions, including Chilgok Kyungpook National University Hospital, from April 2022 to May 2024. Patients were eligible if they had undergone RP for localized prostate cancer and were presented with CPPS symptoms. Inclusion criteria were as follows: NIH-CPSI total score ≥15, indicating moderate to severe CPPS, ability to complete study questionnaires and comply with study requirements and provision of written informed consent. Exclusion criteria included: Biochemical recurrence of prostate cancer requiring additional treatments (radiation or hormone therapy), structural abnormalities, such as bladder stones or urethral stricture, identified on imaging studies and severe comorbidities that could confound the results. Our study included patients who were already on standard treatments, such as alpha-blockers or other medications, before enrollment. Despite receiving these treatments, all enrolled patients had NIH-CPSI scores of 15 or higher, indicating persistent symptoms. When these patients were enrolled in the study, they continued their existing medications while additionally receiving Urovaxom as an adjunct therapy. This study was designed to assess whether Urovaxom could provide additional symptom relief beyond standard treatments.

2. Sample Size Calculation

Based on a prior study, a sample size of 64 patients was calculated to detect a statistically significant reduction in NIH-CPSI scores with a power of 80% and a significance level of 5%. Allowing for a 25% dropout rate, 52 patients were completely included in the analysis.

3. Treatment

Patients received Urovaxom (Aju Pharm Co., Ltd., Pyeongtaek, Korea), administered orally at a dose of 60 mg once daily for 12 weeks. The study did not involve concomitant changes to patients' ongoing treatments unless deemed medically necessary.

4. Assessment of Outcomes

Primary outcomes included changes in total NIH-CPSI

scores from baseline to 12 weeks. Secondary outcomes were changes in individual NIH-CPSI domains (pain, urination, and QoL), changes in overactive bladder symptom score (OABSS) and International Prostate Symptom Score (IPSS). Laboratory measures of inflammation, including white blood cell (WBC) counts and C-reactive protein (CRP) levels.

5. Data Collection

Data were collected at baseline and after 12 weeks of treatment. Patients completed standardized questionnaires (NIH-CPSI, OABSS, and IPSS) at both visits. Laboratory evaluations included complete blood count and CRP levels.

6. Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics ver. 26.0 (IBM Co., Armonk, NY, USA). Changes in scores and laboratory parameters were assessed using the Wilcoxon signed-rank test for paired data. A p-value of <0.05 was considered statistically significant.

Table 1. Patients' baseline characteristics (n=52)

Variable	Value
Age (yr)	67.5±5.4
Initial PSA	19.9±38.7
Prostate volume (mL)	28.9±10.7
Operation method	
RARP	50 (96.2)
RRP	2 (3.8)
Foley keep duration (day)	5.7±1.1
Postoperative cystograms	
Leakage (+)	0 (0)
Leakage (-)	52 (100)
Total GS	
GS 6	5 (9.6)
GS 7	36 (69.2)
GS 8	8 (15.4)
GS 9	3 (5.8)
T stage	
T1	23 (44.2)
T2	24 (46.2)
T3	5 (9.6)

Values are presented as mean±standard deviation or number (%).
PSA, prostate-specific antigen; RARP, robot-assisted radical prostatectomy; RRP, retropubic radical prostatectomy; GS, Gleason score.

RESULTS

A total of 52 patients were included in the analysis, with a mean age of 67.5±5.4 years. The majority (96.2%) underwent robotic-assisted RP, while 3.8% underwent open RP. The mean prostate volume was 28.9±10.7 mL, and the median initial prostate-specific antigen level was 19.9 ng/mL. None of the patients exhibited postoperative leakage on cystogram, and the mean Foley catheter duration was 5.7±1.1 days. Detailed baseline characteristics are summarized in Table 1.

1. Primary Outcomes

Significant improvements were observed in the total NIH-CPSI scores after 12 weeks of Urovaxom treatment (median, 19–12.5; p<0.001). Subdomain analysis revealed significant reductions in pain (6–1, p<0.001), urination symptoms (6–4, p<0.001), and QoL scores (4.0–3.5, p<0.001) (Table 2).

2. Secondary Outcomes

OABSS total scores decreased significantly from a median of 8 to 5 (p<0.001). Individual subdomains, including urinary frequency, urgency, and nocturia, showed consistent improvements (p<0.05) (Table 3).

IPSS total scores improved significantly (median, 13.5–10.5; p=0.001), with reductions observed in both voiding (p=0.008) and storage symptoms (p=0.001) (Table 4).

Inflammatory markers: A slight but statistically significant increase in WBC count was observed (mean: 2.26±0.31 to 2.32±0.32; p=0.028), while CRP levels remained unchanged (0.16±0.02 to 0.09±0.01; p=0.274) (Table 5).

DISCUSSION

CPPS is a prevalent and complex urological condition characterized by persistent pelvic pain lasting at least

Table 2. Difference in NIH-CPSI score after 12 weeks of treatment compared to baseline

Variable	Pretreatment	Posttreatment	p-value†
Pain or discomfort			
Q1	1 (0–2)	0 (0–1)	0.003
Q2	0 (0–1)	0 (0–1)	0.66
Q3	2 (0–2)	0 (0–1)	0.001
Q4	3 (1–5)	0.5 (0–3.0)	0.001
Total	6 (3–9)	1.0 (0–5.8)	<0.001
Urination			
Q5	3 (1–4)	2 (1–2)	<0.001
Q6	3 (2–4)	2 (1–3)	<0.001
Total	6 (4–7)	4 (2–5)	<0.001
Impact of symptoms			
Q7	2 (1–3)	1.0 (0.3–2.0)	<0.001
Q8	2 (2–3)	1 (1–2)	<0.001
Total	4 (3–5)	2 (1–4)	<0.001
Quality of life			
Q9	4 (4–5)	3.5 (2.0–4.0)	<0.001
Total score	19 (16–23)	12.5 (8.0–16.8)	<0.001

Values are presented median (interquartile range).
NIH-CPSI, National Institutes of Health Chronic Prostatitis Symptom Index.
†Wilcoxon signed-rank test.

Table 3. Difference in OABSS score after 12 weeks of treatment compared to baseline

OABSS	Pretreatment	Posttreatment	p-value†
Q1	1.0 (0.3–1.0)	1 (0–1)	0.049
Q2	2 (2–3)	2 (1–3)	0.006
Q3	2 (1–4)	1.0 (0–2.8)	<0.001
Q4	2 (1–4)	1.0 (0–2.8)	0.001
Total	8 (4–11)	5.0 (3.0–7.8)	<0.001

Values are presented median (interquartile range).
OABSS, overactive bladder symptom score.
†Wilcoxon signed-rank test.

three months, often accompanied by lower urinary tract symptoms (LUTS), sexual dysfunction, and psychological distress. The pathophysiology of CPPS is multifactorial, involving chronic inflammation, neuropathic pain, pelvic floor muscle dysfunction, and psychosocial factors [3]. Due to its heterogeneous nature and unclear etiology, managing CPPS remains challenging, necessitating a multimodal treatment approach [9].

CPP following RP is a significant but often underrecognized complication. Previous study reported that

Table 4. Difference in IPSS score after 12 weeks of treatment compared to baseline

IPSS	Pretreatment	Posttreatment	p-value†
Voiding score	7 (3–10)	4.3 (1.3–9.0)	0.008
Q1	2.5 (1.0–4.0)	1 (1–3)	0.007
Q3	1 (0–3)	1 (0–2)	0.15
Q5	2 (0–4)	2 (0–3)	0.16
Q6	1.0 (0– 2.8)	0 (0–1)	0.01
Storage score	8.0 (5.0–10.8)	5.5 (3.3–8.0)	0.001
Q2	3 (2–5)	2 (1–3)	0.001
Q4	2 (1–3)	1 (0–3)	0.014
Q7	3 (1–3)	2 (1–3)	0.01
IPSS total score	13.5 (10.0–22.8)	10.5 (5.0–17.0)	0.001
QoL score	4.0 (2.3– 5.0)	3.5 (2.0–4.0)	0.04

Values are presented median (interquartile range).
IPSS, international prostate symptom score; QoL, quality of life.
†Wilcoxon signed-rank test.

Table 5. Difference in WBC and CRP after 12 weeks of treatment compared to baseline

Variable	Pretreatment	Posttreatment	p-value†
WBC ($10^3/\mu L$)	2.26±0.31	2.32±0.32	0.028
CRP (mg/dL)	0.16±0.02	0.09±0.01	0.274

Values are presented as mean±standard deviation.
WBC, white blood cell; CRP, C-reactive protein.
†Student t-test.

57% of patients experienced pelvic pain at 1 month postoperatively, 33% at 3 months, and 21% continued to have symptoms at 6 months [10]. Post-RP CPPS symptoms can be influenced by multiple physiological and structural factors. While psychological factors such as anxiety and depression may further exacerbate symptom perception and chronicity [11].

Current therapeutic strategies include pharmacological treatments such as alpha-blockers, anti-inflammatory drugs, antibiotics, neuromodulators, and antidepressants, along with nonpharmacological interventions like pelvic floor physical therapy, cognitive-behavioral therapy, acupuncture, and mindfulness-based stress reduction [12]. Previous studies on CPPS and Urovaxom have reported mixed findings regarding its therapeutic efficacy. Wagenlehner et al. [13] conducted a placebo-controlled trial evaluating OM-89 (Urovaxom) in CP/CPPS patients and found a reduction in NIH-CPSI scores. However, both

the Urovaxom and placebo groups demonstrated similar improvements, suggesting a strong placebo effect in CPPS management. In contrast, Lee et al. [8] reported that Urovaxom significantly reduced the recurrence rate of CPPS when administered for 12 weeks following initial treatment .

Our study demonstrates that Urovaxom significantly alleviates symptoms of CPPS following RP. Our findings indicate a substantial reduction in NIH-CPSI scores, particularly in the pain and QoL domains, supporting its potential as a therapeutic option for post-RP CPPS management. Furthermore, improvements in urinary symptoms, as evidenced by reductions in OABSS and IPSS scores, suggest that immune modulation may play a role in both pain relief and bladder function recovery.

Although Urovaxom is primarily recognized as an immune-modulating agent, it may influence CPPS symptoms through its effects on immune regulation. Chronic inflammation and immune dysregulation have been implicated in CPPS pathophysiology with elevated pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-α contributing to neurogenic inflammation and bladder hypersensitivity [14,15]. Previous studies suggest that immune-based interventions can influence sensory pathways and bladder function, potentially reducing LUTS symptoms [16,17]. By modulating immune responses, Urovaxom may reduce neuro-inflammation and alleviate LUTS symptoms.

Despite these promising findings, several limitations must be acknowledged. First, the lack of a placebo-controlled group prevents definitive attribution of symptom improvement solely to Urovaxom. Given the high placebo response rate in CPPS, a randomized placebo-controlled trial is necessary to validate our results. Second, the study's follow-up period was limited to 12 weeks, preventing assessment of long-term efficacy and sustainability of symptom relief. Whether the beneficial effects of Urovaxom persist beyond the treatment period or require maintenance therapy remains unknown. Third, psychological factors such as anxiety and stress are known to influence CPPS symptoms. Future studies should consider a multidisciplinary approach, incorporating psychological interventions alongside immunomodulatory therapy, to optimize treatment outcomes.

Future research should focus on conducting large-scale, placebo-controlled trials to provide more definitive evidence of Urovaxom's efficacy in post-RP CPPS management. Further mechanistic studies are needed to elucidate how Urovaxom interacts with immune and neural pathways involved in CPPS pathophysiology. Additionally, evaluating its potential to mitigate other postoperative complications associated with RP, such as persistent pain syndromes and lower urinary tract dysfunction, may broaden its clinical applicability. Given the increasing recognition of CPPS as a systemic condition rather than a localized disorder, future studies should adopt comprehensive, multidisciplinary study designs to optimize therapeutic outcomes.

CONCLUSIONS

This study highlights the significant benefits of Urovaxom in managing CPPS symptoms and improving the QoL in postoperative prostatectomy patients. These findings suggest that Urovaxom may serve as a novel therapeutic option for post-RP CPPS, potentially improving patient QoL and filling an unmet clinical need. While further studies are necessary, these findings provide a foundation for incorporating Urovaxom into evidence-based guidelines for CPPS after RP management.

NOTES

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• **ORCID**
Jun-Koo Kang: 0000-0002-8857-3406
Yun-Sok Ha: 0000-0003-3732-9814

Sungchan Park: 0000-0002-2337-983X
Tae Gyun Kwon: 0000-0002-4390-0952
Tae-Hwan Kim: 0000-0003-4924-4826

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