Original Article

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Obstetrics and Gynaecology Section

# Effectiveness of Solifenacin versus Mirabegron in the Treatment of Overactive Bladder: A Prospective Cohort Study

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## ABSTRACT

**Introduction:** Overactive Bladder (OAB) syndrome is a symptom-complex defined as urinary urgency, usually accompanied by increased daytime frequency and nocturia, with or without urgency incontinence, in the absence of urinary tract infection or other obvious pathology.

**Aim:** To compare the efficacy and safety between Solifenacin and Mirabegron in treatment of OAB.

**Materials and Methods:** A prospective cohort study was conducted in the Department of Obstetrics and Gynaecology at Medical College, Kolkata, West Bengal, India from May 2020 to April 2021. The study was conducted on 110 willing patients divided into two groups, with Solifenacin 5 mg given to Group-1 and Mirabegron 50 mg given to Group-2, respectively. The sampling frame was women of age > 40 years visiting the hospital's urogynaecology clinic. Study variables were age, the difference between baseline and post-treatment number of urination episodes in 24 hours and at night, urgency, leakage episodes and side-effects experienced in each group. Mann-Whitney U Test was used for comparison between two groups while Chi-square test was used for side-effect comparison.

**Results:** The mean age of the study population was approximately 61.41 years. After nine weeks of treatment, the reduction in total number of urinations in 24 hours was 54.17% in Group-1 and 9.71% in Group-2, which is statistically significant, reduction in the number of urination at night was 79.53% and 76.79%, the reduction in number of leakage episodes was 78.19% and 75.49%, reduction in urgency episodes was 76.96% and 75%, frequent adverse effects were constipation (43.64% vs 7.27%) and dry mouth (56.36% vs 9.09%).

**Conclusion:** The study showed that both drugs are effective in reducing OAB symptoms. Regarding adverse effects, dry mouth was more common with Solifenacin.

**Keywords:** Nocturia, Overactive bladder syndrome, Symptom relief, Urinary bladder

## INTRODUCTION

The OAB is characterised by a sudden, uncontrollable urge to urinate (urinary urgency), often with increased daytime frequency and nocturia, with or without urgency incontinence. The International Continence Society defines OAB as urgency with or without urge incontinence, usually with more than eight voids per day and nocturia, without identifiable causes like infections or bladder diseases [1].

The diagnosis of OAB is made in the absence of urinary tract infections, metabolic disorders affecting urination, or urinary stress incontinence caused by physical effort or overexertion. Only about a third of OAB patients experience urge incontinence, also known as wet OAB [2]. It significantly affects quality of life, causing poor sleep, chronic fatigue and difficulty in daily activities, leading to increased psychological distress.

The OAB involves the inappropriate contraction of the detrusor muscle during bladder filling. Causes can be neurogenic, such as spinal cord injuries and neurological diseases, or non neurogenic, like rapid bladder filling and postural changes. Certain medications and conditions like heart failure can also contribute [3].

The National Overactive Bladder Evaluation (NOBLE) study [4] found 16.5% of US adults have OAB, affecting millions worldwide. In India, the prevalence of urinary incontinence ranges from 8-45%, influenced by cultural and socioeconomic factors.

The European Association of Urology recommends both non-pharmacological and pharmacological treatments for OAB. For idiopathic OAB, the three main treatment approaches are behavioural therapy, pharmacotherapy and surgery, with the choice depending on symptom severity and impact on the patient's lifestyle [5].

The American Urological Association (AUA) and the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) [6] recommend behavioural therapies and education as first-line treatments. Second-line therapies include antimuscarinic drugs, such as Solifenacin and beta-3 adrenoceptor agonists, like Mirabegron, with dose adjustments as needed.

Solifenacin is a competitive muscarinic receptor antagonist that selectively targets the M3 receptor subtype [7] in bladder smooth muscles. By preventing Acetylcholine (Ach) from binding to the M3 receptor, it reduces bladder smooth muscle tone, allowing the bladder to hold more urine and reducing episodes of micturition, urgency and incontinence.

Mirabegron is a beta-3 adrenergic receptor agonist that is the first new drug licensed for the management of OAB in over 30 years. It relaxes the bladder during the storage phase of micturition, increasing bladder capacity [8]. Mirabegron is a novel, once-daily, orally active, first-in-class, potent β (3)-adrenoceptor agonist approved by Food and Drug Administration for OAB therapy [9].

With this background, this study aimed to compare the efficacy of Solifenacin and Mirabegron in treating OAB and to evaluate the safety of these medications in OAB patients.

## MATERIALS AND METHODS

A prospective cohort study was conducted in the Department of Obstetrics and Gynaecology at Medical College and Hospital, Kolkata, West Bengal, India from May 2020- April 2021. The study was conducted after getting approval from the Institutional Ethical Committee (Ref No: MC/KOL/IEC/NON-SPON/723/03/2020 Dated

03/07/2020). The sampling frame was women of age >40 years visiting the hospital's urogynaecology clinic.

**Sample size calculation:** Sample size (N) was measured by calculating the difference of proportions. Proportions were taken from (Sachiavi MC et al., 2018) [10]. In that study, 12% and 2.3% of patients had constipation with solifenacin and mirabegron respectively. So P1 was 12 and P2 was 2.3. The study population thus calculated from the stated formula, consisted of 110 patients.

Calculating Difference in proportion

$$N=\frac{15.7\times\rho\times Q}{(P_1-P_2)^2}$$

Where

- $P_1$ and $P_2$ are the proportion of the 2 groups
- $\rho$ is the average of $P_1$ and $P_2$
- Q is 100-$\rho$

**Inclusion criteria:**

- Ambulatory and able to use toilet without difficulty;
- History of OAB symptoms for >3 months;
- An average of >8 micturition per 24 hours;
- More than one urgency episode (with or without incontinence) per 24 hours;
- Subjects who were bothered by said symptoms.

**Exclusion criteria:**

- Patient with stress or mixed incontinence, Type II diabetes mellitus, history of hypertension, recurrent Urinary Tract Infections (UTIs), painful bladder syndrome or chronic pelvic pain, cardiac disease, stroke, seizures or major neurological disorders, faecal incontinence and/or continuous urine leakage;
- Patient who had surgery to correct pelvic organ prolapse within six months of starting study;
- Patients requiring a catheter;
- Patients taking Tricyclic Anti-Depressants (TCAs) Serotonin/Norepinephrine Reuptake Inhibitors (SSRIs/SNRIs), Calcium Channel Blockers (CCBs), ephedrine/pseudoephedrine/diuretic therapy < eight weeks before the study started

### Study Procedure

Initially, 135 women who appeared to meet the study criteria were assessed for eligibility. Of these, 25 women were excluded: 17 declined to participate and 8 did not meet the inclusion criteria after a thorough clinical assessment. Ultimately, 110 patients were selected for the study and randomly assigned into two groups of 55 each. A computer-generated randomisation schedule was used to allocate 110 patients equally into two groups: Group-1 received Solifenacin 5 mg once daily and Group-2 received Mirabegron 50 mg once daily for nine weeks. Patients were asked to return for follow-ups at 3, 6 and 9 weeks. There were no dropouts. One of the authors conducted in-person interviews to complete the data collection questionnaire. At each follow-up, patients were assessed for reductions in the number of urinations in 24 hours, night-time urinations, night-time leakage episodes, urgency episodes in 24 hours and the occurrence of side-effects such as constipation, dry mouth, blurred vision/photophobia, hypertension and palpitations.

## STATISTICAL ANALYSIS

For statistical analysis, Statistical Package for Social Sciences Version 27.0 and GraphPad Prism version 5 was used. Demographic and other variables were analysed by descriptive statistics {mean, Standard Deviation (SD), proportion} comparison of study variables including efficacy outcomes was done by Mann-Whitney U Test, Chi-square test compare categorical data.

## RESULTS

Both groups (Group-1- Solifenacin and Group-2- Mirabegron) had similar age distributions [Table/Fig-1]. At nine weeks, the reductions in total number of urinations in 24 hours were 54.17% for Group-1 and 52.79% for Group-2, with no significant difference (p=0.9563) [Table/Fig-2]. Regarding night-time urinations, after nine weeks, the reductions were 79.53% for Solifenacin and 76.79% for Mirabegron, with no significant difference [Table/Fig-3].

| Age group | Group-1 (Solifenacin) n (%) | Group-2 (Mirabegron) n (%) | Total |
|---|---|---|---|
| 40-49 y | 7 (12.73) | 10 (18.18) | 17 |
| 50-59 y | 17 (30.91) | 15 (27.27) | 32 |
| 60-69 y | 18 (32.73) | 19 (34.55) | 37 |
| 70-79 y | 10 (18.18) | 6 (10.91) | 16 |
| 80-89 y | 3 (5.45) | 5 (9.09) | 8 |

**[Table/Fig-1]:** Age distribution among the two groups.

| Parameters | Group-1 | | Group-2 | | Mann-Whitney U test p-value (Group-1 vs Group-2) |
|---|---|---|---|---|---|
| | Average value | Reduction % | Average value | Reduction % | |
| Pretreatment | 20.03 | - | 20.56 | - | |
| Post-treatment (3 weeks) | 14.33 | 28.49 | 15.53 | 24.31 | 0.9541 |
| Post-treatment (6 weeks) | 11.69 | 41.65 | 12.42 | 39.61 | 0.9458 |
| Post-treatment (9 weeks) | 9.18 | 54.17 | 9.71 | 52.79 | 0.9563 |

**[Table/Fig-2]:** Total number of urinations in 24 hours.

| Parameters | Group-1 | | Group-2 | | Mann-Whitney U test p-value (Group-1 vs Group-2) |
|---|---|---|---|---|---|
| | Average value | Reduction % | Average value | Reduction % | |
| Pretreatment | 3.91 | - | 4.07 | - | - |
| Post-treatment (3 weeks) | 2.71 | 30.69 | 2.91 | 28.57 | 0.9774 |
| Post-treatment (6 weeks) | 1.6 | 59.06 | 1.67 | 56.69 | 0.9983 |
| Post-treatment (9 weeks) | 0.81 | 79.53 | 0.95 | 76.79 | 0.9430 |

**[Table/Fig-3]:** Total number of urinations at night.

Regarding leakage episodes {including Cough-Associated Detrusor Overactivity (CADO)}, at nine weeks, the reductions were 76.96% for Solifenacin and 75% for Mirabegron, with no significant difference [Table/Fig-4].

For urgency episodes in 24 hours, after nine weeks, reductions were 78.19% for Group-1 and 75.49% for Group-2, with no significant difference (p=0.9305) [Table/Fig-5].

Regarding adverse events constipation was reported in 43.64% of patients in the Solifenacin group compared to 7.27% in the Mirabegron group [Table/Fig-6].

## DISCUSSION

From the results of the present study, it can be inferred that while both Solifenacin and Mirabegron effectively reduced OAB symptoms, including urination frequency, night-time urinations, leakage episodes and urgency episodes, with no statistically significant difference between the groups at 3, 6 and nine weeks, adverse events were more frequent in the Solifenacin group, with higher incidences of constipation, dry mouth, blurred vision and photophobia. In contrast, hypertension and palpitations were more common but less frequent overall in the Mirabegron group. This suggests that while both drugs are equally effective, Mirabegron may have a more favorable side-effect profile.

| Parameters | Group-1 | | Group-2 | | Mann-Whitney U test p-value (Group-1 vs Group-2) |
|---|---|---|---|---|---|
| | Average value | Reduction % | Average value | Reduction % | |
| Pretreatment | 6.95 | - | 7.92 | - | - |
| Post-treatment (3 weeks) | 4.98 | 28.27 | 5.87 | 25.92 | 0.9663 |
| Post-treatment (6 weeks) | 3.13 | 54.97 | 3.76 | 52.52 | 0.9545 |
| Post-treatment (9 weeks) | 1.6 | 76.96 | 1.98 | 75 | 0.9444 |

**[Table/Fig-4]:** Total number of leakage episodes in 24 hours.

| Parameters | Group-1 | | Group-2 | | Mann-Whitney U test p-value (Group-1 vs Group-2) |
|---|---|---|---|---|---|
| | Average value | Reduction % | Average value | Reduction % | |
| Pretreatment | 5.42 | - | 5.49 | - | - |
| Post-treatment (3 weeks) | 3.87 | 28.52 | 4.04 | 26.49 | 0.9742 |
| Post-treatment (6 weeks) | 2.33 | 57.05 | 2.53 | 53.97 | 0.9492 |
| Post-treatment (9 weeks) | 1.18 | 78.19 | 1.35 | 75.49 | 0.9305 |

**[Table/Fig-5]:** Number of urgency episodes in 24 hours.

| Side-effects | Group-1 n (%) | Group-2 n (%) | Chi-square Va value lue | Chi-square test p-value |
|---|---|---|---|---|
| Constipation | 24 (43.64) | 4 (7.27) | 25.8154 | <0.00001 |
| Dry mouth | 31 (56.36) | 5 (9.09) | 31.2466 | <0.00001 |
| Blurred vision | 8 (14.55) | 1 (1.8) | 12.0082 | <0.00001 |
| Hypertension | 2 (3.64) | 8 (14.55) | 8.7428 | 0.012634 |
| Palpitation | 3 (5.4) | 10 (18.18) | 8.5375 | 0.01399 |

**[Table/Fig-6]:** Comparison of side-effects in both the groups.

In a similar study by Schiavi MC et al., both solifenacin and mirabegron groups showed a significant reduction in the mean number of voids per 24 hours and episodes of urgent micturition per 24 hours after 12 weeks of treatment [10]. Detrusor overactivity decreased from 58.3% to 13.1% in the solifenacin group and from 58% to 11% in the mirabegron group. This study also showed that adverse effects are more with Solifenacin. The present study results are comparable to this study.

In study of Nitti VW et al., significant improvement in symptoms with Mirabegron is seen in patients with OAB which was also seen in the present study [11]. The result is also comparable to a study by Kelleher C et al., (2018) who found 50% reduction in incontinence episodes with Mirabegron [12].

The study by Batista JE et al., (2015) also demonstrated a reduction of over 50% in incontinence episodes with both Solifenacin and Mirabegron [13]. Another trial showed a 72% reduction in incontinence episodes after 12 weeks of treatment in the Mirabegron group [14]. The present study yielded comparable results. Warren K et al., reviewed results of different phase 3 trials and concluded that Mirabegron is a safe and effective medication for OAB and it is well tolerated [15].

Karram MM et al., demonstrated that Solifenacin treatment significantly reduced episodes of urgency and other key symptoms of OAB [16]. Additionally, the SYNERGY II study showed that Mirabegron was statistically significantly more effective than placebo in reducing the number of severe urgency episodes {Patient Perception of Intensity of Urgency Scale (PPIUS) grade 3 or 4} per 24 hours [17]. These findings are consistent with the present study, which also found both drugs to be effective in treating OAB.

When adverse events were compared between the two drug groups, Solifenacin was more associated with dry mouth (56.36% vs. 9.09% in Mirabegron), constipation (43.64% vs. 7.27% in Mirabegron), photophobia and blurred vision (14.55% vs. 1.8% in Mirabegron). Mirabegron was more associated with hypertension (14.55% vs. 3.64% in Solifenacin) and palpitations (18.18% vs. 5.4% in Solifenacin).

The present results are similar to those found by Batista JE et al., (dry mouth in 5.8% and constipation in 2.5% of Solifenacin-treated patients compared to 3.1% and 2.2%, respectively, in Mirabegron-treated patients) [13].

In a study by Gratzke C et al., 5.9 % of patients of Mirabegron group developed dry mouth [17]. Yamaguchi O et al., showed 23.3 % of treatment-related adverse effects in the Solifenacin group and the most common of them is constipation [18].

In a study by Scaldazza CV and Morosetti C, Solienacin and Mirabegron were equally effective in improving OAB symptoms [19]. However, Mirabegron offered a better balance between efficacy and tolerability in women with OAB.

A meta-analysis of five Randomised Controlled Trials (RCTs) comparing Solifenacin (5 mg) and Mirabegron (50 mg) over 12 weeks for OAB found similar outcomes in daily incontinence episodes, micturition frequency, urgency episodes and urine volume per void. Although the Solifenacin group had a higher incidence of drug-related adverse events, there was no significant difference in overall side-effects between the groups. The mean post-void residual volume was higher in the Solifenacin group [20].

By incorporating multiple follow-up points at 3, 6 and 9 weeks, the study allowed for a detailed analysis of the progression and consistency of treatment efficacy over time. Additionally, the study conducted a comprehensive symptom assessment, evaluating key OAB parameters. A thorough side-effect analysis provided insights into the tolerability differences between Solifenacin and Mirabegron, contributing to a better understanding of their safety profiles. Recommendations for future research include studies with larger sample sizes, longer follow-ups, double-blind design, subgroup analyses, quality of life assessments and cost-effectiveness analysis for improving generalisability, safety and treatment adherence. It also suggests exploring combination therapy for refractory OAB symptoms and evaluating cost-effectiveness for resource-limited healthcare settings.

### Limitation(s)

The study was conducted in a tertiary care hospital, so hospital bias cannot be ruled out. Long-term follow-up was not performed.

## CONCLUSION(S)

In the present study, the authors observed that Solifenacin and Mirabegron are both effective in reducing OAB symptoms. Solifenacin is slightly more effective than Mirabegron although the difference in efficacy is not statistically significant. With regards to adverse effects of the drugs in question- quite a high percentage of patients experienced anticholinergic side-effects like dry mouth, constipation, or blurred vision in the Solifenacin group and these are much less in treatment with Mirabegron.

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