

Correlation between Clinical and Urodynamic Improvement in Patients with Overactive Bladder Syndrome on Anticholinergic Drugs

Mahmoud Ezzat Ibrahim, Ahmed Mohamed Tawfeek, Sherief Saad Mohamed *

Urology Department, Faculty of Medicine, Ain Shams University

*Corresponding Author: Sherief Saad Mohamed; Email:ahsd0307@gmail.com

ABSTRACT

Background: the International Continence Society (ICS) defined overactive bladder syndrome (OAB) as urinary urgency with or without urge incontinence, often accompanied by frequency and nocturia in absence of infection. Urinary urgency is the complaint of a sudden compelling desire to void which is difficult to defer with patients often suffering from anxiety due to fear of leakage. Urge urinary incontinence is defined as involuntary leakage of urine, accompanied or immediately preceded by urgency. Overactive bladder syndrome is a symptomatic diagnosis. On the other hand, detrusor overactivity (DO) is an urodynamic finding, characterized by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked. These terms aren't interchangeable, as overactive bladder syndrome patients may not have detrusor activity on urodynamic testing.

Aim of the Work: to determine the relation between clinical improvement and urodynamic based improvement in patients with overactive bladder syndrome receiving anticholinergic drugs.

Patients and Methods: this study included thirty eight patients, who presented to the Outpatient Urology Clinic at Ahmed Maher Teaching Hospital with symptoms of OAB syndrome. This study design was prospective. Patients clinical histories were taken, they were examined thoroughly, and completed an IPSS questionnaire. This was followed by a urinalysis, free uroflowmetry and a pelvi-abdominal ultrasound.

Results: this study included thirty eight patients who were divided into two groups. Group A included twenty one patients, fifteen females and six males with mean age of 48.2 years old (21-60), who did not have detrusor overactivity in the first urodynamic study. On the other hand, group B included seventeen patients, ten females and seven males with mean age of 43.7 years old (18-58), who had detrusor overactivity in the initial urodynamic study. Patients in both groups received Solifenacin 10 mg once daily for twelve weeks before completing another IPSS questionnaire and undergoing a follow up urodynamic study.

Conclusion: in this study, we concluded that there was strong correlation between urodynamic and clinical improvement in OAB patients after Solifenacin treatment as patients who were improved urodynamically reported improvement of their symptoms while those with poor urodynamic response reported that their symptoms were either the same as before treatment or worse. We also concluded that Solifenacin 10 mg once daily led to significant improvement in IPSS results of OAB patients with significant increase in volume to first desire and maximum cystometric capacity.

Keywords: Urodynamic Improvement, Overactive Bladder Syndrome, Anticholinergic Drugs.

INTRODUCTION

The International Continence Society (ICS) defined overactive bladder syndrome (OAB) as urinary urgency with or without urge incontinence, often accompanied by frequency and nocturia in absence of infection. Urinary urgency is the complaint of a sudden compelling desire to void which is difficult to defer with patients often suffering from anxiety due to fear of leakage. Urge urinary incontinence is defined as involuntary leakage of urine, accompanied or immediately preceded by urgency ^[1]. Overactive bladder syndrome is a symptomatic diagnosis. On the other hand, detrusor overactivity (DO) is an urodynamic finding, characterized by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked. These terms aren't interchangeable, as overactive bladder syndrome patients may not have detrusor activity on urodynamic testing ^[2]. The National

Overactive Bladder Evaluation (NOBLE) program was developed to estimate the prevalence of OAB and its burden in the United States, assess the influence of sex on OAB and its symptoms and determine the impact of OAB on quality of life, sleep, and general mental health. 5,204 participants completed the study that showed an overall OAB prevalence of ~16% with no significant differences between the two sexes. (16% in men, 16.9% in women) ^[3]. The study demonstrated that OAB without urge incontinence (OAB dry) was more common in men than in women. OAB with urge incontinence (OAB wet) increased with age in both sexes, increasing from 2% to 19% in women after the age of 44 years and from 0.3% to 9% in men with a marked increase after 64 years. While the prevalence of OAB with and without urge incontinence in women was similar (9.3% and 7.6%), in men the prevalence of OAB wet (2.6%) was much lower than the prevalence of OAB dry (13.4%) ^[3]. The difference

between males and females in urge incontinence could be attributed to the anatomical and physiological differences in urinary continence mechanisms such as a shorter female urethra and the effect of pregnancy and vaginal delivery on the pelvic floor ^[4]. It also revealed that men and women with OAB had clinically and statistically significant lower quality of life and poorer quality of sleep than did controls after adjusting for co morbid illnesses ^[5]. An online survey of US women with OAB, 39 % reported that OAB interfered with daily activities, with 12% staying at home because of their symptoms; 38 % reported decreased physical activities, while 34 % attributed weight gain to OAB because of an inability to exercise. Women with OAB were also significantly more likely than those without OAB to report disturbed sleep, decreased self-esteem, decreased sexuality, and feelings of overall declining health ^[6]. An important public health consideration of OAB is the gap between the onset of symptoms and seeking and receiving treatment for symptoms as few individuals who have OAB seek care. In fact, OAB patients often delay seeking treatment or even discussing their symptoms with healthcare providers. A study found that women who had discussed OAB symptoms with a care provider had waited on average 3.1 years after the onset of symptoms with increased symptom severity as the driving force for patients to seek treatment ^[7]. OAB not only diminish overall quality of life, but also create additional health problems for patients. These include an increased risk of falls and fractures, urinary tract infections, sleep disturbances, and depression ^[8]. Some studies have identified urinary urgency and urge incontinence as risk factors for recurrent falls and fractures in the elderly. A study established that the odds ratio of a hip fracture in urinary-incontinent elderly women was twice that in the general population while women suffering from urge incontinence once weekly had a 26% greater risk of sustaining a fall and a 34% greater risk of fracture. When incontinence occurred daily, these risks increased to 35% and 45%, respectively ^[9]. The economic burden of any disease is determined by direct costs, indirect costs, and intangible costs. Direct costs include routine care, treatment and diagnostic costs. Indirect costs are those suffered from lost wages to patients and

caregivers and lost productivity as a result of morbidity. Intangible costs consist of the value of pain and the decreased quality of life associated with an illness. The total national costs of OAB in the U.S are estimated to be \$12 billion with 9 billion more as an indirect cost ^[10]. Anti muscarinic drugs represent the cornerstone of medical treatment of OAB. They offer significant improvements in patients' symptoms and quality of life. They are generally well tolerated with predictable side effects. They exert their action through inhibiting acetylcholine, which stimulates detrusor contraction via muscarinic receptors. They vary according to receptor selectivity and adverse effects ^[11]. Solifenacin succinate is a once-daily, oral antimuscarinic agent with two dosage forms, 5mg and 10mg. it showed significant reduction in symptoms of OAB (urgency, incontinence, and frequency), and was associated with a favorable tolerability profile ^[12].

AIM OF THE WORK

To determine the relation between clinical improvement and urodynamic based improvement in patients with overactive bladder syndrome receiving anticholinergic drugs.

PATIENTS AND METHODS

This study included thirty eight patients, who presented to the Outpatient Urology Clinic at Ahmed Maher Teaching Hospital with symptoms of OAB syndrome. **The study was approved by the Ethics Board of Ain Shams University and an informed written consent was taken from each participant in the study.** **Inclusion criteria:** Patients aged between 18 - 60 years old, patients who their IPSS results were moderate to severe. (Eight or more). **Exclusion criteria:** patients with maximum flow rate less than 15 ml/s on free flowmetry, patients with pyuria (pus cells >5 WBCs / HPF) whose symptoms improved after receiving appropriate medications, patients with history of neurological disease, neurological surgery or abnormal neurological finding during examination, patient who are under medical treatment for BPH, patients who suffer from bladder lithiasis, patients with history of bladder tumors, patients with OAB symptoms and mild IPSS score (Seven or less). **Methodology:** This study design was prospective. It included thirty eight patients. Patients who were complaining from OAB symptoms had their clinical history taken, were examined thoroughly, and completed an IPSS

questionnaire. This was followed by a urinalysis, free uroflowmetry and a pelvi-abdominal ultrasound. Those who met the aforementioned criteria were enrolled in the study after informing them of the nature and purpose of the study and obtaining their consent. They underwent an urodynamic study using a 7f double lumen urethral catheter in a seated position. Filling was done by room temperature normal saline. The starting filling rate was 10 ml/min and increased gradually to 40 ml/min. Patients were divided into two groups. Group A included patients without detrusor overactivity on urodynamic study while group B included those suffering from detrusor overactivity (DO was defined as uninhibited detrusor contractions during filling phase that had any of the following criteria : amplitude more than 10 cm h₂O, associated with discomfort or led to leakage). Afterwards Solifenacin 10 mg once daily was prescribed for patients and another urodynamic study scheduled three months later. Before the second urodynamic study, patients were asked to complete an IPSS questionnaire and repeat the urinalysis to exclude infection. After the second study, data regarding changes in IPSS results, urge urinary incontinence, volume to first desire, maximum bladder capacity, PVR and drug side effects was collected. Comparison between the two groups was done regarding initial IPSS results, improvement in IPSS results after treatment, number of patients with urge urinary incontinence, changes in urodynamic findings after treatment and drug related side effects.

Statistical analysis: Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23 (SPSS Inc., 2017 South Wacker Drive, Chicago, USA). The quantitative data were presented as mean plus or minus standard deviations (SD) and ranges when their distribution found parametric. Also qualitative data were presented as number and percentages.

RESULTS

Table (1): Showing the demographics of the patients included in the study.

		Group A No.= 21	Group B No.= 17
Sex	Male	6 (28.6%)	7 (41.2%)
	Female	15 (71.4%)	10 (58.8%)
Age	Mean	48.2	43.7

Comparison between group A and group B regarding sex and age.

Table (2): Showing the results in group A before and after treatment

		Group A		Difference	Test value	P-value
		Before	After			
IPSS results	Mean	15.3	9.7	-5.6	-6.108	< 0.001
Volume to first desire	Mean	180	260	+80	11.06	< 0.001
Maximum capacity	Mean	400	460	+60	7.153	< 0.001
PVR	Mean	20	40	+20	0.067	0.796

Comparison between before and after in group A regarding IPSS results, Volume to first desire, maximum capacity and PVR showing improvement in IPSS and increase in all urodynamic parameters after treatment.

Table (3): Showing the results in group B before and after treatment

		Group B		Difference	Test value	P-value
		Before	After			
IPSS results	Mean	20.7	13.8	-6.9	-5.651	< 0.001
Number of patients with urge urinary incontinence		2 (11.8%)	1 (5.9%)		0.366	0.545
Volume to first desire	Mean	150	240	+90	12.043	< 0.001
Maximum capacity	Mean	280	370	+90	7.730	< 0.001
PVR	Mean	30	50	+20	-0.614	0.543

Comparison between before and after in group B regarding IPSS results, Number of patients with urge urinary incontinence, Volume to first desire, maximum capacity and PVR showing improvement in IPSS and increase in all urodynamic parameters after treatment.

Table (4): Comparing the percentage of change in group A and group B

Mean % change	Group A	Group B	Test value	P-value
IPSS results	-36.60	-33.33	0.859	0.596
Volume to first desire	44.44	60.00	2.028	0.051
Maximum capacity	15.00	32.1	7.045	0.0001

The volume to first desire and maximum cystometric capacity significantly increased more in group B with insignificant difference between the two groups in IPSS results denoting that group B patients had more improvement in their urodynamic parameters although both groups had a similar improvement in IPSS results.

DISCUSSION

Overactive bladder (OAB) is a common condition that affects both physical and mental health, with symptoms such as sleep disturbance, fall-related injuries, depression and lower quality of life. OAB patients are more likely to limit social outings, physical activity, and participation in social events^[13]. The annual direct costs of OAB in the US – including diagnostic tests, physician visits, medications, treatment procedures, and supplies such as pads, diapers, and home care – total over \$12 billion. This estimated cost is comparable to the annual costs of breast cancer (\$12.7 billion)^[14]. Anti-muscarinics are the mainstay of treatment of OAB syndrome. They relieve patients' symptoms and improve their quality of life. Solifenacin is a once daily anti-muscarinic that has more selectivity on detrusor M3 receptors than older anti-muscarinics resulting in fewer side effects, so it is associated with better compliance^[15]. Our study aimed to determine the relation between urodynamic findings and clinical improvement in OAB patients after Solifenacin 10 mg once daily for 12 weeks. **Hsiao et al.** used Solifenacin 5 mg once daily for 12 weeks on 648 OAB patients in order to find the patients' factors associated with better therapeutic outcome. They found that Female gender, high urgency severity score, high Q max, and low PVR were associated with better response to Solifenacin^[16]. In our work, we assessed the outcome of Solifenacin 10 mg once daily for 12 weeks on thirty eight OAB patients clinically and urodynamically. There was significant decrease in IPSS results after treatment in both groups. In group A, three patients had the same IPSS after treatment and one reported a higher IPSS while all the other patients had a lower IPSS. In group B, all patients had a better IPSS except three patients two of them had a higher IPSS, high amplitude uninhibited detrusor contractions and diminished volume to first desire and maximum bladder capacity. The other patient had the same IPSS as before treatment despite

having improved urodynamic parameters. Burger et al. measured the improvement in IPSS in 799 OAB patients after administering solifenacin 5 or 10 mg for 12 weeks according to severity of symptoms. There was significant decrease in IPSS results after treatment with 20.4% reporting severe IPSS results (> 20) before treatment reduced to 2.3% after treatment^[17]. In our study, the follow up urodynamic study showed significant increase in the volume to the first desire ($P < 0.001$) in both groups. **Schiavi et al.** used Solifenacin 5mg on 168 OAB patients for 12 weeks and found significant increase in the volume to first desire ($P < 0.0001$)^[18]. On the contrary, **Kosilov et al.** found a significant increase in PVR after Solifenacin 10 mg administration in 52 patients for six weeks but the average age of the patients was 71.2 years old suggesting that the effect of Solifenacin on PVR is related to patient's age^[19]. Multiple reported side effects including dry mouth, constipation and blurred vision. The most common and the most annoying side effect was dry mouth. In group A, 33.3% of patients complained of dry mouth while 29.4% of group B patients had the same complaint. **Schiavi et al.** found the percentage of DO cure after treatment to be 77.5%, while **Vecchioli et al.** found it 40%^[18, 20]. In this study, we found that OAB patients who had DO on their urodynamic studies had more increase in their volume to first desire and maximum capacity after Solifenacin treatment than patients without DO, although there was no statistically significant difference in IPSS results. The AUA guidelines in 2012 stated that Urodynamics should not be used in the initial workup of the uncomplicated OAB patient. This was agreed upon by **Abrams et al.**, **Ruffion et al.** and **Marinkovic et al.** who found that urodynamic study is indicated after failure of conservative and drug therapy to manage OAB symptoms^[21, 22, 23]. On the other side, **Vecchioli et al.** suggested that it is important to conduct an urodynamic study in patients with OAB, while **Naranjo-ortiz et al.** recommended performing initial urodynamic study for OAB wet patients. **Rovner et al.** suggested doing urodynamic study before starting treatment in OAB patients with neurogenic lesions, history of prior LUT surgery, concomitant bladder outlet obstruction, high PVR, mixed urinary incontinence and after failure of medical treatment^[24, 25, 26]. In this study, there was significant improvement in IPSS results in both groups associated with

significant increase in volume to first desire and maximum bladder capacity, while those patients who reported a higher IPSS after treatment had the same urodynamic parameters or worse denoting strong correlation between clinical and urodynamic improvement in OAB patients.

CONCLUSION

In this study, we concluded that there was strong correlation between urodynamic and clinical improvement in OAB patients after Solifenacin treatment as patients who were improved urodynamically reported improvement of their symptoms while those with poor urodynamic response reported that their symptoms were either the same as before treatment or worse. We also concluded that Solifenacin 10 mg once daily led to significant improvement in IPSS results of OAB patients with significant increase in volume to first desire and maximum cystometric capacity. The effect of Solifenacin on PVR was insignificant and probably related to age. Dry mouth was the most reported side effect. This study added to the available evidence that urodynamic studies is not indicated in the initial management of OAB patients as there was no significant difference between improvements in IPSS results in OAB patients with/without detrusor overactivity. Urodynamic study should be reserved for patients with poor response to medical treatment and neurologic patients.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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