



## Original Article

# Effects of different urodynamic characteristics on therapeutic outcomes of overactive bladder medication in a real-life clinical practice

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## ABSTRACT

**Objective:** This study retrospectively investigated the influence of urodynamic parameters and patient characteristics on success rates among patients with overactive bladder (OAB) and urodynamic detrusor overactivity (DO). **Materials and Methods:** Consecutive patients with OAB and urodynamic DO initially received solifenacin, mirabegron, or combination of both for 1–3 months. If failed, patients were switched to another OAB medication subtype or provided additional OAB medication for a total of 6 months. A successful treatment was defined as an improvement in urgency severity and a global response assessment of  $\geq 1$ . Success rates after initial or modulated OAB medication were analyzed based on patient and urodynamic characteristics. **Results:** A total of 453 patients were enrolled, among whom 144, 255, and 54 received solifenacin, mirabegron, and combined medications, respectively. Among the patients, 259 (57.2%) had OAB dry and 194 (42.8%) had OAB wet. Patients receiving mirabegron alone had a significantly higher initial medication success rate compared to that of others. Patients with a phasic DO (50.7%), bladder outlet obstruction (BOO, 52.5%), and no central nervous system (CNS) lesions (47.5%) exhibited higher success rates than those with a terminal DO (42.0%), no BOO (42.7%), and CNS lesions (31.6%), respectively. After switching or modulating the initial OAB medication following treatment failure, 115 (62.2%) of 185 patients still showed improvement in OAB symptoms, with an overall success rate of 70.2% after 6 months of treatment. **Conclusion:** Initial solifenacin or mirabegron treatment had a success rate of around 50%. In general, patients with a phasic DO, urodynamic BOO, and no CNS lesions have higher success rates than those with a terminal DO, no BOO, and CNS lesions, respectively. Success rates can further be improved by switching or modulating OAB medication.

**KEYWORDS:** *Adverse events, Detrusor overactivity, Pharmacology, Treatment outcome*

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## INTRODUCTION

Overactive bladder syndrome (OAB) is defined as a group of symptoms involving urinary frequency and urgency with or without urgency urinary incontinence (UUI) [1]. Estimates have shown that OAB affects more than 400 million individuals worldwide [2] and around 16% of the adult population in the USA [3] and Europe [4]. Another study reported that 29.9% of adult men across 11 Asian countries exhibited OAB [5].

OAB treatment has been well documented in the American Urological Association (AUA) and European Urological Association (EAU) guidelines [6,7]. All guidelines recommend that patient education and lifestyle modulation should be the first-line treatment for OAB, while pharmacological treatment with oral antimuscarinics or beta-3

adrenoceptor agonists (mirabegron) should be the second-line therapy. Accordingly, patients whose OAB symptoms do not improve adequately after oral medication or those who have intolerable adverse drug events with one antimuscarinic agent should consider receiving a dosage modification, switching to a different antimuscarinic agent, or administering a beta-3 adrenoceptor agonist to achieve a successful outcome [8]. Although the efficacy of antimuscarinics and mirabegron has been considered equal, the 2017 EAU guidelines on urinary incontinence had recommended that mirabegron be used for patients with OAB who have inadequate response to conservative treatment [7].

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OAB had been initially characterized as a group of symptoms without definite etiology or underlying diseases [1]. However, OAB has been widely defined as a group of symptoms with varying etiologies, such as bladder outlet obstruction (BOO), neuropathy due to central nervous system (CNS) lesions (e.g., cerebral vascular accident [CVA], Parkinson's disease, and dementia), mixed intrinsic sphincter deficiency, or systemic diseases (e.g., diabetes mellitus, congestive heart failure, chronic kidney disease, and cardiovascular disease) [8]. Under this concept, OAB has usually been associated with urodynamic detrusor overactivity (DO). Patients with severe urgency or UII have a high prevalence of urodynamic DO, which may be associated with inadequate detrusor contractility (DHIC) [9]. Patients with OAB may develop urinary incontinence during the urge sensation (OAB wet) or only urgency without urinary incontinence (OAB dry).

In actual clinical practice, conservative treatment and initial OAB therapy may not provide symptom relief to all patients with OAB. As such, an increase in the antimuscarinic agent dosage and treatment duration, a shift to or addition of another antimuscarinic [10], a shift to mirabegron [11], a combination between mirabegron and an antimuscarinic agent [12], or the administration of botulinum toxin A injection [13] may be considered. However, higher antimuscarinic agent dosage or the combination of two or more OAB medications may increase adverse events and intolerability. Therefore, determining the underlying etiology and appropriate treatment for OAB is mandatory [7].

Given that urodynamic DO is highly prevalent among patients with OAB who have high urgency severity, urodynamic parameters and patient demographics might have an influence on treatment outcomes of OAB medication. Acceptingly, the current study retrospectively investigated the influence of urodynamic parameters and patient characteristics on therapeutic outcomes of patients with OAB who received OAB medication that was subsequently modulated after initial medication failure. The results presented herein can serve as a reference for urologists and general practitioners in the treatment of OAB.

## MATERIALS AND METHODS

From January 2017 to December 2018, all consecutive patients who experienced symptoms of urgency and frequency with or without UII were retrospectively enrolled in this study. Patients who had undergone video urodynamic study (VUDS) confirming urodynamic DO were specifically selected for analysis on the therapeutic efficacy of initial OAB medication and modulation to other OAB medications after initial medication failure to improve OAB symptoms. Patients should have received VUDS before or immediately after the initial medication had been provided. They should not have received any type of OAB medication 6 months before enrollment and should have undergone more than 6 months of continuous treatment. Some patients who had been treated with OAB medication but have discontinued the medication for more than 6 months were also enrolled. This study was approved by the Ethics Committee of the hospital (IRB:

104-15-B) who waived the need for informed consent due to the retrospective nature of the study.

OAB was defined based on the terminology of International Continence Society [1]. Urgency with or without UII was identified as the key symptom of OAB. Patients were then classified as OAB wet when they had at least one UII episode in their 3-day voiding diary and OAB dry when no UII episode occurred during the same 3 days. After confirmation of OAB, initial OAB medication, including antimuscarinics (e.g., solifenacin [5 mg QD]), mirabegron (50 mg QD), or a combination of solifenacin (5 mg) and mirabegron (25 mg QD), was prescribed for 1–3 months. Although the selection of OAB medications was not regular and rigid, some considerations were taken according to the incontinence guidelines of AUA and EAU [6,7]. For instance, male patients without previous prostate surgery or elderly men with moderate postvoid residual (PVR) usually received mirabegron as the initial medication, whereas women with severe UII and small bladder capacity usually received a combination of solifenacin and mirabegron.

Patients who received the initial OAB medication were followed up for therapeutic efficacy and adverse events at the outpatient clinic 1, 3, and 6 months after the initial treatment. Clinical efficacy was considered successful if their global response assessment (GRA, scoring from -3 to +3, indicating markedly worsened, -3 to markedly improved, +3) after medical treatment was  $\geq 1$ , including symptoms improved from UII to urgency, from urgency to frequency without urgency, or from any OAB symptom to symptom free. Patients whose OAB symptoms had improved continuously received the same OAB medication for up to 6 months. However, those who did not experience OAB symptom improvement after 1–3 months' treatment were considered to have failed initial medication and were switched to another mode of OAB medication, that is, from solifenacin to mirabegron (50 mg); from mirabegron to solifenacin; from combined OAB medication to mirabegron (50 mg) or solifenacin alone; or the addition of more than two OAB medications, such as tolterodine (detrusitol, 4 mg QD) or oxybutynin (5 mg TID), to solifenacin (5 mg QD) and mirabegron (50 mg). The mode of OAB medication was modulated after 1–3 months, while OAB medication was continued until 6 months (end of the study), after which treatment outcomes were assessed.

Patients with CNS lesions, such as CVA, Parkinson's disease, or early dementia, were identified. Those with enlarged prostates and voiding dysfunction besides OAB received an alpha-blocker with or without a 5-alpha reductase inhibitor at least 1 month before OAB therapy. All patients underwent VUDS for a definitive diagnosis of DO before or after initial medication. VUDS was performed in accordance with the recommendations of the International Continence Society [1]. Details regarding the VUDS had been well described and reported in a previous study [14]. Patients with equivocal pressure flow results were diagnosed with bladder outlet dysfunction based on the features of the bladder neck, prostatic urethra, and external sphincter during voiding cystourethrography [14]. Detrusor underactivity (DU) in patients

with DO was defined as DHIC, which was diagnosed according to the findings of characteristic low detrusor contractility, low  $Q_{max}$ , and large PVR, without bladder outlet narrowing during the voiding phase [1,14]. No patient had an active urinary tract infection during the VUDS.

Patients were then subgrouped according to their initial OAB medication prescription (solifenacin [5 mg QD], mirabegron [50 mg QD], or a combination of solifenacin [5 mg QD] and mirabegron [25 mg QD]), OAB subtype (OAB wet or dry), and mode of OAB medication modulation after the initial treatment failure. Categorical data were presented as numbers and percentages (%). Statistical comparisons between groups were conducted using the Chi-square test, with statistical significance being set at  $P < 0.05$ . All statistical analyses were performed using SPSS 15.0 statistical software (SPSS Inc., Chicago, IL, USA).

## RESULTS

A total of 453 consecutive patients (315 men and 138 women, mean age  $70.1 \pm 12.3$  years) whose chief complaint was urgency with or without UUI were enrolled. All patients had VUDS-confirmed DO and OAB for  $>3$  months and did not receive OAB medication or botulinum toxin A 6 months before study participation. Patient characteristics are summarized in Table 1. Urodynamic study revealed that among the included patients, 305 (67.3%) and 148 (32.7%) had terminal and phasic DO, respectively. Small cystometric bladder capacity (CBC) ( $<350$  mL) was noted in 383 (84.5%) patients and small PVR ( $<100$  mL) in 358 (79.0%) patients. DHIC was noted in 66 (14.6%) patients, BOO was diagnosed in 99 (21.9%) patients, and 76 (16.8%) patients had CNS lesions.

Patients were initially treated with solifenacin (5 mg QD) ( $n = 144$ , 31.8%), mirabegron (50 mg QD) ( $n = 255$ , 56.3%), and a combination of solifenacin (5 mg) and mirabegron (25 mg QD) ( $n = 54$ , 11.9%). The distribution of OAB medication among different patient characteristics was arbitrary with some concerns regarding OAB severity to avoid potential adverse events and achieve early successful treatment. A combination of solifenacin and mirabegron was usually prescribed to patients with severe UUI who had previously received OAB monotherapy but failed.

Among the included patients, 259 (57.2%) and 194 (42.8%) were classified as OAB dry and wet, respectively. Moreover, 203 (44.8%) patients, including 122 (47.1%) OAB dry and 81 (41.8%) OAB wet, exhibited successful initial OAB treatment. Accordingly, both OAB dry (53.7%) and OAB wet (51.3%) patients receiving mirabegron (50 mg QD) alone had significantly higher initial treatment success rates compared to those receiving solifenacin alone or a combination of solifenacin and mirabegron (25 mg) [Table 2].

Table 3 shows the success rates of initial OAB medication according to baseline patient and urodynamic characteristics. In general, patients with a phasic DO (50.7%), urodynamic BOO (52.5%), and no CNS lesions (47.5%) have higher success rates than those with a terminal DO (42.0%), no BOO (42.7%), and CNS lesions (31.6%), respectively.

A comparison of the success rates among different types of initial OAB medication according to urodynamic variables showed that mirabegron (50 mg QD) remained the best treatment for patients with OAB who had varying urodynamic variables.

After the initial OAB treatment for 1–3 months, 203 patients continued to receive the initial medication to maintain the improved bladder condition until the end of study, whereas 250 (55.2%) failed the initial medication and were advised to switch to another mode of medication. Among such patients, 65 (26%) did not change their mode of medication due to fear of adverse events, polypharmacy, or tolerable current bladder conditions. Table 4 shows the modes of OAB medication modulation after initial treatment failure. A total of 99 patients were switched to another type of OAB medication: 27 patients receiving a combination of solifenacin and mirabegron (25 mg) were switched to solifenacin alone or mirabegron (50 mg alone) and 60 patients receiving OAB monotherapy were prescribed two additional antimuscarinics and mirabegron (50 mg). Surprisingly, after switching from the initial OAB medication, 115 (62.2%) of the 185 patients still exhibited improvement in OAB symptoms. At the end of the study, 203 and 115 patients experienced successful treatment outcomes after initial OAB medication and modulation, respectively. The overall success rate of OAB medication was 70.2% after 6 months of treatment.

## DISCUSSION

The current study revealed the outcomes of oral OAB medications in actual clinical practice. Accordingly, the initial success rate of OAB medication was  $<50\%$  following 1–3 months of treatment. Patients with terminal DO, no BOO, and CNS lesions had lower success rates compared to those with phasic DO, urodynamic BOO, and no CNS lesions, respectively. However, after switching to other modes of OAB medication, 62.2% of the patients who failed after initial treatment still exhibited improvement in OAB symptoms, resulting in an overall success rate of 70.2% after 6 months of oral OAB pharmacotherapy. Our results showed that mirabegron (50 mg QD) seemed to have a better success rate in treating patients with OAB of any urodynamic subtype compared to the other modes of medication.

Antimuscarinics have been considered the first-line pharmacotherapy for OAB [15]. However, fewer than 25% of patients can continue antimuscarinic treatment for up to 1 year [16], with most exhibiting suboptimal responses and some experiencing adverse effects [17]. Mirabegron has been the first  $\beta_3$ -adrenoceptor agonist approved for the treatment of OAB [18]. Pooled data indicate that mirabegron had low rates of common adverse events associated with antimuscarinics [19]. A recent meta-analysis of several Phase III trials also confirmed the efficacy and safety of mirabegron for OAB treatment across various regions worldwide [20]. Currently, either antimuscarinics or mirabegron has been recommended as the first-line oral medication for OAB treatment [6,7], whereas a combination of antimuscarinics and mirabegron can provide additional benefit to patients with severe UUI [12].

**Table 1: Baseline demographics of patients with overactive bladder receiving different initial overactive bladder medications**

Patient characteristics	<i>n</i>	Solifenacin 5 mg QD ( <i>n</i> =144), <i>n</i> (%)	Mirabegron 50 mg QD ( <i>n</i> =255), <i>n</i> (%)	Solifenacin+mirabegron 25 mg ( <i>n</i> =54), <i>n</i> (%)	<i>P</i>
Gender					
Male	315	93 (64.6)	187 (73.3)	35 (64.8)	0.137
Female	138	51 (35.4)	68 (26.7)	19 (35.2)	
Age (years)					
<65	129	51 (35.4)	58 (22.7)	20 (37.0)	0.009
≥65	324	93 (64.6)	197 (77.3)	34 (63.0)	
DO					
Terminal	305	101 (70.1)	167 (65.5)	37 (68.5)	0.624
Phasic	148	43 (29.8)	88 (34.5)	17 (31.5)	
CBC (mL)					
<350	383	119 (82.6)	217 (85.1)	47 (87.0)	0.699
≥350	70	25 (17.4)	38 (14.9)	7 (13.0)	
Compliance					
<30	183	54 (37.5)	110 (43.1)	19 (35.2)	0.699
≥30	270	90 (62.5)	145 (56.9)	35 (64.8)	
PVR (mL)					
<100	358	118 (81.9)	194 (76.1)	46 (85.2)	0.191
≥100	95	26 (18.1)	61 (23.9)	8 (14.8)	
DHIC (DO+DU)					
Yes	66	16 (11.1)	41 (16.1)	9 (16.7)	0.360
No	387	128 (88.9)	214 (83.9)	45 (83.3)	
BOO					
Yes	99	26 (18.1)	69 (27.1)	4 (7.4)	0.003
No	354	118 (81.9)	186 (72.9)	50 (92.6)	
CNS lesion					
Yes	76	27 (18.8)	36 (14.1)	13 (24.1)	0.153
No	377	117 (81.3)	219 (85.9)	41 (75.9)	

BOO: Bladder outlet obstruction, CBC: Cystometric bladder capacity, CNS: Central nervous system, DHIC: Detrusor overactivity and inadequate contractility, DO: Detrusor overactivity, DU: Detrusor underactivity, PVR: Postvoid residual

**Table 2: Treatment outcomes of different initial overactive bladder medications among patients with overactive bladder dry or overactive bladder wet at baseline**

	<i>n</i>	Solifenacin 5 mg QD ( <i>n</i> =144), <i>n</i> (%)	Mirabegron 50 mg QD ( <i>n</i> =255), <i>n</i> (%)	Solifenacin+mirabegron 25 mg ( <i>n</i> =54), <i>n</i> (%)	<i>P</i>
OAB dry					
Success	122	20 (31.7)	95 (53.7)	7 (36.8)	0.007
Failure	137	43 (68.3)	82 (46.3)	12 (63.2)	
OAB wet					
Success	81	31 (38.3)	40 (51.3)	10 (28.6)	0.055
Failure	113	50 (61.7)	38 (48.7)	25 (71.4)	
Total					
Success	203	51 (35.4)	135 (52.9)	17 (31.5)	0.000
Failure	250	93 (64.6)	120 (47.1)	37 (68.5)	

OAB: Overactive bladder

The current study found that successful outcomes can be achieved in <50% of patients with OAB after initial medication. This is not surprising given that patients enrolled herein had urodynamic DO and had generally higher urgency severity. Our previous study had revealed that OAB wet was frequently associated with urodynamic DO [9]. OAB medication might not be capable of adequately relieving urgency symptoms after only 1–3 months of monotherapy. Considering that the present study enrolled only patients with OAB who had urodynamic DO, the treatment outcome may reflect the therapeutic effect of OAB medication on DO-induced UUI.

Our findings also showed that patients who received a combination of solifenacin and mirabegron (25 mg QD) as the initial medication had low success rates. However, most patients initially receiving combination OAB medication likely had very severe UUI, which might not be successfully treated with short-term pharmacotherapy. As such, longer treatment periods and larger dosages might improve treatment outcomes.

Interestingly, our results showed that initial treatment with mirabegron (50 mg) had significantly better success rates than that of solifenacin, not only in OAB wet but also in OAB dry.

**Table 3: Comparison of the success rates of the initial overactive bladder medication according to baseline urodynamic characteristics**

Patient variable	Success rate (%)	Solifenacin 5 mg QD (n=144), n (%)	Mirabegron 50 mg QD (n=255), n (%)	Solifenacin+mirabegron 25 mg (n=54), n (%)	P
DO					
Terminal	42.0	32/101 (31.7)	85/167 (50.9)	11/37 (29.7)	0.002
Phasic	50.7	19/43 (44.2)	50/88 (56.8)	6/17 (35.3)	0.160
CBC (mL)					
<350	44.9	42/119 (35.3)	115/217 (53.0)	15/47 (31.9)	0.001
≥350	44.3	9/25 (36.0)	20/38 (52.8)	2/7 (28.6)	0.291
Compliance					
<30	48.1	18/54 (33.3)	64/110 (58.2)	6/19 (31.6)	0.004
≥30	42.6	33/90 (36.7)	71/145 (49.0)	11/35 (31.4)	0.064
PVR (mL)					
<100	44.7	45/118 (38.1)	100/194 (51.5)	15/46 (32.6)	0.015
≥100	45.3	6/26 (23.1)	35/61 (57.4)	2/8 (25.0)	0.006
DHIC (DO+DU)					
Yes	43.9	3/16 (18.8)	24/41 (58.5)	2/9 (22.2)	0.009
No	45.0	48/128 (37.5)	111/214 (51.9)	15/45 (33.3)	0.009
BOO					
Yes	52.5	11/26 (42.3)	41/69 (59.4)	0/4 (0)	0.033
No	42.7	40/118 (33.9)	94/186 (50.5)	17/54 (34.0)	0.007
CNS lesion					
Yes	31.6	5/27 (18.5)	16/36 (44.4)	3/13 (23.1)	0.070
No	47.5	46/117 (39.3)	119/219 (54.3)	14/41 (34.1)	0.006

BOO: Bladder outlet obstruction, CBC: Cystometric bladder capacity, CNS, Central nervous system, DHIC: Detrusor overactivity and inadequate contractility, DO: Detrusor overactivity, DU: Detrusor underactivity, PVR: Postvoid residual

**Table 4: Treatment outcomes among patients with overactive bladder who failed the initial overactive bladder medication and switched to a different mode of medication\***

	Mode of switch of OAB medication	n	Successful, n (%)	Failure, n (%)	P
Switch OAB medication	From solifenacin to mirabegron 50 mg QD	5s1	28 (54.9)	23 (45.1)	0.181
	From mirabegron to solifenacin 5 mg QD	47	32 (68.1)	15 (31.9)	
Solifenacin 5 mg+mirabegron 25 mg	Switch to solifenacin 5 mg QD alone	11	6 (54.5)	5 (45.5)	0.084
	Switch to mirabegron 50 mg alone	16	14 (87.5)	2 (12.5)	
Add-on≥2 OAB medications	From solifenacin to add-on≥2 anti-M	27	14 (51.9)	13 (48.1)	0.357
	From mirabegron to add-on≥2 anti-M	33	21 (63.6)	12 (36.4)	
Total		185	115 (62.2)	70 (37.8)	

\*Excluding 65 patients who failed the initial medication but did not switch to other mode of treatment. Anti-M: antimuscarinic agent, OAB: Overactive bladder

We also noted the superiority of mirabegron over solifenacin among patients with terminal DO, lower bladder compliance, and small CBC. These results indicated that mirabegron might have an inhibitory effect on bladder contractions during the storage phase. Thus, patients with increased detrusor tonicity and were OAB dry can be effectively treated with mirabegron. Further study is mandatory to reveal this therapeutic mechanism.

A number of patients with BOO had urothelial dysfunction-related DO and increased bladder outlet resistance. Considering the results of a previous urodynamic study revealing that mirabegron therapy did not affect detrusor contractility, it is reasonable to consider mirabegron as the first-line therapy for patients with OAB due to BOO [21]. Current guidelines have suggested that antimuscarinic monotherapy can be used for men without BOO, whereas alpha-blocker and antimuscarinic combination therapy is usually prescribed for men with

concomitant BOO and OAB [22]. However, male patients with BOO may experience persistent OAB symptoms after OAB medical treatment; it is possible that bladder outlet conditions may not be relieved after short-term alpha-blocker therapy. Therefore, the combination of antimuscarinics and mirabegron together with longer alpha-blocker treatment durations is generally more effective than monotherapy. This study also demonstrated a 60% success rate among patients who received a combination of more than two OAB medications after having failed the initial OAB treatment, thereby suggesting that the combination of OAB medications can increase treatment success rates.

Patients with CNS lesion-related DO usually have terminal DO and coordinated sphincter function. These patients generally do not have phasic DO during bladder storage, while patients might not precisely feel the bladder fullness until the bladder capacity is reached where the uninhibited detrusor

contraction-associated UUI occurs. Therefore, antimuscarinics might not effectively reduce their UUI episodes. Mirabegron has been demonstrated as safe and effective in improving OAB symptoms without impairing voiding efficacy among this group of patients [23]. Moreover, cognitive dysfunction and impaired bladder emptying during treatment with non-selective antimuscarinics for OAB have become a growing concern [24]. Under such considerations, mirabegron seems to be a better OAB medication for the CNS lesion-related OAB.

Patients with DHIC or elderly individuals usually have low detrusor contractility, low  $Q_{max}$ , and large PVR. Antimuscarinic treatment among patients with DHIC might increase the risk for voiding dysfunction and large PVR, as well as subsequent urinary tract infection. Although antimuscarinics can decrease urgency sensation, the reduced detrusor contractility and increased PVR after treatment might not effectively decrease frequency episodes. Patients who do not experience satisfactory UUI symptom relief usually attribute the dissatisfaction to treatment failure. Although patients with DHIC may experience improved perception of bladder condition, voiding efficiency may still remain inadequate despite no increase in PVR after antimuscarinic treatment. Our recent study revealed that the use of mirabegron among elderly patients was safe and effective in improving OAB symptoms without increasing PVR [25]. Therefore, mirabegron may be considered the drug of choice for elderly patients with OAB.

Patients with OAB usually do not have high persistence rate and usually switch from one medication to another to improve therapeutic efficacy or reduce adverse events [26]. Solifenacin (5 mg QD) or the beta-3 adrenoceptor agonist mirabegron (50 mg QD) can be a feasible first-line medication for OAB treatment. Patients who demonstrated less favorable responses to solifenacin or mirabegron may experience improved success rates by switching to mirabegron or antimuscarinics, respectively. This result reflects the possibility for the multifactorial pathophysiology of OAB wherein different etiologies cause functional receptor alterations and consequent DO and urgency symptoms. One study showed that a small starting dose of mirabegron (25 mg) can be feasible for OAB [11]. However, patients with suboptimal responses to 25 mg of mirabegron may experience improved therapeutic efficacy by escalating to 50 mg of mirabegron or using combination with antimuscarinics. Interestingly, our results found that patients with OAB not responding to the combination of solifenacin and mirabegron (25 mg QD) can still experience improvement after switching back to mirabegron (50 mg QD) or solifenacin (5 mg QD) for longer periods. This suggests that a longer duration of pharmacotherapy is necessary prior to determining therapeutic outcomes.

There are some limitations of this study. First, in this study, we included only patients with urodynamic DO, but not patients with OAB. It might be difficult to translate the current result into clinical practice for the entire OAB population. Second, the treatment outcome was measured by GRA but not by an OAB questionnaire, therefore factors such as adverse events might interfere the true therapeutic effects of OAB medication in certain subtypes of OAB.

## CONCLUSION

The present study found that initial treatment with solifenacin or mirabegron had a success rate of around 50% in actual clinical practice involving the treatment of patients with OAB who had urodynamically confirmed DO. Our findings showed that mirabegron promoted better therapeutic efficacy compared to other modes of medication regardless of patient and urodynamic characteristics. In general, patients with a phasic DO, urodynamic BOO, and no CNS lesions have higher success rates than those with a terminal DO, no BOO, and CNS lesions, respectively. An overall success rate can be improved by treatment modulation if initial treatment fails.

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## Conflicts of interest

Dr. Hann-Chorng Kuo, an editorial board member at *Tzu Chi Med J*, had no role in the peer review process of or decision to publish this article. The other author declared no conflicts of interest in writing this paper.

## REFERENCES

- Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardization of terminology of lower urinary tract function: Report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn* 2002;21:167-78.
- Irwin DE, Kopp ZS, Agatep B, Milsom I, Abrams P. Worldwide prevalence estimates of lower urinary tract symptoms, overactive bladder, urinary incontinence and bladder outlet obstruction. *BJU Int* 2011;108:1132-8.
- Stewart WF, Van Rooyen JB, Cundiff GW, Abrams P, Herzog AR, Corey R, et al. Prevalence and burden of overactive bladder in the united states. *World J Urol* 2003;20:327-36.
- Milsom I, Abrams P, Cardozo L, Roberts RG, Thüroff J, Wein AJ, et al. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. *BJU Int* 2001;87:760-6.
- Moorthy P, Lapitan MC, Quek PL, Lim PH. Prevalence of overactive bladder in Asian men: An epidemiological survey. *BJU Int* 2004;93:528-31.
- Gormley EA, Lightner DJ, Faraday M, Vasavada SP, American Urological Association, Society of Urodynamics, Female Pelvic Medicine. et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. *J Urol* 2015;193:1572-80.
- 2017 EAU Guidelines on Urinary Incontinence. *European Association of Urology*; 2017. p. 147-74.
- Chiu AF, Liao CH, Wang CC, Wang JH, Tsai CH, Kuo HC, et al. High classification of chronic heart failure increases risk of overactive bladder syndrome and lower urinary tract symptoms. *Urology* 2012;79:260-5.
- Chung SD, Liao CH, Chen YC, Kuo HC. Urgency severity scale could predict urodynamic detrusor overactivity in patients with overactive bladder syndrome. *Neurourol Urodyn* 2011;30:1300-4.
- Wang CC, Jiang YH, Kuo HC. Efficacy and adherence of flexibly adding on a second antimuscarinic agent for patients with refractory overactive bladder. *Low Urin Tract Symptoms* 2017;9:27-32.
- Liao CH, Kuo HC. High satisfaction with direct switching from antimuscarinics to mirabegron in patients receiving stable antimuscarinic treatment. *Medicine (Baltimore)* 2016;95:e4962.

12. Abrams P, Kelleher C, Staskin D, Kay R, Martan A, Mincik I, et al. Combination treatment with mirabegron and solifenacin in patients with overactive bladder: Exploratory responder analyses of efficacy and evaluation of patient-reported outcomes from a randomized, double-blind, factorial, dose-ranging, phase II study (SYMPHONY). *World J Urol* 2017;35:827-38.
13. Apostolidis A, Averbeck MA, Sahai A, Rahnama'i MS, Anding R, Robinson D, et al. Can we create a valid treatment algorithm for patients with drug resistant overactive bladder (OAB) syndrome or detrusor overactivity (DO)? Results from a think tank (ICI-RS 2015). *Neurourol Urodyn* 2017;36:882-93.
14. Kuo HC. Videourodynamic analysis of pathophysiology of men with both storage and voiding lower urinary tract symptoms. *Urology* 2007;70:272-6.
15. Chapple CR. Muscarinic receptor antagonists in the treatment of overactive bladder. *Urology* 2000;55:33-46.
16. Sexton CC, Notte SM, Maroulis C, Dmochowski RR, Cardozo L, Subramanian D, et al. Persistence and adherence in the treatment of overactive bladder syndrome with anticholinergic therapy: A systematic review of the literature. *Int J Clin Pract* 2011;65:567-85.
17. Benner JS, Nichol MB, Rovner ES, Jumadilova Z, Alvir J, Hussein M, et al. Patient-reported reasons for discontinuing overactive bladder medication. *BJU Int* 2010;105:1276-82.
18. Igawa Y, Michel MC. Pharmacological profile of  $\beta_3$ -adrenoceptor agonists in clinical development for the treatment of overactive bladder syndrome. *Naunyn Schmiedebergs Arch Pharmacol* 2013;386:177-83.
19. Nitti VW, Khullar V, van Kerrebroeck P, Herschorn S, Cambronero J, Angulo JC, et al. Mirabegron for the treatment of overactive bladder: A prespecified pooled efficacy analysis and pooled safety analysis of three randomised, double-blind, placebo-controlled, phase III studies. *Int J Clin Pract* 2013;67:619-32.
20. Sebastianelli A, Russo GI, Kaplan SA, McVary KT, Moncada I, Gravas S, et al. Systematic review and meta-analysis on the efficacy and tolerability of mirabegron for the treatment of storage lower urinary tract symptoms/overactive bladder: Comparison with placebo and tolterodine. *Int J Urol* 2018;25:196-205.
21. Nitti VW, Rosenberg S, Mitcheson DH, He W, Fakhoury A, Martin NE. Urodynamics and safety of the  $\beta_3$ -adrenoceptor agonist mirabegron in males with lower urinary tract symptoms and bladder outlet obstruction. *J Urol* 2013;190:1320-7.
22. McVary KT, Roehrborn CG, Avins AL, Barry MJ, Bruskewitz RC, Donnell RF, et al. Update on AUA guideline on the management of benign prostatic hyperplasia. *J Urol* 2011;185:1793-803.
23. Chen SF, Kuo HC. Therapeutic efficacy of low dose (25 mg) mirabegron therapy for the patients with mild to moderate overactive bladder symptoms due to central nervous system diseases. *Low Urin Tract Symptoms* 2019;11:O53-8.
24. Kay GG, Abou-Donia MB, Messer WS Jr., Murphy DG, Tsao JW, Ouslander JG, et al. Antimuscarinic drugs for overactive bladder and their potential effects on cognitive function in older patients. *J Am Geriatr Soc* 2005;53:2195-201.
25. Lee YK, Kuo HC. Safety and therapeutic efficacy of mirabegron in very old patients with overactive bladder and multiple comorbidities. *Geriatr Gerontol Int* 2018;18:1330-3.
26. Chen HW, Chen YC, Wu WJ, Li CC, Chang YH, Geng JH, et al. Comparative persistence, switch rates, and predictors for discontinuation of antimuscarinics for overactive bladder: A 10-year nationwide population-based study in Taiwan. *Urol Sci* 2018;29:223-8.