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***Original Research Article***

# THE SAFETY AND EFFICACY OF SOLIFENACIN AS COMPARED TO MIRABEGRON IN OVERACTIVE BLADDER SYNDROME PATIENTS IN THE ADULT POPULATION OF DERA ISMAIL KHAN

**SEERWAN M[1], ADNAN M[*2], SHAFI H[3], JAVED N[4], ILYAS M[1], HUSSAIN M[5]**

*[1]Department of Urology, Gomal Medical College D.I Khan, Pakistan*
*[2]Department of Urology, Bakhtawar Amin Medical & Dental College Multan, Pakistan*
*[3]Department of Urology, Sheikh Zayed Hospital Lahore, Pakistan*
*[4]Department of Urology, The Children's Hospital & the University of Child Health Sciences Lahore, Pakistan*
*[5]Department of Urology, Sharif Medical & Dental College Lahore, Pakistan*
**Correspondence author email address: adnanshaheen123@yahoo.com*

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**Abstract:** *An overactive bladder syndrome is a group of symptoms, i.e., frequency, urgency, nocturia, and sometimes accompanied by urge incontinence. The recent pharmacological options are some drugs, mainly used anti-muscarinic. However, anti-muscarinic drugs have different adverse effects, i.e., constipation and dry mouth. In 2011, a β3 receptor agonist, mirabegron, was studied to treat overactive bladder syndrome. This non-randomized trial was conducted in the Department of Urology, Gomal medical college, D.I. Khan, KPK Pakistan. The study was done from June 2018 to January 2022. We divided 4220 patients into two equal groups. Group a used solifenacin 5 mg for 6 weeks, while group B used mirabegron 50 mg for the same duration. We assessed safety and efficacy after 6 weeks. Most of the adverse effects were mild to moderate severity. Dry mouth occurred in 125 patients out of 2110 (5.92%) in group A and 66 out of 2110 (3.12%) in group B. p-value = 0.0001. Constipation occurred in 53 (2.51%) patients in group A and 46 (2.18%) patients in group B. p-value=0.5417. The improvement in overactive bladder symptoms score (OBSS) occurred in 1443 out of 2110 (68.38%) patients in group A and 1409 out of 2110 (66.77%) patients in group B. p-value=0.2778. Based on the results, it can be concluded that Mirabegron has fewer adverse effects than solifenacin, while both drugs are approximately similar in efficacy.*

**Keywords:** Overactive bladder syndrome; Solifenacin; Mirabegron; Adult population; Pakistan.

## Introduction

Overactive bladder syndrome (OAB) is a group of symptoms, i.e., frequency, urgency, nocturia, and sometimes accompanied by urge incontinence (Haylen et al., 2010). It is more common in women as compared to men (Homma et al., 2005). It affects the quality of life profoundly (Coyne et al., 2008). The recent pharmacological options for overactive bladder syndrome are some drugs, mainly used anti-muscarinic. However, anti-muscarinic drugs have different adverse effects, i.e., constipation and dry mouth. In 2011, a β3 receptor agonist, mirabegron, was studied to treat overactive bladder syndrome. It has a distinct mechanism of action, different from the anti-muscarinic. Mirabegron promotes relaxation of the detrusor muscles and hence increases the urine storage capacity of the urinary bladder (Condino and Calvi, 2015; FUJIMURA et al., 1999; Takeda et al. 2003; Takeda et al., 1999). Mirabegron demonstrated significant efficacy in treating the symptoms of OAB and had a low rate of adverse events. The incidence of dry mouth with mirabegron is significantly less than the tolterodine (an anti-muscarinic) (Chapple et al., 2014). Different studies show similar efficacy of the mirabegron and the different anti-muscarinic (statistically no significant difference between the two groups (Batista et al., 2015; Kreydin et al., 2021; Maman et al., 2014; Yamaguchi et al., 2014).

Although anti-muscarinic are considered the 1st line medications for the overactive bladder syndrome, they have significant adverse effects, leading to poor compliance in such patients. Especially dry mouth is one of the most common adverse effects of this (Maman et al., 2014). This study aims to compare the safety and efficacy of solifenacin to our population to improve the treatment outcomes of overactive bladder syndrome patients.

## Methodology

This non-randomized trial was conducted in the Department of Urology, Gomal medical college, D.I. Khan, KPK Pakistan. The study was done from June

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2018 to January 2022. We enrolled the patients from the OPD of our institute. We calculated the sample size with an online calculator, i.e., https://www.openepi.com/SampleSize/SSCohort.htm . By taking the expected percentages of safety and efficacy as 47% and 43 % of both the drugs. 13 Calculated Sample size of our study was 4180 with a 95% level of confidence and 80 % power of the test. We have done the sampling by nonprobability consecutive sampling technique.

The Inclusion criteria included any patient between the ages of 14 and 40 years with overactive bladder syndrome. The exclusion criteria were any patient with a vesical stone, active urinary tract infection, and neurogenic bladder disease.

After taking informed written consent from all the patients, we divided the 4400 patients into two groups by the lottery method, i.e., group A, which used the solifenacin 5 mg, and group B which used mirabegron 50 mg daily, each containing 2200 patients. Both groups used the medicines for at least six weeks.

We assessed the safety by VAS of different side effects, i.e., dry mouth and constipation. VAS range was a minimum of zero (no symptoms) and a maximum of 10 (severe symptoms). We assessed the efficacy using the Overactive Bladder Symptoms Score (Homma et al., 2006) (including the number of incontinence episodes during the 24 hours) after six weeks of treatment with either drug.

The age of the patients and their gender were our matching variables. Our two research variables were safety (having no significant adverse effects) and efficacy (improvement in the symptoms). We analyzed the age (on a ratio scale) by the mean and the standard deviation. The counts and the percentages assessed gender and safety, and efficacy (on nominal scale).

The hypothesis testing was performed by using McNemar chi-square test (Pagano et al., 2022; Zar, 1999) at alpha 0.5 by using the online statistical calculator GraphPad (Ahmad et al., 2022).

## Results

Of the 4400 patients divided equally into two groups, 180 didn't complete the study. In group A, 690 out of 2110 patients (67.30%) were males, and 1420 (32.70%) were female patients, while in group B, 720 out of 2110 patients (34.12%) were males and 1390 (65.88%) female patients; almost similar.

In group A, the mean age of the patients was 25.45±11.22 years; in group B, it was 27.38±12.27 years, comparable between the two groups.

Most of the adverse effects were mild to moderate in severity with both treatments. Dry mouth occurred in 125 patients out of 2110 (5.92%) in group A and 66 patients out of 2110 (3.12%) in group B as shown by the p-value of 0.0001 in Table-1

**Table-1 Occurrence of a dry mouth.**

| Groups | Dry mouth | | Total | Chi-square value | Degree of freedom | p-value |
|---|---|---|---|---|---|---|
| | Yes | No | | | | |
| A | 125 | 1985 | 2110 | 18.448 | 1 | 0.0001 |
| B | 66 | 2044 | 2110 | | | |
| Total | 191 | 4029 | 4220 | The null hypothesis was rejected | | |

Constipation occurred in 53 (2.51%) of the patients in group A and 46 (2.18%) patients in group B as p-value=0.5417 (Table 2)

**Table-2 Occurrence of Constipation**

| Group | Constipation | | Total | Chi-square value | Degree of freedom | p-value |
|---|---|---|---|---|---|---|
| | Yes | No | | | | |
| A | 53 | 2057 | 2110 | 0.372 | 1 | 0.5417 |
| B | 46 | 2064 | 2110 | | | |
| Total | 99 | 4121 | 4220 | Null hypothesis accepted | | |

The improvement in overactive bladder symptoms score (OBSS) occurred in 1443 out of 2110 (68.38%) patients in group A and 1409 out of 2110 (66.77%) patients in group B. p-value=0.2778

**Table-3 The improvement in overactive bladder symptoms score**

| Group | Constipation | | Total | Chi-square value | Degree of freedom | p-value |
|---|---|---|---|---|---|---|
| | Yes | No | | | | |
| A | 1443 | 667 | 2110 | 1.178 | 1 | 0.2778 |
| B | 1409 | 701 | 2110 | | | |
| Total | 2852 | 1368 | 4220 | Null hypothesis accepted | | |

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## Discussion

Mirabegron is a β3-receptor agonist used for the treatment of overactive bladder syndrome. Its mechanism of action is the relaxation of detrusor muscles which is different from the anti-muscarinic. Our study shows that solifenacin and mirabegron are approximately equal in efficacy, but mirabegron has fewer adverse effects than solifenacin.

Similar results to our study were noted by Khaled et al.(Maman et al., 2014). They evaluated and compared the efficacy and the tolerability of different drugs used to treat overactive bladder. They noted that mirabegron 50mg was nearly equal in efficacy compared to anti-muscarinic drugs in decreasing the frequency and urgency and urge incontinence. They also noted that solifenacin 10mg was more effective than mirabegron 50mg.

Inouea M et al (Inoue and Yokoyama, 2019). Demonstrated in their study that both the drugs used have almost similar efficacy after four weeks of the treatment. They also switched the patients from the solifenacin group to the mirabegron group and vice versa. The patients who switched from the solifenacin to the mirabegron group showed no significant difference in efficacy. But when they switched oppositely, i.e., mirabegron to solifenacin, there was a significant improvement in the symptoms.

Nitti et al. (Nitti et al., 2013) showed that the patients less commonly reported the adverse effects of mirabegron, i.e. dry mouth and constipation, compared to the anti-muscarinic, which are the main cause of the treatment discontinuation. We also noted similar results in our study. He also reported that hypertension was a more common adverse effect noted in the patients that used mirabegron.

B3-receptors are also expressed in the cardiovascular system; their stimulation may result in the elevation of B.P. In our study, we have not noted serious hypertension in our patients. Gian et al.(Rosa et al., 2016) revised almost 20 publications, and they observed that mirabegron is safe from a cardiovascular point of view, and adverse effects are acceptable at 25-50 mg of the doses. They also observed that the adverse effects of mirabegron were comparable to that of the anti-muscarinic. Kobayashi et al. (Yeowell et al., 2018) also compared the efficacy and safety of mirabegron and anti-muscarinic drugs for treating patients with overactive bladder syndrome. They demonstrated that mirabegron might be selected as the initial treatment option due to its tolerability and efficacy. We also noted in our study that mirabegron is comparable to solifenacin in efficacy but has fewer side effects than solifenacin.

## Conclusion

Both the drugs, i.e., solifenacin and mirabegron, are effective in overactive bladder syndrome.Mirabegron has fewer adverse effects than solifenacin, especially dry mouth. Therefore, we recommend that irabegron be prescribed initially in patients with overactive bladder syndrome. If the patients are unsatisfied with the mirabegron, we can switch to solifenacin.

## Conflict of interest

The authors declared absence of conflict of interest.

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