

The Bladder in MS: A Review

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Abstract

Urinary complaints are common in Multiple Sclerosis (MS), representing a large source of morbidity and financial burden for these patients. These issues can be complex and difficult to manage for the care provider. As new treatments develop, it is important to have a structured but flexible approach to the diagnosis and treatment of urinary symptoms. In this article we review the pathophysiology, symptoms, work up, and management options for the bladder in MS.

Keywords: Multiple sclerosis; Urinary incontinence; Neurogenic bladder

Background

Multiple Sclerosis (MS) is a progressive inflammatory demyelinating disease of the central nervous system well known to significantly impact both bladder and bowel function [1,2]. Accordingly, rates of urinary complaints in MS patients are significantly higher than in the general population, with up to 14% of patients presenting with urinary complaints as their first symptoms of disease [3]. With increased disease duration, urinary symptoms tend to become more prevalent and severe: 39% of patients with a five year disease history report symptoms, versus 64% of patients with a disease history of 17.1 years [4-9]. A review of the North American Research Committee on Multiple Sclerosis (NARCOMS) database showed that 50% of respondents reported a minimum complaint of mild disability from their urinary or bowel symptoms [7].

Urinary symptoms related to MS significantly impact quality of life for MS patients and increase economic consequences related to nursing care, supplies for management of incontinence, and resulting UTIs [1,8]. The effects of MS on the bladder and their management will be discussed in this review.

Physiology of Micturition

Normal micturition involves complex reflex pathways organized in the brain and spinal cord. Their role is to provide coordination between the urinary bladder and the urethra during the storage and voiding stages of the bladder. Some reflexes promote urine storage, whereas others facilitate voiding.

During urine storage, mechanoreceptors in the wall of the bladder respond to stretch as the bladder fills and produce low-level bladder afferent firing via pelvic nerves (S2-S4). Via spinal reflex pathways representing "guarding reflexes", the sympathetic outflow (T11-L2) to the bladder base and urethra and the pudendal outflow (S2-S4) to the external urethral sphincter are activated, thereby preventing involuntary loss of urine by closing the bladder neck [10,11]. Concomitantly, during urine storage under parasympathetic control

(S2-S4), the detrusor muscle is inhibited, promoting bladder relaxation.

As bladder filling continues, increased afferent neuron firing within the pelvic nerve activates the spinobulbospinal reflex pathway which relays neurons through the periaqueductal grey (PAG) to the pontine micturition center (PMC). At a critical level of tension created by elevated bladder pressure with increased urine content, PMC neurons, which are off during storage, become maximally activated and voiding ensues due to detrusor contraction and urethral sphincter relaxation. Voiding is the result of parasympathetic outflow to the bladder and to the urethral smooth muscle and is associated with inhibition sympathetic and pudendal bladder control, resulting in opening of the bladder neck allowing the outflow of urine [10,12].

In addition to autonomic and somatic control, cerebral circuits above the PAG control the generation of conscious bladder sensations and mediate the conscience switch from storage to voiding. The prefrontal cortex, insula, and hypothalamus, all play a role in controlling micturition [10,12].

Symptoms

In MS patients, a lesion anywhere in the aforementioned pathways can cause urinary dysfunction, but symptoms will depend on the location of the lesion. Symptoms can range from urinary incontinence to urinary retention, with mixed symptoms being the most predominant. In a recent study, up to 70% of respondents reported both urinary incontinence and retention symptoms [4]. In their review, Ruffion et al. reported urge incontinence complaints in over 50% of patients with MS and detrusor overactivity in 27-91% of patients with MS [6].

Urinary incontinence (UI) is a widespread complaint in patients with MS, primarily caused by overactive bladder (OAB) [4]. According to the International Continence Society (ICS), OAB is characterized by urinary urgency, which can be accompanied by frequency and nocturia, with or without UI [13]. Spinal cord lesions may interrupt the spinobulbospinal pathway and create a sacral segmental reflex arc, resulting in detrusor hyperreflexia, or OAB [14]. These uninhibited detrusor contractions may cause episodes of incontinence when intra-detrusor pressure surpasses urethral sphincter closure pressure.

Patients with MS are particularly susceptible to this form of incontinence due to their limited mobility resulting in prolonged times to get to a toilet. Urgency, UI and frequency have all been correlated to the severity of pyramidal damage, however no link between MRI data and clinical symptoms has been established [8]. Therefore, patients with apparently mild disease on imaging, may still present with severe urinary symptoms.

Urinary incontinence may also result from a loss of urethral sphincter tone, termed intrinsic sphincter deficiency (ISD). Low urethral sphincter pressure may cause passive neuropathic incontinence due to an open bladder neck, resulting from lesions often found in the PMC [15,16]. In contrast, stress urinary incontinence (SUI) was recently reported to be less prevalent in patients with MS than in the general population, possibly due to decreased activity in this population or increased urethral sphincter tone resulting from detrusor sphincter dyssynergia (DSD) preventing SUI [17].

Conversely, dysfunctional voiding and/or urinary retention may result from detrusor hypoactivity, acontractility or bladder outlet obstruction (ie, DSD). The prevalence of obstructive voiding symptoms is 34-79%, and can result in chronic urinary retention [8]. Detrusor hyporeflexia or acontractility may occur when the innervation to the bladder wall is interrupted. Poor stream and post void dribbling have also been seen in patients with detrusor hyporeflexia, likely resulting from a disruption of the spinal pathway at S2-S4, leading to a loss of control from the PMC [11,15]. Detrusor sphincter dyssynergia occurs when the urethral sphincter exhibits increased tone simultaneously during voluntary voiding efforts, resulting in obstructed voiding and low urinary flow rate [15]. Cervical spinal cord lesions below the PMC can result in DSD or other obstructive symptoms [12].

Sometimes, lesions that are found rostral to the pons can alter the tension set-point of the voiding reflex, causing micturition to occur at larger or smaller amounts of bladder distension, leading to retention like symptoms or incontinence, depending on the location of the lesion [10]. The result is urinary retention manifesting as an inability to void and overflow incontinence or frequent urges to pass small amounts of urine.

Urinary tract infections (UTI) are another serious concern in MS. One study of the NARCOMS data reported 65% of patients with a UTI within the past six months [7]. Urinary tract infections can result from the involuntary retrograde flow of urine into the urethra, resulting in the introduction of bacteria into the bladder [12]. Additionally, strong detrusor contractions against a closed sphincter may cause disruption in the protective glucosaminoglycan layer of the urothelium, allowing bacteria to adhere [12]. Increased frequency of UTI may cause upper urinary tract damage, putting patients at risk for bacteremia, and activates the immune system, which can worsen the symptoms of MS [2,12]. In addition, some of the therapies for urinary incontinence are complicated by risk of UTI. Catheterization, injection of botulinum toxin, and surgical therapies all carry UTI as an associated adverse effect [18].

The management of UTIs should be handled carefully as untreated infections can lead to further complications, and overuse of antibiotics can lead to resistance [Table 1; 19]. Asymptomatic bacteriuria in patients who are self catheterizing does not require antibiotic treatment, as this has not been associated with UTI [19]. However, it may be useful to perform a urine dipstick analysis to assess for nitrites and leukocyte esterase prior to treating MS relapses with high dose

steroids, which can unmask an infection if asymptomatic bacteriuria is present [20]. Prophylactic antibiotic therapy can be considered for patients who catheterize with recurrent proven UTIs, after excluding other causes for infection [1, 19]. Commonly utilized medications for UTI prophylaxis may include a daily dose of nitrofurantoin (50 or 100 mg), cephalexin (500 mg), or trimethoprim (100mg). Caution should be used with prolonged antibiotic prophylaxis due to the risk of developing drug resistance and the risk of long term adverse effects, particularly pulmonary fibrosis with prolonged nitrofurantoin use.

| Condition | Treatment | Risks | Cautions |
|-------------------------------|--|---------------------------|--|
| Acute urinary tract infection | Treat based on culture results | Minimal | |
| Asymptomatic bacteriuria | No treatment indicated | | Screen urine for infection prior to starting immunosuppression |
| Recurrent UTI | Antibiotic suppression (i.e. daily nitrofurantoin, trimethoprim, cephalexin) | Development of resistance | Drug related complications from prolonged use |

Table 1: Treatments for lower urinary tract infections

Upper urinary tract (UUT) complications were very common among MS patients 50 years ago, however with heightened awareness and early treatment efforts, these complications are becoming more scarce [21]. Recently, UUT complications were reported in only 0-25% of patients, including upper UTI, dilatation of the upper urinary tract, and vesicoureteral reflux. The risk of developing UUTs increases with the longer MS disease duration, being more common after the 15th year of disease [8]. Other risk factors for the deterioration of the UUT include the presence of an indwelling catheter, high maximum amplitude of detrusor contractions, and permanent high detrusor pressures during filling [8,19]. Fletcher et al found that of MS patients screened for UUT, 6% were found to have an abnormality seen on a renal ultrasound. Development of UUT was related to patient age and abnormal bladder compliance identified on urodynamics [21].

Evaluation and Findings

Awareness of lower urinary tract dysfunction (LUTD) in MS is growing, however some studies suggest that these symptoms may be under treated [5,7]. Unfortunately, many patients and their caregivers avoid discussing this sensitive topic with their providers, leaving patients and their families to cope with these disabling issues with little to no assistance. A review of the NARCOMS database showed that despite high prevalence rates, only 43% of patients with self-reported moderate to severe bladder dysfunction had ever been evaluated by a urologist. The same study found that of this same group, only 51% had ever been prescribed an anticholinergic medication for management of their symptoms [4,5]. Marrie et al. 2007 found that the length of disease, the higher degree of disability, and the female sex were independently associated with higher levels of self reported symptoms on questionnaire [7]. These findings suggest a role for both neurologists and urologists in addressing and evaluating urinary symptoms with patients in the clinical setting [22].

Guidelines for how to evaluate LUTD in patients specifically with MS have been suggested by several organizations [22]. All guidelines recommend measurement of PVR and screening for UTI. However, recommendations vary with regard to advanced testing for symptomatic patients [22]. The most common modalities for evaluating LUTD in MS patients include voiding diary and quality of life questionnaires, screening for UTI, uroflow, measurement of PVR, renal and bladder ultrasound (US), serum creatinine measurement, identifying upper urinary tract risk factors, and urodynamics [22]. For the primary care provider, the FLUE-MS algorithm, which utilizes many of the testing modalities mentioned above, is available to guide management of LUTD in patients with MS [23]. This algorithm starts with evaluation for 'red flags', such as recurrent UTI, presence of structural anomalies on ultrasound, or elevated PVR. The presence of these risk factors requires the attention of a specialist, as they can complicate care [23]. The decision tree format helps guide the general practitioner through evaluation and management of LUTD in this patient population [23].

Bladder function is an important component of care and should be discussed with all MS patients. Often, starting the conversation may be the hardest part of caring for patient these patients. Since bladder function is integrally related to the patient's mental, cognitive, and functional status, it should be assessed at the first visit. Some guidelines recommend a thorough history including neurological, sexual, and bowel function history, as well as documenting sensation and reflexes in the urogenital area with anal sphincter and pelvic floor function [22]. Patient mobility can affect his or her ability to get to the bathroom in a timely manner, potentially resulting in incontinence, termed functional incontinence. Understanding the patient's baseline functional status can help guide treatment choices. For example, options such as clean intermittent catheterization (CIC) can only be offered to patients with sufficient manual dexterity to maintain personal hygiene or a willing caregiver to assist [4].

In general, many bladder symptoms can be successfully treated with behavioral changes and medications, while surgery is rarely necessary. Therefore, it is very important to review the individual's diet and lifestyle, as many of these choices that contribute to incontinence are easily modifiable [4]. A bladder diary, often for 24 hours or up to three days, can be implemented in order to characterize symptoms and assess the severity and frequency of incontinent episodes. Recording the volumes of daily fluid intake and voided urine allow the clinician to understand patients' habits and lifestyle related patterns.

To avoid missing urinary symptoms in MS, de Seze et al. recommend the use of a voiding questionnaire in asymptomatic patients [8]. There are many available questionnaires, including the Urogenital Distress Inventory (UDI-6), the Short Form 36 (SF-36), the Short Form (SF-12), Qualiveen, and the Incontinence Impact Questionnaire (IIQ-7). Another such questionnaire is the Actionable Bladder Symptoms Screening Tool (ABSST), which has been validated for identifying MS patients with incontinence symptoms, who may benefit from referral to a specialist [24]. Bates et al. reported that a shortened version of the ABSST was able to maintain sensitivity and specificity in identifying MS patients with urinary symptoms, making this tool easier and quicker to use in the office setting [24]. The International Prostate Symptom Score (IPSS) has also been used to characterize the severity of bladder symptoms in males with MS, however this tool was originally designed to describe symptoms of benign prostate hyperplasia [24]. The Incontinence Quality of Life Questionnaire (I-QOL) and the Overactive Bladder-Patient

Satisfaction with Treatment Questionnaire (OAB-PSTQ) have both been used to assess health related quality of life (HRQoL) in patients with neurogenic bladder symptoms [25].

For those with a known MS diagnosis but no urinary complaints, evaluation yearly or at each follow-up visit is recommended [8]. For those with urinary complaints, a referral to a urologist or urogynecologist who is familiar with MS is recommended. A urinalysis with a dipstick should be performed on all patients who present with new urinary symptoms, and a post void residual (PVR) measurement should be performed in patients prior to treatment if incomplete emptying is suspected [1,8,19,22]. A PVR residual volume below 100-150 mL is considered normal, and screening is recommended in all symptomatic patients [22]. Urine cultures should be sent when clinically indicated, and all patients should be screened for common treatable causes of urinary incontinence, including delirium, infection, urethral atrophy, medications, depression, polyuria from other medical conditions (i.e. diabetes), difficult ambulation, and constipation or stool impaction. These modifiable issues can be addressed individually when present, and are important to keep in the differential diagnosis when dealing with new symptoms in MS patients.

Urodynamic testing (UDS) is often used for the evaluation of patients with voiding dysfunction or other urinary complaints. However, symptoms do not always correlate with a specific UDS finding, limiting the value of the test. Different lesions can present with similar symptoms [2]. For example, one study by Koldewijn showed that in patients with obstructive symptoms, etiologies included detrusor hypoactivity, DSD, and unspecified bladder outlet obstruction [26]. Overactive bladder (OAB) symptoms generally correlated with the finding of unsolicited bladder contraction with or without urine leakage on urodynamic testing, termed detrusor overactivity (DO), although not all affected patients with OAB complaints will demonstrate DO on a single urodynamic study. Furthermore, multiple types of voiding dysfunction can coexist simultaneously in patients with MS, depending on the location of specific lesions. MS can be a progressive disease with urodynamic findings that may change over time. Accordingly, some authors recommend serial UDS monitoring as the disease progresses [2]. In contrast, others believe that urodynamics should be reserved for patients whose symptoms have been refractory to conservative management, have obstructive symptoms, urinary retention, or who wish to undergo further, more invasive, interventions [1,2,8,19,22].

Further steps in the evaluation of LUTD can be guided using existing algorithms for individual patients, as described previously. Additional tools for measuring the effects of MS include serum creatinine and ultrasonography of the genitourinary tract. Serum creatinine can be measured to monitor the extent of renal damage, if present. Bladder and renal ultrasound are utilized to assess for the presence of nephrolithiasis, bladder diverticula and hydronephrosis [23]. Evaluation and treatment should be tailored to each patient individually with attention to the severity of their MS.

Treatment

Lifestyle modification is the first-line treatment for urinary complaints in patients with MS once infection and urinary retention have been ruled out [1,4] (Table 2). These modifications include limiting fluid intake to one to two liters per day and moderating caffeine intake [19]. These interventions are generally very useful in all

patients with bladder complaints, regardless of neurogenic dysfunction. Many patients with neurogenic LUTD, however will likely have refractory symptoms which require more intensive management. Pelvic floor physical therapy has been recommended to patients with mild disability from MS [1,2,4,12,22]. Biofeedback and pelvic floor electrical stimulation have been shown to be useful in the

treatment of frequency and incontinence [2,12]. McClurg et al. found that the addition of pelvic floor training together with biofeedback and neuromuscular electrical stimulation was useful in reducing the number of incontinent episodes reported [27]. Patient information sheets outlining these treatments should be routinely distributed to patients for education.

| Behavioral modifications for Urinary symptoms | |
|---|--|
| Fluid modification | Limit fluid intake to 1-2 liters per day, or about 4-6 ounces per hour. |
| Avoid bladder irritants | Avoid alcohol, caffeine, citrus juices and artificial sweeteners |
| Restrict fluids before bed | Decrease episodes of voiding at night or nocturia. |
| Change medication timing | Avoid diuretics in the evening. Bedtime medications can be taken 2-3 hours earlier. |
| Scheduled voiding | Voiding at specific times during the day to avoid incontinent episodes |
| Bladder retraining | Teaching patients with urinary frequency was to control urge and lengthen time between voids |
| Kegel exercises | Training pelvic floor muscles to control urinary urge and incontinence |

Table 2: Common behavioral changes to treat urinary incontinence complaints

For those patients in whom a post-void residual has been checked and found to be less than 150 ml, medications are commonly utilized as a second line therapy or as a first line treatment in conjunction with behavioral changes. Anticholinergic medications are the most common medications used for the management of OAB and work by inhibiting detrusor contractions and increasing bladder capacity [7,28]. Side effects of these medications however, can make compliance difficult, and can include: blurry vision, dry mouth, dry eyes, constipation, and mental status changes [11]. Caregivers should be advised to monitor for signs or symptoms of cognitive impairment in patients beginning treatment with anticholinergics, and medications that do not cross the blood brain barrier should be considered [19]. Patients should be started on the smallest dose and gradually increased based on efficacy and tolerability.

Recently, β_3 adrenergic agonists have been introduced as an alternative treatment for OAB symptoms. These medications can be useful in patients who have failed anticholinergic therapy, or cannot tolerate their side effects. Beta-3 adrenergic agonists induce detrusor relaxation during the storage phase of the voiding cycle, thereby increasing bladder capacity without affecting voiding [29]. Mirabegron, a β_3 agonist, is the first beta agonist to be approved for use in OAB. However, it has not yet been studied in patients with MS.

Alpha-1 adrenergic antagonists have been used in patients with detrusor-sphincter dyssynergia (DSD) to help with urethral relaxation and alleviate the symptoms of obstruction. Tamsulosin has been shown to decrease PVR, strength of involuntary detrusor contractions, and increase the urine flow and quality of life scores in patients with MS [29]. Unfortunately, their use is limited by side effects including dizziness, drowsiness, hypotension, and syncope. These medications are best taken at bedtime to minimize their side effects during the day.

Cannabinoids have been investigated for medical treatment of bladder symptoms in MS. Cannabinoids are thought affect muscle stiffness, spasticity and neuropathic bladder pain [31]. Recent studies have shown cannabinoids to be effective in reducing urge incontinence, frequency and and nocturia in MS patients [32-35].

Desmopressin, an analog to ADH or vasopressin, has been used for symptoms of nocturia as it decreases frequency within the first 6-8 hours of administration [12,19,35]. However, caution is recommended as patients must restrict fluid intake in order to avoid possible life-threatening fluid overload while taking desmopressin [12].

Those who do not respond to oral medications and are willing to use clean intermittent catheterization (CIC) or another catheterization method if necessary should be offered intra-detrusor injections with botulinum toxin [1]. Onabotulinumtoxin-A (OnaBoNT-A) (Botox®, Allergan, Inc., Irvine, CA) has been approved by FDA for the treatment of idiopathic and neurogenic OAB. Botox® is the most commonly used formulation in the United States. However other formulations and serotypes of botulinum toxin are available, including: abobotulinum toxin A (Dysport®, Ipsen Biopharmaceuticals, Basking Ridge, NJ), incobotulinum toxin A (Xeomin®, Merz, Germany), and rimabotulinumtoxin B (Myobloc®, botulinum B toxin, US World Meds, Louisville, KY) [18]. All forms of botulinum toxin act via blockade of presynaptic cholinergic nerves, thereby preventing the release of acetylcholine into the synapse, resulting in temporary inhibition of detrusor muscle contraction. Each formulation is structurally similar, however they differ in molecular weight and potency, making dose conversion between different formulations an important consideration [18]. Common dosing regimens for neurogenic patients include 200-300 units of onabotulinumtoxin-A injected in 20-30 different locations in the bladder, sparing the trigone. No difference in efficacy was seen when comparing a dose of 200 versus 300 units of OnaBoNT-A, however adverse side effects were more frequent in the higher dose [18,25]. In patients with MS, a dose of 200 units of OnaBoNT-A as been approved [18]. OnaBoNT-A has been shown to significantly reduce the number of incontinence episodes in MS patients with neurogenic detrusor overactivity (NDO), with 58% to 100% of treated patients with neurogenic OAB reporting complete continence after treatment [36,37,38]. The duration of effect is on average ten months, and onset of effect is usually within two weeks from the time of injection [28].

The most common risks of botulinum toxin injection include infection and urinary retention, which varied widely between 0% and 30% depending on the study [4]. Phase 3 trials on intradetrusor injection of botulinum toxin treatment have reported rates of UTI to be as high as 50% and rates of urinary retention up to 29% in patients with MS [18,39]. Given the high risk of associated urinary retention with treatment, patients must be willing and able to perform CIC or tolerate some form of urinary catheterization (i.e. transurethral foley) before receiving intradetrusor botulinum toxin treatment. Other potential but rare side effects include generalized weakness, dysphagia, diplopia, and blurred vision. Although occurring in the natural history

of the disease of botulism (from uncontrolled toxin dosing), to date there have been no reported cases of respiratory paralysis following therapeutic lower urinary tract injection of botulinum toxin [40]. Cost was previously an important consideration that limited the availability of the therapy, as the toxin itself can be very expensive and not be covered by insurance [28]. However, with recent FDA approval of intra-detrusor Onabotulinum A injection for the treatment of neurogenic and idiopathic detrusor overactivity, this therapy has generally become universally covered for patients with refractory detrusor overactivity.

Sacral neuromodulation (SNM) has been reported in a small number of MS patients as effective and safe option in patients with refractory OAB symptoms, with 50% of patients reporting significant symptomatic improvement, and another 25% moderate improvement after implantation [40]. However larger, randomized studies are needed [14, 41- 44]. Although the exact method of action on SNM remains unclear, spinal inhibitory systems appear to be activated by the stimulator device, thereby preventing detrusor contraction by stimulating the afferent pathways of the anorectal branches of the pelvic nerve, somatic fibers in the pudendal nerve, and muscle afferents from the limbs, as they pass through the sacral spinal nerves [14]. Of the sacral spinal nerves, S3 is the most practical one for use in chronic electrical stimulation. The InterStim® (Medtronic, Inc., Minneapolis, Minnesota) system uses a lead implanted transcutaneously into S3 sacral foramina under fluoroscopic guidance to send electrical pulses from a neurostimulator (pulse generator) inserted under the skin through a small incision in the upper buttock. However, care must be taken when recommending InterStim® to patients with MS, as it precludes the use of magnetic resonance imaging while the device is in place and removal requires surgical intervention.

Percutaneous tibial nerve stimulation (PTNS) is the least invasive form of neuromodulation and uses no permanent lead or pulse generator implanted. It is an easily administered office procedure that delivers retrograde neuromodulation through the tibial nerve (L4-S3) to the sacral nerve plexus via a percutaneous thin needle electrode. The needle electrode is inserted cephalad to the medial malleolus and slightly posterior to the tibia and connected to a handheld external stimulator. Usually, the therapy is initiated with 30-minute treatments weekly for a total 12 weeks. The responders to treatment are advised to continue therapy to sustain their OAB symptom improvement with approximately one treatment per month [45]. PTNS has been shown to improve symptoms of urgency, frequency, and detrusor overactivity secondary to MS [12]. One large randomized control trial showed significant improvement of urinary symptoms in patients using PTNS (54.5% PTNS patients vs. 20.9% sham) [46]. Gobbi et al. also report improvement in frequency, nocturia and PVR with the use of PTNS [47]. Complications of PTNS are mild, transient, and relatively uncommon, occurring in 1%–2% of patients, but include bruising or bleeding at the site, tingling, and pain [4,46].

Investigation is ongoing regarding chemical neuromodulation with vanilloids, capsaicin and resiniferatoxin [28]. These work by blocking c-fiber afferent pathways in the bladder, which are postulated to contribute to pathological reflex pathways [12]. Some studies have shown improvement in incontinence with treatment; however side effects like pelvic pain and burning limit their clinical applicability [28].

Collecting devices have also been described for use in patients with nocturia, for whom ambulation to the bathroom can be difficult. A bedside commode is a simple and helpful option in patients with

limited ambulation and nighttime voiding complaints. Penile sheaths in men can reduce distress from incontinence, especially in those who share a bed with a partner. For women who lack manual dexterity, urine collection devices, some of which can be affixed to the perineum using adhesive used for ostomy bags, can also be utilized when ambulation to the bathroom is problematic [11,48]. Advantages to this method include that the patient is not exposed to a urethral catheter, with its risk of infection, and the patient does not have to ambulate to the bathroom. A study of 26 women found that 78% of those studied were leak free in the first 24 hours of wearing the perineal collection device, the devices were well tolerated, and did not exacerbate pre-existing decubitus ulcers [49]. Follow up studies are lacking, however, on bacteriologic implications of female external urinary collection systems.

Clean intermittent catheterization (CIC) or a long-term indwelling catheter, suprapubic or transurethral, may be necessary in patients with severe OAB refractory to other treatments or urinary retention. Often a combination of clean intermittent self-catheterization or a long-term indwelling catheter and oral antimuscarinics or botulinum toxin intradetrusor injections is effective in managing severe urinary incontinence in MS patients with refractory detrusor overactivity [1]. For these patients, quality of life can be significantly improved as they achieve socially acceptable continence, and remain sexually active [28,50]. A recent review of the 2005 NARCOMS data showed that about one in four patients with MS use a catheter for symptom management [50]. Additionally, it was estimated that up to 25% of patients with MS will experience urinary retention and require urinary catheterization during the course of their disease [4]. Medications are generally not helpful for urinary retention. For these patients CIC tends to be the preferred method of bladder emptying [51] and avoids complications related to long-term use of indwelling catheters such as chronic infection, leakage around the catheter due to detrusor overactivity, necrosis of the bladder neck with potential fistula development, stone formation, and bladder cancer. Castel-Lacanal et al. report that initiating CIC when appropriate is well accepted by patients, decreases bother with limitation scores and improves overall quality of life scores as indicated by the Qualiveen questionnaire [52]. However, for patients who lack the dexterity, flexibility, cognitive function to self catheterize, or a helpful caregiver, a long-term indwelling catheter can be an option for managing urinary symptoms. Suprapubic catheters may be useful as a minimally invasive option. Compared with transurethral indwelling catheters, suprapubic catheters allow for sexual function while avoiding the risk of urethral erosion [28]. Antibiotic prophylaxis may be considered in patients with recurrent infections after catheterization and education and support must be available to all catheterized patients.

When more conservative measures fail, surgical interventions may be considered. Surgical options are invasive and irreversible, making counseling an important part of the treatment. Bladder augmentation with or without catheterizable stoma can be used to increase bladder capacity and decrease pressure, thereby promoting continence. The risks of bladder augmentation include persistent leakage, bladder perforation, bladder stone formation, vitamin B12 deficiency, catheter obstruction and risk of bladder cancer [28]. Urinary diversion and continent urinary diversion are procedures in which the ureters are diverted to a pouch made of ileum, which can then be brought to the abdominal wall as a continent stoma [28]. Advantages to this procedure include reported increased quality of life. Cutaneous ileovesicostomy can also be performed whereby a segment of the ileum

is anastomosed to the bladder and brought to the lower abdominal wall as a stoma.

Numerous potential complications of these drastic procedures have been described in the literature, including: infection, leaking of urine, strictures, stomal stenosis, parastomal hernia, bowel obstruction, and renal calculi [28]. However, improvement has been seen in patients with secondary progressive MS who have undergone urinary diversion and reconstruction. A small study of 26 patients showed that other covariates were likely to increase the morbidity of the procedure including preoperative indwelling catheters, diabetes, high body mass index and high operative blood loss [53]. For these reasons, careful patient selection and counseling are important aspects of management.

Conclusion

MS can have profound effects on the urinary tract, which can significantly impact patient quality of life. Careful assessment of urinary complaints must be performed and continued throughout the course of MS treatment, as the disease can present with many different symptoms and may progress over time. There are many available treatment options, ranging from lifestyle modification to invasive surgical procedures. The treatment should be tailored to the individuals' specific goals and needs.

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