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State-of-the-art office evaluation and treatment options for symptoms of an overactive bladder

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The defining symptom of an overactive bladder (OAB) is urgency. OAB is a condition that 16% of Americans suffer from. There is a direct cost of more than $6 billion annually. Symptoms of an OAB affect both men and women in almost equal percentages, especially with advancing age. Most medical offices have the ability to offer state-of-the-art evaluations in a painless and efficient manner. There have been significant breakthroughs in minimally invasive technology that provide practitioners with specific data to help customize treatment for each individual patient.

Over the past 15 years, there have been multiple advances in treatment options for OAB. We have seen several new medications that are more selectively geared toward the urinary bladder. There have also been advances in surgical and nonsurgical modalities. We see that most of these advances benefit patients who have refractory symptoms. The greatest advances have occurred in the area of neuromodulation. We now are able to improve our patients' quality of life, even in the most extreme cases.

Many other symptoms are seen in patients with an OAB. Using state-of-the-art technologies, we can quickly evaluate most of these patients in the office setting. The medical history and physical remain the mainstays of evaluating these patients. As osteopathic physicians, we have the unique ability to focus our evaluations by fully understanding the neurologic and muscular physiology for this condition. The osteopathic physician has an advantage when applying a complete musculoskeletal examination as part of the physical. We can potentially uncover other contributing conditions that are perhaps easier to treat. As our research and the osteopathic profession expand, perhaps we can formulate newer treatment opportunities using manipulative medicine. This article focuses on the current and practical treatments available to our patients.

Introduction

More than 30 million Americans are estimated to have an overactive bladder (OAB).[1] The direct cost of this is approximately $6.9-$12.6 billion annually.[2,3] The pharmaceutical and device companies have improved our success with regard to the treatment of OAB; however, the cost of research and development is reflected in the rising cost of therapy. This condition becomes more prevalent with advanced age, so as the population ages, we can expect to see a higher number of people affected by this condition. Unfortunately, this will also lead to higher costs in treating these patients.

Prior to 1980, the medical community used terms such as unstable bladder, detrusor instability, or detrusor hyperreflexia. These terms are extremely confusing and very difficult to properly use in diagnosing patients without invasive testing. In 1980, the International Continence Society (ICS) began to use the term overactive detrusor as a generic term to simplify terminology. The term OAB was first used in 1997. Today, the term OAB reflects this very specific con-

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dition with an appropriate treatment option by a trusted medical provider.[4]

Direct patient advertising exposes more people to the term and symptoms of OAB. These same advertisements include specific treatment modalities. Our population is receiving its education from the advertising community and may not only be receiving inaccurate, but biased information. In turn, the medical community must be prepared to address questions and help our patients better understand the information they see and hear from non–medical sources. Primary care physicians (PCPs) are in the unique position of being the primary educator for our patient population. With the help of the PCP, the patient can be properly educated and directed to an appropriate treatment by a trusted medical provider.[5]

Definition

The definition of the OAB requires a patient to have the complaint of urgency with or without the presence of incontinence.[1-3] Urgency is the sudden desire to urinate with difficulty deferring the sensation. Urge incontinence is the involuntary leakage of urine accompanied by or immediately following a feeling of urgency.

In 2002, the ICS came to a consensus replacing the criteria that required a urodynamic finding of a spontaneous involuntary contraction of the detrusor during the storage phase of filling.[4] The second major change ICS recognized is that incontinence is not a prevalent feature. The current ICS standardized definition does not require incontinence to be present in a patient with OAB.[2] Associated symptoms may include frequency and nocturia. Frequency is the complaint of voiding too often during the day, usually more than 8 times. Nocturia is the complaint of having to urinate at night, waking the individual from sleep 1 or more times.[5]

We need to avoid confusing stress urinary incontinence (SUI) with OAB. SUI is leakage that is involuntary and associated with exertion and other causes that increase intra-abdominal pressures.[3] SUI is physiologically very different from OAB. SUI typically has a defective sphincter mechanism, allowing for urine to leak when the abdominal pressures exceed the ability of the sphincter to hold back the urine. SUI is frequently treated by increasing the urethral sphincter pressures with bulking agents, urethral sling procedures, or bladder neck suspension. Patients with mixed incontinence have signs or symptoms of stress incontinence and urge incontinence. Treatment starts by correcting the most pronounced part of the condition.

Similar symptoms with urgency are also seen in patients with neurologic conditions, such as recent stroke or spinal cord injuries. Patients with neuropathic origins are classified as having a neurogenic bladder (NGB). Lapides identified the following 5 subcategories of NGB: sensory NGB, motor NGB, uninhibited NGB, reflex NGB, and autonomous NGB. The remainder of this paper focuses on patients with the primary diagnosis of OAB and excludes those who have either SUI or NGB, including any of Lapides' subcategories.[4]

Prevalence

The NOBLE study in 2001 showed that the overall prevalence of OAB in the United States was approximately 16%. An estimated 34 million people have this condition.[1,6,7] The ranges of OAB vary in developed countries from 7%-17%. In 2006, EPIC trial identified the range to be from 11%-13% in Canada and Europe.[8]

A common misconception is that OAB is a female condition. Women do have a slightly higher prevalence than men—when all age groups over the age of 18 are reviewed, the prevalence in women is 17% and in men it is 16%.[1] The incidence increases with age in both men and women, but we start to see men affected more than women with increasing age. For ages over 60, women have an 18.3% incidence and men are at 19%.[9] When we look at ages over 75, the condition affects men more, with women at 31% and men at 42%.[10]

Obesity plays a role in patients with bladder symptoms. Women experience higher rates of incontinence with higher body weights. This association occurs in all subtypes of incontinence. Interestingly, women with higher body mass index (BMI), but not men, have an increased incidence of wet OAB. The NOBLE study showed a direct correlation of BMI levels over 30 and incontinence associated with OAB. There is a 2.2 times greater rate of wet OAB in women with BMI over 30 compared with women with a BMI under 24.[11] There is no significant difference in African-American women compared with Caucasians or Hispanics.[12]

Etiology

The exact etiology of OAB is not fully understood. We do know that urothelial cells possess properties—both sensory and signaling—that allow communication with each other and the neurologic system via chemical pathways. They respond to chemical changes and the physical environment. Afferent activity is disproportionately higher in relation to the amount of bladder distention in someone with OAB.

There are 3 prominent theories for OAB. The first is the neurogenic model, which is primarily due to nerve–mediated activity. It is commonly seen in cases of increased sensitization of peripheral afferent nerve endings. This increased sensitization leads to a triggering of an abnormal detrusor response, which leads to bladder function being overactive.

The myogenic model suggests that a spontaneous smooth muscle contraction will be followed by a prolonged propagation of abnormal activity in the detrusor. In the laboratory, this model has been demonstrated using strips of de-

trusor muscle tissue. The degree of overactivity was able to be altered using pharmacologic agents.

Lastly, the peripheral theory suggests that there is an increase in the sensitivity from exaggerated smaller modular contractions. The concept accepts that the muscle units exist as small modules. It is believed that these smaller modules of tissue synchronize and then result in a stronger, coordinated contraction.[4]

Evaluation

History and physical examination remain the most important components of evaluating the patient with OAB. Crucial information needed to make a diagnosis and initiate therapy can be obtained from an appropriate history and focused exam. Chronic and acute neurologic conditions, recent injuries, or pelvic procedures may suggest other causes for the patient's condition.

History of acute symptoms with urgency, frequency, dysuria, and blood in the urine may suggest an infection. This information may direct the practitioner to treat the condition and correct the symptoms using an appropriate short course of antibiotics. Symptoms of SUI are related primarily to increases in the intra-abdominal pressure. The rise in pressure exceeds the ability of the sphincter to overcome these pressures. The patient may complain of small spurts of urine with coughing, laughing, or sneezing. Patients experiencing larger volumes of leakage with urgency would suggest wet OAB. Blood in the urine in an adult patient in the absence of an infection warrants a workup for malignancy. There is a higher degree of suspicion when the hematuria is painless and involves a smoker.[4,5,13]

Medications also can alter a previously normal urinary pattern. Over-the-counter medications containing decongestants for upper respiratory infections as well as alpha blockers for hypertension can affect bladder emptying. Diuretics usually result in increasing frequency and can even worsen the symptoms of OAB.

Medical providers should ask patients if they have a strong and unexpected desire to urinate. Is there loss of control of urine? How often do they wake up at night to urinate? We need to ask about the number of times they urinate during the day. Does the patient use protective pads, and if so, how often are they changed? A focused examination should be able to demonstrate abnormalities with neurologic deficits, which would suggest neurogenic conditions causing these symptoms. Pelvic floor abnormalities, such as cystocele or vaginitis, would suggest gynecologic issues. Bladder neck hyper-mobility with reproducible incontinence would identify SUI. Rectal examinations should be performed in all males. The exam might demonstrate an enlargement seen in benign prostatic hyperplasia or a prostate nodule that may suggest a malignancy. Abdominal or pelvic scars or markings may suggest previous surgeries or radiation therapy, which could affect normal functioning.[5]

Some very simple studies can guide the practitioner on the further workup or treatment for the patient presenting with urinary symptoms. An office urine test may find abnormalities, such as leukocytes, that may suggest an infection. Elevated glucose can be a sign of diabetes. Blood in the urine can be a sign of malignancy. Elevated post void residuals identify a patient with urinary obstruction. The most common tools to identify obstruction include a bladder scanner, ultrasound, or catheter. A normal post void residual should be less than or equal to 50-100 mL.[13] Uroflow and urethral calibration are also used to identify patients with obstruction. These patients have a low urinary flow rate or a narrow urethra. The number of pads a patient uses or the weight of these pads along with a voiding diary can help determine the complexity and severity of incontinence.[14]

A urinary culture will identify particular organisms that may be causing an infection. Cytology is used in identifying patients who have a malignancy. More invasive studies, such as cystoscopy, will identify obstruction, tumors, and other unusual causes for urinary complaints. Urodynamic testing can verify detrusor instability, bladder capacity, and bladder pressure changes. These more invasive tests are helpful when trying to assess the patient with a more complex and confusing presentation. Not every patient with OAB needs these more advanced and invasive studies.

Treatments

Patients with mild forms of OAB may respond to conservative management. Those who do not want medication or experience side effects from medicine should at least be offered these lesser invasive options. Simple dietary changes that avoid irritants can be helpful. Products that contain caffeine and other stimulants have been shown to worsen urinary bladder symptoms.[1] Weight loss through diet and exercise has shown positive outcomes through the Program to Reduce Incontinence by Diet and Exercise (PRIDE). Unfortunately, the evidence to support improvement in UUI is not as strong as the evidence of weight loss in people with SUI. Another identified concern showed that maintaining weight loss long-term is not very successful.[11] Behavioral modifications may also help patients lessen the frequency and degree of incontinence. These techniques include timed voiding on a fixed schedule and bladder retraining with pelvic floor exercises. The goal is to attempt to increase the voiding time intervals. A slow increase in intervals range from 15-30 minutes as they slowly try to reach a 60-minute delay in urination.[1,14]

The combined use of the peri-urethral musculature and tightening techniques along with inhibiting contractions has shown measurable improvement. The use of biofeedback has been used to increase the success rate with the above techniques. When suppression techniques are combined with attempts to increase voiding intervals, 80% of patients have reported a reduction of UUI vs 39% in placebo groups.

Success rates using conservative therapy will increase with the addition of pharmaceuticals.[14]

Antimuscarinics are the pharmacologic agents of choice.[15] They have anticholinergic properties that relax the detrusor muscle allowing the patient to either retain larger volumes or inhibit detrusor contractions. The vast majority of bladder muscarinic receptors are in the detrusor and the bladder neck. The most prevalent receptor in the bladder is the M3 receptor.

Oxybutinin is one of the oldest anticholinergic drugs. Due to its generic formulation, it is found on most insurance plans. It is also one of the least expensive agents in its oral form. There are also patches and gel formulations, but they are more expensive. All formulations have proven to decrease the amount of voids per day and UUI. There also has been a significant improvement in the quality of life metrics. Oxybutinin is a nonselective agent, which results in a less desirable side effect profile.[8] The adverse effect profile of oxybutinin rises significantly with doses of more than 10 mg/day.[12] Some of the more severe side effects are higher rates of memory loss and poor cognitive function. These side effects are more prevalent in the immediate-release formulation.[11] Common side effects of all antimuscarinics include dry mouth, drowsiness, and constipation. The side effect profile will vary with each agent.[15,16]

Some of the more recent medications include tolteradine, darifenacin, solifenacin, fesoterodine, and tropsium. Tolteradine has been used in combination with alpha blockers for men having symptoms of benign prostatic hyperplasia along with symptoms of OAB with few side effects. Darifenacin is a selective M3 antimuscarinic.[17] In theory, this should lead to fewer side effects as the agent focuses on the M3 bladder receptors.[16] Tropsium is a quaternary structure. This property lowers its potential permeability with the blood-brain barrier. This also should lessen neurologic side effects. Each product should be initiated at the lowest possible dose and then titrated as needed.[2,13]

Regardless of which product is used, they all have been shown to be effective in treating the symptoms associated with OAB. There have been head-to-head studies with fesoterodine and tolteradine showing superiority in effectiveness in the former in patients with UUI.[15] None of the other products has been studied in this fashion.

Advances have also been made with refractory OAB—up to 40% of all patients with OAB have refractory symptoms.[18,19] Treatments using botulinum-A toxin (Botox) and neuromodulation have been effective in many of these cases.

Botox requires invasive cystoscopy with multiple injections of 8-10 sites into the trigone. This causes the striated smooth muscle to relax. A possible side effect may cause the patient to experience urinary retention that will require intermittent catheterization. For motivated individuals, this is a reasonable alternative to surgery and other invasive therapies. Most patients respond to doses of 100-150 units. Symptoms improve, including UUI. No further UUI is experienced by 30%-57% of patients.[18,20] On August 25, 2011, the Food and Drug Administration (FDA) approved the use of Botox for symptoms of OAB in neurologic conditions.[21] Any other use is considered off-label at this time. This may result in a large out-of-pocket expenses for off-label use.

The first reported use of neuromodulation for lower urinary tract symptoms was in 1987. The treatment is currently used in patients with refractory OAB and those unable or unwilling to take medication.[6] Neuromodulation targets specific nerves in the sacral plexus. These treatments include peripheral tibial nerve stimulation and sacral nerve stimulation. Peripheral tibial nerve stimulation involves placing a needle into the area of the posterior tibial nerve as an electric impulse is generated and conducted to the nerve from a small portable generator. Most patients respond after 12 weeks of weekly treatment. MacDiarmid et al demonstrated a 71% improvement in frequency, nocturia, urgency, and UUI. Peters et al demonstrated a 54% improvement in symptoms and 96% sustained improvement.[7]

Sacral nerve stimulation involves the placement of a treatment wire into the S3 foramen using either landmarks, palpation, fluoroscopy, or sonography.[2,13] Studies done in the 1990s led to an approval by the FDA to Medtronic for release of this product in 1997. Either continence or improved UUI has been achieved by 70%-80% of patients. The mechanism of action is uncertain. It is thought to be an inhibition of somatic afferent activity. The cost of this treatment exceeds $22,000. Ideal candidates should first have a temporary test lead placed. This is referred to as a stage 1 procedure. If there is more than 50% improvement, then the patient should be offered a permanent implant.[13,19]

More invasive surgery involves the excision of a part of the bladder, an incision that creates a mucosal bulge or complete urinary diversion. These are better used in patients with neurologic conditions. Patients with non-neurogenic etiology have a poor result. Side effects include self-catheterization, bladder stones, recurrent infections, and electrolyte abnormalities.[4]

Discussion

In the last 2 decades, there have been several advances to help people with OAB symptoms. With this progress comes an increase in the cost of treatment. The total cost, including indirect costs, exceeds $26 billion annually. This not only includes the cost of progress with medication and therapies, but also other comorbidities.[5] The cost of OAB treatment rises proportionately with the associated morbidity of this disease.[1] Morbidities that increase indirect costs include the risk of falls, fractures, and skin complications in the elderly. Any one of these can lead to hospital admission, and in the most severe cases, even death.[4,12,14]

Patients also may suffer from many other conditions, including depression and sleep disorders.[20] Women with frequency are more bothered than men, while men with

incontinence are more bothered than women, 77% vs 67%. Overall, women cope better than men with these conditions, 73% vs 67%.[15] Quality of life decreases with incontinence, and many of these previously productive patients experience loss of work and income. Patients with incontinence are partly responsible for 50% of all nursing home admissions.[4]

Many patients with UUI experience severe leakage. This can result in complete bladder emptying in a single episode, which leads to a risk of damage to clothing and furniture. The embarrassment can lead to isolation and further psychological injury. Relationships can be lost due to this isolation. The patient may also experience a loss of intimacy. Many of these same patients limit their physical activity, which can lead to further morbidity with the musculoskeletal system. These losses lead to further financial burdens to the patient, family, and society.

We cannot cure every patient experiencing symptoms of OAB, but we can offer an improvement in the quality of life. One of the most important goals we need to keep in mind for our patients is to maintain a level of physical activity and the maintenance of good function. We cannot stop the aging process, but we do have options to help our patients with this condition. When starting treatment, take into consideration age and other comorbidities. When choosing a medication, try to find one that would offer the least adverse effects. It is important to always start with the lowest possible dose.

The PCP is in the unique position of offering the patient the first line of defense for proper treatment and education about this and other conditions. It is our responsibility to guide the patient to the proper treatment modality. Supervision of these treatments is uniquely inherent to the role of the PCP. With the concept of the medical home model, PCPs will find their role invaluable in the treatment and diagnosis of OAB.

Although currently there are no published treatments using manipulation specifically for OAB, Walton refers to craniosacral and thoracolumbar supply to the urinary bladder. He demonstrates visceral reflexes that can be used to evaluate and plan treatment for issues with the urinary bladder.[22] As the research arm of the osteopathic profession makes advances, we may find the ability to offer further alternative treatments with fewer side effects for patients with OAB.

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