



Overactive bladder

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Abstract

Overactive bladder (OAB) is known to affect millions of people worldwide, with a subsequent deleterious impact on the quality of life. The clinical diagnosis of OAB requires, at a minimum, a meticulous history, physical examination, and urinalysis. The American Urological Association views OAB as a symptom complex, not a life-threatening disease, and recommends conservative measures and behavioral therapies as first-line treatment, including bladder training, bladder control strategies, pelvic floor muscle training, and fluid management. Current medical management approved by the US FDA include anti-muscarinics and beta3-agonists. Anti-muscarinics should be avoided in patients with narrow-angle glaucoma, and used with extreme caution in patients with impaired gastric emptying or a history of urinary retention. Surgical interventions may be offered, if second-line therapy using medications is not successful in obtaining adequate symptom control of OAB, and the patient is motivated and healthy. In uncomplicated patients, OAB may be clinically diagnosed and treated with conservative measures; however, the armamentarium for the diagnosis and treatment continues to expand for more complicated patients.

Keywords: Overactive bladder, Definition, Pathophysiology, Diagnosis, Treatment

Prevalence

Overactive bladder (OAB) is known to affect millions of people worldwide, with a subsequent deleterious impact on the quality of life. The EPIC study, which focused on four European countries and Canada, reported the prevalence of OAB to be 11.8%, and 64.3% of people studied reported at least one lower urinary tract symptom [1]. An analysis of the population in the United States in the NOBLE study showed that 16% of men and 16.9% of women had OAB, and the prevalence increased in both sexes with age [2]. In the Chinese population, one large questionnaire-based study

reported a prevalence of 8.0% among Fuzhou women, and 70% of these women had associated incontinence [3]. While the exact prevalence varies geographically, it is apparent that this urologic disorder carries a significant burden worldwide.

Definition

OAB is defined by the International Continence Society (ICS) as “urgency, with or without urgency incontinence, usually with frequency and nocturia, if there is no proven infection or other obvious pathology” [4]. Because OAB is a symptom complex and not a life-threatening

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disease, it is important that any other possible causes, such as malignancy or infection, are ruled out prior to diagnosing a patient with OAB [5]. Nocturia is defined as the need to wake up one or more times per night to void. This must be distinguished from those who wake up during the night for other reasons, then void because they are awake. Daytime frequency is defined as a patient's subjective opinion that they are voiding too frequently during the day. Adding to these difficult-to-quantify characteristics, OAB does not commonly exist in isolation. Patients may present with symptoms of stress and urge incontinence, also known as mixed urinary incontinence (MUI) [6]. MUI is typically associated with increased incontinence compared with OAB alone.

Pathophysiology

These highly-subjective definitions used to diagnose OAB make it difficult to develop suitable animal models [6]. There are three theories, however, that have been advanced to explain the actual pathophysiology of the detrusor overactivity (DO) observed during urodynamics in patients diagnosed with OAB. The first theory is a neurogenic hypothesis that explains DO as a result of damage to the central or peripheral nervous system that unmasks primitive voiding reflexes and triggers bladder overactivity [7]. The myogenic hypothesis holds that the detrusor smooth muscle may be primed, possibly by partial denervation, to have a higher likelihood than normal smooth muscle to contract spontaneously, as well as an increased propensity for exaggerated propagation of excitation, thus resulting in DO [6, 8]. Finally, the integrative hypothesis states that "detrusor overactivity results from exaggerated symptomatic expression of peripheral autonomous activity, resulting from a shift in the balance of excitation and inhibition in smooth muscle modules" [9].

Diagnosis

The clinical diagnosis of OAB requires, at a minimum, a meticulous history, physical examination, and urinalysis [5]. The presence or absence, severity, and degree of nuisance for all lower urinary tract symptoms should be recorded [6]. Validated questionnaires, such as the International Consultation on Incontinence Modular Questionnaire (ICIQ), may be used to delineate a patient's symptoms in more

detail [10]. Concurrent bowel symptoms should be queried. Standard past medical, surgical, obstetric and gynecologic, as well as medication histories should be obtained. A basic neurologic exam should be completed to rule out the presence of an occult neurogenic cause for the OAB. A genitourinary exam is especially relevant. If the diagnosis is not apparent, some patients may require a urine culture, determination of the post-void residual (either by bladder scan or catheterization), a voiding diary, and/or a more thorough symptom score, depending on the specific areas of ambiguity in the evaluation. Urodynamics, cystoscopy, and renal and bladder ultrasounds are not warranted for uncomplicated cases [5].

In more complicated cases, or in patients who fail conservative bladder management, urodynamics may be considered [5]. The diagnosis of DO can only be made based on urodynamics, and is defined as "involuntary contractions during the filling phase, which may be spontaneous or provoked" [6]. It should be specifically stated in the urodynamics report whether or not the testing accurately reproduced the patient's symptoms. The symptoms most consistent with OAB include DO and increased sensation during filling. Bladder outlet obstruction and incomplete emptying must be screened for, because treatment aimed to improve storage function may worsen these symptoms [6]. A diagnosis of neurogenic DO is made when these symptoms have a known neurologic cause, such as central nervous system or spinal cord injury.

Treatment

The American Urological Association recently released treatment guidelines for non-neurogenic OAB. They view OAB as a symptom complex, not a life-threatening disease, and recommend conservative measures and behavioral therapies as first-line treatment. Such therapies include bladder training, bladder control strategies, pelvic floor muscle training, and fluid management [5]. Additionally, avoidance of dietary irritants, smoking cessation, and weight loss (for obese patients), should be pursued [6]. When behavioral modification is not sufficient to control a patient's symptoms, medical management may be used in combination [5]. Current medical management approved by the US FDA includes anti-muscarinics and beta3-agonists. However, anti-muscarinics should be avoided in patients with narrow-angle glaucoma,



and used with extreme caution in patients with impaired gastric emptying or a history of urinary retention [5]. Different medications from this class may be tried prior to declaring treatment failure, because patients may respond better or worse to various medications within this class. Attempts should be made to manage side effects, such as constipation or dry mouth, prior to discontinuing the medication [5]. Mirabegron is the first beta3-agonist to be approved by the US FDA. Randomized control trials have shown significant improvements in the frequencies of voiding and incontinence episodes, as well as quality of life, with only mild side effects (e.g., small elevations in pulse rate and blood pressure) [11].

If second-line therapy using medications is not successful in obtaining adequate symptom control of OAB, and the patient is motivated and healthy, surgical interventions may be offered [5]. Onabotulinum toxin A has recently been FDA-approved for the treatment of OAB. Injection of onabotulinum toxin A is the least invasive surgical option, although re-injection is required when OAB symptoms return. Additionally, patients must be willing to return to the clinic for assessment of the post-void residual volume and possibly perform clean intermittent catheterization, if necessary [5]. Although no standard injection technique exists, a total of 100 units of onabotulinum toxin A injected into 20 locations, without trigone sparing, has been proposed [12]. Patients who received onabotulinum toxin A detrusor injections had a 62.8% improvement based on the Treatment Benefit Scale (TBS) and significant improvements in quality of life scores [13]. The most common risks associated with injection are infection (15.5%–20.4%) and urinary retention (5.4%–5.8%) [13, 14]. This treatment is not ideal for people previously diagnosed with myasthenia gravis, Eaton-Lambert syndrome, amyotrophic lateral sclerosis, or any other disorder that may interfere with neuromuscular function.

A third-line surgical option is the implantation of neuronal modulation. Sacral nerve stimulation may be offered to patients in whom symptoms are not controlled with first- or second-line therapies, and who are willing to undergo a surgical procedure [5]. Sacral nerve stimulation is performed by implanting temporary percutaneous electrodes into the sacral nerve roots. If the patient's symptoms are improved by >50% during an initial trial period (typically 2–4 weeks), the

electrodes are permanently implanted into the subcutaneous fat of the buttock [15]. One longitudinal study reported a sustained cure rate of 40%, and a partial success rate of 20% in patients who qualified for permanent implantation, although the repeat intervention rate was 37.7% [16]. The risks of these procedures include infection, erosion, migration, and pain, as well as technical failure or device malfunction. Implantation is not recommended for patients who may require magnetic resonance imaging in the future.

Fourth-line management does exist for patients who continue to have severe, refractory OAB symptoms. These methods include various forms of bladder augmentation, with or without methods to increase bladder outlet resistance, such as mid-urethral slings [5]. In extreme cases, urinary diversion may be considered. However, patients must be healthy enough to tolerate these major procedures. Additionally, indwelling catheters, such as urethral or suprapubic tubes, are not recommended, as the risks of these devices outweigh any benefits, except as a last resort in selected patients [5].

Conclusion

OAB is a constellation of symptoms that affects millions of people worldwide. Because the symptoms of OAB become more prevalent as people get older and the population continues to age, the diagnosis and treatment of OAB is becoming ever more important. In uncomplicated cases, OAB may be diagnosed clinically and treated with conservative measures; however, the armamentarium for the diagnosis and treatment continues to expand for more complicated cases.

Conflict of interest

The authors declare no conflict of interest.

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