STRESS INCONTINENCE AND PROLAPSE (R DMOCHOWSKI, SECTION EDITOR)

Diagnosis and Management of Stress Urinary Incontinence in Females With Neurogenic Disease

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Abstract Women with a wide variety of neurological conditions, including multiple sclerosis (MS), Parkinson's disease (PD), cerebrovascular accidents (CVA), and spinal cord injury (SCI) frequently develop neurovesical dysfunction, commonly resulting in what is often called neurogenic bladder (NGB). The most common manifestations of NGB are urinary urgency, frequency, and urgency urinary incontinence (UUI). However, because many women with NGB conditions lead active lifestyles and are at an age when stress urinary incontinence (SUI) is prevalent, indeed, SUI is not uncommon in affected women. It is also true that, in some conditions, SUI may be a direct result of the neurological insult, for example, patients with low thoracic or lumbar SCI. Thus, deciphering the cause of urinary incontinence in patients with NGB is often complex, yet vital to developing optimal management strategies. This review focuses on the recent literature regarding both the diagnosis and treatment of SUI in women with NGB. In particular, specific strategies that may be essential in evaluating women with NGB and urinary incontinence (UI) will be discussed. Additionally, we will discuss both treatments uniquely applicable to patients with NGB and SUI as well as common treatments that might have unique risks

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and adaptations in women with NGB. From this review, it is clear that, as standardized practice and technologies continue to grow for management of SUI in patients with comorbid neurological conditions, additional research and analysis may be required to determine the complexities of this unique disease process.

Keywords Neurogenic bladder · Multiple sclerosis · Parkinson's disease · Spinal cord injury · Stress urinary incontinence · Urodynamics · Pubovaginal sling

Introduction

Stress urinary incontinence (SUI) is a common condition that can affect women as early as their teenage years. Approximately 10 to 25 % of women aged 15–64 develop SUI [1•]. However, for patients with neurogenic bladder conditions, the incidence of SUI is more difficult to define and has been evaluated only in certain populations [2], since urgency urinary incontinence (UUI) is more typically the focus of studies in women with neurogenic bladder (NGB) [3••].

Recent studies suggest that the prevalence of SUI in women with neurogenic disease such as multiple sclerosis (MS) is lower than expected, though the actual frequency of MS patients with SUI is unclear [4•]. Dillon et al. found that 45 of 280 (16 %) women with MS had SUI demonstrable on UDS or pelvic exam. This number was lower than the 30–50 % prevalence of SUI in an age-matched MS population [4•]. It remains unclear if this relative reduction in SUI prevalence is due to diminished physical activity associated with certain MS conditions, increased bladder neck tone resulting in enhanced resistance, or some other physiological mechanism related to the underlying neurological condition. A prospective study

used the Urogenital Distress Index-6 (UDI-6) and Incontinence Inventory Questionnaire-7 (IIQ-7) to determine the rate of stress incontinence among MS patients. This study found a higher proportion of patients than expected; 80 of 143 (55.9 %) of women reported incontinence with exertion [2]. However, the study admits possible bias towards women seeking urological care. In addition, the group noted that overactive bladder (OAB) is observed more frequently in this patient population (101 of 143 or 70.6 %) [2]. Data is less abundant with regard to the prevalence of SUI in Parkinson's disease (PD) and spinal cord injury (SCI). Patients with very low thoracic (T10-T12) and lumbar level SCI have been consistently shown to have a higher likelihood of intrinsic sphincteric deficiency resulting in SUI [5].

Diagnosis

Guidelines

In 2012, the National Clinical Guidelines Centre published the NICE Guidelines for evaluating and managing lower urinary tract symptoms in neurogenic patients, including SUI. A detailed history of any urinary tract symptoms, post-void residual, urine dipstick analysis, focused neurological exam, evaluation of hand function and mobility, and input from caregivers are vital to assessing any patient with a neurogenic bladder. Upper tract studies must also be considered in highrisk patients, specifically those with spinal cord injuries and spina bifida [6]. These guidelines do not delineate specific diagnostic algorithms for female patients or necessarily those with SUI though they are useful guides for the general evaluation of any new patient with neurogenic bladder.

Validated Questionnaire Data for Patient-Reported Symptoms

In addition to a thorough physical exam including a pelvic exam, validated patient-reported questionnaires data are the vital in the initial diagnostic assessment. Non-condition specific yet validated lower urinary tract questionnaires are frequently used in NGB patients to evaluate LUTS. The Urinary Distress Inventory-6 (UDI-6), which assesses the bothersomeness of various LUTS on daily life, is one commonly used questionnaire that has been utilized successfully in patients with NGB [2, 7...]. It has been noted, in particular, that question 3 of UDI-6 is independently associated with the urodynamic finding of SUI among women with MS [7••]. The Incontinence Impact Questionnaire-7 (IIQ-7), which assesses the impact of LUTS on daily life activities, has also been similarly used [2, 8] A profound impact of urinary incontinence (UI) on quality of life related to reduction in physical recreation has been noted among patients with NGB conditions [2, 8].

Condition-Specific Instruments

Currently, there are no widely accepted patient-reported outcome measures specifically for patients with NGB. Welk et al. recently created and validated the Neurogenic Bladder Symptom Score (NBSS) to measure urinary symptoms and consequences among patients with acquired or congenital neurogenic bladder [9•]. A total of 230 patients (men and women grouped together) with neurogenic bladder conditions (136 with MS, 80 with SCI, 14 with congenital neurogenic bladder) were given the 22-question questionnaire including items focusing on incontinence, storage, and voiding symptoms. The questionnaire compared favorably with non condition-specific LUTS scales such as AUA-SS, ICIQ-UI, and Qualiveen scales [9•]. In addition, in 2007, the Incontinence Quality of Life (I-QoL) was validated for patients with neurogenic bladder [10]. Fifty-nine patients, mostly with SCI or MS, demonstrated appropriate I-QoL response to symptom improvement after a single Botox injection [10]. While mainly used for assessing treatment impact on quality of life, the I-QoL may still have widespread applicability for a variety of interventions in patients with NGB conditions.

Urodynamic Studies for Diagnosing SUI

Urodynamic investigations have important predictive value in the management of patients, including those with neurogenic disease. Historically, urodynamic (UDS) have been vital in determining intravesical pressures in patients with NGB (via measuring detrusor leak point pressure) and in so doing, assessing the potential risk of renal damage over time [6]. Adding fluoroscopic monitoring during video UDS gives a more precise view of the bladder neck during filling and voiding, assesses for vesicoureteral reflux, and is of particular use in patients with NGB. NICE guidelines recommend UDS testing in patients with NGB prior to any surgical intervention. While SUI can be diagnosed accurately without the use of UDS and indeed, UDS may not enhance the outcome of non-NGB patients undergoing surgery for SUI [11], the same may not be true for patients with NGB conditions. Not only is establishing the diagnosis of SUI crucial, but also a careful assessment of the voiding phase is essential to minimizing the risk of voiding dysfunction that may be associated with surgical intervention for SUI. Subtle forms of dyssynergia, while perhaps unnoticeable to the patient, may result in severe voiding dysfunction following surgical intervention, and thus, patients should be carefully screened with EMG and video monitoring at the time of UDS, particularly prior to considering surgery. Additionally, a careful assessment of bladder compliance is critical in patients with NGB conditions, as the ramifications of untreated poorly compliant bladders are potentially devastating particularly if there is a risk of inducing bladder outlet obstruction by the surgical intervention. Other



aspects of the evaluation, including voiding diaries and pad tests, also likely have a role in select populations [8, 12].

Role of Functional Neuroimaging for Evaluation of SUI

Functional neuroimaging has been used to evaluate brain control of bladder storage and micturition and has been studied to assess the potential impact of deep brain stimulation (DBS) on urinary control in patients with PD. In a literature review on the topic, Fowler et al. found that, among patients with SUI, functional MRI can be used to observe how pelvic floor exercises can alter motor and somatosensory cortex involvement of micturition. Pelvic floor exercises helped focus the primary motor and somatosensory cortical responses [13]. Though clearly not yet ready as a preferred primary diagnostic modality, the possibility of utilizing these types of imaging modalities to predict symptom patterns and progression in patients with NGB is an intriguing one.

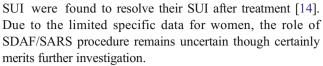
Management

Pelvic Floor Muscle Training and Pelvic Floor Electrical Stimulation

Various methods of pelvic floor muscle training and nerve stimulation have been examined for the treatment of SUI in patients with NGB. McClurg et al. evaluated the effectiveness of pelvic floor training, electromyography biofeedback, and neuromuscular electrical stimulation (NMES) via an intravaginal probe, used in combination, for lower urinary tract symptoms in women with MS. Their findings indicate that the combination therapy was more effective in reducing incontinence episodes leakage volumes than pelvic floor training alone or combined with EMG biofeedback among patients with MS. The results also indicate that a program of pelvic floor training with EMG biofeedback is more successful at relieving these symptoms than pelvic floor training alone [8]. Although taken from a relatively small study (n=30), these findings suggest that in certain patients with MS and SUI, non-medical and non-surgical interventions are still viable options.

Spinal and Deep Brain Stimulation

For those without intact voluntary pelvic floor control, other methods of nerve stimulation have been studied. Krasmik et al. investigated sacral intradural deafferentation and sacral anterior root stimulation (SDAF/SARS) via an implantable device in SCI patients with a variety of LUTS. While the patients in this studied were mixed in terms of baseline LUTS type and severity as well as gender, 44 of 70 patients with



An interesting functional neuroimaging study of patients with PD, though not exclusive to females, demonstrated the potential benefit of DBS of the subthalamic nucleus (STN) in those with UI. By using PET signals to observe regional cerebral blood flow (rCBF), bladder filling was found to significantly increase rCBF in the anterior cingulate gyrus and lateral frontal cortex. DBS improved the coordinated cortical control of pelvic floor muscle activity and eliminated supplemental motor and pre-motor activity resulting in the potential for improved UI in PD patients [15]. Further study of functional incontinence outcomes appears to be warranted by this initial innovative trial.

Implantable Continence Devices

Artificial Urinary Sphincter (AUS) has been recommended in specific populations of neurogenic patients suffering from SUI due to ISD, though has largely been studied in men. One group studied 51 patients with spinal cord lesions (37 with SCI, 8 with myelomeningocele, and 8 with other spinal cord lesions) and SUI who underwent AUS placement. Pre-operatively, 41 patients used CIC to empty their bladders, while 10 voided by sacral anterior root stimulation. Thirty-six patients (70.6 %) reported postoperative continence [16]. It is important to note that 38 of 41 patients continued to require intermittent catheterization, which may be a concern for patients with implanted AUS, due to the risk of cuff erosion in patients requiring lifelong CIC. The authors further note that there were additional pump concerns in women undergoing AUS, such as labial skin erosion and deactivation of the pump during straddling activities (i.e., bicycle riding) [16]. Thus, while the AUS seems to be a potential treatment option for SUI in patients with SCI, a consideration of the ongoing need for CIC and a thorough discussion of the potential complications associated with AUS placement are mandatory.

Mehnert et al. studied implantation of an adjustable continence device (ACT) in 37 patients (24 women and 13 men) with NGB. The majority of patients had SCI (51 %), spina biffida (19 %), or cauda equina syndrome (11 %). The device was placed via a minimally invasive approach (under local anesthesia in the majority of patients), and patients were followed for 4 years. Pad use and number of incontinence episodes were significantly reduced postoperatively, with greater than 50 % improvement in incontinence noted in 67.6 and 64.8 % of patients at 1 and 2 years, respectively. Only 21 % gained full continence, 39.4 % had the device permanently removed, either due to insufficient efficacy of



adverse event, and 24 % of patients went on to further surgeries, including AUS, bladder neck closure, and ileal conduit [12]. While ACT is an interesting option for patients who might be at significant surgical risk due to other comorbidities, its role in this patient population remains unproven.

Mid Urethral Synthetic and Pubovaginal Fascial Sling

As mid urethral slings (MUS) have been widely accepted as a standard surgical option for management of SUI in female populations, their specific success in patients with neurogenic bladder has also been studied. Hamid et al. conducted a retrospective review of 12 women with NGB (3 with SCI, 3 with spinal stenosis, and 6 with disc surgery) who underwent retropubic mid urethral sling placement (RMUS) for urodynamically proven SUI. Prior to surgery, 9 women used CIC to empty their bladders, while the other 3 used suprapubic compression to void. Each of the 12 women continued her prior voiding method post-operatively, with no patient needing to start self-catheterization. Overall, 10 patients resolved their SUI and were considered successes, while one developed worsening neurogenic detrusor overactivity and one had no SUI improvement [17]. Ongoing evaluation of 9 of these patients followed for 10 years demonstrated that 7 remained continent with a significant decrease in the number of pads per day. All 9 patients were satisfied with results at 10 years $[1 \bullet]$.

Others have investigated the use of transobturator tape mid urethral slings (TMUS). Pannek et al. conducted a study of 9 women with SUI due to intrinsic sphincteric deficiency in the setting of SCI who underwent TMUS. Of the 9 women, 7 managed their bladders with CIC, one voided voluntarily, and one had a suprapubic catheter and all 9 patients had SUI observed on VUDS. Overall, 2 patients gained continence, while one patient had a 50 % improvement in pad use, and 6 patients had no improvement. Furthermore, one patient developed urethral erosion. Five of these patients went on to have further surgeries for their incontinence [18•]. These findings clearly question the efficacy of TMUS in the NGB population, perhaps due to more severe ISD in the setting of neurogenic disease

Pubovaginal sling (PVS) utilizing rectus fascia has also been studied for the treatment of SUI in patients with NGB. In general, those patients with NGB undergoing PVS are on CIC, but leak between catheterizations due to ISD. In a retrospective chart review, Athanasopoulos et al. assessed 33 women (21 with myelomenigocele and 12 with SCI) who underwent placement of a rectus fascial sling. Of the 33 patients, 30 were cured, and as expected, all continued to require intermittent catheterization [4•]. PVS remains the most widely accepted method of managing the incompetent outlet in patients with neurogenic bladder due to its long-term durability, minimized risk of mesh-related

urethral events, and superior ability to safely raise intraurethral pressures. The theoretical concern of ongoing catheterization in a patient who has had a synthetic sling placed is mitigated by the use of autologous tissues. And, the usual concern of sling overtightening (and potential resultant urinary retention) in patients who must void normally after sling placement is a non-issue in patients requiring lifelong CIC due to their neurogenic bladder condition. Ongoing urodynamic and upper tract evaluations are necessary to maintain safe intravesical pressures and reduce the risk of long-term renal damage.

Conclusions

Although relatively few studies have focused on diagnosing and managing SUI in the neurogenic bladder population, patients and clinicians do have a handful of options. A complete clinical examination including urodynamics and physical exam is vital for assessing many patients with NGB and SUI. In addition, validated (though often non-condition specific) questionnaires can be used to monitor quality of life and patient perception over time. Neuroimaging, while having a promising future, does not yet play a major role in SUI evaluation.

With regard to therapies, no current medical treatments are FDA-approved for the treatment of SUI in the US. Pelvic floor muscle training has had positive results for those patients with intact pelvic floor function and may be a good first-line option in the MS and stroke populations. Biofeedback and nerve stimulation have also proven to be reasonable early therapies that also avoid major surgery. AUS is effective and durable, particularly in men with ISD, though has unique risks in this patient population who frequently require intermittent catheterization. Sling procedures, when performed via a retropubic approach are effective in treating SUI, though are associated with a greater likelihood of de novo voiding dysfunction than non-neurogenic populations, and patients should be carefully assessed for this risk preoperatively. The authors favor fascial slings, particularly when ongoing CIC is believed to be likely following surgery.

Compliance with Ethics Guidelines

Conflict of Interest Arthi Satyanarayan and Louise Gliga declare that they have no conflict of interest.

Gary E. Lemack declares a consultancy fee from Allergan, payment for development of educational presentations from Allergan, Astellas, and Pfizer, stock in Pfizer, and expense reimbursement from Allergan and Astellas, not related to this article.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.



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