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URODYNAMIC FINDINGS AFFECTING INITIAL MEDICAL TREATMENT OUTCOMES IN PATIENTS WITH OVERACTIVE BLADDER: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT **Introduction and Objective:** Treatment of overactive bladder is challenging due to its distressing symptoms and complications associated with medical management. This study aims to prospectively evaluate the effects of the various findings during urodynamic evaluation of overactive bladder (OAB) on success of initial medical management. **Methods:** Patients with OAB underwent urodynamic studies at index presentation and those with urodynamic detrusor overactivity (DO) were started on solifenacin, mirabegron, or combination of both for 1-3 months. Success of these drugs was evaluated using ICIQ OAB questionnaire and regression of symptoms and was according to bladder capacity, compliance, post void residue, and presence of phasic or terminal DO, DHIC, bladder outlet obstruction (BOO) and central nervous system (CNS) lesions. **Results:** Out of 150 patients, those with phasic DO (69%), BOO (67%) and no CNS lesions (62%) had higher success rates at follow-up. No significant difference in efficacy was noted between three types of drug therapy. **Conclusions:** Presence of terminal DO, absence of BOO and presence of CNS lesion have a negative correlation with success of initial OAB pharmacotherapy.

KEYWORDS : urodynamics, overactive bladder, pharmacotherapy, anticholinergics, mirabegron

INTRODUCTION

The International Continence Society (ICS) diagnoses overactive bladder (OAB) as "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence (UUI), in the absence of urinary tract infection (UTI) or other obvious pathology." [1] OAB and its associated symptoms are all associated with significantly decreased health-related quality of life. [2] The prevalence of OAB symptoms is 11.8% (10.8% in men and 12.8% in women) according to the EPIC study. [3] Diagnostic evaluation of OAB includes the use of a bladder diary and urodynamic testing. [4]

First-line therapy for this condition includes lifestyle changes such as fluid reduction, weight loss, caffeine reduction, and behavioral therapies such as pelvic floor muscle training and bladder training. [5] Patients who fail first-line therapy are usually switched to oral pharmacologic therapy that includes antimuscarinics and β3-adrenergic agonists (either as an alternative treatment or as combination therapy). [6] Antimuscarinics are associated with adverse effects such as dry mouth, constipation, cognitive effects, and visual disturbances, which can be dose-limiting and lead to noncompliance. [7]

Although the exact etiology of OAB is unknown, factors such as aging, bladder outlet obstruction (BOO), psychological, CNS, and systemic disorders are thought to play a role in pathogenesis. [8] Urodynamic studies help identify features commonly associated with the cardinal symptoms of OAB and may also reveal bladder outlet obstruction. These features include detrusor overactivity (DO), bladder conformity, the presence of detrusor hyperactivity with impaired contractility (DHIC), and post-void residual urine (PVR). [9] Urodynamic testing prior to initiation of OAB treatment has been associated with improved treatment satisfaction [10], but a clear improvement in outcomes has not been demonstrated. [11] A well-informed decision before starting treatment also helps in the prudent use of oral pharmacotherapy and limiting its adverse effects. Therefore, this study aims to prospectively evaluate the various urodynamic findings in the evaluation of OAB and their association with the initial results of medical treatment.

MATERIALS AND METHODS

The study was conducted at the Institute of Urology, Rajiv Gandhi Government General Hospital, Chennai, over an 18-month period from January 2021 to June 2022, after institutional ethics committee approval. Patients provisionally diagnosed with OAB based on clinical features underwent urodynamic testing at the start of the study. The urodynamic testing was performed according to ICS Good Urodynamic Practices. [11] Those who had urodynamic DO were included in the study. Patients with equivocal pressure flow results were diagnosed with bladder outlet dysfunction, which was clarified by further investigations using cystourethrography and cystoscopy, depending on suspicion. Detrusor underactivity (DU) in patients with DO was defined as DHIC diagnosed on the basis of findings of characteristic low detrusor contractility, low Qmax, and large PVR without narrowing of the bladder outlet during voiding. No patient had an active urinary tract infection during the study. Patients who had taken OAB medication within 6 months before the examination were excluded. CNS lesions and bladder outlet obstruction were documented.

Alpha blockers with or without 5-alpha reductase inhibitors started one month before OAB medication in male patients with BOO due to prostate enlargement. Patients were classified as dry or wet OAB according to the presence of UUI in their voiding diary. Initial OAB medication, including antimuscarinics, mirabegron, or their combination, was prescribed for 3 months depending on the severity of symptoms, concomitant diseases, and discretion of the treating physician. Patients who were not compliant were excluded.

Patients were followed up at 1and 3 months after initial treatment. Therapeutic efficacy and adverse events related to treatment were documented. ICIQ OAB questionnaire at baseline, 1 and 3 months was used to analyze treatment efficacy. [12] Treatment was considered successful there was a significant decrease in the ICIQ score (≥3) or if symptoms improved from UUI to urgency, from urgency to frequency without urgency, or from an OAB symptom to symptom-free.

Categorical data were expressed as numbers and percentages (%). Statistical comparisons between groups were performed with the chi-square test, with statistical significance set at $P < 0.05$. All statistical analyses were performed with SPSS 15.0 statistical software (SPSS Inc., Chicago, IL, USA).

RESULTS

Table 1: Demographic Characteristics Of Observed Oab Patients And Their Medications

	n	Solifenacin 5mg	Mirabegron 50mg	Solifenacin + Mirabegron	P
		n=57	n=66	n=27	
Gender					0.36
Male	84(56)	32(56.1)	40(60.6)	12(44.4)	
Female	66(44)	25(43.9)	26(39.4)	15(55.6)	
Age					0.02
<65	58(38.67)	30(52.6)	20(30.3)	8(29.6)	
≥65	92(61.33)	27(47.4)	46(69.7)	19(70.4)	

DO					0.2
Terminal	89(59.33)	39(68.4)	35(53.0)	15(55.6)	
Phasic	61(40.67)	18(31.6)	31(47.0)	12(44.4)	
Bladder capacity					0.01
<300ml	103 (68.67)	31(54.4)	51(77.3)	21(77.8)	
>300ml	47(31.33)	26(45.6)	15(22.7)	6(22.2)	
Compliance					0.001
<30	54(36)	17(29.8)	19(28.8)	18(66.7)	
>30	96(64)	40(70.2)	47(71.2)	9(33.3)	
PVR					0.14
<100ml	106 (70.67)	35(61.4)	51(77.3)	20(74.1)	
>100ml	44(29.33)	22(38.6)	15(22.7)	7(25.9)	
DHIC					0.007
Yes	28(18.67)	5(8.8)	13(12.1)	10(37.0)	
No	122 (81.33)	52(91.2)	53(80.3)	17(63.0)	
BOO					0.02
Yes	58(38.67)	28(49.1)	25(37.9)	5(18.5)	
No	92(61.33)	29(50.9)	41(62.1)	22(81.5)	
CNS lesion					0.22
Yes	45(30)	15(26.3)	26(39.4)	7(25.9)	
No	105(70)	42(73.7)	40(60.6)	20(74.1)	

In this study, a total of 150 patients (84 men and 66 women) were studied. This included all patients who presented with symptoms of OAB with urodynamic evidence of DO within the time frame of the study. The characteristics of the patients are summarized in Table-1. As indicated, 61.3% of the patients were in the older age group of ≥65 years. Detrusor overactivity on urodynamic evaluation was terminal in 59.3%, whereas it was phasic in the remaining 40.7%. Other features such as decreased bladder capacity (< 300ml), decreased compliance (<30), high PVR (> 100ml) were found in 68.9%, 36% and 70.7%, respectively. DHIC was noted in 18.7% of patients, while bladder outlet obstruction and CNS lesions were noted in 38.7% and 30% of cases, respectively.

The choice of drug for therapy was made taking into account the severity of symptoms and the ability of patients to tolerate adverse effects. Patients with severe UUI (22.7%) were started on combination therapy unless there was a contraindication. The drug distribution pattern is also shown in Table-1.

Table-2: Comparison Of Success Rates Of Initial OAB Medication According To Urodynamic Characteristics

Variable	Success rate(%)	Solifenacin 5mg	Mirabegron 50mg	Solifenacin + Mirabegron	P
Terrminal	40.45%	15/39(38.46)	15/35 (42.86)	6/15(40)	0.0006
CBC					0..87
<350	52.43%	15/31(48.39)	29/51 (56.86)	10/21(47.62)	
>350	51.06%	14/26(53.85)	7/15 (46.67)	3/6(50)	
Compliance					
<30	50.00%	7/17(41.18)	11/19 (57.89)	9/18(50)	0.71
>30	53.13%	22/40(55)	25/47 (53.19)	4/9(44.44)	
PVR					
<100ml	43.40%	17/35(48.57)	29/51 (56.86)	10/20(50)	0.75
>100ml	51.16%	12/22(54.55)	7/15 (46.67)	3/7(42.86)	
DHIC					
Yes	53.57%	3/5(66.67)	7/13 (53.85)	5/10(50)	0.8 5
No	51.64%	26/52(50)	29/53 (54.72)	8/17(47.06)	
BOO					0.003
Yes	67.24%	20/28(71.42)	16/25 (64)	3/5(60)	
No	42.39%	9/29(31.03)	20/41 (48.78)	10/22(45.45)	
CNS lesion					0.02
Yes	37.78%	4/15(26.67)	10/26 (38.46)	3/7(42.86)	
No	62.22%	25/42(59.52)	26/40(65)	10/20(50)	

After three months, patients were reassessed and classified into treatment success or failure based on the criteria described previously. The distribution of success rates among the different patient characteristics is shown in Table-2. Success rates were analyzed separately for each of the characteristics studied, and the P -value was calculated using the chi-square test.

The overall success rate for the initial treatment was 52%. There was no statistically significant difference between success rates with either drug or their combination. It was found that phasic DO (68.9%), the presence of BOO (67.3%), and the absence of a CNS lesion (62.2%) were associated with significantly higher initial treatment success rates, regardless of the treatment method used.

DISCUSSION

The aim of our study was to evaluate the characteristics that influence the outcomes of initial therapy in OAB patients. In this regard, the overall success rate was just above 50%. This could be due to a number of reasons, including the selection of patients who only have urodynamic DO, in whom symptoms are generally more severe. [9] Nevertheless, there were no significant differences in the success rate of the three types of treatment offered.

The factors that significantly decreased the success of initial treatment were terminal DO, absence of BOO, and presence of CNS lesions. These results are consistent with a retrospective study by Wang et al. in 2022 that showed similar results, in which they also compared the three drug modalities after switching drugs after three months if they were ineffective and further compared their efficacy. They also compared dry and wet OAB for each drug and showed the superiority of mirabegron. [13]

Terminal DO occurs when the bladder volume approaches its maximum capacity. This volume dependent change is thought to be less responsive to pharmacotherapy as the functional bladder capacity is reported to be lower in these patients as reported by Valentini et al. [14] Also there is a higher association of terminal DO with history of neurological diseases. This may suggest that higher neuronal pathways play a role in the pathophysiology of terminal DO which cannot be completely opposed by the current line of drugs, leading to inadequate treatment response.

Bladder outlet obstruction presents with a dilemma as alpha-blocker therapy alone at times helps in alleviating storage LUTS in a section of cases. Reportedly, 40% cases show no improvement in OAB despite resolution of obstruction. [15] Abrams et al proposed denervation due ischemia, physiological changes in the bladder wall, and neural control of bladder contraction induced by BOO as possible mechanisms of OAB in these cases. [16] Studies evaluating anticholinergic and beta 3 agonist (mirabegron) therapies have shown that both can be safely administered in men with BOO and OAB without negative effects on voiding or urodynamic pressures. [17]

None of the three treatment modalities showed any significant statistical superiority over another. Even though antimuscarinics are considered first-line therapy, many patients are unable to tolerate their adverse effect profile. Mirabegron as first-line therapy in patients at high risk of these adverse effects is definitely worth considering. Dual pharmacotherapy as initial treatment has shown to be of considerable efficacy and selective usage in severe cases is warranted. [4]

Limitations of this study include the selection of patients with urodynamic DO alone which does not extend its validity to clinically diagnosed OAB. Also a longer follow-up period is needed further substantiate of effect of the above risk factors on the success of various treatments.

CONCLUSIONS

In patients having urodynamic DO, presence of terminal DO, absence of BOO and presence of CNS lesion have a statistically significant negative correlation with success of initial OAB pharmacotherapy irrespective of the drug or combination used.

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