

Diagnosis and treatment of overactive bladder in menopausal women

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Financial Disclosure: The authors have no financial disclosures pertinent to this research.

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Text word count: 2,078

Introduction

Overactive bladder (OAB) is a common and embarrassing problem that affects many women during and beyond menopause. Overactive bladder can present with or without incontinence, and has a constellation of symptoms including urgency, usually with urinary frequency and nocturia.(1) A diagnosis of OAB is made when a patient presents with urgency in the absence of pathologic or metabolic conditions that might explain this symptom. OAB is a bladder storage disorder caused by an increase in bladder pressure from an uninhibited contraction of the detrusor muscle.

Overactive bladder is a serious health condition that affects 16.6% of the general U.S. female population.(2) The prevalence of OAB is higher than that of stress incontinence in the aging female population. The inability to control the involuntary loss of urine is one of the most unpleasant and distressing symptoms a woman can experience and may significantly affect her quality of life. Ultimately, these alterations in the physical, occupational, and sexual quality of life may result in depression or loss of self-esteem. Unfortunately, women affected by OAB may attempt to cope with symptoms on their own instead of seeking treatment for a variety of reasons including poor access to healthcare, embarrassment, and lack of knowledge about OAB treatments.

Diagnosis of OAB

A presumptive diagnosis of OAB can be made with a careful history and physical exam. Typical symptoms of OAB include voiding more than eight times per day (urinary frequency) or more than once at night (nocturia) and a strong and sudden desire to urinate (urinary urgency). One simple question illicit a response confirming urge urinary

incontinence is, “Do you feel the need to urinate but cannot get to the toilet fast enough?” In addition, validated questionnaires such as the Incontinence Impact Questionnaire measure symptom distress in women with this complaint.(3)

A physical examination should include a focused neurologic examination in which the physician evaluates sacral nerve function by testing the bulbocavernosus reflex and/or an anal wink. Used over a period of 72 hours, a temporal log of urination can gauge progress following treatments and is well correlated with urodynamic diagnosis.(4) A urinalysis, and possibly a urine culture, should be performed to rule out a urinary tract infection as the etiology of the OAB. A post-void residual should also be performed to rule out voiding dysfunction.

Cystometry is the only way to quantitatively diagnose the amplitude of detrusor contractions and thus make the diagnosis of detrusor overactivity. The most cost-effective diagnostic method is office cystometrics in which the bladder is retrograde filled with saline, and the meniscus of fluid in a graduated syringe is observed for fluctuations. Subtracted multi-channel urodynamics can be used to make a diagnosis with a history of mixed urinary incontinence or other provocative maneuver defined as stress provoked detrusor overactivity.

Conservative Therapy

At the Cleveland Clinic, we have recommended noninvasive approaches prior to pursuing invasive approaches for treatment of incontinence. Behavioral modification such as reduction in consumption of bladder irritants, bladder training, and pelvic floor muscle exercises all heavily rely on compliance of the patient. Scheduled voiding (bladder

training) is a mainstay of treatment for OAB. Pelvic floor muscle rehabilitation focuses on strengthening the levator ani muscles in order to help the patient suppress detrusor contractions. Although anticholinergic medicines, as will be discussed below, may decrease the frequency of urge episodes, medicine will not stop an urge once it starts. When an urge starts, contraction of the levator ani muscles may be the only method to relax the detrusor muscle and prevent urinary incontinence. Many patients will require a concurrent second treatment option, which has been shown to be more effective than a single treatment alone.(5)

Pharmacologic Therapy

Anticholinergics/Antimuscarinics

The goal of pharmacotherapy is to limit frequency and the number of leakage episodes by decreasing bladder contractions. Anticholinergic medications block the action of acetylcholine receptors in the bladder smooth muscle to prevent strong bladder contractions at low volumes of urine. The efficacy of various anticholinergics-antimuscarinics has been evaluated by a comprehensive Agency for Healthcare Research and Quality (AHRQ) meta-analysis.(6) The results produced by behavior modifications are similar to the impact of antimuscarinics. A 2006 Cochrane Collaboration systematic review showed at the end of the treatment period, the improvement in leakage episodes in 24 hours was statistically significant favoring medication (relative risk (RR) 1.39, 95% CI 1.28 to 1.51).(7) The placebo effect (33-56%) is strong in this patient population because patients may be somewhat desperate for a solution. The role of antispasmodic, antidepressant, and calcium channel blocking medications is still under review.

Estrogen Replacement Therapy

The efficacy of estrogen replacement therapy for OAB has been debated, and the majority of the data regarding estrogen for treatment of OAB are derived from studies with mixed results. Some of the highest quality data comes from the randomized and placebo-controlled Heart and Estrogen/progestin Replacement Study (HERS). Data from HERS showed that the major predictors of urge incontinence were increasing age, diabetes, and urinary tract infections in a postmenopausal population.(8) Both stress and urge incontinence had a statistically significant worsened for 37% of the population after a four-month treatment with estrogen and progesterone compared to placebo. In contrast, these conditions worsened for 27% of the placebo group which was statistically significant as well.

Surgical Therapy

There are several surgical techniques available to treat refractory OAB including detrusor injection of Clostridium botulinum A-toxin, neuromodulation, and other methods. Surgeons' views differ as to when using invasive techniques for this indication of refractory OAB is justified. We recommend pursuing invasive techniques when behavioral interventions and at least two pharmacologic therapies fail, are contraindicated, or cannot be tolerated. Women who fail conservative and pharmacologic management and are diagnosed with refractory undesired bladder contractions may consider surgery. Even in the subset of hard-to-treat women, the decision to treat OAB surgically should not be made lightly.

Clostridium botulinum A-toxin (Botox, Allergan, Inc., Irvine, CA) intradetrusor injections are not FDA approved and are currently being studied as a chemodenervation agent for temporary paralysis of the muscle.(9) Using a cystoscope, the physician injects 100 to 200 units of botulinum toxin within the detrusor muscle or bladder submucosa. Data from two randomized controlled trials illustrated that 200 units of botulinum A toxin decreased urge incontinence in women with idiopathic detrusor overactivity and refractory urge incontinence; however, one trial was halted because of a statistically significant increased risk of urinary retention.(10-11) Women who received botulinum A-toxin were more likely to report improvement on a validated questionnaire, a 3-day urinary diary, and had a median duration of response that was significantly longer than for placebo ($p<0.0001$). However, the clinical significance of the resultant urinary retention is unclear as it was temporary and the majority of patients did not complain of voiding dysfunction.

Sacroneuromodulation is another surgical method employed to treat urinary incontinence. Several anatomic sites for neuromodulation have included the placement of electrodes adjacent to the dorsal clitoral nerve, sacral nerve roots, and tibial nerve.(12-13) Six months after placement of a sacral nerve stimulator the number of daily heavy incontinence episodes decreased from 3.4 ± 3.8 to 0.3 ± 0.9 ($p<0.0001$) in one randomized controlled trial.(14) Posterior tibial nerve stimulation is a percutaneous therapy is technically simple placement of leads based on the insertion of acupuncture needles over these sites to affect bladder activity. Multiple treatment sessions are scheduled in the

office and may be helpful in patients who desire not to take more medications. Sacral nerve stimulation was FDA approved for use with refractory voiding dysfunction in 1997. The exact mechanism of action of sacral nerve stimulation is not known.

Placement of a sacral nerve stimulator (Interstim Therapy System®, Minnetonka, MN) is a two stage process whereby a subcutaneous implantable pulse generator is connected to a lead electrode that lies along the third sacral nerve. The first stage can be performed either as an office percutaneous nerve stimulation or as an outpatient procedure. The neuromodulation device is commonly described to patients as a “bladder pacemaker” (Figure 1).

In extreme cases of OAB with urge urinary incontinence, bladder augmentation with bowel establishes an acontractile bladder or bladder-intestine-reservoir. However, this procedure is rarely performed given the associated morbidity. Given the high cost associated with sacral neuromodulation, a thorough preoperative evaluation should be performed to ensure the patient is a suitable candidate. Prior to any operative procedure, the physician should document that an adequate trial of medical or conservative management has been offered and attempted or refused (informed refusal). Patients should understand that they need to turn off the generator if they are going to undergo a surgical procedure, they cannot have magnetic resonance imaging with the device in place and they cannot undergo a procedure employing diathermy. Unknown durability and operative reversibility are the unique risks of sacral nerve stimulators and should be discussed.⁽¹⁵⁾ Physicians who have a strong understanding of the consent process and

the variety of various OAB options will be best prepared to illustrate this risk versus benefit relationship.

Conclusions

In conclusion, given the growing number of OAB cases treated annually it is encouraging to see that during the past five years new drugs and procedures have been developed to treat these patients. There remains little data regarding the ideal OAB management that minimizes morbidity while maximizing subjective outcomes for the menopausal patient. Thus, treatment should be individualized, based on provider experience and patient preference, depending on both the patient's and provider's tolerance for risk.

Legend

Figure 1: A sacral nerve stimulator with a tined lead placed in the second sacral nerve root.

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