

GENITOURINARY DYSFUNCTION IN PERSONS WITH MULTIPLE SCLEROSIS

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Genitourinary symptoms may affect up to 90% of persons with Multiple Sclerosis (MS), and may be the presenting symptom in up to 15% of patients. They are a significant cause of morbidity, non-participation in activities of daily living, time lost from work outside the home, and decreased quality of life. After participating in this educational activity the learner will be able to:

1. Describe the neurophysiology of normal micturition
2. Elicit and recognize common symptoms of bladder dysfunction
3. Prescribe appropriate pharmacologic and non pharmacologic treatment strategies to treat bladder dysfunction
4. List contributing factors to bowel dysfunction in persons with MS
5. Describe approaches to assessment & treatment of sexual dysfunction in persons with MS

Neurophysiology of micturition

The primary function of the urinary bladder is to store urine and then expel it completely at a socially appropriate time & place. Bladder neurons are contained in the frontal lobes, basal ganglia and midbrain, but ultimately pass through the two main neural control centers of voiding, the Pontine Micturition center (PMC) and Sacral Micturition Center (SMC). The output of the frontal lobes and midbrain are primarily inhibitory, the PMC facilitates voiding, the SMC is more responsible for storage.

The sympathetic innervation to the bladder arises in the thoracolumbar (T10-L2) spinal cord, and innervates the bladder as the **hypogastric nerve**. The parasympathetic innervation to the bladder is primarily carried in the **pelvic nerve**. Somatic motor innervation is carried in the **puddendal nerve**, which arises from cell bodies at S2-S4 in Onuf's nucleus, and innervates the urethral sphincter, and pelvic floor. During bladder filling the SMC facilitates continence by increasing bladder wall accommodation and blocking parasympathetic impulses that stimulate bladder wall contractility, increasing outlet resistance and increasing activity in the pelvic floor muscles, the "guarding" reflex. The PMC promotes voiding by inhibiting the guarding reflex, stimulating parasympathetic transmission (to facilitate bladder wall contractility), and relaxing the urethral sphincter. Voiding thus requires coordination between increased contractility of the bladder smooth muscle and simultaneous relaxation of the sphincter to permit emptying.

MS bladders may be broadly classified as "failure to empty", "failure to store" or "mixed" (Lapides, et al 1972). These different conditions may in fact produce similar symptoms, namely frequency, urgency, nocturia, hesitancy, urge incontinence or overflow incontinence.

A failure to store bladder results from detrusor overactivity, and is commonly associated with other pyramidal tract signs such as hyperreflexia or spasticity. Failure to empty bladders may be associated with demyelination in the SMC, and are a result of acontractile bladder activity. Failure to empty and mixed bladders are also associated with frequent UTIs and may also lead to upper urinary tract damage by producing hydronephrosis. Mixed bladders are most commonly a result of detrusor sphincter dyssynergia (DSD) where a hypercontractile bladder cannot effectively empty through a non-compliant sphincter.

Diagnosis of Bladder dysfunction

Assessment of urinary function in persons with MS begins with a thorough history. In addition to symptoms, it is important to inquire about habits as they may contribute to bladder dysfunction and may be ameliorated through behavior modification (*vide infra*). The Actionable 8 item questionnaire developed by Bates *et al* has been shown to be a short & useful screen to determine who may benefit from urologic assessment & treatment (Bates et al 2013)

The next step is screening for infection (UA/C&S) and determination of post voiding residual(PVR). PVR of ≤ 100 cc is generally regarded as a failure to store bladder(MS Council for Clinical Practice Guidelines,1999). First line treatment would include behavioral modification, e.g. limiting fluids before bedtime, limiting bladder irritants such as caffeine, and timed voiding. If these measures are not sufficient, pharmacologic agents may be added. Anticholinergic agents are generally effective; newer formulations have longer half lives and somewhat less systemic side effects e.g. xerostomia. Other strategies for treating a failure to store bladder include percutaneous tibial nerve stimulation(PTNS), an implanted sacral stimulator, and instillation of intravesicular botulinum toxin. There is now level III evidence suggesting that botulinum toxin A injection into detrusor muscle in MS patients is efficacious in improving symptoms, urodynamic parameters, and quality of life (Cruz *et al.*, 2011, Ginsberg *et al* 2012).

PTNS is a minimally-invasive treatment found to be effective in the treatment of detrusor overactivity. This is accomplished by stimulating the tibial nerve near the medial malleolus. Electrical stimulation is performed for 30 minutes, with sessions occurring once a week for 6-12 weeks. Although the mechanism of action of PTNS has not been clearly elucidated, multiple randomized controlled studies have shown its efficacy in reducing symptoms and improving urodynamics measures (Kim JH & Choi, J. 2016).

The Interstim ® sacral modulator is a newer modality used to treat overactive bladder. It provides stimulation to the S3 nerve root, and is thought to have several actions, including interrupting the guarding reflex, and blocking transmission of peripheral afferents, thus modulating filling sensations and urge to void. It may also have an impact on detrusor contractility. Clinical trials indicate up to 70% success rate of the Interstim® in reducing frequency, incontinence, reducing PVR and increasing voiding volume(Minardi & Muzzonigro 2012, Van Kerrebroeck & Marcellessen,2012). It is primarily suggested for patients with refractory failure to store bladder or DSD. However, patients with this device will not be able to have MRI.

Failure to empty bladders(PVR ≥ 100 cc) (MS Council for Clinical Practice Guidelines,1999). may be addressed by clean intermittent catheterization (CIC); sometimes the addition of an alpha adrenergic antagonist will also facilitate emptying by relaxing the bladder neck. In patients for whom CIC is not feasible, an indwelling catheter may need to be placed. Suprapubic tubes are preferred over indwelling urethral catheters, as the latter can lead to urethral erosion and higher rates of infection. The only way to diagnose detrusor sphincter dyssynergia is by formal urodynamic studies. These should be done prior to prescribing agents to promote bladder contractility, e.g. bethanechol, as this would be contraindicated in the case of a non-compliant sphincter. Valsalva or Crede maneuvers should also be used with caution as if they are done in the presence of DSD they could transmit increased pressure to the kidneys & cause renal damage.

Patients whose primary complaint is nocturia, and who are still symptomatic after limiting fluids in the evening may respond to bedtime administration of intranasal desmopressin (DDAVP). Bedtime doses of long acting anticholinergic agents, or tricyclic antidepressants such as amitriptyline or imipramine are also useful in this regard.

Bowel Dysfunction

Bowel dysfunction is estimated to affect 50% of the MS population. Defecation reflexes are coordinated at the S3-S5 level. In addition to impairment caused by the disease itself, i.e. slowed intestinal transit time, and decreased mobility, other factors contribute such as constipating effects of medications, and decreased fluid intake which is usually due to bladder dysfunction, but may also be due to dysphagia.

As with bladder dysfunction, behavioral modification is the first line of therapy in addressing bowel complaints. For constipation, encouraging fluid (ideally 2000cc/day) and fiber (20-35gms/day) intake, setting aside protected time for bowel evacuation e.g. after a warm meal or warm beverage consumption, and digital rectal stimulation are all helpful. Use of stool softeners and bulk agents may be added. Laxatives and enemas should be used sparingly; suppositories are preferable to induce a planned evacuation. Diarrhea is usually addressed by identifying dietary components that may irritate the bowel, and using bulk agents to produce formed stools.

Sexual Dysfunction

Sexual dysfunction is present in a majority of persons with MS, and can have a significant deleterious effect on quality of life in this patient population. Unfortunately, there is often a “don’t ask, don’t tell” mentality about this topic, i.e. health care professionals don’t ask about it and patients do not volunteer information, although they are much more likely to do so if asked directly.

Sexual dysfunction has been categorized as primary, secondary & tertiary (Foley 2016). Primary dysfunction is directly due to nerve damage along CNS pathways, especially in the S3-S5 area. Secondary sexual dysfunction is a result of other signs and symptoms of MS including pain, fatigue, depression, spasticity, bladder problems, sensory disturbance and cognitive issues. Several classes of medication also can aggravate primary sexual dysfunction. Tertiary symptoms are the psychosocial consequences, including distortion of body image, change in self esteem, performance anxiety and inability to please partner.(Foley FW, 2016)

Strategies for addressing sexual dysfunction obviously begin with establishing a dialogue about it. The Multiple Sclerosis Intimacy & Sexuality Questionnaire(MSISQ) is a 15 item list of primary, secondary and tertiary issues that is useful in identifying which factors are producing sexual dysfunction in a particular individual.(Foley et al,2013)

Primary symptoms may respond to a combination of pharmacologic and non-pharmacologic modalities. For example, erectile dysfunction is treated with agents such as phosphodiesterase-5 inhibitors(Viagra®, Cialis,®etc.)vacuum pumps or implants. A new agent for women, flibanserin has been approved to treat decreased libido in women. Mechanical aids to increase sensory stimulation such a vibrators or other devices are also useful. Sexual counseling is often very effective for both sexes.

Secondary and factors should be identified and treated, including a careful assessment of medications that may be contributing to problems.

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