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Invited Review

Lower urinary tract dysfunction in common neurological diseases

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ABSTRACT

The lower urinary tract has the main function of urine storage and voiding. The integrity of the lower urinary tract nerve supply is necessary for its proper function. Neurological disorders can lead to lower urinary tract dysfunction (LUTD) and cause lower urinary tract symptoms (LUTS). Common causes of neurogenic LUTS or LUTD include spinal cord injury, multiple sclerosis, Parkinson's disease, cerebrovascular accidents, cauda equina syndrome, diabetes mellitus, and multiple system atrophy. The pathophysiology is categorized according to the nature of the onset of neurological disease. Assessment requires clinical evaluation, laboratory tests, imaging, and urodynamic studies. Impaired voiding is most often managed by clean intermittent self-catheterization if the postvoid residual urine exceeds 100 ml, whereas storage symptoms are most often managed by antimuscarinic medications. Intradetrusor injection of botulinum toxin type A is emerging as an effective treatment for managing refractory neurogenic detrusor overactivity. This review provides an overview of the clinical characteristics, diagnosis, and management of LUTD in patients with central and peripheral common neurological diseases.

Keywords: Cerebrovascular accident; multiple sclerosis; lower urinary tract symptoms; parkinson's disease; peripheral nervous system diseases; spinal cord injuries.

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Introduction

Lower urinary tract symptoms (LUTS) are progressively age-related and comprise a combination of storage, voiding, and postmicturition symptoms. It has been recognized that patients often have underlying and overlapping pathophysiologic mechanisms that may be related to the expression of LUTS.[1] Their prevalence increases with age, and severe LUTS are found more commonly in either older men or women.[2] Although for many years we believed that LUTS were mainly caused by benign prostatic hyperplasia (BPH), there are several other causes of LUTS in men including prostatitis, bladder dysfunction, urinary tract infections, and prostate or bladder cancer.[3] The storage and periodic voiding of urine depend on the coordinated activity of two functional units in the lower urinary tract: (a) the reservoir (the urinary bladder) and (b) the outlet consisting of the bladder neck, the urethra, and the urethral sphincter, as well as the prostate gland in men. Coordination between these organs is mediated by a complex neural control system located in the brain, spinal cord, and peripheral ganglia.[4] As a result, LUTS suggest common and morbid consequences of neurological diseases, best known as neurogenic LUTS or lower urinary tract dysfunction (LUTD), and the patterns of bladder storage and voiding dysfunction depend on the level of the neurological lesion.

Herein, we present an overview of the clinical characteristics, diagnosis, and current management of LUTD, focusing on patients with common neurological conditions affecting the central and peripheral nervous systems.

General considerations

LUTD evaluation includes general medical, bowel, and sexual dysfunction history; bladder/voiding diary; thorough physical examination of the urogenital system and neurological examination; ultrasonography; urodynamic testing when indicated; and validated questionnaires.[5] The risk of developing upper urinary tract failure and concomitant renal failure is much lower in patients with slowly progressive nontraumatic neurological disorder than

in those with spinal cord injury (SCI) or spina bifida.[6] Impaired emptying is most often managed by clean intermittent self-catheterizations (CISC), which should be initiated if the postvoid residual urine (PVR) exceeds one-third of the bladder capacity, if it exceeds 100 ml, or if spontaneous voiding occurs due to high detrusor pressure. Storage symptoms are most often managed by antimuscarinic medications or β3-agonists.[7,8] In the general population, an overactive bladder (OAB) is described as a status of urgency, with or without incontinence, associated with frequency and nocturia.

In patients suffering from a variety of neurological diseases such as SCI, Parkinson's disease (PD), and multiple sclerosis (MS), the OAB develops as neurogenic detrusor overactivity (NDO), which currently lacks a universally effective therapy.[9] Detrusor sphincter dyssynergia (DSD) is the urodynamic description of bladder outlet obstruction (BOO) from detrusor muscle contraction with concomitant involuntary urethral sphincter activation. DSD is associated with neurologic conditions such as SCI, MS, and spina bifida, and some of these neurogenic bladder patients with DSD may be at risk for autonomic dysreflexia, recurrent urinary tract infections (UTIs), urinary incontinence (UI), vesicoureteral reflux or upper urinary tract dilatation, and renal failure.[10] NDO with or without DSD is the main cause of increased storage pressure and long-term damage to the upper and lower urinary tracts, particularly in neurological patients.[11] It has been demonstrated that neurological disorders can lead to common and morbid urological complications, including UI, UTIs, urolithiasis, urosepsis, ureteric obstruction, vesicoureteral reflux, and renal failure.[12]

LUTS in patients with SCI

Traumatic SCI is a devastating condition that can cause a serious dysfunction in sensation, motor ability, and autonomic function, with a significant negative impact on the patient's quality of life (QoL). The estimated annual incidence of SCI varies from 10.4 per million to 83 per million in North America and Western Europe, respectively.[13] SCI typically affects the cervical (50%), thoracic (35%) and lumbar (11%) level of the spinal cord (50%), with the single most common level affected being C5.[14] The most common urological complications following SCI are UTIs, upper and lower urinary tract dysfunction, and bladder or renal stones.[15]

Main Points:

- All aspects of lower urinary tract dysfunction suggest common consequences of several neurological disorders, depend mainly on the level of the lesion and need regular urological assessment on, at least, yearly basis.
- Antimuscarinics and β3-adrenoreceptor agonists may be helpful in most of the cases and remain as the first line of therapy.
- Incomplete bladder emptying is currently managed by clean intermittent self-catheterization.
- Botulinum toxin A is the current second line of treatment option for neurogenic detrusor overactivity (NDO).
- Neuromodulators offer promising results regarding the management of both storage and voiding dysfunction, while surgical interventions, such as bladder augmentation, are indicated in cases where there is reduced compliance or NDO refractory to all other nonsurgical treatments.

LUTD following SCI can be divided into 2 phases: an initial period of spinal shock and a chronic phase. Initially, the urinary bladder is hypotonic; therefore, urinary retention and overflow incontinence occur in the absence of management. This phase usually resolves within the first 2 weeks, although it can last up to 1 year.[16]

Initial urological management in SCI cases includes safe urine storage, efficient bladder emptying, maximal urinary continence and minimal risk of urological complications. Physicians must ensure an appropriate bladder emptying immediately after SCI. Spontaneous voiding and/or CISC must be considered in selected patients once they are medically stable.[17] In a recent study, 76% of the patients with SCI who could not voluntarily void were able to at least perform CISC with appropriate assistance.[18]

CISC are recommended for the management of neurogenic bladder in patients with SCI. Alternative treatment options are condom and indwelling urethral or suprapubic catheters, reflex voiding, and voiding using Valsalva or Credé maneuvers. Noninvasive medical therapies are used to improve incontinence, urodynamic parameters, and (QoL) in this population.[19] Usually antimuscarinic drugs are given to adults suffering from NDO. Most of the studies, especially randomized trials, were performed with oxybutynin immediate release (IR), trospium chloride IR, propiverine IR, and propiverine extended release and demonstrated that these drugs are effective in NDO, normalizing the intravesical pressure and increasing cystometric bladder capacity.[20] Mirabegron, a β3-adrenoceptor selective agonist, has been proven to have similar efficacy as the antimuscarinic drugs. Adding mirabegron to the conventional antimuscarinic therapy further improved urodynamic parameters in patients with chronic SCI, and sustained efficacy was observed with a long-term use.[21]

The administration of botulinum toxin A (BTX-A) has revolutionized the treatment of LUTD over the past three decades. BTX-A has shown to be effective and safe in treating NDO after SCI. There were no statistically significant differences between dosage schemes (200 U or 300 U) or between injection sites (into the detrusor or submucosa).[22] Transcutaneous electrical

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stimulation of the neurogenic bladder in patients following SCI improves the lower urinary tract function within 2 years after completion of the electrical stimulation treatment.[23] Patients who fail the treatment either because of decreased efficacy or from intolerance due to side effects can be treated with various other surgical methods, such as augmentation cystoplasty with the use of a colonic segment or urinary diversion with the use of an ileal conduit.[15]

DSD is the urodynamic description of BOO caused by detrusor muscle contraction with concomitant involuntary urethral sphincter activation. DSD is associated with neurological conditions such as SCI. CISC remains a mainstay in managing symptoms/signs related to DSD. Other than urinary diversion, endoscopic urethral sphincterotomy is the most invasive treatment for symptomatic DSD.[24]

SCI at or above the 6th thoracic (T6) spinal cord segment often results in the development of a potentially life-threatening syndrome called autonomic dysreflexia (AD). AD is clinically defined as acute hypertension generated by unmodulated sympathetic reflexes below the injury level. AD is precipitated by noxious visceral or somatic stimulation below the level of injury. The most common triggers are overdistension of the bowel or bladder. The most common treatment regimen involves the use of vasoactive drugs intended to resolve the acute hypertensive crises rather than preventing them from occurring. Some evidence suggests that prazosin and BTX-A may provide prophylactic management of AD associated with normal and iatrogenic urogenital stimulations.[25]

LUTS in patients with cerebrovascular accidents

UI can affect 40% to 60% of the patients admitted to the hospital after a stroke, with 25% reporting problems when discharged from the hospital and 15% remaining incontinent after 1 year.[26] It is well established that this condition is a strong prognostic marker of stroke severity and is associated with poor functional outcomes.[27] In a cross-sectional, clinical survey of 519 stroke patients, the most frequent symptom was nocturia (76%) followed by urgency (70%) and daytime frequency (59%). Among respondents who had at least one symptom, the prevalence of bother was 78%.[28] Urodynamic studies are essential in order to manage LUTD in stroke patients. The comparison of the urodynamic parameters in ischemic and hemorrhagic stroke patients with bladder dysfunction revealed significant differences between the two group of patients. In the ischemic group, NDO was present in 70% and detrusor underactivity (DU) in 29% of the patients, respectively, while in the hemorrhagic group NDO was reported in 35% and DU in 65% of the patients, respectively.[29]

Improvement in continence status can help to enhance the overall and health-related QoL.[30] Nonpharmacologic treatment, such as behavioral therapy, and pharmacologic agents including antimuscarinics and β-adrenergic medications have not been well studied in post-stroke patients. UI in stroke patients needs to be further studied to help decrease morbidity and mortality rates within this population.[31] Although not infrequent mainly in old stroke patients, a pattern named "detrusor hyperactivity with impaired contractility" (DHIC syndrome) is described, characterized by simultaneous urge incontinence and increased PVR. If PVR is significant (≥100 ml), CISC are required in association with low doses of antimuscarinic drugs.[32] Transcutaneous electrical nerve stimulation improved incontinence symptoms and promoted activities of daily living of post-stroke patients.[33]

LUTS in patients with PD

Parkinson's disease is the most common neurodegenerative motor disorder. The etiology of the disease in most patients is unknown. The cardinal motor symptoms of PD are tremor, rigidity, bradykinesia/akinesia, and postural instability, but the clinical picture includes other motor and nonmotor symptoms.[34] NDO occurs in up to 70% and underactive bladder in up to 50% of the patients with PD, which has been suggested to reflect an altered frontal-basal ganglia circuit.[35] Irritative symptoms predominate, and urodynamic studies confirm a high prevalence of NDO in patients with PD. LUTD is present early and more common in patients with PD than in age-matched controls, while the incidence of erectile dysfunction (ED) of more than 60% in men with PD is bothersome and the most distressing of their various disabilities imposed by the disease.[36]

The assessment of LUTD in patients with PD is complicated by coexisting bradykinesia and cognitive impairment. Although LUTD becomes more troublesome as PD progresses, it remains unclear if its severity correlates with motor symptoms and/or duration of PD.[37] Urodynamics is a key investigative tool. The bladder dysfunction complex pathophysiology in PD is usually not responsive to levodopa, and add-on therapy is necessary.[38] The PVR volume is minimal in patients with PD, which differs significantly from that in multiple system atrophy (MSA) patients who have a more progressive disease that leads to urinary retention. However, subclinical detrusor weakness during voiding may also occur in PD.[39]

Dopaminergic drugs can improve or worsen LUTD in PD patients. Therefore, add-on therapy with antimuscarinics is required. β3 adrenergic agonists suggest a potential treatment option because they have little to no central cognitive events. Novel interventions, such as deep brain stimulation, are expected to improve bladder dysfunction in patients with PD. BTX-A injections can be used to treat intractable UI in patients with PD. Transurethral resection of the prostate for comorbid BPH in PD patients is indicated provided that MSA is excluded.[39] Office cystoscopy and low-dose BTX-A injection treatment is

a potential long-term management strategy for patients with PD and UI who fail oral medications. The treatment seems to be safely utilized in older men with BPH as well as women with potential hypoactive detrusor function.[40] In a recent study, solifenacin succinate treatment led to an improvement in UI, despite persistence in other LUTD symptoms.[40] Transcutaneous tibial nerve stimulation is effective in the treatment of LUTD in patients with PD, reducing urgency and nocturia episodes and improving urodynamic parameters.[41]

LUTS in patients with MS

MS is the most common progressive inflammatory demyelinating neurological disorder in young people, whose pathological hallmark is the disruption of myelin sheaths. The prevalence and severity of urinary system involvement closely correlate with the severity of the underlying disease,[42] duration of disease, and extent of spinal cord involvement.[43] Although urological symptoms are rare in the first presentation of MS (3%–10%), almost two-thirds of MS patients will suffer from moderate-to-severe urinary disturbances and almost all patients report LUTD 10 years or more after symptom onset. [5] Nocturia followed by urinary urgency and frequency are the most prevalent signs. UI and poor bladder emptying are noticed less frequently.[44] Over 90% of the patients with MS reported experiencing LUTD regardless of gender, with symptoms reflective of the NDO.[45]

Brain deficits in MS can also lead to a loss of voluntary control of initiation and NDO. Other LUTD symptoms secondary to MS are mediated by axonal damage in the pons and the spinal cord. Damage to the lateral corticospinal and reticulospinal cords can result in DSD, NDO, and detrusor hypocontractility. The evaluation of LUTD in patients with MS should include history, physical and neurological examination, voiding diaries, history of bowel or sexual dysfunction and two validated questionnaires: the actionable bladder symptom and screening tool [46] and the neurogenic bladder symptom score.[47] For patients with new bladder symptoms, urine testing to exclude hematuria or urinary tract infection and measurement of a PVR volume and renal ultrasound are both recommended, while urodynamic studies and cystoscopy are reserved for selected patients.[8,48]

A number of treatment options can be used for MS-LUTD. The treatment is tailored according to the type of dysfunction: storage (NDO) or voiding (DU or DSD). First-line treatments include behavioral modifications, fluid intake management, biofeedback, and pelvic floor muscle training along with physical therapy. Medical management of storage symptoms includes antimuscarinic drugs, desmopressin, and β3-adrenoreceptor agonists. In cases with limited effectiveness or discontinuation due to side effects of first-line oral treatment, second-line treatments are available and include BTX-A injections, intravesical therapies, invasive and noninvasive neuromodulators, and catheterization.[49] The latter in terms of CISC or indwelling catheterization suggests treatment options for voiding symptoms. The use of antimuscarinics in NDO is widespread, while the use of β3-agonists seems an advantageous alternative to antimuscarinics in this population because of a more favorable side effect profile including less cognitive effects, impairment of bladder emptying, and gastrointestinal motility, although there are currently no published randomized controlled trials assessing the efficacy of mirabegron in MS patients.[50] Systematic reviews have not concluded superiority of one agent over others and suggest that the only difference between drugs is their side effect profiles. Measurement of the PVR volume should be done preferably before antimuscarinic treatment is started.[51-53] For voiding problems, only α-blockers are currently considered for medical therapy, and in refractory cases neuromodulators, indwelling catheterization, or CISC is considered.[44]

A study demonstrated for the first time that daily administration of tadalafil 5 mg in patients with MS improved the storage symptoms and PVR volume without urodynamic changes.[54] Intradetrusor BTX-A injection is an approved treatment modality for urge incontinence secondary to NDO. In a randomized trial, BTX-A significantly reduced UI and improved urodynamics and QoL in MS and SCI patients with NDO. Doses of 200 U and 300 U were well-tolerated with no clinically relevant differences in efficacy nor duration of effect between the two doses.[55] Also, BTX-A may be used in the treatment of DSD in MS patients. A placebo-controlled double-blinded study failed to demonstrate that a single injection of BTX-A toxin (100 U allergan) did not decrease PVR.[56] The sacral nerve modulation (SNM) is an alternative treatment for voiding dysfunction in patients with MS in a medium- to long-term follow-up. Urinary retention due to DU is a contraindication for SNM. This treatment option should be offered to MS patients with refractory urgent UI and MS patients with urinary retention due to DSD.[57] SNM may be an option in selected cases of storage and voiding symptoms refractory to conservative treatments, which have been caused by a stable or slowly progressive MS considering its minimal invasiveness and reversibility.[58] Chronic posterior tibial nerve stimulation is effective in the management of severe NDO in MS, without compromising bladder emptying or inducing side effects.[59]

Some patients with MS, especially those who are in a stable disease status, may benefit from surgery. The options include augmentation cystoplasty, a continent and non-continent urinary diversion. Augmentation cystoplasty is a major surgical procedure with high potential morbidity, but data suggest that it is efficacious in MS patients with refractory LUTD for the long term.[60] Non-continent urinary diversion with ileal conduit ap-

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pears to be an effective end-stage solution in MS patients. The 26% rate of perioperative morbidity and the 31% rate of late complication should be considered in order to inform patients prior to the operation.[61]

LUTS in patients with peripheral neuropathy

Diabetic bladder dysfunction (DBD) is currently referred to an "umbrella" description for a group of clinical symptoms that encompasses storage problems such as NDO and urge incontinence, and voiding problems such as poor emptying or overflow incontinence. Its prevalence among diabetic individuals has been estimated to be between 43% and 87%. The most common urodynamic findings in diabetic patients are impairment of bladder sensation, increased PVR, and decreased detrusor contractility.[62] The pathogenesis of DBD is multifactorial. Alterations in the detrusor muscle physiology, neuronal impairment, and urothelial dysfunctions are considered as participating factors. The choice regarding a specific treatment related to DBD depends on the urodynamic abnormalities found.

The 2 main goals of treatment are to avoid overdistension of the bladder and to decrease PVR. In the first stage of treatment, noninvasive strategies should be considered, such as weight reduction or changes in diet, assessing the amount and timing of fluid intake, and bladder and pelvic muscle training.[63] Antimuscarinic agents represent the cornerstone of treatment for patients who present with NDO symptoms. A multicenter, prospective study confirmed that the management with solifenacin was equally effective for both DM-related NDO and idiopathic OAB.[64] α-blockers have shown some benefit in diabetic cystopathy concomitant with BOO.

Bethanechol chloride has been used with inconsistent results in DBD.[65] In patients with consistent residual volumes of over 100 ml but not exceeding 500 ml, treatment with bethanechol (10 mg–20 mg orally 3–4 times a day) may be beneficial.[63] Autonomic and sensory neuropathy with diminished bladder sensation and bladder contractility is the predominant urologic manifestation of diabetic cystopathy. Common treatment options include double void or straining to void and CISC or indwelling catheterization.[65] Cell-based therapies for DBD have shown promising results. Transplantation of ex vivo-cultured healthy smooth muscle cells into the bladders of diabetic rats resulted in increased bladder contractile responses and decreased PVR.[66] Adipose tissue–derived stem cells (ADSCs), a type of mesenchymal stromal cells, have shown promising results as a novel tissue regenerative technique that may be beneficial in DBD. Improved voiding function was noted in ADSC-treated rats as compared with phosphate-buffered saline-treated rats. ADSCs differentiated into smooth muscle cells resulting in a reduction of apoptosis and preservation of "suburothelial capillaries network." [67]

LUTS in patients with herniated disc

There is a correlation between the neurogenic bladder and the disc disease. Approximately 40% of the patients with lumbar disc disease have shown abnormal urodynamic testing and an even larger proportion complain of voiding symptoms. The most common urodynamic finding is detrusor areflexia, but DO or DU can also be observed. The overactive detrusor is related to early nerve roots stretching causing an irritative state responsible for overstimulation and NDO.[68]

Cauda equina syndrome (CES) is most commonly caused by herniation of a lumbar disc, especially in middle-aged patients (40 years-60 years).[69] Acute disc herniation produces bilateral sacral, buttock, perineal and posterior leg pain, tingling, and numbness as well as LUTD, with variable motor and sensory involvement of lower extremities.[70,71] The syndrome can progress to paraplegia with rectal incontinence and UI indicating a need for urgent surgical intervention. Surgical treatment within 48 hours after onset leads to a 70% probability that the lost bladder function will be regained at 2 years; whereas with delayed care, the probability is only 40%. Up to 90% of the patients who receive timely treatment may regain the lost bladder function within 5 years.[72] Sudden urinary retention is considered the most important clinical feature heralding the onset of CES.[73] Urine retention may result in "overflow" incontinence, which may also be the presenting symptom. Although constipation may occur in acute CES, this and other anorectal or sexual symptoms often take much longer to become apparent to patients and physicians.[74] On urodynamic evaluation, underactive detrusor and urinary retention with loss of bladder sensation are shown. Rarely, insensitive bladder with poor compliance and detrusor overactivity can also occur.[75]

Electrically induced bulbocavernosus reflex (E-BCR) using electromyography examination has given excellent positive and negative predictive values for the recovery of bladder function in patients with CES. Determining the preservation of E-BCR in the subacute stage of CES is useful in predicting the eventual bladder dysfunction recovery.[76] A retrospective study demonstrated that a decompressed surgery within 24 hours of the onset of autonomic symptoms in incomplete CES reduces bladder dysfunction at initial follow-up, but no statistically significant difference in outcome was observed in CES with retention regarding the timing of operation.[77]

LUTS in patients with MSA

MSA is an adult-onset, fatal neurodegenerative disease characterized by progressive autonomic failure, parkinsonian features, and cerebellar and pyramidal features in various combinations.[78] Several studies have demonstrated that MSA is a rather primary oligodendrogliopathy; however, the exact pathogenic mechanisms underlying MSA remain unclear.[79,80] MSA is char-

acterized by a prodromal premotor phase in 20% to 75% of the cases, including sexual dysfunction, urinary urge incontinence or retention, orthostatic hypotension, inspiratory stridor, and rapid-eye-movement sleep behavior disorder, months to years before the first motor symptoms appear.[81] These symptoms include parkinsonism, with slowness of movements, rigidity, and a tendency to fall, while the cerebellar subtype of MSA consists of a wide-based gait, uncoordinated limb movements, action tremor, and spontaneous, gaze-evoked, or positional downbeat nystagmus.[78] As far as the nonmotor features of MSA are concerned, the most frequently affected domains are the urogenital and the cardiovascular ones. Regarding the former, ED typically occurs at disease onset in male patients, while genital hyposensitivity during intercourse characterizing the sexual dysfunction in women. Urinary dysfunction includes urinary urgency and frequency, urge incontinence, nocturia, and, less commonly, incomplete bladder emptying. The most frequent cardiovascular symptoms include severe orthostatic hypotension, recurrent syncopic episodes, light-headedness (dizziness), weakness, nausea, tremulousness, headache, or "coat-hanger pain" (pain in the neck and shoulder region) on standing. Additionally, respiratory disturbances are characteristic of MSA, with diurnal or nocturnal inspiratory stridor developing in as many as 50% of the patients at some time.[82]

The diagnosis of MSA is based on the medical history and neurologic findings, with ancillary investigations, such as CT, MRI, PET, urodynamic studies, ultrasonography, and neuropsychological testing.[78]

Unfortunately, there are no specific treatment options for MSA, but only symptomatic therapy is available at present and most of the available prescribed drugs are off-label. In cases of parkinsonian predominance, levodopa is advisable.[82,83] There is no specific therapy available for the cerebellar symptoms. Clonazepam, gabapentin, and buspirone have also been effective treatment options in selected cases, and neurorehabilitation programs can be helpful.[84,85] In cases with neurogenic bladder symptoms, UTIs should be ruled out, while UI due to NDO can be treated with antimuscarinic agents. BTX-A injections in the detrusor muscle may be performed in patients whose condition does not improve with antimuscarinics and CISC as first-line therapy for urinary retention with PVR >100 ml. Sildenafil can reverse ED in men with MSA, but deterioration of the orthostatic hypotension is a side effect.[86,87] Intracavernous injection of vasodilatory prostaglandins (e.g., alprostadil) can be used as an alternative approach.[88]

Conclusions

The lower urinary tract is regulated by a coordinated, multilevel, neurological input that requires an intact central and peripheral nervous system. LUTD is a common sequela of neurological disease, and the patterns of bladder storage and voiding dysfunction depend on the level of the lesion. The lower urinary tract is sensitive to various diseases, such as cerebrovascular accidents, PD, MS, SCI, peripheral neuropathy, and herniated disc or MSA. Incomplete bladder emptying is most often managed by CISC, and storage dysfunction by antimuscarinic drugs or β3-agonists. Intradetrusor injections of BTX-A have transformed the management of NDO. Neuromodulators offer promising results regarding the management of both storage and voiding dysfunction. Bladder augmentation surgery is indicated in cases where there is reduced compliance or NDO refractory to all other nonsurgical treatments. A regular and yearly clinical assessment of all neurogenic LUTD patients with their urologists is done to assess urological complications. Bladder recovery using stem cell-based therapy is promising in experimental settings; however, its role in clinical neurogenic LUTD management continues to evolve.

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Turk J Urol 2020; 46(Supp. 1): S70–S78
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Turk J Urol 2020; 46(Supp. 1): S70–S78
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