

# Effect of Mirabegron to Reduce Lower Urinary Tract Symptoms in Prostatitis

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## ABSTRACT

**Aim:** To investigate effectiveness and safety of mirabegron in a patient's symptoms associated with prostatitis in routine practice.

**Study Design:** Prospective, pilot study

**Place and Duration of Study:** Department of Urology, Liaquat University Hospital Jamshoro between 1<sup>st</sup> October 2020 and 30<sup>th</sup> November 2021

**Methodology:** Fifteen male subjects in two groups (control and treatment group with Mirabegron), 18 to 50 years old, with acute and chronic prostatitis according to the operational definition were recruited. The overactive bladder started with mirabegron at daily doses of 25mg, 50mg, and 100 mg respectively.

**Results:** The mean ages were 47.7±2.1 years and 33.8±7.0 years respectively in the control and mirabegron groups. The significant efficacy in treating OAB symptoms such as frequent urination, urge incontinence, and urgency. For mirabegron 50 and 100 mg, the mean volume of urine passed per micturition was observed as early as the first assessment after 4-week's duration and remained stable throughout treatment for up to 12 months. In terms of dry rates, our analyses revealed a considerable improvement with mirabegron 50mg and 100 mg. Patients considered their treatment with mirabegron to be worthwhile, according to an analysis of patient's satisfaction treatment criteria. Mirabegron observed to be safe in OAB clinical trials with prostatitis that lasted up to 12 months.

**Conclusion:** When contrasted with existing antimuscarinics that restricted due to associated adverse effects and insufficient effectiveness, mirabegron found improved compliance with balance between effectiveness and safety in Pakistani patients with associated symptoms in prostatitis.

**Key words:** Prostatitis, Mirabegron, Effectiveness

## INTRODUCTION

Globally, prostatitis contributed to the third most common urogenital disease among males which seriously affects the patient's quality of life<sup>1-3</sup>. The disease especially affects young and middle-aged males, with common clinical presentations including Frequency, burning/painful micturition or discharge, rectal and lower back pain, fever with chills, loss of libido, and erectile dysfunction<sup>4,5</sup>. Chronic prostatitis/chronic pelvic pain syndrome accounts for up to 90-95% of all prostatitis cases.<sup>6,7</sup> For the management of prostatitis, the conventional treatment approach includes antibiotics, antioxidants, and surgery. However, conventional management is less effective and with the complaint of reoccurrence. Biofeedback, hyperthermia, and magnetic therapy were recently used as physical therapies, but the effectiveness and associated adverse effects are controversial<sup>8-11</sup>.

Presently, the management of prostatitis is still complex and the diagnostic methods are still lacking. The challenges to managing prostatitis are owed to the complexity of the pathogenesis of the prostate disorders. Psychological variables, pathogen infection, sex hormone imbalance, symptoms of the lower urinary tract, inflammation, and aberrant immune response all have an impact on the pathogenesis, with the inflammatory microenvironment reaction being the primary pathogenic mechanism of prostatitis.<sup>12-14</sup> In the recent era, numerous investigations into the pathogenesis and aetiology of prostatitis have been conducted, and new therapeutic approaches have been identified to increase its effectiveness. The pathology behind the ineffectiveness of traditional pharmacological treatments is because of challenging to access the prostatitis due to its deep placement in the pelvic cavity, the prostate has a unique milieu that is categorized by inflammatory hyperplasia, a increased pH, bacterial build-up, and a disruption of the blood-prostate barrier<sup>16,17</sup>.

Clinically, obstructive and irritable voiding symptoms are frequently combined with prostatitis associated with discomfort. Inhibitors of 5-alpha reductase and alpha-1 adrenoceptor antagonists are frequently used salts to treat the blockage of the bladder outflow brought on by prostatitis and prostatic hypertrophy. Unfortunately, the anticholinergic medications demonstrate bothersome diarrhoea, dry mouth, and impaired vision are some of

the negative effects<sup>18-19</sup>. The treatment of lower urinary tract symptoms in patients with BOO associated with prostatitis using the new family of pharmaceutical salt mirabegron, a 3-adrenoceptor agonist, has been studied recently. It has a reduced risk of urine retention and other adverse effects. In addition, mirabegron considerably reduces the frequency of adverse effects such impaired vision, dry mouth, and constipation when compared to conventional anticholinergic medications<sup>20-23</sup>.

In a patient with OAB and additional lower urinary tract storage symptoms related to prostatitis, the effectiveness and safety of mirabegron were evaluated in routine clinical practise.

To investigate the effectiveness and safety of mirabegron in a patient's symptoms associated with prostatitis in routine practice.

## MATERIALS AND METHODS

This prospective, pilot study was conducted at the Urology Department of Liaquat University Hospital Jamshoro between 1<sup>st</sup> October 2020 and 30<sup>th</sup> November 2021. A total of 15 male subjects, two groups (control and treatment group with Mirabegron), 18 to 50 years old, with acute and chronic prostatitis according to the operational definition were recruited. The overactive bladder started with mirabegron at daily doses of 25mg, 50mg, and 100 mg respectively. Patients with significant bladder diverticulum or urethral stricture, a history of urine retention, clean intermittent catheterization, a previous diagnosis of neurogenic bladder, or other disorders were excluded from the study. The data was collected on the design Case Report Form (CRF) as per the criteria and symptoms of prostatitis. The lower urinary tract symptoms were recorded in the designed questionnaire form for analysis. The mean number of micturition episodes per 24 hours was modified from baseline to the conclusion of therapy as the primary outcome. Secondary outcomes included changes in the average amount of urine passed per micturition, the average number of episodes of urgency, nocturia, and urinary incontinence per day, and quality of life indicators. Before the trial started, all baseline laboratory analyses were completed. The fourteen patients on mirabegron were examined alone and with other medications for a period of 1 month to 12 months. The overall OABSS, Qmax, and PVR were recorded. The data was entered and analyzed through SPSS-25. This study was approved by LUMHS Ethical Review Board.

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## RESULTS

The ages of the participants were  $47.7 \pm 2.1$  and  $33.8 \pm 7.0$  years respectively in control and mirabegron groups. The two groups' average prostate volumes were 29.514.0 mL and 37.38.7 mL, respectively. The baseline characteristics were not significantly different. The total international Prostate Symptom Score in control group was reduced from 15.5 to 13.3 ( $p=0.289$ ) and from 19.7 to 15.5 ( $p=0.025$ ) in the treatment group after the eight-week of therapy with mirabegron. In the median international Prostate Symptom Score storage, 69 (19.4 percent) of the 286 participants were female. Age was 56.2911.04 on average. The mean quality of life sub-score fell from 3.6 to 3.2 ( $p=0.053$ ) and 3.7 to 3.3 ( $p=0.026$ ), respectively, and the symptom sub-scores decrease from 8.4 to 7.8 ( $p=0.584$ ) and 9.3 to 7.8 ( $p=0.015$ ) in the control and mirabegron groups. In the control and mirabegron groups, the mean overall Over Active Bladder Symptoms Score decreased from 8.4 to 7.2 ( $p=0.173$ ) and 8.8 to 7.3 ( $p=0.005$ , respectively). In the third quarter, the mean OABSS reduced from 3.6 to 2.9 ( $p=0.073$ ) and from 3.5 to 2.7 ( $p=0.002$ ), respectively. In the fourth quarter, the mean OABSS (as measured by the questionnaire) decreased from 2.4 to 2.0 ( $p=0.306$ ) and from 2.7 to 2.0 ( $p=0.016$ ) (questions and answers) Mean Qmax increased from 12.9 to 14.2 mL/s ( $p=0.308$ ) and from 15.3 to 14.9 mL/s ( $p=0.749$ ) in the control and mirabegron groups, respectively, whereas mean PVR increased from 18.0 to 20.6 mL ( $p=0.472$ ) and from 23.7 to 42.9 mL ( $p=0.581$ ) [Table 1].

Mirabegron 50 and 100 mg significantly improved dry rates, the proportion of patients with eight or fewer urinations per day at the final visit, and the mean number of incontinence episodes per day by about 50% (12 months). Patients under 50 and those who had previously stopped receiving antimuscarinic therapy clearly benefited from mirabegron 50 and 100 mg. Therefore, these data show that mirabegron has a clinically significant advantage in the OAB objective endpoints. Patients considered their treatment with mirabegron to be worthwhile, according to an analysis of health-related quality of life and treatment satisfaction criteria. Mirabegron appeared to be well tolerated in OAB clinical trials with prostatitis that lasted up to 12 months. The control group experienced nasal stuffiness ( $n=1$ ), headache ( $n=1$ ), and dizziness ( $n=1$ ). In the mirabegron group, dyspepsia ( $n=1$ ), dizziness ( $n=1$ ) and headache ( $n=1$ ) were reported (Table 2).

Table 1: Comparison of mean age, IPPS score, symptoms score, quality of life, OABSS, Q-Max, PVR (control group vs mirabegron)

Variable	Control Group	Mirabegron Group	P value
Age (years)	$47.7 \pm 2.1$	$33.8 \pm 7.0$	0.003
Prostate size (ml)	$29.5 \pm 14.0$	$37.3 \pm 8.7$	0.004
IPSS reduce after 8 weeks treatment	15.5–13.3	19.7 - 15.5	0.0298
Symptoms sub scores decreased after 8 weeks treatment	8.5–7.9	9.1–7.6	0.584
Mean quality of life sub scores decreased after 8 weeks treatment	3.7 – 3.1	3.6 – 3.2	0.452
Mean OABSS Q3 decreased after 8 weeks treatment	3.6 – 2.9	3.5 – 2.7	0.373
Mean OABSS Q4 decreased after 8 weeks treatment	2.4 – 2.9	3.5 – 2.7	0.073
Mean Q-Max decreased after 8 weeks treatment	12.9 – 14.2	15.3-14.9	0.749
Mean PVR decreased after 8 weeks treatment	18.0-20.6	23.7-42.9	0.851

Table 2: Comparison of Adverse event reported (control group and mirabegron group)

Adverse Event	Control Group	Mirabegron Group
Nasal stiffness	1	-
Headache	1	1
Dizziness	1	1
Dyspepsia	-	1

## DISCUSSION

The current study investigates the safety and effectiveness of Mirabegron to reduce lower urinary tract symptoms in prostatitis in actual clinical practice in a leading tertiary care hospital in Jamshoro. Mirabegron showed significant effectiveness in treating the exhibiting typical OAB symptoms. International guidelines acknowledge these symptoms as crucial indications of therapy success for OAB<sup>31</sup>.

As early as the first evaluation at week 4, mirabegron at dosages of 50 and 100 mg also showed significant benefits over placebo on important secondary endpoints, and these were maintained throughout the course of treatment. Mirabegron appeared to be well tolerated in OAB clinical trials lasting up to 12 months. As demonstrated in earlier studies examining medications for typical Over-Active-Bladder symptoms, the alteration in placebo was apparent after 7 days therapy, and a maximal benefit was attained and persisted from eight to twelve weeks.<sup>32</sup> At the end of treatment, 50% of the incontinent subjects in each mirabegron therapy group were dry. As a result, mirabegron showed significantly effective in the therapy for OAB indicators. It was found to be equally well tolerated as a placebo and tolterodine, with a minimal frequency of adverse events. The most prevalent and annoying side effect of antimuscarinic therapy is dry mouth<sup>33-36</sup>

Therefore, a key advantage of mirabegron therapy may be the low reported of dryness of mouth found with this medication than with tolterodine. A clinically meaningful rise in cardiovascular adverse events was not linked with our investigational drug, which was less apparent than that described in other studies.<sup>37,38</sup> No patient left the trial due to symptoms linked to greater exposure to these events, and there was no indication that there was a dose-response relationship for them.

## CONCLUSION

When contrasted with existing antimuscarinics that restricted due to associated adverse effects and insufficient effectiveness, mirabegron found improved compliance with balance between effectiveness and safety in Pakistani patients with associated symptoms in prostatitis.

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