TELE-REHABILITATION GUIDELINE
Neurogenic Bladder Management in Spinal Cord Injuries

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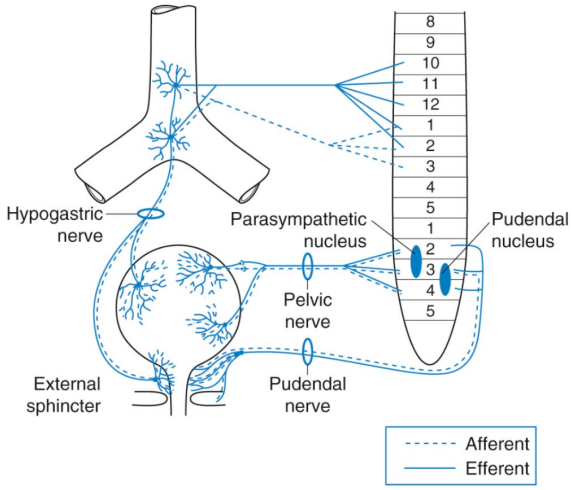
70-84% of people with SCI will have some level of bladder dysfunction with a risk of upper and lower urinary tract complications (1). Therefore, formulating an individualized comprehensive bladder retraining and management program is essential. The goals are to protect renal function, preserve the upper urinary tracts, minimize lower urinary tract complications and minimize bladder incontinence.

I. Lower urinary tract innervation

A. Peripheral innervation

1. The bladder receives innervation from both parasympathetic and sympathetic nervous system.
2. Sympathetic innervation (SI) to the lower urinary tract arises from the T11-L2 cord level.
   a. SI synapses are located in the inferior mesenteric and hypogastric plexuses.
   b. Sympathetic efferent nerve fibers travel through the hypogastric nerve to alpha (α-1) and beta (β-2) adrenergic receptors within the bladder and urethra.
   c. Activation of the SI produces norepinephrine to be released in the lower urinary tract, resulting in detrusor relaxation, bladder neck and internal sphincter contraction.
3. Parasympathetic innervation (PI) to the lower urinary tract arises from the S2-S4 cord level and is located within the pudendal nucleus.
   a. Parasympathetic efferent nerve fibers travel through pelvic nerves to parasympathetic receptors of detrusor muscle.
   b. Activation of the PI results in the release of acetylcholine and nitric oxide in the lower urinary tract, causing detrusor contraction and relaxation of the proximal urethra.
4. Somatic nervous system innervation to the external urethral sphincter arises from the pudendal nucleus at the S2–S4 cord level, which courses through the pudendal nerve to the sphincter striated muscle. Somatic innervation enables voluntary contraction of external urethral sphincter.
5. The majority of sensory afferent fibers are small myelinated A fibers and unmyelinated C fibers. The A fibers have a graded response to bladder distention, while C fibers detect painful stimuli, temperature and chemical stimuli.
6. The loss bulbospinal control and coordinated interaction between the autonomic and somatic nervous systems results in urinary bladder dysfunction termed “neurogenic bladder”

The parasympathetic, sympathetic, and somatic nerve supply to the bladder, urethra, and pelvic floor (6)



B. Voiding centers
   1. Normal micturition allows proper function of both the bladder and urethra. Micturition reflex coordinates detrusor contraction with internal and external urinary sphincter relaxation, enabling adequate voiding of the bladder.
   2. The pontine micturition center (PMC)
      a. Lies in the pons along with other autonomic centers
      b. Modulates the opposing effects of the parasympathetic and sympathetic nervous systems on the lower urinary tract
      c. In the emptying stage, the PMC sends excitatory signal to the sacral spinal cord, results in detrusor contraction while simultaneously sending inhibitory signal to the thoracolumbar cord to relax the internal urethral sphincter.
      d. In the storage stage, the PMC is inhibited, which in turn suppresses the sacral outflow, resulting in detrusor relaxation. The thoracolumbar spinal cord is activated simultaneously, allowing internal urethral sphincter contraction.
   3. The sacral micturition center (SMC)
      a. Located at the level of S2-S4
      b. Modulates efferent parasympathetic impulses to the bladder, causing bladder contraction
      c. Afferent impulses to the SMC provide feedback regarding bladder fullness
   4. Supraspinal centers
      a. A facilitatory reflex with afferent axons originating from the bladder and synapsing on the pudendal nucleus at S2,3 and 4
      b. Allows inhibition of pelvic floor activity during voiding

II. Pathophysiology and classification of neurogenic bladder

A. Mechanical or physiologic defects in the bladder could result in an inability to regulate filling pressure.
B. Neurogenic bladder is the loss of normal bladder function caused by damage to part of the nervous system.
C. The damage can cause the bladder to be underactive, resulting in loss of contraction and complete emptying.

D. The damage can also cause the bladder to be overactive, resulting in frequent and uninhibited contractions, with loss of synergy in bladder contractions and sphincter relaxation.
E. Neurogenic bladder can be classified based on different criteria. The following classification is mainly formulated based on the level of injury in the central nervous system and helps guide pharmacologic and surgical intervention.
    1. Uninhibited bladder
        a. Lesion is above the pontine micturition center (i.e. stroke, brain injury, or brain tumor).
        b. There is reduced awareness of bladder fullness with a low pressure filling system, resulting in a low bladder capacity.
        c. Since the PMC is intact, the normal opposition of detrusor and internal/external sphincter tonus is maintained and does not put the upper urinary tract at risk of high pressure injury, which can occur with detrusor sphincter dyssynergia (DSD).
    2. Upper motor neuron bladder
        a. Supraconal Lesion is between the pontine micturition center and sacral spinal cord (i.e. traumatic spinal cord injury or multiple sclerosis).
        b. The spinal cord damage renders the bladder and sphincters spastic, especially if lesions are above T10 level.
        c. It is characterized by detrusor sphincter dyssynergia (DSD), where simultaneous detrusor and urinary sphincter contractions create a high pressure system.
        d. Over time, DSD can lead to vesicoureteral reflux and renal damage.
        e. The bladder capacity is usually reduced due to the high detrusor tone and loss of compliance.
    3. Lower motor neuron bladder
        a. Conal/Infraconal Lesion is at the level of sacral cord (i.e. traumatic spinal cord injury, multiple sclerosis or sacral nerve root injuries).
        b. The SMC or related peripheral nerves are usually damaged while the sympathetic outflow is intact; resulting in low detrusor tone with normal internal sphincter innervation. Bladder capacity tends to increase above normal threshold, with associated overflow urinary incontinence.

III. Evaluations

A. Detailed history and physical examination is essential for accurate diagnosis and appropriate management.
B. Neurological examination should include mental status, reflexes, strength, and sensation, including sacral dermatomes, to determine if there are neurologic conditions present that may contribute to the voiding dysfunction.
C. Detailed genitourinary history needs to be taken.
D. Medication history is also essential to eliminate any reversible causes.
E. Urologic examination (6)
    1. Upper Tract Tests
        a. Ultrasonography, KUB (kidney, ureter and bladder), CT with or without contrast
        b. Creatinine Clearance Time
        c. Isotope studies
    2. Lower Tract Tests
        a. Post void residual (PVR)
        b. Urinalysis with culture and sensitivity testing
        c. Cystography
        d. Urodynamic evaluation (gold standard for the evaluation of lower urinary tract function)

e. Urethral pressure profiles
f. Sphincter Electromyography
g. Video urodynamics/ Fluoro urodynamics
h. Cystoscopy

F. Abnormal residual volume is 100 ml or greater than 20% of the voided volume. Residual urine volumes under 100 ml are associated with a reduced risk of development of bacterial cystitis.(7)

G. Urodynamic evaluation is recommended to assess urinary function, including urinary flowmetry, bladder cystometrogram/electromyogram (CMG/EMG), Valsalva leak point pressure (LPP) measurement, and urethral pressure profile (UPP).

H. Urodynamic studies are the most definitive and objective means to determine abnormalities in the bladder and urethra in the filling/storage phase and voiding phase in neurogenic bladder dysfunction. In one cross sectional observation study, 47.9% of individuals required at least one type of intervention based on urodynamic studies. (20)

J. Normal filling pressure is 40 cm of H_20 or less.(12) If a high detrusor leak point pressure is above 40 cm H2O, the upper tract is endangered.(25)

IV. Goals of management

A. Achieve/maintain continence
B. Prevent development of a high pressure detrusor that can lead to upper urinary tract damage
C. Minimize symptomatic urinary tract infections and over-distension of the bladder.
D. In a literature review with low level evidence, the use of intermittent sterile catheter was associated with lower rates of bladder infections in patients with neurogenic bladder. Comparisons of bladder infection rates between patients using indwelling urethra catheter or suprapubic catheters and suprapubic catheters and intermittent sterile catheter were inconclusive. (26)

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V. Non pharmacologic intervention

A. Intermittent catheterization
1. Requires sufficient hand skills or willing care giver
2. Not recommended in patients with abnormal urethral anatomy, bladder capacity less than 200 ml, poor cognition/motivation or high fluid intake
3. May require fluid schedule and restrictions (1800 ml/day, 400 cc with meals, 200 cc TID)
4. Hydrophilic catheters may decrease the number of bladder infections and decrease urethral trauma and improve quality of live and from a societal aspect be less expensive in the long term. (21)
5. Complications: UTI, urethral trauma, incontinence with over distention.

B. Credé and Valsalva
1. For individuals with lower motor injury with low outlet resistance.
2. Avoid in patients with detrusor sphincter dyssynergia, bladder outlet obstruction, vesicoureteral reflux or hydronephrosis.
3. Complications: incomplete bladder emptying, high intra-vesical pressure, vesicoureteral reflux, hydronephrosis, abdominal bruising, possible hernia, pelvic organ prolapse or hemorrhoids.

C. Indwelling urethral catheterization
1. For patients with poor hand skills, high fluid intake, cognitive impairment, active substance abuse, elevated detrusor pressures, lack of success with other less invasive bladder management methods.

2. Complications: bladder stones, kidney stones, urethral erosions, epididymitis, recurrent symptomatic urinary tract infections, incontinence, pyelonephritis/hydronephrosis from bladder wall thickening, fibrosis or bladder cancer.

D. Suprapubic catheterization: For patients with urethral abnormalities, stricture, false passages, bladder neck obstruction, urethral fistula, urethral discomfort, perineal skin breakdown as secondary to urine leakage/urethral incompetence, personal preference, desire to improve sexual genital function, prostatitis, urethritis or epididymo-orchitis

E. Reflex voiding
1. For male patients who, post-spinal shock, demonstrate adequate bladder contractions and adequate hand skills or have a willing care giver to change a condom catheter.
2. Requires a periodic urodynamic study to monitor bladder pressures.

F. Timed voiding: For patient with uninhibited bladder and a low pressure system

G. Electrical nerve stimulation (18, 19)

1. A clinical option for promoting micturition in SCI patients.
   a. Sacral Anterior Root Stimulation and Sacral Deafferentation
   b. Pudendal Nerve Stimulation
   c. Sacral Neuromodulation -InterStim® (Medtronic Inc., Minneapolis, MN, USA) was approved by the FDA in 1997 for urge urinary incontinence and in 1999 for urinary retention
   d. Percutaneous tibial nerve stimulation (PTNS) - a less invasive treatment alternative to SNS, as surgical implantation is not required. Urgent® PC Neuromodulation System (Uroplasty, Inc., Minnetonka, MN, USA) received FDA 510(k) clearance in 2007 for the treatment of urinary urgency, urinary frequency, and urge urinary incontinence.
   e. Transcutaneous electrical stimulation for bladder control - surface stimulation of the dorsal nerve of the penis to inhibit bladder activity, targets peripheral nerves through a less invasive approach.
   f. S1 nerve transfer- with unilateral proximal end of the S1 ventral root (VR) anastomosed to the distal end of the S2 and S3 VRs has been shown to be effective in atonic bladder function caused by low conus medullaris injuries. (22)
2. Well-designed, randomized and controlled studies are essential to bring more of these treatment strategies from the research bench to the patient.

VI. Pharmacologic interventions

A. Alpha-1 Adrenergic Antagonists
1. Peripheral postsynaptic blockade of alpha-adrenergic receptors in the bladder neck and proximal urethra to reduce urinary outflow resistance.
2. Dibenzyline, terazosin, tamsulosin, alfuzosin, and doxazosin
3. Reduction in blood pressure due to vasodilating effect on arterial smooth muscle.
4. Side effects include fatigue, dizziness, lightheadedness, dry mouth and constipation.
5. Can be used in conjunction with transurethral sphincterotomy.

B. Anticholinergic (antimuscarinic) medications reduce reflex (involuntary) detrusor activity by blocking cholinergic transmission at muscarinic receptors and are the first-line option for treating neurogenic detrusor overactivity. (9) One contraindication is untreated narrow angle glaucoma. (16) A long term side effect, may be early onset dementia. (15)
1. Non-selective
   a. Oxybutynin (Ditropan), tolterodine (Detrol LA), and trospium chloride

b. Side effect includes QT interval prolongation and memory and cognition impairments.

2. Selective for M2 and M3 receptors
   a. Solifenacin (Vesicare) and darifenacin (Enablex)
   b. Fewer cognitive side effects, should not be used in patients with severe hepatic impairment, and dosing adjustment is needed when used concomitantly with ketoconazole or erythromycin (23)

C. Selective beta-3 adrenergic Agonist. Stimulation of the beta-3 pathway promotes smooth muscle relaxation of the bladder to increase urine storage. (17)
   1. Mirabegron (Myrbetriq)
   2. Side effects of HTN, headache, tachycardia.
   3. May provide synergistic effect with anticholinergic medications in patients who do not respond well to monotherapy (16)

D. Botulinum toxin (8, 10)
   1. Blocks neuromuscular junction presynaptic vesicle fusion and prevents acetylcholine release. It is an invasive procedure with intramuscular injections via a cystoscope procedure.
   2. Acts on sensory afferent neurons and prevents the excitatory effects of nerve growth factor; effects can last for up to six-to-nine months.
   3. Studies have demonstrated that botulinum-A toxin inhibits ACh release at the presynaptic cholinergic nerve terminals, decreases substance P and CGRP release in afferent nerves, and reduces the expression of transient receptor potential vanilloid subfamily 1 (TRPV-1), as well as purinergic receptor P2X expression in the bladder wall. Thus, botulinum-A toxin can be effective in treating neurogenic detrusor over activity, DSD, and motosensory urgency. (24)

E. Vanilloids such as capsaicin and resininferatoxin
   1. Detrusor overactivity can be inhibited in spinal-injured human patients by directly suppressing the C-fiber-mediated bladder afferent hyperexcitability by administrating vanilloids such as capsaicin and resininferatoxin. Vanilloid receptors, or VR1, can become upregulated after spinal cord injury.
   2. Inflitrating the bladder with caspsaicin or resininferatoxin in solution can trigger transient depolarization in the afferent neurons followed by a prolonged period of inactivation, which leads to C-fiber afferent desensitization and reduced excitability in response to bladder wall distention and spasticity with filling. (27, 28)

F. Antibiotic medications should be used only to treat symptomatic urinary tract infections (UTI).
   1. An UTI may manifest differently in patients with SCI than in the general population. The complaints of dysuria, frequency, and urgency are usually absent in infected patients with SCI (4). Common manifestations of UTI in patients with SCI include unusual fatigue, worsening muscle spasms, increasing autonomic dysreflexia**,** urinary leakage, and change in voiding habits. Fever is usually, but not always, present.
   2. The definition of symptomatic UTI:
      a. The presence of significant bacteriuria ($\geq 10^5$ CFU/ml); pyuria ($> 10^4$ WBC/ml of uncentrifuged urine or > 10 WBC/hpf for spun urine); and
      b. Fever (> 100°F) plus
      c. More than one of the following signs and symptoms: suprapubic or flank discomfort, bladder spasm, change in voiding habits, increased spasticity, and worsening dysreflexia, provided that no other potential etiologies for these clinical manifestations are identified. (5)

3. Most cases of bacteriuria in patients with SCI represent asymptomatic bladder colonization.

VII. Surgical procedures to enhance detrusor storage

A. Enterocystoplasty increases bladder capacity (13) - This procedure creates an anastomosis to join a part of the ilium or ileocecal segment to the detrusor. High complication rate post-surgery, mucus production which can clog catheters
B. Myomyotomy or myomectomy creates a large detrusor diverticulum

VIII. Surgical procedures to help detrusor emptying

A. Unilateral or bilateral sacral nerve root stimulation
B. Dorsal rhizotomy
C. Urinary diversion
D. Continent abdominal stoma for clean intermittent catheterization (CIC)
E. Appendicovesicostomy anastomosis (Mitrofanoff)

IX. Bladder sphincter procedures to enhance emptying

A. Sphincterotomy
B. Internal/external sphincter resection
C. Urethral stents/balloon dilatation
D. Artificial urinary sphincter devices
E. Botox injections into the internal/external sphincter muscles.

This guideline was developed to improve health care access in Arkansas and to aid health care providers in making decisions about appropriate patient care. The needs of the individual patient, resources available, and limitations unique to the institution or type of practice may warrant variations.

Guideline Developers

Guideline developed by Noadia Worku, D.O in collaboration with the TRIUMPH team led by Thomas Kiser, MD, and Rani Lindberg, MD. 2014
Revised: Yen Nguyen, MD and Thomas Kiser, MD 2018
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