Sir Salimullah Medical College Journal

Sir Salimullah Med Coll J 2022; 30: 55-60

Original Article

A Quasi Experiment on Outcome of Mirabegron and Solifenacin in the Treatment of Primary Over Active Bladder in A Tertiary Hospital in Dhaka, Bangladesh

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Article information
Received: 01.11.2021
Accepted: 01.12.2021

Cite this article:
Sarkar MI, Islam MS, Azad AK, Alam R, Alam M, Gupta SD. A Quasi Experiment on Outcome of Mirabegron and Solifenacin in the Treatment of Primary Over Active Bladder in a Tertiary Hospital in Dhaka, Bangladesh. Sir Salimullah Med Coll J 2022; 30: 55-60

Key words:
OAB, Mirabegron, Solifenacin

Abstract

Background: *Overactive bladder (OAB) syndrome is a common symptom complex that affects millions of people worldwide, with an increasing prevalence with increased age in primary overactive bladder.*

Objective: *The study was done to find out the efficacy and outcome of Mirabegron and solifenacin on primary overactive bladder.*

Methodology : *This study was a quasi-experimental study conducted on 100 study population (Group A-50 Group B-50) in Urology Outpatient Department, Sir Salimullah Medical College Mitford Hospital, Dhaka from July 2017 to December 2018. Study population were total 100 men and women aged at least 18 & up to 60 years (Group A -50 and Group B-50) with persistent primary overactive bladder (OAB) symptoms for 3 months or more were enrolled in this study. Patients were eligible for the study who were able to give a written informed consent before starting the intervention & was also able to complete a voiding diary. Patients were recruited at the urology outpatient department, SSMCMH, Dhaka and were selected by the following inclusion and exclusion criteria. A data sheet was completed for each patient which included particulars of the patient, history, examination findings and baseline investigations. Half of the patients were enrolled in each group. Mirabegron group was experimental group and Solifenacin group was control group. Cases of Mirabegron group was given once daily dose of Mirabegron 25 mg and Solifenacin group was also given single dose of Solifenacin succinate 5 mg, at for 12 weeks.*

Result: *The result of age distribution of the study patients belonged to age 31-40 years in group A (Mirabegron 25 mg) 21(42.0%) and 16(32.0%) in group B (Solifenacin 5 mg). The mean voided volume of each micturation at 12 week of treatment was more increased in group A (Mirabegron 25 mg) than group B (Solifenacin 5 mg). The mean change in micturition frequency per 24 hours, episodes of urgency per 24 hours, urge incontinence episodes per 24 hours and nocturia episodes per 24 hours were statistically significant ($p<0.05$) between group A (Mirabegron 25 mg) and group B (Solifenacin 5 mg).*

Conclusion: *The study shows that Mirabegron is more effective than Solifenacin in the treatment of primary over active bladder and can be used in without organic and pathological diseases of urinary bladder.*

Introduction

Overactive bladder (OAB) is "urgency, with or without urge incontinence, usually with frequency and nocturia in the absence of an underlying metabolic or pathologic condition[1].Overactive bladder (OAB) syndrome is a common symptom complex that affects millions of people worldwide, with an increasing prevalence with increased age [2]It is a chronic symptom complex that can substantially impair quality of life [3].This chronic

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condition affects both men and women, with slightly more prevalent in women[4]. Treatment approaches for OAB include behavioral modification, pharmacological and surgical therapy[5]. In recent decades OAB was treated by some antimuscarinic agents like solifenacin a newer antimuscarinic agent which has proved to be bladder selective and M3 receptor selective. It is a long acting muscarinic receptor antagonist and is metabolized by the cytochrome P450 system[6]. But anticholenargic like solifenacin also causes some anticholenargic adverse effects such as dry mouth, constipation, nausea, upper abdominal pain, headache, UTI, blurred vision which along with lack of efficacy, is the most frequently cited reason for discontinuation of antimuscarinic treatment[7]. Different investigators define OAB in different ways the international Continence Society, (ICS) committee defined Overactive bladder (OAB) as urgency, with or without urge incontinence usually with frequency and nocturia[8]. It occurs as a result of involuntary detrusor contractions during bladder filling [9]. Overactive bladder (OAB) is a symptom complex that is characterized by urinary urgency, with or without urgency-associated urinary incontinence.

OAB is often associated with urinary frequency and nocturia in the absence of pathologic or metabolic conditions that may cause or mimic OAB, such as urinary tract infections, polyuria, transitional cell carcinoma, underlying neurologic abnormalities, and certain drug treatment[10].

Methodology

This study was a quasi-experimental study conducted on 100 study population(group A-50 Group B-50) in urology outpatient department, Sir Salimullah Medical College Mitford Hospital, Dhaka from July 2017 to December 2018.Study population was total 100 men and women aged at least 18 & up to 60 years with persistent primary overactive bladder (OAB) symptoms for 3 months or more were enrolled in this study.Patients were eligible for the study who were able to give a written informed consent before starting the intervention & was also able to complete a voiding diary. Sample Technique: After proper evaluation based on history, clinical examination and other investigations, patients were diagnosed as primary over active bladder in the out-patient Department of Urology, SSMCMH. Patients who fulfilled the selection criteria were randomized into two groups. One group (Group-A) was the odd number of the patients were treated with Mirabegron and another group (Group -B) even number of the patients were treated with Solifenacin. In this way patients were selected as Group –A (Mirabegron 25mg) and Group –B (Solifenacin 5 mg). Selection criteria: Patients were recruited at the urology outpatient department, SSMCMH, Dhaka and were selected by the following inclusion and exclusion criteria. Inclusion criteria: The patients fulfilling the following criteria was selected for this study-Male or female aged 18-60 years with persistent OAB symptoms ≥3 months who were able to complete the voiding diary correctly ,an average of ≥8 micturition per 24 hours. An average of ≥1 urgency episode per 24 hours. An average of ≥1 nocturia episode per 24 hours. Exclusion criteria: Stress or mixed urinary incontinence, Neurological cause of abnormal detrusor activity. Pregnant and lactating women or those who intended to become pregnant during the study. Clinically significant bladder outflow obstruction (PVR >100 ml), symptomatic urinary tract infection, bladder stones, diabetic neuropathy. Significant hepatic, renal or other medical diseases. Previous pelvic radiation therapy for malignant disease of the pelvic organs. Patients with urinary retention, uncontrolled narrow angle glaucoma. Patients with severe uncontrolled hypertension which is defined as a sitting average systolic blood pressure ≥180 mmHg and /or average diastolic blood pressure ≥110 mmHg.

Procedure: This study was conducted in the department of Urology, SSMCMH, Dhaka from July 2017 to December 2018. The study sample was selected on the basis of selection criteria from the patients attended in the outpatient department of Urology, SSMCMH, Dhaka.

Data collection: A data sheet was completed for each patient which included particulars of the patient, history, examination findings and baseline investigations. Half of the patients were enrolled in each group. Mirabegron group was experimental group and Solifenacin group was control group. Cases of Mirabegron group was given once daily dose of Mirabegron 25 mg and Solifenacin group was also given single dose of Solifenacin succinate 5 mg, at for 12 week. The study subjects were selected on the basis of selection criteria from the

patients attending the outpatient department of Urology, SSMCMH, Dhaka. The demographic information, history, examination findings, investigation reports and outcome of treatment of all the study subjects was recorded in the data collection sheet.

Data processing and data analysis: Statistical analyses were carried out by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA. Ethical consideration: Prior to commencement of this study, the Ethical Clearance Board approved the research protocol. All the patients included in this study were informed about the nature, risk and benefit about the study and written informed consent was taken.

Result

Table I shows age distribution of the study patients, it was observed that majority of the (42.0%) patients belonged to age 31-40 years in group A (Mirabegron 25 mg) and 16(32.0%) in group B (Solifenacin 5 mg). The mean age was found 36.7±10.7 years in group A and 38.5±10.9 years in group B. The mean age difference was not statistically significant ($p>0.05$) between two groups. (Group A= Mirabegron 25 mg Group B= Solifenacin 5 mg) (Table I)

Table II shows that mean change in micturition frequency per 24 hours, episodes of urgency per 24 hours, urge incontinence episodes per 24 hours and nocturia episodes per 24 hours were statistically significant ($p<0.05$) between group A (Mirabegron 25 mg) and group B(Solifenacin 5 mg). (Table II)

Table I

Age distribution of the study population (n=100)

Age (years)	Group A(n=50)		Group B(n=50)		P value
	n	%	n	%	
≤ 20	7	14.0	2	4.0	
21-30	8	16.0	12	24.0	
31-40	21	42.0	16	32.0	
41-50	12	24.0	12	24.0	
51-60	2	4.0	8	16.0	
Mean±SD	36.7±10.7		38.5±10.9		0.416^{ns}

ns= not significant

P value reached from unpaired t-test

Table II

Mean change from baseline to after 12 weeks of treatment.

Variables	Group-A (n=47)	Group-B (n=45)	p value
	Mean±SD	Mean±SD	
Micturition frequency per 24 hours	4.32±1.58	2.73±1.37	0.001^{s}
Episodes of urgency per 24 hours	2.51±0.98	1.73±0.58	0.001^{s}
Urge incontinence episodes per 24 hours	1.94±0.48	1.51±0.55	0.001^{s}
Nocturia episodes per 24 hours	1.89±0.43	1.51±0.66	0.002^{s}
Voided volume of each micturation (ml)	-67.66±30.38	-57.56±25.40	0.088^{ns}
Pad usage per 24 hours	0.93±0.89	0.31±2.39	0.099^{ns}

s= significant, ns= not significant

P value reached from unpaired t-test

Figure 1 shows mean voided volume of each micturation at 12 week of treatment was more increased in group A (Mirabegron 25 mg) than group B (Solifenacin 5 mg).

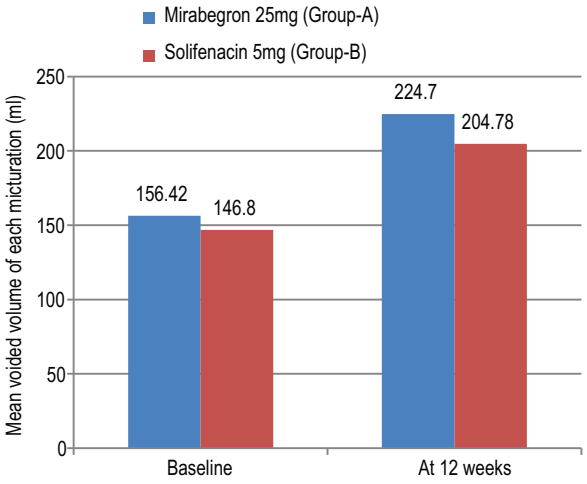

Fig.-1: *Bar diagram shows mean voided volume of each micturation baseline and at 12 weeks.*

Discussion

This quasi-experimental study was conducted in urology outpatient department, Sir Salimullah Medical College Mitford Hospital, Dhaka from July 2017 to December 2018.

A total 100 cases were initially enrolled in this study. Among them 50 cases were treated with Mirabegron 25 mg and 50 cases were treated with Solifenacin 5 mg tablet once daily for 3 months. Then the patients were followed up at 1st week and 12th week and compared between two groups. At 12th week follow up 3 cases were lost in group A (Mirabegron 25 mg) and 5 cases were lost for follow up in group B (Solifenacin 5 mg).

In present study the mean age was found 36.7±10.7 years in group A (Mirabegron 25 mg) and 38.5±10.9 years in group B (Solifenacin 5 mg) (Table I). Higher mean age was observed by Batista et al.[11] (2015), Wagg et al.[12] (2014) and Khullar et al.[13] (2013). The higher mean age may be due to geographical variations, racial, ethnic differences, and genetic causes may have significant influence on overactive bladder in their study subjects.[11-13]

The present study shows that mean micturition frequency per 24 hours - at 12th week follow up was statistically significant ($p<0.05$) within the both group (group A & group B) compared with baseline . Similar decrease was observed at Scaldazza and Morosetti[14] (2016). Some authors Yamaguchi et al.[15] (2014) and Wagg et al.[17] (2014) have found the primary efficacy measure showed a statistically significant reduction from baseline in mean micturition frequency with mirabegron compared with placebo and majority of the findings are consistent with the present study regarding the reduction of frequency of micturitions in 24 hours.[12,14,15]

This study shows mean change in micturition frequency per 24 hours compared with baseline to at 12th week follow up was statistically significant ($p<0.05$) between two groups .

The current study shows that mean episodes of urgency per 24 hours-at 12th week follow up was statistically significant ($p<0.05$) within the both group (group A and group B) compared with baseline . Scaldazza and Morosetti (2016) studied the mean number of urgency episodes per 24 hours significantly decreased in patient treated with Mirabegron compared with patient receiving Solifenacin, which is consistent with this study[14].

This study showed mean change in episodes of urgency per 24 hours compared with baseline to at 12th week follow up was statistically significant ($p<0.05$) between two groups . The similar results obtained by a number of investigators (Khullar et al. 2013; Nitti et al. 2013) demonstrated that mirabegron significantly improves the number of urgency episodes/24 h, compared with placebo after 12th week of treatment. The above mentioned findings are consistent with the current study[13,16].

This study shows mean change in urge incontinence episodes per 24 hours compared with baseline to at 12th week follow up was statistically significant ($p<0.05$) between two groups . Yamaguchi et al. (2014) found a statistically significant difference in the 25, 50 and 100 mg mirabegron groups compared with placebo from baseline to end of study in the mean number of incontinence episodes/24 h ($p<0.001$, all groups), which support with the present study[15].

This study shows mean change in nocturia episodes per 24 hours compared with baseline to at 12th week follow up was statistically significant ($p<0.05$) between two groups. Barista et al. (2015) shows

that adjustment change from baseline was -0.95 and -0.94 in mirabegron and solifenacine group, which is consistent with this study[11].

This study shows mean change in pad usage compared with baseline to at 12th week follow up was not statistically significant (p>0.05) between two groups .

This current study shows that the mean voided volume of each micturition at 12th week follow up was statistically significant (p<0.05) within the group A compared with baseline similar observation was found done by Scaldazza and Morosetti, (2016). Abrams et al. (2015) reported that combined therapy had greater efficacy than solifenacin 5 mg alone on the change from baseline to end of treatment in the mean voided volume / micturition was well tolerated compared with the monotherapies or placebo[14].

This study shows mean change in mean voided volume of each micturition compared with baseline to at 12th week follow up was not statistically significant (p>0.05) between two groups . Wang et al. (2018) shows that the mean volume voided per micturition (P = 0.05) suggested that mirabegron and solifenacin had no significant differences in terms of OAB treatment which are comparable with the current study[17].

Conclusion

This study shows both Mirabegron and Solifenacin are effective in improving primary over active bladder symptoms. Mirabegron shows greater outcome over solifenacin in primary overactive bladder in all age group for solution of micturition frequency per 24 hours, episodes of urgency per 24 hours, urge incontinence episodes per 24 hours and nocturia episodes per 24 hours is satisfactory. Therefore, at present, Mirabegron can be considered as the drug with the better outcome in the treatment of primary over active bladder.

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