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An overview of overactive bladder

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ABSTRACT

Overactive bladder (OAB) is a common multifactorial disease that can cause a burden to the patient. Despite being a symptomatic diagnosis, several urological examinations need to be done to rule out other possible causes. The management of OAB is specific to each individual, from the very first line of behavioral therapy to surgical for an extremely rare case of OAB. This overview will look out for OAB thoroughly from the epidemiological burden, pathophysiology, clinical presentation and diagnosis, and the current treatment of OAB.

Keywords: Overactive Bladder, Urinary Incontinence, Urodynamics.
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INTRODUCTION

Overactive bladder (OAB) is defined by the International Continence Society (ICS) as a syndrome of urinary urgency, usually accompanied by frequency and nocturia, with or without the presence of urgency incontinence, in the absence of urinary tract infection (UTI) or other obvious pathology.[1] A prevalence study estimated over 455 million individuals aged ≥20 years experienced OAB, with that Asia as the highest, followed by Europe, Africa, North America, and South America.[2] Two questionnaire-based surveys were conducted to analyze the numbers of men and women affected by OAB in Asia. Among Asian women, the prevalence of OAB was 53.1%, while Asian men were 29.9%.[3,4] A burden-of-illness study showed the economic burden of OAB worldwide is estimated at 65.9 billion USD, and the number varies amongst countries. In the United States, the estimation of mean annual OAB-specific costs ranged between 655 and 860 USD per patient. In Spain, the cost estimated at 492 USD, and 1237 USD in Italy.[5]

PATHOPHYSIOLOGY OF OVERACTIVE BLADDER

The etiology of OAB is still unclear. However, current literature suggests seeing OAB as a multifactorial symptom syndrome caused by several pathophysiological mechanisms. Several hypotheses propose the cause of OAB, which are a myogenic factor, neurogenic factor, and urotheliogenic factors.[6]

Myogenic Factor

An early study by Brading suggests that an abnormal electrical coupling in detrusor smooth muscle can stimulate involuntary contraction. This unstable electrical coupling spread through the bladder wall, increasing unstable pressure inside. This event is a result of a histological change of the detrusor smooth muscle.[7]

Neurogenic Factor

A disturbance to the central inhibitory pathway in the central nervous system or an increased sensitization of peripheral afferent terminal in the bladder will result in detrusor overactivity. Patient with central nervous system diseases such as Parkinson's Disease, cerebrovascular event, and multiple sclerosis had been shown to experience OAB symptoms. The involvement of unmyelinated C-fibers of the bladder neurons can trigger detrusor overactivity in a patient with bladder ischemia resulting from severe obstruction or peripheral vascular disease affecting the bladder.[7]

Urotheliogenic Factor

In a normal bladder, a release of Acetylcholine (Ach) from the parasympathetic nerve to the bladder can activate the muscarinic receptor (M_2 and M_3) that can trigger bladder contraction. A recent study also describes that urothelium can also produce Ach by itself. In urothelium, hypotheses suggest that there is increased production of Ach in the bladder and the muscarinic receptor expression in the pathological state. This mechanism believed to be the main underlying pathophysiology of OAB.[7]

CLINICAL PRESENTATION AND DIAGNOSIS

Patients with OAB generally complain of symptoms of urinary frequency, both daytime and night, and urgency, with or without urgency incontinence. The diagnosis of OAB is generally made based on patient symptoms. The use of bladder diaries that document the

intake and voiding behavior may helpful for both patient and clinician. Several questionnaires, such as Urogenital Distress Inventory (UDI), the Incontinence Impact Questionnaire (II-Q), and the Overactive Bladder Questionnaire (OAB-q) have been made to validate OAB symptoms.[8]

Despite being a symptomatic diagnosis, several diagnostic assessments should be carried out. A urine examination should be carried out to rule the lower urinary tract. Urine culture is unnecessary unless there is an indication of infection. In a complicated and refractory OAB, the clinician can do urodynamics, cystoscopy, and ultrasound examination to exclude other possible causes of the symptoms.[9]

TREATMENT

Behavioral Therapies

The first line of intervention for OAB is behavioral treatment. The first is weight loss, which is proved to be effective in several studies at managing OAB symptoms. Additionally, patient education regarding fluid intake and caffeine consumption, pelvic floor muscle training (PFMT) and bladder training programs.[10,11] The bladder training programs includes scheduled voiding and way to increase the interval between voiding episodes. This approach is considered first-line by The American Urological Association because of its effectiveness in reducing symptom levels compared to pharmacological medications. It can also be modified to meet each patient's needs and capacities.[11]

Pharmacological Therapies

Anti-muscarinic

Anti-muscarinic drugs are widely used for urinary incontinence (UI) treatment. A systematic review and meta-analysis of six different anti-muscarinic drugs (trospium, tolterodine, fesoterodine, oxybutynin, solifenacin, and propiverine) showed a significantly higher chance a return to continence and a reduction of incontinence episode compared to placebo. Based on The European Association of Urology, there is no superiority between anti-muscarinic drugs on relieving OAB symptoms on the patient and on improving quality of life (QoL). An individualized approach considering the patient's medical history has to be noted to achieve an optimum result.[12]

The common adverse effect of anti-muscarinic treatment is dry mouth. Some patients also experience constipation, blurred vision, and fatigue. Some of them also have long-term cognitive dysfunction and dementia related to anti-muscarinic action to the central nervous system.[9] Recent prospective cohort study revealed that prolonged use of Oxybutynin could cause cognitive deterioration in elderly patients.[12] The clinician has to be very careful in prescribing anti-muscarinic drugs, especially in the elderly with reduced cognitive function.

Mirabegron

In 2013, mirabegron was introduced commercially as the first available β3-agonist for OAB management. Stimulation of β3-adrenoceptors in detrusor smooth muscle cells can cause detrusor relaxation.[13] Several studies have evaluated mirabegron's efficacy and safety profile. In previous Phase III trials, mirabegron significantly decreased voiding frequency per day and an episode of incontinence compared to placebo, at a dose of 50 mg and 100 mg once daily.[8]

The most common adverse events of mirabegron are hypertension, nasopharyngitis, and UTI. Some patients receiving mirabegron also experienced dry mouth. However, it is significantly lower compared to anti-muscarinic drugs. There were also minor reports of cardiac arrhythmia that happens in a 12-months mirabegron used. However, this event is dose-dependent, relatively low, and comparable to placebo.[8]

Mirabegron can also be used as a combination therapy with anti-muscarinic drugs. The SYNERGY trial showed that there was a significantly reduce incontinence episode per day in combination therapy compared to monotherapy/placebo.[13]

Intradetrusor Botulinum Toxin A (BTX-A) therapy

A recent meta-analysis of randomized controlled trials of BTX-A analyzed five dosage groups of BTX-A (50U, 100U, 150U, 200U, and 300U) compared to placebo for managing OAB. The 300U and 200U BTX-A showed a short-term (2 to 12 weeks) positive result on the management of urinary incontinence. However, BTX-A dose of 300 U showed no superiority to 200 U with increased BTX-A associated adverse events (urinary retention, urinary tract infection, hematuria, and muscle weakness). Therefore, BTX-A 300U is not recommended. The study also found that BTX-A with a dose higher than 50U showed a significant improvement of the symptom of OAB in 12 to 36 weeks compared to placebo.[14]

Neuromodulation

There are two neuromodulation techniques that can be chosen for OAB based on AUA/SUFU Guideline, percutaneous posterior tibial nerve stimulation (PTNS) and sacral neuromodulation (SNM).[11]

The posterior tibial nerve is stimulated by inserting a 34-gauge needle connected with an electrode 4-5 cephalad to the medial malleolus. After that, an electrical current with a frequency of 200hz is introduced through the needle for 200 Us. The flexion movement of the big toe or other toes indicates the correct positioning of the needle.[15]

A systematic review of four RCTs analyzing the efficacy of PTNS compared to Placebo, tolterodine, sham stimulation, and vaginal electrical stimulation. The result showed that PTNS improvement rate higher than Placebo, Tolterodine, Sham, and vaginal electrical stimulation. The long-term efficacy of PTNS was assessed in several retrospectives, and prospective studies showed PTNS improve not only symptoms but also QoL and cost-effectiveness.[16]

In SNM, the electrodes are placed at the same level as the third sacral nerve (S3) and connected to an implanted electrical stimulator. The device will trigger the sacral nerve that stimulates the bladder, sphincter of the urethra, and the muscle of the pelvic floor. The clinician should do a screening test to see the clinical effect of sacral nerve stimulation before doing SNM. The screening can be done by doing either one-stage stimulation or two-stage stimulation. However, several previous RCTs showed that two-stage stimulation has a higher success rate.[17]

A prospective 6-month, randomized multicenter trial comparing SNM with

standard medical therapy (SMT) for OAB patients with mild to moderate symptoms revealed the superiority of SNM with InterStim therapy over SMT.[18] The ROSETTA trial was one of the studies that compared SNM with BTX-A. The BTX-A was slightly better than SNM in reducing urgency incontinence. However, the difference was not clinically meaningful. The use of BTX-A also associated with higher UTI than SNM.[16]

Surgical Therapy

The surgical methods that can be used are augmentation cystoplasty and urinary diversion. Because of the high risk of this approach, surgical treatment only appropriate for an extremely rare case of OAB.[11]

CONCLUSION

Overactive Bladder is a common multifactorial symptom syndrome with unclear etiology that posed burden to the patient's quality of life. The OAB diagnosis is based on clinical symptoms. However, the clinician has to exclude the possible causes with several urological examinations. The management of OAB is personalized, which include behavioral therapy, pharmacological therapy, and invasive treatment including neuromodulation and surgical techniques.

CONFLICT OF INTEREST

None to Declare.

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AUTHOR CONTRIBUTION

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