Overactive Bladder: A Better Understanding of Pathophysiology, Diagnosis and Management

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Purpose: We reviewed current information regarding the updated definitions, prevalence, etiologies, disease burden, and management of OAB from a number of perspectives, including professional impact and patient quality of life.
Materials and Methods: Published literature and current treatment concepts were reviewed regarding the understanding and management of OAB.
Results: OAB is a symptom syndrome including urinary urgency with or without urinary incontinence, usually with frequency and nocturia. Approximately 17% of the adult population experience OAB. There are evolving theories regarding its pathophysiology and the mechanism of action of the most commonly prescribed pharmacological therapy (antimuscarinic agents). Treatment primarily revolves around improving quality of life.
Conclusions: Behavioral therapy combined with pharmacological therapy often will bring about acceptable outcomes for patients with OAB. Modalities such as botulinum toxin injections, neuromodulation, and various surgical interventions also are showing encouraging results in more refractory patients.

Key Words: bladder, urinary incontinence, muscarinic antagonists, behavioral medicine

The definition of OAB has been evolving over the years as the syndrome has come to be studied more diligently. The ICS now defines OAB as urgency, with or without urge UI, usually associated with frequency and nocturia.[1] The symptoms must be exhibited in the absence of pathological or metabolic disorders (eg urinary tract infection, bladder cancer or benign prostatic enlargement) that might otherwise cause such symptoms. Urgency is the primary symptom; OAB would not be diagnosed without the complaint of urgency. It can, however, be diagnosed without the complaint of incontinence. Approximately two-thirds of patients with OAB do not experience involuntary leakage of urine; OAB in the absence of UI is termed "OAB dry." Note that a component of the previous definition, fear of leakage and/or fear of pain from a full bladder, is no longer included in the definition of OAB.[2]

Since urgency is the key symptom, it becomes important to define it. The ICS defines urgency as a "sudden compelling desire to void that is difficult to defer."[1] The word desire is used rather than urge, because urge is a normal phenomenon that we all feel when the bladder is full. The desire is termed as "sudden" to avoid confusion with the gradual increase in sensation that is also a normal phenomenon.

Despite the availability of a formidable definition, clinicians often find that patients, especially in clinical practice, do not understand exactly what is meant by "urgency." Likewise, in many studies purporting to measure or record urgency, an incorrect definition was used, most commonly a strong desire to void. This is something to take into consideration when reading literature regarding studies that evaluate "urgency."

Urgency is the primary driver of all symptoms of OAB. It leads to frequency and OAB related nocturia, as well as to urge UI in the approximately one-third of patients with OAB who suffer from UI.[1,3] According to the ICS definition, frequency is defined as urination 8 times or greater per 24 hours. Nocturia, which is simply waking to urinate during sleep hours, generally is only considered a clinical problem if the frequency is greater than 2 times per night. (Nocturia will be discussed in greater detail elsewhere in this supplement.)

EPIDEMIOLOGY OF OAB

OAB overlaps with other subtypes of LUT dysfunction (fig. 1). As noted, approximately a third of all patients with OAB experience incontinence and, thus, they are classified as having urge UI, which is synonymous with "OAB wet." Stress UI, which involves failure of the urethra and pelvic floor to withstand pressure created by such stressors as sneezing or laughing, does not fall within the OAB syndrome; however, many patients suffer from UI and/or urgency with mixed symptoms (urgency and stress). The combination of stress UI with urge UI constitutes "mixed UI," while stress UI accompanied by urgency but not urge UI constitutes "mixed symptomatology." As figure 1 illustrates, a large portion of patients suffer from OAB dry. These patients experience urgency and frequency but not UI.

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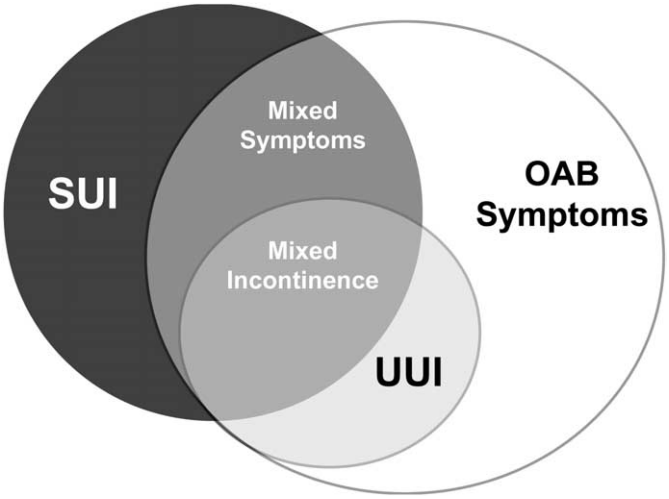

FIG. 1. Spectrum of OAB. *SUI*, stress UI. *UUI*, urge UI

Two major epidemiological studies have been performed regarding the prevalence of OAB, 1 in Europe and 1 in the United States. Both indicate a similar prevalence of approximately 17% of the general adult population. The United States study, which was done by the National Overactive Bladder Evaluation program, found that 16.5% of adults (18 years or older), or approximately 33 million people, met the criteria for OAB.[4] The portion of patients with OAB in the European study was 16.6% in a population of adults 40 years or older in 6 countries.[5] This does not mean that 17% of the population requires treatment for OAB, because not everyone will have severe uncontrollable symptoms. This issue of what level of symptoms warrant treatment is a subject of ongoing discussion.

Data from the National Overactive Bladder Evaluation study indicate that 37% of patients with OAB experience incontinence, while 63% do not.[4] The prevalence of both OAB wet and OAB dry increases with age. OAB dry is more common in men (13.6% vs 7.6% in women overall), and OAB wet is more common in women (9.3% vs 2.4% in men overall). Urge UI in men is often associated with benign prostatic hyperplasia or benign prostate obstruction, which will both be discussed in another section of this supplement.

The impact of OAB on QOL is considerable. The highly validated Short Form with 36 questions, a health related QOL survey, shows OAB to cause QOL limitations and/or impairment in domains including physical activity, psychological well-being, social activity, sexual activity, occupational productivity, and domestic logistics.[6] Psychological well-being is commonly mentioned. Patients often express loss of self-esteem, fear of becoming incontinent in public, and depression. As discussed by Abrams et al, the incidence of depression associated with OAB is on the same scale as that of numerous other chronic conditions, including diabetes, rheumatoid arthritis, and hypertension.[7]

OAB also can be a contributing factor to fall related injuries in the elderly population. In a study of Brown et al, 19% to 42% of community dwelling women 65 years or older experienced falls; 4% to 9% of those falls resulted in fractures.[8] The high incidence of urge UI in this population was determined to be an independent risk factor in women experiencing 1 or greater urge UI episode per week, with the risk of falls and fractures being increased by 26% and 34%, respectively. The authors noted frequency, nocturia, and "rushing to the bathroom" as being likely to increase the risk of falling in elderly women. In consideration of the morbidity and mortality associated with hip fracture in older women, it is important to identify these individuals with OAB and properly treat them.

PATHOPHYSIOLOGY

Because the bladder is a smooth muscle organ attached to the CNS, it is logical to assume that the pathophysiology of OAB is neurogenic and/or myogenic in origin. The neurogenic etiology is easier to conceptualize,[9] and within that realm, the simplest to understand is that of decreased suprapontine inhibition of the micturition reflex, such as that following a cerebrovascular accident. Other examples of neurogenic etiology of OAB would be damaged axonal paths in the spinal cord, increased LUT afferent nerve input, loss of peripheral inhibition, and enhancement of excitatory neurotransmission in the micturition reflex pathway. Common causes of these phenomena include stroke, spinal cord injury and multiple sclerosis.

The myogenic theory[10] is applicable mostly to patients with bladder outlet obstruction, owing to an increase in intravesical pressure, which subsequently causes partial neurological denervation of the bladder smooth muscle. Spontaneous action potential generation is generally limited in bladder smooth muscle and is not propagated from cell to cell. However, when the smooth muscle is denervated, there is an increase in the number of spontaneous action potentials and in the ability of the action potentials to propagate from cell to cell. Rather than causing a normal detrusor contraction that would empty the bladder, this denervation results in "micromotions" of the detrusor smooth muscle that give rise to increased intravesical pressure and stimulation of afferent receptors in the detrusor smooth muscle. The receptors provide feedback to the CNS and cause the sensations associated with OAB.

Another of the new ideas being proposed is that ACh is released from the urothelium in an amount greater than normal during bladder distention, or the sensory receptors in the urothelium are more sensitive to the ACh that is released. The subsequent feedback to the CNS creates the sensation of urgency that drives OAB. There is increasing evidence that the urothelium is involved in sensory function, including the release of neurotransmitters in response to stimuli.[11]

Another hypothesis is that, rather than experiencing no activity in the postganglionic efferent nerve during filling/storage (the normal state), patients with OAB experience an abnormal leak of ACh from efferent fibers, causing micromotions in bladder smooth muscle and stimulate the CNS, creating the sense of urgency.[12]

DIAGNOSIS AND TREATMENT

Understanding that not all patients will require treatment for OAB, it is important to determine the severity and precise symptomatology. The initial evaluation should include a thorough history, physical examination, urinalysis, and bladder diary (fig. 2). Since OAB symptoms can be early signs of underlying and/or remediable conditions, special attention should be focused on detecting them. The most