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Diagnosis and management of patients with overactive bladder syndrome and abnormal detrusor activity

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SUMMARY

Overactive bladder syndrome (OABS) is a widely recognized syndrome with symptoms that can include urinary urgency, frequency, nocturia, and incontinence. Although there may be several causative factors for OABS, detrusor overactivity is the most common. In addition, urinary incontinence can also be due to a distinct but equally bothersome condition underactive bladder syndrome, or detrusor underactivity. The incomplete bladder emptying that characterizes detrusor underactivity often arises from impaired contractile function of the detrusor muscle. The variations in etiologies of the two syndromes necessitate patient evaluations tailored to individual symptom presentation. Increased awareness of the differences between the manifestations of OABS and underactive bladder syndrome call for specific approaches to the management of bladder dysfunction.

KEYWORDS detrusor underactivity, neurogenic bladder dysfunction, overactive bladder syndrome, urinary incontinence

REVIEW CRITERIA

Medline was searched for records between 1966 and 2004, under the terms "overactive bladder" and "detrusor underactivity". Of the 415 citations identified by the searches, papers were selected on the basis of clinical results, and preference was given to randomized clinical trials and articles that best described the diagnosis and treatment currently used. Only papers published in English have been cited in this review.

CME

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Received 31 August 2004 **Accepted** 29 October 2004
www.nature.com/clinicalpractice
doi:10.1038/ncpuro0054

INTRODUCTION

Bladder dysfunction is common and continues to increase in prevalence, particularly in the aging population. Patients may suffer from either OABS or DETRUSOR UNDERACTVITY. The cardinal symptom of OABS is urgency, with or without urge incontinence.[1] This syndrome has both neurogenic and myogenic causes. OABS is well known to the international urology community as a widespread and bothersome condition that can significantly limit daily activities. However, the pervasiveness of poor bladder emptying, possibly owing to detrusor underactivity, which is the hallmark of underactive bladder syndrome may be less appreciated by urologists.

Detrusor underactivity is used to denote the opposite condition from OABS. Detrusor underactivity can be more challenging to diagnose and treat than OABS. Unlike OABS, detrusor underactivity is often asymptomatic until a patient presents late with chronic retention of urine. The differential diagnosis of detrusor underactivity is vast, and includes both bladder and urethral etiologic factors. This article reviews the bladder etiologies of both OABS and detrusor underactivity. The causes of these two syndromes as well as their respective evaluation and screening techniques, and overall treatment options are discussed.

OVERACTIVE BLADDER SYNDROME

OABS is defined by the International Continence Society as a syndrome suggestive of lower urinary tract dysfunction characterized by urinary urgency, with or without urge incontinence, usually with frequency and nocturia.[1] Urgency, the complaint of a sudden compelling desire to void that is difficult to avoid and may precede incontinence, is the cardinal symptom. The combination of symptoms relating to OABS suggests detrusor overactivity, but the condition can result from other forms of urethrovesical dysfunction as well. After other abnormalities are ruled out

by diagnostic evaluation, no precise cause for OABS is identifiable; it is thus generally treated as being caused by detrusor overactivity.[1–3]

Pathophysiology

Detrusor overactivity can have both myogenic and neurogenic bases, which can include detrusor muscle instability and damage to or malfunction of neuronal pathways. Neurogenic and myogenic causes of idiopathic OABS most likely interact to produce its clinical symptoms.[4,5]

Myogenic causes

OABS can be caused by hyperactivity of the smooth detrusor muscle and defective control of detrusor activity by the cerebral cortex, brain stem, and spinal cord. Denervation of the bladder can increase spontaneous action potentials, resulting in more frequent bladder contractions. Triggers for this hyperreflexia also include damaged inhibitory pathways in the central nervous system (CNS), sensitization of afferent peripheral nerve terminals in the bladder,[6] and denervation caused by aging or peripheral neuropathy, often from diabetes, in which the bladder gradually expands to an overlarge capacity of more than 500 ml owing to a sensory deficit.[7] Idiopathic detrusor overactivity may actually be the result of changes in the detrusor muscle brought about by denervation.[5,8] Emerging myogenic mechanisms include leakage of acetylcholine from neurons in the bladder wall during storage or micromotion that causes afferent nerve stimulation.

Neurogenic causes

Normal bladder function requires autonomic and somatic pathways from the lumbosacral spine to the urethral outlet, bladder neck, and detrusor muscle. Changes in any of these can produce OABS, as can sensitization of peripheral afferent nerves from the bladder. The alteration in innervation of the bladder wall, or the pelvic floor and urethra can also trigger overactivity.[4,5] Patients with neurologic and other disorders can also have OABS symptoms associated with the activation of secondary excitatory pathways, such as unmyelinated afferent sensory C-fibers in the parasympathetic nerves.[5,6,8]

Another possible cause of OABS stems from microscopic structural changes in the bladder. Altered cell-to-cell connections leading to degeneration of muscle and nerve fibers can result in impaired contractility and reduced bladder compliance.

Diagnosis

Primary care physicians can usually diagnose patients suspected of having OABS on the basis of a thorough history that includes past and present medications, a physical examination, and urinalysis. A medication history is important because some medications, including diuretics, antidepressants, α-agonists, α-antagonists, β-antagonists, sedatives, anticholinergics, and analgesics can affect the ability to void. A general physical examination should have genitourinary, abdominal, pelvic, rectal, and neurologic aspects, and a urinalysis should rule out infection, hematuria, pyuria, bacteriuria, glucosuria, or proteinuria.

Bladder diaries are useful in determining the frequency, volume, and pattern of voiding. Assigning a relative measure of symptom intensity (i.e. a symptom scale) can also help. Together, these tools can pinpoint the pattern of symptoms and help to identify underlying causes or contributing factors.[3]

A diagnosis of OABS is appropriate when other diseases, such as infection, a bladder stone or genitourinary cancer have been excluded.[9] The differential diagnosis of OABS can include pelvic floor prolapse, bladder outlet obstruction caused by medical conditions such as benign prostatic hyperplasia (BPH), bladder neck dysfunction, posterior urethral valve dysfunction, uncoordinated sphincter activity, postsurgery iatrogenic obstruction, atrophic vaginitis, pelvic floor dysfunction, painful bladder syndrome or interstitial cystitis, and diabetes, in addition to neurological illness and injury such as multiple sclerosis, stroke, Alzheimer's disease, spinal stenosis, spinal cord injury or myelodysplasia.[5,8]

OABS can occur alone or with stress urinary incontinence (involuntary leakage on effort or exertion, or on sneezing or coughing), in which case it is called mixed urinary incontinence. Women with stress urinary incontinence can present with OABS symptoms because they often have a weak, poorly coapted, or poorly supported proximal urethra, and their urine flow can trigger a micturition reflex.[5,8]

Treatment options

Primary treatment options for OABS include the following: medication, BEHAVIORAL THERAPY, or

GLOSSARY

DETRUSOR UNDERACTIVITY
Impaired contractile function of the detrusor muscle leading to incomplete and/or prolonged bladder emptying

BEHAVIORAL THERAPY
A method of educating the bladder by documenting and timing micturitions, managing liquid intake, and controlling bladder contractions

GLOSSARY

URODYNAMICS
Catheter-based test measuring bladder sensation and involuntary detrusor contractions

PARURESIS
A form of social phobia expressed through the physical symptom of being unable to urinate whenever the person desires (i.e. in a public restroom)

IDIOPATHIC DETRUSOR SPHINCTER DYSSYNERGIA
Nonobstructive retention or voiding dysfunction due to functional bladder outlet obstruction at the external sphincter striated muscle

a combination of both. Strong clinical evidence indicates that antimuscarinic receptor antagonists are the treatment of choice, as they block the cholinergic muscarinic receptors (predominantly M_2 and M_3 receptor subtypes) that modulate and initiate bladder contraction. The antimuscarinic receptor antagonists available in the USA include oxybutynin (oral immediate-release and long-acting formulations, and in a transdermal patch), tolterodine (oral immediate-release and long-acting formulations), and trospium chloride (twice-daily oral formulation).

Antimuscarinics are generally effective in reducing symptoms of OABS, including urinary incontinence, frequency, and volume voided per toilet visit. For example, a primary outcome of improved continence of OABS would be 60–75% reduction in incontinence episodes. Adverse effects typical of antimuscarinic drugs include dry mouth, constipation, blurred vision, and CNS effects, including dizziness, somnolence and cognitive dysfunction, all of which can limit their use.[3,9]

Trospium choloride is a quaternary amine, making it poorly lipophilic and, therefore, it has a limited ability to cross the blood–brain barrier.[10,11] In addition, trospium is minimally metabolized by liver cytochrome P450 isoenzymes, and thus has no known metabolic drug–drug interactions.[12] Interestingly, of the trospium that is absorbed by the body, 60% is eliminated unchanged by the kidney[12] and is therefore available to act in the bladder. In a rat model of cholinergically induced OABS, twice-daily dosing, to produce the same level of trospium that has been measured in the human bladder, inhibited detrusor hyperactivity by decreasing the frequency of bladder contractions after intravesical carbachol stimulation. The exact mechanism of this action is not completely known, but might be due to the inhibition of an M_2 muscarinic receptor blockade of bladder-afferent pathways.[13]

Behavioral training that can improve OABS symptoms include educational reinforcement, use of bladder diaries, managing fluid intake, delayed and timed voids, and pelvic floor exercises to inhibit detrusor contractions. Behavioral therapy can reduce the number of incontinence episodes by approximately 50%, somewhat higher than the 30% improvement in symptoms seen in control groups not undergoing behavioral training.[3,14–16]

A combination of drug therapy and behavioral modification is usually the best approach when treating OABS. Older women (≥55 years of age) with OABS who changed from behavioral treatment to combination therapy significantly reduced incontinence by 58–89% ($P = 0.034$). Similarly, women who added behavioral therapy to their existing drug therapy significantly improved incontinence by 73–84% ($P = 0.001$).[17]

Cases that are more difficult to diagnose are referred for specialized tests involving URODYNAMICS that measure relative bladder pressure during the time of a 'sudden compelling desire to void'. This treatment strategy is usually recommended only if initial treatment fails.[3]

Promising investigational therapies include intravesically administered vanilloid receptor blockers to inactivate sensory neurons, and botulinum toxin injection directly into the detrusor muscle.[9,18–20] New orally administered pharmacotherapies include selective β_3-agonists to relax the detrusor muscle, and potassium channel openers that reduce spontaneous bladder contractions.[4,18] A summary of causes, diagnosis and management of OABS is given in Box 1.

UNDERACTIVE BLADDER SYNDROME

Pathophysiology

Incomplete bladder emptying indicative of detrusor underactivity is less well known, and is under-diagnosed compared with OABS; however, evaluation and effective management of a patient with chronic urinary retention can often be the more challenging of the two conditions.

Incomplete bladder emptying and urinary retention can be caused by abnormal bladder contractility, bladder outlet obstruction, or both. Bladder outlet obstruction has a number of causes, including BPH and PARURESIS, which is retention owing to IDIOPATHIC DETRUSOR SPHINCTER DYSSYNERGIA. Complete bladder emptying is dependent on the CNS, detrusor smooth muscle activity, coordinated bladder and urethral sphincter function, and voluntary initiation of voiding. Should any of these components go awry, incomplete bladder emptying could result.[21]

Urinary retention can be either obstructive or nonobstructive. Obstructive retention can be anatomical; for example, bladder outlet obstruction, or functional, as with idiopathic detrusor sphincter dyssynergia. Nonobstructive retention is generally caused by detrusor

underactivity.[22] Detrusor underactivity can lead to recurrent urinary tract infections and eventual kidney damage.[23]

Box 1 Evaluation and treatment of OABS.

Motor causes
Neurologic diseases damaging the nerves that innervate the bladder
Detrusor muscle damage
Anticholinergic drugs used to treat OABS possibly inducing a high residual urine volume and impaired bladder emptying

Sensory causes
Gradual expansion of the bladder to a large capacity due to sensory deficit (commonly seen in patients with diabetic neuropathy)

Evaluation
History (including medication history)
Physical examination
Urinalysis (to rule out infection)
Bladder diary
OABS symptoms and OABS symptom indexes
Residual urine screening
Urodynamics

Treatment
Medical therapies:
- Oxybutynin
- Tolterodine
- Trospium chloride

Behavioral therapy
Combinations of behavioral and drug therapies
Botulinum toxin injection into bladder
Neuromodulation (sacral nerve stimulation)
Investigational treatments:
- Selective β_3-agonists
- Potassium channel inhibitors

Sensory failure

The most common known cause of bladder sensory dysfunction is diabetes, which can result in sensory and autonomic polyneuropathy. When neurons innervating the bladder are damaged it can result in bladder dysfunction, characterized by impaired sensation of bladder fullness, increased bladder capacity, reduced detrusor contractility, and increased residual urine volume.[24] The prevalence of DIABETIC CYSTOPATHY is related to the duration of diabetes in the patient, although it can occur early in the course of the disease.

Myogenic failure

Detrusor muscle degeneration or damage can induce detrusor underactivity. Neurologic conditions such as lumbosacral radiculopathy are among the most common causes of impaired detrusor contractility. Detrusor myogenic failure can be secondary to chronic bladder overdistension, even if the neurologic disease is treated or reversed. Intermittent catheterization can protect the bladder from permanent myogenic damage.[22]

Neurogenic bladder defects

Detrusor underactivity can also be caused by acontractility of the bladder muscle owing to a CNS abnormality, although myogenic factors may contribute. Such neurogenic bladder defects can develop from various conditions in which the neurologic pathways innervating the bladder are damaged.[22]

Spinal cord injury can cause voiding dysfunction. Cauda equina and peripheral sacral nerve injury can have devastating effects on bladder function.[22] Trauma such as pelvic and transverse sacral fractures can result in cauda equina and pelvic plexus injury.[25] Most injuries from trauma are incomplete, so the majority of patients with neurourologic injury will improve over time. Again, intermittent catheterization to avoid overdistention of the bladder can prevent permanent myogenic damage.

A number of surgical procedures can often be the cause of postoperative vesicourethral dysfunction, including abdominal perineal resection, radical hysterectomy and proctocolectomy.[25] Voiding dysfunction can also be the presenting symptom of a herniated disc.[26] Recovery of detrusor function with treatment is uncommon once patients show evidence of bladder dysfunction following lumbar disc herniation.[25] Therefore, cauda equina syndrome from lumbar disc herniation should be considered a surgical emergency.

Infection of the CNS is another common cause of neurogenic bladder dysfunction. Among the infectious causes of bladder dysfunction are AIDS, neurosyphilis (tabes dorsalis), herpes zoster, herpes simplex, and Lyme disease.[25,27]

Medical therapies, such as anticholinergics that are used for OABS, block neurotransmission of acetylcholine and can also cause urinary retention particularly in those that are already at risk (e.g. men with bladder outlet obstruction).[27] RESIDUAL URINE SCREENING to check the residual urine volume after initiation of therapy can rule out potential problems.

There is also a condition commonly described as idiopathic urinary retention that usually occurs after a urinary tract infection or prostatitis.[22] Discussion of this topic is beyond the scope of this article.

GLOSSARY

DIABETIC CYSTOPATHY
Polyneuropathy characterized by impaired sensation of bladder fullness, increased capacity and residual urine volume, and reduced detrusor contractility

RESIDUAL URINE SCREENING
Noninvasive ultrasonographic assessment of residual urine volume rather than catheterization for residual volume

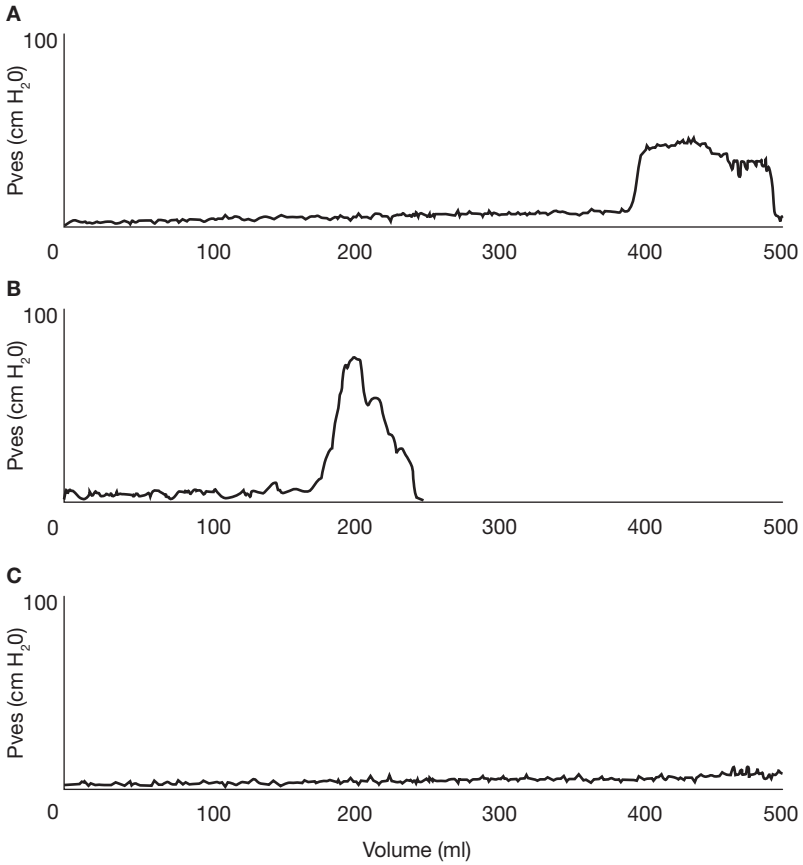

Figure 1 Cystometrograms (CMG) in normal urination, OABS, and detrusor underactivity. (**A**) Normal CMG in a woman 52 years of age without any voiding complaints. Bladder capacity was 400 ml, at which time she was told to void. She developed a voluntary bladder contraction of 48 cm H_20 magnitude. The bladder was stable during the filling phase. (**B**) OABS on a CMG of a woman of 58 years of age with day and night-time urgency, urinary frequency, and urge incontinence. She felt full at a volume of 185 ml, at which time she developed an involuntary bladder contraction. She was unable to inhibit this bladder spasm and leaked urine. (**C**) Detrusor underactivity of a woman with insulin-dependent diabetes who is 61 years of age, she voids only three-times a day. She strains to void but does not feel empty, leaks between voids, and has had recurrent urinary tract infections. On CMG she had no voluntary or involuntary bladder contractions to >800 ml. Pves, intravesical pressure.

GLOSSARY

UROFLOWMETRY
A noninvasive private test to screen for diminished flow rate; can predict impaired contractility, bladder outlet obstruction, or both

Diagnosis

Evaluation always begins with a careful history and physical examination. General symptoms of impaired bladder emptying are a feeling of fullness in the bladder area, straining to void, hesitancy, interrupted or diminished stream, double voiding, sensation of incomplete emptying, lower abdominal discomfort, constant dribbling, and recurrent urinary tract infections.[22] Physical examination might reveal a distended bladder, but the most characteristic features are elicited by a careful neurourologic examination. Evaluating the sacral dermatomes includes assessing perianal sensation, anal sphincter tone, and the bulbocavernosus reflex. Deep tendon reflexes in the lower extremities, clonus, and plantar responses should also be routinely evaluated.[22]

Once the history and physical examination is complete, evaluation consists of urinalysis to rule out infection, screening of postvoid residual urine volume with an ultrasonographic bladder scanner, UROFLOWMETRY that screens for diminished flow rate, and urodynamics.[22]

Urodynamics is a catheter-based test that measures bladder sensation and contractility. Detrusor underactivity is the typical cystometrogram finding of neurogenic bladder dysfunction (Figure 1). On uroflowmetry, a sawtooth pattern is generally seen, suggesting abdominal straining.[22] In some patients with cauda equina injury, urodynamic abnormalities may be the only findings, with no other obvious neurologic manifestations. For example, patients with complete cauda equina lesions will have shorter latency of sacral-evoked potentials, as recorded by stimulating penile skin with a needle electrode in the bulbocavernous muscle.[28] Therefore, these patients have an absent or diminished bulbocavernosus reflex, detrusor underactivity, neuropathic changes on perineal floor electromyography, and absent evoked electromyographic responses. Fluoroscopic evaluation of the bladder outlet appearance is also possible during this testing.[29]

In a patient with a high residual urine volume (≥300 ml), bacteria can quickly multiply in the bladder, overgrow, and become stagnant, even if sterile techniques are used.[22] Ultrasound scanning of the bladder, which assesses residual urine volume, is important to avoid unnecessarily catheterizing these patients.

Treatment

One approach to treating detrusor underactivity is to drain the bladder by indwelling urethral or suprapubic catheters or clean intermittent catheterization. There is a consensus that intermittent self-catheterization is the preferred treatment. Indwelling catheters are used when patients are either unable to or refuse to intermittently catheterize themselves. Generally, suprapubic tubes are more comfortable than urethral catheters, are easier to change and allow the patient to remain sexually active. In female patients, long-term urethral catheterization can cause erosion damage and fistula formation to the vagina and should be avoided.[22] Those patients with sensory uropathy, for example from diabetic cystopathy,

should void at routine times to prevent chronic overdistention of the bladder.[30]

Sacral nerve stimulation can promote voiding in patients with idiopathic detrusor sphincter dyssynergia and incomplete bladder emptying.[31] The stimulation suppresses sphincter guarding reflexes, thereby facilitating bladder contraction.[32] Pharmacologic therapy with a parasympathetic cholinergic agonist facilitates detrusor muscle contraction.[33,34] Although no prospective randomized clinical studies support the efficacy of bethanechol, it is nevertheless the only approved drug to treat detrusor underactivity. Bethanechol works rapidly after administration, so efficacy for a particular patient can be determined within days (Figure 2). Adverse effects include upset stomach, vomiting, dizziness, wheezing, sweating, and flushing.[22]

Alpha-1 adrenergic antagonists are also used to treat urinary retention. These drugs relax the bladder neck and prostate, and have been shown to decrease residual urine in neuropathic and non-neuropathic bladders, as well as to subjectively improve symptoms of BPH.[35,36]

Biofeedback and botulinum toxin injection into the urethral sphincter muscles can be considered as treatment options for functional and anatomical bladder outlet obstruction, respectively.[22,31,37–39] A summary of causes, diagnosis and management of underactive bladder syndrome is given in Box 2.

CONCLUSION

The future of diagnosis and treatment for OABS and detrusor underactivity looks bright. Advances in diagnostic tools such as radiofrequency urodynamic telemetry could improve how we monitor bladder and urethral function without catheterization. This would allow a much improved assessment of how the lower urinary tract functions under more natural conditions. We speculate that with improved diagnosis of detrusor underactivity, the number of patients with this condition would increase significantly, and will stimulate the medical community to develop even better treatment options.

With the rapid advances being made in the areas of human genomics and molecular medicine, we can envision a time when transplantation of muscle stem cells will restore muscle contractility in patients with detrusor myogenic failure. A patient with neurogenic bladder denervation might be able to void again because of gene therapy that will allow the expression of neurotrophic growth factors to repair the damaged nerves. For refractory OABS, we foresee gene therapy that could compensate and correct the abnormal sensory and motor neurotransmitter receptors, and inhibit the abnormal micturition reflexes.[31,40]

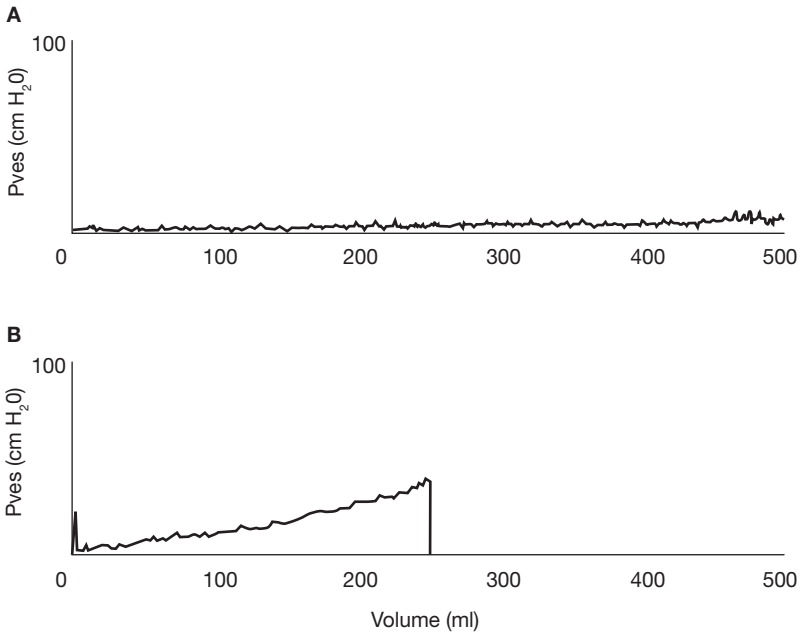

Figure 2 Effect of bethanechol in the diabetic woman (as described in Figure 1C). (**A**) Baseline CMG demonstrating detrusor underactivity. (**B**) Repeated CMG 30 minutes after oral ingestion of 25 mg bethanechol. Bladder pressure increased to 35 cm H_20 at a volume of 250 ml. Pves, intravesical pressure.

Box 2 Evaluation and treatment of underactive bladder syndrome.

Causes

Urethral obstruction:
- Mechanical obstruction (BPH and urethral stricture)
- Functional obstruction at the pelvic floor external sphincter (paruresis)

Bladder motor dysfunction:
- Neurologic diseases damaging the nerves that innervate the bladder
- Detrusor muscle damage
- Anticholinergic drugs used to treat OAB possibly inducing high residual urine and impaired bladder emptying

Bladder sensory dysfunction (gradual expansion of the bladder to large capacity owing to sensory deficit, commonly seen in patients with diabetic neuropathy)

Evaluation

Urinalysis (to rule out infection)
Residual urine screening
Uroflowmetry
Urodynamics

Treatment

Catheterization
- Indwelling urethral catheters
- Suprapubic catheters
- Clean intermittent catheterization

Biofeedback
Pharmacotherapy (bethanechol chloride, 25 mg three/four times daily is only drug approved for urinary retention)
Urethral sphincter botulinum toxin injection
Neuromodulation (sacral nerve stimulation)

Competing interests
The authors have declared competing interests, go to the article online for details.

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