

## Original Research Article

# Comparison of efficacy of mirabegron and darifenacin in overactive bladder- a prospective study

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### ABSTRACT

**Background:** Overactive bladder (OAB) is under reported yet distressing symptoms which can be managed effectively by the drugs available. Aim was to study and compare the efficacy of two drugs, mirabegron and darifenacin in controlling the symptoms of overactive bladder.

**Methods:** This prospective study included a total of 120 cases of overactive bladder reported at Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar from January 2018 to December 2019. This comparative study was done by giving Mirabegron to first five patients and next five patients were given darifenacin up to 120 patients. The drug treatment with once daily administration of 25 mg mirabegron and 7.5 mg of darifenacin was given for a total of 12 weeks. The signs and symptoms were noted at the beginning of the therapy and then follow up was done at 4, 8, 10 and 12 weeks.

**Results:** Total 54 out of 60 patients (90%) on miragaberon and 59 of 60 patients (98.33%) on darifenacin were relieved of symptom of increased frequency of micturition. 53 of 60 patients (88.33%) on miragaberon and 59 of 60 patients (98.33%) on darifenacin were relieved of symptom of decreased average voiding volume. 28 of 60 patients (46.67%) on miragaberon showed nocturia as compared to 25 of 60 patients (41.67%) on darifenacin.

**Conclusions:** It has been concluded that both mirabegron as well as darifenacin are highly efficacious newer treatment options for the management of OAB. Our study found Darifenacin to be relatively more efficacious in the treatment of OAB at a lesser dose and statistically significant differences were observed between the two drugs.

**Keywords:** Overactive Bladder, Darifenacin, Mirabegron

### INTRODUCTION

Overactive bladder (OAB) syndrome is defined as presence of increased urinary frequency (>8 micturitions/24 hours), urgency with a difficulty to defer and nocturia with or without urge incontinence, in the absence of local pathological or metabolic factors.<sup>1</sup>

The international continence society (ICS) defines OAB as an involuntary rise in detrusor pressure during filling of the bladder in a laboratory situation in a conscious co-operative patient.<sup>2</sup> Approximately 400 million people worldwide suffer with symptoms of urgency and

frequency (dry OAB) and a proportion will have associated urgency incontinence (wet OAB).<sup>3</sup>

OAB is a highly prevalent disease and can be associated with a numerous risk factors such as age, post-menopausal status, incontinence surgery, neurogenic diseases, lifestyle factors such as BMI, Smoking, Caffeine Intake, behavioral factors such as fluid Intake.

OAB has consequences on physical as well as mental health of an individual, with symptoms such as skin breakdown due to leakage, sleep disturbance, fall-related injuries, depression and prolonged hospital stays.<sup>4</sup> People

with OAB are more likely to limit social outings, physical and recreation activity.<sup>5</sup>

The diagnosis of OAB requires thorough examination of the patient and an analysis of the signs and symptoms excluding the pre-existing illness, if any. History, examination and laboratory testing aid in formation of the diagnosis.<sup>6</sup> The history must include information about the daily fluid intake, intake of potential irritants such as caffeine, carbonated beverages, spicy food and artificial sweeteners, baseline urinary function and the duration of OAB. A major component of concern is if the patient is bothered by the urgency and frequency as no intervention is required in case the patient isn't bothered.<sup>7</sup>

Mirabegron, a  $\beta_3$  adrenoceptor agonist is the first drug of this class to be used for OAB. It has proved to be highly efficacious due to lesser side effects and can be used alone or in combination with antimuscarinics.<sup>8</sup>

Darifenacin is a novel M3 selective antagonist which has been developed with a dosage regimen of once daily administration and has very high efficacy and tolerability in all age groups. It has even proved to be effective in chronic debilitating patients. It has shown a good safety profile for the treatment of OAB.<sup>9</sup>

This prospective study was undertaken to compare the efficacy of the two novel drugs mirabegron and darifenacin in the effective treatment of OAB considering the improvement in the key clinical presentation features of OAB namely, frequency of micturition, average voiding frequency, nocturia and urge incontinence.

### Aim

Aim was to compare the efficacy of mirabegron and darifenacin in treatment of overactive bladder.

### METHODS

This prospective study was conducted in the department of General Surgery at Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar from January 2018 to December 2019. A total of 120 cases of overactive bladder were included in this study. This comparative study was done by giving Mirabegron to first five patients and next five patients were given darifenacin and so on till the total count was completed. The drug treatment with once daily administration of 25 mg mirabegron and 7.5 mg of darifenacin was given for a total of 12 weeks. The signs and symptoms were noted at the beginning of the therapy and then follow up was done at 4, 8, 10 and 12 weeks after administration of the medication to assess the response of the patient's symptoms. The patients were asked to maintain a daily diary of total number of micturitions per day and amount of urine per micturition using a urine pot as well as to note down the episodes of nocturia and periodic comparison of the efficacy of the two drugs was made.

Ethical committee approval was taken for carrying out this study in our tertiary care centre

Statistical analysis was done using SPSS version 21.0. To compare prevalence chi-square test was used. P value of <0.05 was considered to be statistically significant.

### RESULTS

In this study, patients from the age group of 30-80 years were included. It was observed that a majority of patients presenting with OAB were from the age group of 51-60 years followed by the patients in the age group of 61-70 years, as depicted in Table 1.

**Table 1: Age wise distribution of patients affected with OAB.**

Age distribution (years)	Number of patients	Percentage
30-40	11	9.16
41-50	20	16.67
51-60	42	35
61-70	28	23.33
71-80	19	15.83
Total	120	100

Amongst a total of 120 patients included in this study, a preponderance of female patients was observed. In this study 86 patients were females (71.66%) while 34 patients were males (28.33%) as depicted in the Table 2.

**Table 2: Gender distribution of the patients affected with OAB.**

Gender	No. of patients	Percentage
Male	34	28.33
Female	86	71.67
Total	120	100

**Table 3: Relief of symptom of increased frequency of micturition comparing effects of mirabegron and darifenacin at various time intervals.**

Time of therapy	Patients relieved with mirabegron		Patients relieved with darifenacin		P value
	No.	%	No.	%	
0 week	0	0.00	0	0.00	-
4 weeks	38	63.33	55	91.67	0.001
8 weeks	46	76.67	56	93.33	0.011
10 weeks	50	83.33	58	96.67	0.015
12 weeks	54	90.00	59	98.33	0.051

Firstly, the symptom of increased frequency of micturition was evaluated. As stated by ICS, more than 8 episodes of micturition were considered as increased frequency of micturition. On comparison of the two

drugs, a statistically significant difference was observed at 4 weeks (p value=0.001), 8 weeks (p value=0.011) and 10 weeks (p value=0.015) while no significant difference was observed at 12 weeks (p value=0.051) as depicted in Table 3.

**Table 4: Relief of symptom of decreased average voiding volume comparing effects of mirabegron and darifenacin at various time intervals.**

Time of therapy	Patients relieved with mirabegron		Patients relieved with Darifenacin		P value
	No.	%	No.	%	
0 week	0	0.00	0	0.00	
4 weeks	36	60.00	49	81.67	0.009
8 weeks	45	75.00	57	95.00	0.002
10 weeks	48	80.00	58	96.67	0.004
12 weeks	53	88.33	59	98.33	0.028

All the 120 patients were asked to record the voiding volume with the help of a urine pot. An average of this

voiding volume per was calculated at the end of 4, 8, 10 and 12 weeks. The average voiding volume of more than 100 ml was considered to be efficaciously treated for OAB. This evaluation was done for mirabegron and darifenacin receiving groups separately and on comparison of the two drugs, a statistically significant difference was observed at 4 weeks (p value=0.009), 8 weeks (p value=0.002), 10 weeks (p value=0.004) and 12 weeks (p value=0.028). The comparison is depicted in Table 4.

OAB has been associated with night episodes of micturition causing awakening of the patients at night to empty the bladder causing sleep disturbances. It has been defined by various studies that  $\leq 1$  episode of micturition during the night can be taken as normal. This evaluation was done for mirabegron and darifenacin receiving groups separately. 53 people were affected with nocturia and were randomly distributed into treatment groups as follows. (Table 5) On comparison of the two drugs, a statistically significant difference was observed at 4 weeks (p=0.001), 8 weeks (p=0.002), 10 weeks (p=0.017) and 12 weeks (p=0.033) (Table 6).

**Table 5: Distribution of patients with night episodes in group A and B.**

Groups	Nocturia Present	Percentage	Nocturia Absent	Percentage
Group A (treated with mirabegron)	28	46.67	32	53.33
Group B (treated with darifenacin)	25	41.67	35	58.33

**Table 6: Relief of symptom of nocturia comparing effects of mirabegron and darifenacin at various time intervals.**

Time of therapy	Patients relieved with mirabegron		Patients relieved with Darifenacin		P value
	No.	%	No.	%	
0 week	0	0.00	0	0.00	-
4 weeks	4	6.67	21	35.00	0.001
8 weeks	17	28.33	24	40.00	0.002
10 weeks	20	33.33	24	40.00	0.017
12 weeks	21	35.00	24	40.00	0.033

**Table 7: Distribution of patients with urge incontinence.**

Groups	Urge Incontinence Present	Percentage	Urge Incontinence Absent	Percentage
Group A (treated with mirabegron)	13	21.67	47	78.33
Group B (treated with darifenacin)	9	15	51	85

**Table 8: Relief of symptom of urge incontinence comparing effects of mirabegron and darifenacin at various time intervals.**

Time of therapy	Patients having side effects with mirabegron		Patients having side effects with Darifenacin		P value
	No.	%	No.	%	
0 week	0	0.00	0	0.00	-
4 weeks	5	8.33	4	6.67	0.779
8 weeks	6	10.00	8	13.33	0.040
10 weeks	8	13.33	9	15.00	0.157
12 weeks	10	16.67	9	15.00	0.121

Amongst a total of 120 patients, only 23 presented with the symptom of urge incontinence. They were randomly distributed into group A and B and received treatment with mirabegron and darifenacin respectively. It was observed that 13 of them received mirabegron while 9 of them were chosen into group B and received darifenacin. (Table 7) On comparison of the two drugs, a statistically non-significant difference was observed at 4 weeks ( $p$  value=0.779), 10 weeks ( $p$  value=0.157) and 12 weeks ( $p$  value=0.121) while a significant difference was observed at 8 weeks ( $p$  value=0.040) as depicted in Table 8.

## DISCUSSION

In this study, we have performed a non-randomized comparative trial using Mirabegron and Darifenacin for the treatment of OAB along with the comparison of the two drugs in relieving the symptoms of OAB and side effects of each drug have been evaluated as compared to the other at the time intervals of 4 weeks, 8 weeks, 10 weeks and 12 weeks. The symptoms evaluated were frequency of micturition, average voiding volume, nocturia and urge incontinence.

Warren et al conducted a study on “mirabegron in overactive bladder patients: Efficacy review and update on drug safety” and reported mirabegron to be effective in curing the increased frequency of micturition.<sup>8</sup> In our study, mirabegron was able to cure increased frequency of micturition in 63.3% of patients at just 4 weeks of treatment and 90% of patients were relieved of the symptoms at the end of the study period i.e. 12 weeks. Although, mirabegron was effective in treating 90% patients, relapse of the symptom was observed in 2 patients at the end of therapy.

Zinner et al conducted a study to evaluate the effect of Darifenacin treatment for OAB in patients who expressed this satisfaction with treatment with prior antimuscarinics drugs and concluded that more than 85% patients reported to be satisfied after treatment with Darifenacin which is consistent with our observation.<sup>10</sup> In our study, we found darifenacin to be furthermore effective in the cure of the same symptom, i.e. increased frequency of micturition. Also, the effect of darifenacin was observed as early as 4 weeks with 91.6% of patients being relieved at the first follow up, 93.3% at the period of 8 weeks, 96.6% at 10 weeks and 98.03% of the patients at the end of therapy. Only 1 patient in the group B persisted with the symptom of increased frequency of micturition at the end of therapy which is similar to the findings of Zinner et al.

Khullar et al conducted a trial on the efficacy and tolerability of mirabegron vs a placebo and measured post voiding residual volume. They reported mirabegron to be effective in decreasing the post voiding residual volume.<sup>11</sup> Hesch et al conducted a study on the agents for treatment of overactive bladder and concluded that Darifenacin was effective in relieving the symptom of

decreased voiding volume per micturition in more than 90% of the patients.<sup>12</sup> In our study, 60% of patients treated with mirabegron reported normal average voiding volume at the end of 4 weeks, while 88.3% of them were efficaciously treated at the end of the study period i.e. 12 weeks. This was found to be less effective as compared to darifenacin in which 81.67% of patients reported normal average voiding volume as early as first follow up visit at 4 weeks and 98.33% of the individuals reported normal volumes at the end of study period leaving behind only 1 patient whose average voiding volumes were still below 100ml per micturition. Therefore, both the drugs were effective in the relieving symptom of decreased average voiding volume and these findings were similar to the findings observed in previously conducted clinical studies.

Nocturia is a disabling symptom of OAB which affects the quality of life of the patients to a great extent. Coyne conducted a study to evaluate the prevalence of nocturia in OAB and concluded that a prevalence rate of 42.2% to 66.8%. They also reported increased prevalence of nocturia in women and Caucasians with an increase in the prevalence associated with advancing age.<sup>13</sup> In our study, nocturia was prevalent in 41.66% of the patients of OAB which is consistent with the previously reported findings.

Andersson et al conducted a study on the pharmacotherapy of nocturia and described mirabegron to be an effective agent for the treatment of nocturia associated with OAB based on phase 2 dose-ranging trial of Mirabegron.<sup>14</sup> Salazar et al conducted a study on Darifenacin and its therapeutic efficacy and concluded that it effectively relieved nocturia in the patients of OAB.<sup>15</sup> In our study, the patients suffering from nocturia were randomly distributed in group A and B and treated with mirabegron and darifenacin respectively. 46.67% of the patients were given mirabegron while 41.67% of patients received darifenacin for the treatment of OAB. Amongst the patients receiving mirabegron, 75% were relieved of nocturia while darifenacin was able to treat nocturia in 96% of the patients at the end of study period of 12 weeks showing both the drugs to be effective in the management of nocturia which is in concordance to the previously mentioned studies.

Irwin et al conducted EPIC study and concluded that urgency was present in 21% of men and 23% of women affected with OAB which is consistent with the finding of our study. Coyne et al conducted Epi Luts study which devised that the prevalence rates of urge incontinence were found to be between 10.9% to 15.6%.<sup>16</sup> In this study, amongst the 120 patients, only 23 presented with urge incontinence. The prevalence of urge incontinence was evaluated 19.17% in our study which is comparable to results of aforementioned studies.

Herschorn et al conducted a double blind randomized multicenter trial for the efficacy of mirabegron in the patients of OAB and found mirabegron to be effective in



relieving the symptoms of urgency in the patients with OAB.<sup>17</sup> Zinner et al also reported darifenacin to be highly effective in the treatment of urge incontinence with more than 85% of patients being satisfied on treatment with Darifenacin.<sup>10</sup> Similarly, in our study, urge incontinence was relieved in 76.92% of patients with mirabegron while all the patients treated with darifenacin were relieved of urge incontinence at 10 weeks of treatment without any relapse.

## CONCLUSION

It has been concluded that both mirabegron as well as Darifenacin are highly efficacious newer treatment options for the management of OAB. The once daily oral administration of both the drugs makes them a highly tolerable and compliant treatment modality. The relief of symptoms begins as early as 4 weeks gradually progressing and is retained with minimal relapses of the symptoms throughout the therapy. We found darifenacin to be relatively more efficacious in the treatment of OAB at a lesser dose and statistically significant differences were observed between the two drugs.

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