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Review Article

Overactive Bladder: Causes, Investigations and Management

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Abstract

An overview of the symptoms, diagnosis and management for overactive bladder syndrome in the female population. Identify the symptoms, risk factors, diagnosis and the different strategies for management of OAB bladder syndrome and provide professional advice in overactive bladder syndrome.

Keywords: Overactive Bladder Syndrome; Conservative Treatment; Pharmacologic Treatment

Introduction

A considerable portion of the population suffers with OAB syndrome, a chronic illness that significantly lowers their quality of life. OAB is a disorder that is characterized by "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency incontinence, in the absence of urinary tract infection or other obvious pathology," according to the International Continence Society's 2010 update" [1]. Daily activities and social functions like employment, travel, exercise, sleep, and sexual function are all impacted by OAB. Those who have an overactive bladder may experience self-consciousness. As a result, they may avoid others or restrict their social and professional lives. Although OAB is more prevalent in older persons, it is not a typical outcome [2].

What causes overactive bladder?

The etiology of OAB is still under investigation and is not well understood. However, different theories have been proposed to explain the pathophysiology of OAB [3,4]. OAB was historically thought to be caused by either "myogenic" or "neurogenic" conditions. Recently another theory suggested a new mechanism with the role of urothelium "urotheliogenic" hypothesis. OAB should be seen as a complex, multifactorial symptom syndrome, resulting from multiple potential pathophysiological mechanisms [5]. There are several causes of overactive bladder. In some cases, however, the cause is unknown. Conditions or injuries that affect the detrusor muscle cause a malfunction of the detrusor muscle.

These conditions may include:

- A family history of urinary incontinence;
- Urinary tract infections;
- Drinking too many fluids, taking diuretics, eating spicy foods, smoking, obesity, diabetes;
- Pregnancy, menopause and ageing;
- Anxiety, depression, trauma or injury, such as sexual assault;
- Irritable bowel syndrome, chronic constipation;
- Bladder stones, bladder cancer, bladder obstruction, pelvic organ prolapse;
- Neurological disease: multiple sclerosis, Parkinson's disease, stroke, Alzeimer's disease, herniated discs L5-S1;
- Any kind of pelvic surgery;

Most cases of OAB are idiopathic, i.e. in the absence of any underlying neurologic, metabolic, or other causes.

What are the symptoms of overactive bladder

OAB represents a collection of symptoms. These symptoms include:

- To feel the need to urinate more than 7 times daily;
- Frequent urination at night more than 2 times (nocturia);
- Urgency is defined as a sudden, overwhelming urge to void;
- Urinary urge incontinence occurs due to overactivity of the detrusor muscle and the urge is accompanied by loss of urine.
- Bed wetting, incontinence during intercourse.

Diagnosis of overactive bladder

To get a diagnosis of OAB, a medical history, a physical examination, a neurological exam and other specific tests are necessary [6-9].

- A thorough medical history;
- A physical examination;
- Urinalysis to exclude infection, haematuria and glycosuria;
- Postvoid residual volume (upper limit of normal being 50 mL);
- Frequency/volume chart for at least 3 days and ladder diary for a minimum of 3 days;

When there is diagnostic doubt, sophisticated testing like urodynamics, cystoscopy, or urinary tract imaging may be used in the initial examination of individuals with OAB.

Medical history

Health care provider should take a focused history and perform a primary evaluation for assessment for urinary tract conditions, including bladder tumors, calculi in the bladder, and recurrent UTIs. To rule out general conditions and risk factors that contribute to incontinence OAB, such evaluation is required.

Certain medications

They may contribute to urinary incontinence. Based on our present understanding of the mechanisms involved in continence and the transmitters that play a role, attempts have been made to identify the mechanism causing urine incontinence, which has been linked to a number of medicines. Drug classes that induce urinary incontinence include α1- adrenoceptor antagonists, antihypertensives, antipsychotics, benzodiazepines, antidepressants hormone replacement therapy, and antiepileptics (Table 1).

Diuretics: Diuretics increase urinary frequency and may cause urinary urgency and incontinence by overwhelming the patient's bladder capacity. There is a link between diuretics and/or conditions associated with their use and urinary incontinence in community-dwelling women.

Antipsychotics: A number of antipsychotics have been associated with urinary incontinence. Incontinence occurs over a broad range of antipsychotic dosages. Antipsychotics also cause incontinence by one or more of the following mechanisms: alpha-adrenergic blockade, dopamine blockade, and cholinergic actions on the bladder

Narcotics such as oxycodone, meperidine, morphine cause sedation or drowsiness; relax the bladder, causing it to retain urine

Other Drugs: Alpha-adrenergic antagonists or alpha blockers, in women, they can relax the bladder.

Several laboratory tests

They are recommended and simple office testing should also be a part of the initial assessment and work-up, including urinalysis and culture, levels of creatinine for kidney function evaluation and assessment of post-void residual urine. Infections should be treated and any hematuria thoroughly investigated. A follow-up test should be performed to confirm any abnormal post-void residual (PVR), which may also be useful.

Bladder diary

It is also known as a voiding diary, is indispensable for the evaluation of symptoms associated with OAB.

Each time a fluid is consumed, the patient will indicate this by date, time, what type of fluid was consumed, and how much of each fluid. This document will provide the maximum amount of relevant information to the physician (Table 2). Heath care providers usually ask patients to keep a bladder diary for at least 3 days, It is important to know if the patient had any wetting accidents while keeping their bladder diary.

- To begin the diary when the patient wakes up each day
- How often is a patient urinating?
- What time of day?
- To measure urine by peeing into a measuring jug during both the day and nigh
- What is the patient doing when she feels the need to urinate?
- How strong is the urge to urinate?
- To record the time, as well as a rating of how urgently the need to urinate using the following scale:
- 0 = No urgency - 1= An urgency to urinate, but could easily tolerate it - 2 = To need to urinate so urgently which interfer with ability to carry out everyday activities - 3 = To urinate very urgently, which caused abruptly to stop from doing an everyday activity.
- How much urine is being released?
- Are there any accidental urine leaks?
- What is the patient eating and drinking? How much?
- How do the circumstances affect the patient's daily routine?

Table 2

Physical examination

It should begin with observation of the patient and a general assessment should be focused on the posture, the scars of previous surgery, hernias, pelvic floor muscles testing, anal sphincter tone and grade of pelvic organ prolapse. Neurological exam to look for sensory issues or reflex problems.

Urodynamic tests

Urodynamic investigations are an important tool helping the clinical evaluation of patients with lower urinary tract symptoms such as OAB. The aims of urodynamics are to reproduce patients' symptoms, and to provide a lower urinary pathophysiological explanation in order to propose the best management. They are some tests which are used in this evaluation: uroflowmetry, postvoid residual measurement, cystometry, urethral pressure profilometry, pressure flow study and electromyography.

Ultrasound imaging

They are considered to be a safe non-invasive procedure which can provide clinicians with information to aid diagnosis of a wide range of conditions. These techniques have used both 2D and 3D ultrasound techniques. Bladder ultrasound can give information about the bladder wall, bladder stones and bladder tumors. Ultrasound imaging can detect bladder muscle thickness of the bladder wall.

Cystoscopy

They include: bladder cancer or tumor, polyps, bladder stones, scarring and damage caused by frequent urinary tract infections and urinary tract injury. OAB can be a symptom of CIS, bladder cancer, bladder stones or stricture. If there is a need to exclude other causes for symptoms, such as cancer, a cystoscopy may be considered.

Conservative management

Non-surgical treatment designed as conservative treatment is the mainstay of the non-invasive therapy. This can be initiated in the primary care setting. It includes a combination of lifestyle interventions, bladder training, behavioral modification, biofeedback and electrical stimulation. Antimuscarinic medications can be added if these measures fail to control symptoms. These therapies are the first choice in helping manage an OAB.

Lifestyle interventions and Management of fluid intake

Both reduce incontinence and frequency, increasing to improve urine concentration. Restriction of fluids may result in an increase in urine concentration that may irritate the bladder mucosa and promote urgency, frequency and urinary tract infections. Bladder irritants can exacerbate OAB symptoms and UUI [10-13]. Caffeine in particular has been shown to have a diuretic effect and is natu-

rally found in tea leaves, cocoa beans, coffee beans and a variety of foods and drinks, including ice cream and energy bars. To reduce nocturia, it is generally recommended to reduce to drink after 6.00 pm and to manage the ingestion of fruits and vegetables while avoiding caffeine and high-salt diet [14].

Bladder irritants

Dietary modification to eliminate possible bladder irritants (eg. reducing caffeine, alcohol and carbonated
beverages). Caffeine is a mild diuretic and bladder irritant, and reducing intake can reduce both urge and stress incontinence. Caffeine-containing products (foods and fluids) may increase OAB symptoms by increasing detrusor pressure and by promoting detrusor muscle excitability. In women, there is some anecdotal evidence that eliminating these from the diet may promote continence [10,11,12].

Smoking cessation

Chemicals in cigarette smoke alter the composition of urine, making it more acidic which can irritate the bladder wall, further aggravate bladder problems. There is an increased detrusor activity induced by nicotine. Smoking cessation may result in decreased symptoms.

Weight reduction

Central obesity places pressure on the bladder and may worsen urge incontinence and increases the risk of onset of OAB in women [11]. Obesity is associated with increased risk for the onset of OAB symptoms, and having a body mass index > 30 kg / m2 is an independent risk factor for OAB in women [12].

Regulating bowel function

Constipation is defined clinically as passing < 3 stools per week; however, from the patient's perspective, this definition also includes straining while passing a stool. Regular bowel function to avoid constipation and straining during bowel movements is important in managing OAB.

Behavioural modifications and bladder training

Behavioral modifications include counseling the patient that the bladder should be emptied every 2 to 3 hours, and that it is not necessary to void with every sensation of bladder fullness. Patients are advised to keep bladder diaries [15].

Behavioural training requires a highly motivated patient, and 20–30% will become dry. As behavioral treatments work gradually at first, it is important to follow patients regularly to see sustained behavioural changes [16].

Bladder training is widely used for the treatment of urinary incontinence in both primary and secondary care. Bladder drill, another term is often recommenced for patient's symptoms (such as urgency, frequency, nocturia, or mixed urinary incontinence). Bladder training aims to increase the time interval between voids, either by an adjustable schedule and teaching techniques to suppress urgency such as relaxation, distracting techniques and pelvic floor muscles contractions. The duration of the diary has a minimum of three days need recording, to give the frequency volume chart validity.

Pelvic floor muscle training and biofeedback

Pelvic floor muscle training (PFMT) is a mainstay of behavioral treatment for urinary incontinence and OAB symptoms, such as urgency. In urge incontinence, the biological rationale is that an involuntary detrusor contraction which may be used to control urgency [15,17,18]. Studies have shown that contraction of these muscles leads to suppression of detrusor contraction [19].

Biofeedback therapy can be defined as the use of monitoring equipment to control different body processes. This technique has been proven to be effective in the treatment of urinary incontinence in a number of research studies. The most common modalities of biofeedback involve electro- myography (EMG), manometry.

Biofeedback has now gained several potential applications for urologic conditions, having been successfully used for patients with urologic disorders such OAB. It is a very specific treatment that can restore bladder control by teaching patients to modulate the mechanisms of continence [15,20,21]. The caregiver needs to know how PFMs are able to contract when instructed to squeeze their PFMS. More than 25% of patients performed it improperly which is counter- productive because it increases intra- abdominal pressure on the bladder [20-22]. This false maneuver has been described as a "reversed perineal command" [21]. Thus, caregivers need to assess the ability to contract the PFM. Combination therapy consisting of bladder training, PFMT with biofeedback had the greatest immediate efficacy in the management of OAB [15].

Electrical stimulation

Electrical stimulation has been used since many years is an effective treatment for urge incontinence. This technique uses neurological pathways and its efficacy relies on a preserved reflex arc with complete or partial integrity of the PFM innervation. The mechanism of electrical stimulation for urge incontinence is a reflex inhibition of detrusor contraction. Electrical stimulation can be performed either in the clinic office or at home. While sacral neuromodulation is established third-line treatment, the pudendal nerve offers potential advantages. Electrical stimulation for OAB is a safe and effective way to reduce the muscle contractions that cause the condition [23,24]. The main contraindications to electrical stimulation are as follows: heart pacemakers, pregnancy, post-volume residual > than 100 mL, urinary tract infection or vaginal discharge, complete peripheral denervation of the pelvic floor. Magnetic stimulation provides a novel strategy that is applied to the sacral roots with an activation of pudendal nerve afferents blocking parasympathetic detrusor fibers at the level of S3. The lack of an internal probe in the magnetic chair indicates that the magnetic field can pass through clothing. Extracorporeal magnetic stimulation provides a useful alternative and offers a new effective modality for painless electrical stimulation with no need for a probe, and no need to be undressed for sessions [25,26].

Pharmacologogical treatment

If symptoms don't improve with conservative treatment as described above, medication is usually the next stept.

The anticholinergics

The state of the art pharmacological treatment for OAB is the use of anticholinergics. Anticholinergic drugs are often given to people who OAB. They work by relaxing the muscles and can help some of the symptoms such as frequency and leakage but they can have side effects, in that case it is possible to change the dose or the type of medication might help [27]. Taking an anticholinergic drug probably results in a small reduction in the number of urgency episodes. Several anticholinergic drugs used today are available and anticholinergic medications include (Table 3). Antimuscarinic drugs produced a significant improvement or cure but it can take several weeks before symptoms begin to improve. The most common side effects are dry mouth and constipation which may lead to the discontinuation of medication. Contraindications are patients with closed angle glaucoma, myasthenia gravis, severe ulcerative colitis, or intestinal obstruction. In a recent Cochrane's review, Stoniute., *et al*. [28] concluded that the use of anticholinergic drugs results in important but modest improvements in symptoms compared with placebo treatment and that this is generally associated with only modest improvement in quality of life.

- **Oxybutynin (Ditropan):** This medication comes in immediate - or slow-release tablet form, liquid, gel, or skin patches. People may take it liquid two to three times daily. Using skin patches may be applied twice per week.
- **Solifenacin (Vesicare):** This medication may not be suitable for people with certain health conditions, such as glaucoma, Crohn's disease. A person may typically take one tablet per day.
- **Fesoterodine (Toviaz):** This is a slow-release medication and it comes in tablet form, and a person may take one tablet per day to treat OAB. It may not be suitable if a person is pregnant though.
- **Darifenacin (Enablex):** This is another slow-release medication that may not be suitable if a person is pregnant. Darifenacin comes in tablet form, and a person may take one tablet per day to treat OAB.
- **Tolterodine (Detrusitol):** It may not be suitable if a person has certain health conditions (glaucoma, heart problems). A person may take one immediate-release tablet twice daily, or one slow-release tablet per day.
- **Trospium (Sanctura):** This medication comes in immediate- and slow-release tablet form. A person may take one immediate-release tablet twice daily, or one slow-release tablet per day.

Table 3

Mirabegron

Mirabegron, a β(3)-adrenoceptor agonist, acts mainly via peripheral pathways in detrusor overactivity. The activation of beta-3 receptors relaxes detrusor smooth muscle during the storage phase. Myrbetriq is a prescription medicine for adults approved by the U.S. Food and Drug Administration (FDA) and available in Europe. The main side effects are an increase of blood pressure, headache and allergic reactions (angioderma).

Imipramine

Imipramine (Tofranil) is a tricyclic antidepressant. It is often prescribed along with other medications that help relax the bladder muscle. It may be used to treat mixed incontinence but as it can cause drowsiness, so it may be useful for nighttime incontinence. There are side effects as follows: nausea, vomiting, constipation or diarrhea.

Duloxetine

Duloxetine, a serotonin norepinephrine reuptake inhibitor (Cybalta) is known to have role in the treatment of anxiety disorder and USI. In the randomized control trial by Mirzai., *et al*. the concluded that duloxetine can be a suitable alternative option for overactive bladder treatment, due to the acceptable therapeutic effect and side effects [29].

Management of refractory overactive bladder

Failure in achieving clinical improvement with conservative treatment and drugs is problematic for the patient and challenging for the physician. Therefore, they are some minimally-invasive second line treatment options to be considered.

Botulinum neurotoxin

Botulinum neurotoxin (BoNT/A) is an FDA approved second-line treatment for overactive bladder (OAB) in patients either not responsive or intolerant to anti-cholinergic drugs. Botox is most often injected as an outpatient procedure by cystoscopy under local anaesthetic. BoNT-A injections have been shown to be an effective alternative to anticholinergic medications and to be found to decrease urinary incontinence in OAB. This a temporary treatment and the benefit lasts for 6–9 months. Among the side effects, urinary retention [30]. Patients should be informed the potential adverse effects before BoNT-A treatment.

Sacral nerve stimulation

In more severe cases, SNS nerve may provide relief from frequency-urgency symptoms in patients with severe symptoms of OAB that are refractory to proven behavioral treatment and drugs. Electrical impulses stimulate the nerves and this can help reduce the symptoms. The most commonly described site of neuromodulation for treatment of OAB is the third sacral nerve root [31,32]. SN uses electrical stimulation to stimulate the sacral nerves that innervate the musculature of the pelvic floor and lower urinary tract.

Other approaches

In cases refractory to all previous treatments, bladder augmentation enterocystoplasty is an alternative for patient with refractory OAB with the potential of achieving the above aims [33]. Bladder augmentation cystoplasty or urinary diversion may be offered in patients with who have not responded to all other therapeutic options. IUGA. Augmentation cystoplasty (AC) is surgery that makes the bladder larger to store urine. This detubularizes segment, reduces enteric contractions, and maximizes volume that segment contributes to urinary storage. This procedure is a major surgery which take anywhere from two to six hours with risks include urinary tract infections and bladder stretching.

Conclusion

The causes of OAB are not completely understood, and symptoms may differ between patients and may be confusing. Currently, there are several options for treatment. The first-line therapies include (behavioral modification and PFMT), knowing that these treatment options have a low risk profile, progressing to second-line OAB medications. For those who are poorly responsive or intolerant to prior treatment, other more complicated therapies are also available (neuromodulation and intravesical botulinum toxin). A complete cure is rare and the management of an OAB is a challenging mission for the physician, with the need to tailor treatment options to the patient's condition.

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