Part II: Current Treatment Options for Neurogenic Bladder Dysfunction

Clinicians need to keep abreast of the most current treatment options for NGB, which can result in improved patient outcomes and quality of life.

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Neurogenic lower urinary tract dysfunction—or neurogenic bladder (NGB)—dysfunction may be caused by various diseases and events affecting the nervous system controlling the lower urinary tract. The resulting dysfunction depends on location and extent of the neurologic lesion; thus, the population with NGB dysfunction is quite diverse (Table 1). Two common neurologic causes of neurogenic detrusor overactivity (NDO), which may cause symptoms similar to overactive bladder, are multiple sclerosis (MS) and spinal cord injury (SCI). Limitations imposed by the underlying disease and the broad range of symptoms encompassed by NGB dysfunction can have a significant effect on patient quality of life, necessitating both a multidisciplinary and an individualized approach to management and treatment.

Treatment goals

One proposed treatment paradigm for patients with NGB dysfunction is to optimize oral therapy, provide local bladder treatment, and offer bladder augmentation and urinary diversion. Considerations in managing patients with NGB include the high rates of discontinuation of antimuscarinics, pharmacologic safety, and surgical and emerging therapies that can maximize adherence and minimize risk of systemic effects.

The overarching goal for the patient with NGB dysfunction—including both NDO and detrusor sphincter dyssynergia, which can cause high intravesical pressure, leading to upper urinary tract damage—is to preserve renal function, decrease potential urologic complications, and improve quality of life by relieving symptoms. Patients with SCI or MS often have NDO, which also frequently causes urinary incontinence.

The more independent a patient can become by reducing symptoms of urgency, frequency, and incontinence, the less likely he or she will need to rely on assistance or be institutionalized. Individualized treatment plans should take into account a patient’s history and physical examination, urodynamics, renal function, and personal goals and limitations, including mobility, degree of disability, hand function,
Treatment options

Treatment for dysfunction usually includes a combination of both pharmacologic agents and nonpharmacologic approaches, including noninvasive, minimally invasive, and surgical options.

Noninvasive treatments

Noninvasive treatment options for NGB dysfunction include intermittent catheterization, Crede and Valsalva, and timed voiding, lifestyle changes/behavioral modification, and oral pharmacotherapy.

Lifestyle changes/behavioral modification. These approaches may be helpful for patients with lower urinary tract dysfunction. They include moderate fluid intake, reducing or eliminating caffeine, dietary changes, pelvic floor muscle exercises, biofeedback, timed voiding, toileting assistance, and bladder education/retraining.

Clean intermittent catheterization (CIC). CIC is one of the most commonly used methods for patients with NGB that fails to empty. Adequate hand function or a caregiver willing to perform CIC is necessary for this method to be successful. Abnormal urethral anatomy, strictures, bladder capacity <200 mL, adverse reaction to catheters, or autonomic dysreflexia with high bladder volumes may interfere with the ability to conduct CIC.

Urinary tract infections, one potential side effect of CIC, may be avoided by using hydrophilic-coated catheters; for example, in patients with SCI.12 Strictures, hematuria, and bladder stones are other side effects that can occur.13 Crede and Valsalva. Third-party bladder expression (Crede) and voiding by abdominal straining (Valsalva) may be appropriate for patients with low outlet resistance. Risks include high intravesical pressures, which can lead to worsening vesicoureteral reflux or hydronephrosis; incomplete bladder emptying, leading to chronic urinary tract infections; pelvic organ prolapse; hernia; and hemorrhoids.

Indwelling and suprapubic catheterization. Considered temporary methods, these may be preferred when other approaches have failed. Complications can include bladder stones, infections, and malignancies.

Oral pharmacotherapy. Anticholinergics/antimuscarinics, the most commonly used class of agents for NGB, bind to muscarinic receptors in the detrusor muscle, reducing bladder storage pressure and increasing capacity (Table 2).14-17 They are generally used in conjunction with CIC to treat NGB dysfunction.

Perceived lack of efficacy, costs of medication, polypharmacy, and adverse effects—including dry mouth (a well-known effect), facial flushing, dizziness, constipation, and neurologic deficits—can all lead to patients discontinuing treatment with anticholinergics. Studies have shown that among 6 therapeutic classes—angiotensin receptor blockers, bisphosphonates, oral antidiabetics, overactive bladder agents, prostaglandin analogs, and statins—medication for overactive bladder had the lowest adherence rate.18 One study found that at 1 year after initiating therapy for overactive bladder, <30% of patients are still taking antimuscarinics; another showed that of patients initiated on either oxybutynin and tolterodine, <14% continued for 1 year, with a median of 31 days until discontinuation.19 Individual responses to anticholinergics vary; therefore, patients may find another medication or a combination of agents can increase efficacy or reduce adverse effects. Other oral agents that have been used in patients with NGB include phosphodiesterase type 5 inhibitors, gonadotropin-releasing hormone antagonists, neurokinin receptor-1 antagonists, beta-3 adrenoceptor agonists, and desmopressin.20

Minimally invasive treatments

Patients with NGB who have refractory detrusor overactivity may benefit from minimally invasive treatment. Refractory detrusor overactivity is persistent urgency, frequency, and incontinence, and remains bothersome despite oral pharmacologic therapy.

Sacral neuromodulation. Although this approach is approved by the U.S. Food and Drug Administration (FDA) for the treatment of urinary retention and the symptoms of overactive bladder, its safety and efficacy have not been established for patients with neurologic disease origins. An alternative treatment option in patients with voiding dysfunction and chronic pelvic pain, it is generally performed in stages to identify responders; those who respond proceed to full implantation of pulse generator and leads.

Intravesical drug delivery. Neurogenic overactivity can be decreased for several months by intravesical instillation of agents that desensitize afferent C-fibers in the bladder. Sensation is restored when the sensory nerves regenerate. Higher levels of anticholinergics such as oxybutynin can be increased and adverse effects decreased by avoiding hepatic first-pass metabolism. Vanillic acid compounds, capsaicin, and reslinfera-
**Case Study: Managing Urinary Incontinence in Multiple Sclerosis**

K.A. is a 52-year-old woman with multiple sclerosis (MS) that was diagnosed at the age of 37 years. She has had to take a medical leave of absence from her job as an elementary schoolteacher because of fatigue, lack of adequate bladder control, and urinary incontinence (UI) that impaired her ability to teach. She can walk 50 feet without a cane but must watch her balance, and going up and down stairs is difficult for her. K.A. is currently on beta interferon for her MS and has not had a flare-up for more than 2 years. Her overall health is otherwise stable, with only borderline hypertension and normal lipid profiles.

One year ago, K.A. admitted she was increasingly constipated and often felt dizzy if she stood up too quickly. Her clinician determined she was having involuntary detrusor contractions starting at 79 mL and had a maximal detrusor pressure of approximately 40 cm H2O. She did not have stress incontinence or pelvic prolapse on examination. Several options were suggested, including switching to a different anticholinergic agent, clean intermittent catheterization, and a suprapubic catheter, since increasing her current oxybutynin dose was not a viable alternative.

She agreed to switch to a different anticholinergic and was placed on tolterodine tartrate extended-release tablets 4 mg/day. At her 2-week follow-up, postvoid residual (PVR) was 75 mL, symptoms had improved, and incontinence was 75% better.

However, at her 10-month follow-up, K.A. asks her clinician to discuss any other options, as treatment with this anticholinergic has resulted in blurred vision and drowsiness, interfering with her ability to walk up and down stairs without fear of falling, and her UI seems to be worse. At this visit, her PVR is 35 mL, her incontinence has returned to baseline, and her urgency symptoms have returned.

Three suggested treatment modalities are neuromodulation, bladder injection of botulinum toxin, or augmentation. The efficacy and safety of each of the options are explained. K.A. opts for treatment with intradetrusor injection of onabotulinumtoxinA 200 U because she does not want to undergo a surgical procedure. She understands that the treatment with onabotulinumtoxinA will last approximately 10 months.

**Botulinum neurotoxin (BoNT) injection.** Cystoscopic injections of Botulinum toxin were shown to be effective in refractory urge incontinence in adults with SCI and MS. Further studies are needed to determine long-term efficacy and safety.24 Advances in development of intravesical drug delivery, including the use of liposomal nanoparticles, will help improve management of symptoms of the lower urinary tract.26

An initial 24-week study found that onabotulinumtoxinA 200 U and 300 U clinically significantly decreased signs and symptoms of urinary incontinence caused by NDO in 59 patients due to SCI or MS vs. placebo.72 The studies assigned patients with NDO resulting from SCI or MS not adequately managed with anticholinergics to onabotulinumtoxinA 200 U, 300 U, or placebo. Primary end point was changed from baseline in weekly urinary incontinence episodes at week 6. Patients in the onabotulinumtoxinA 200 U and 300 U arms had significant decreases in weekly frequency of incontinence episodes vs. placebo and had similar improvements in incontinence episodes, urodynamic parameters, and health-related quality-of-life scores (Figure 1).52,74

![Figure 1. Change from Baseline in Incontinence Quality-of-Life Total Score with OnabotulinumtoxinA 200 U or Placebo](adapted from Cruz F, et al. Eur Urol 2011;60(4):742-750.)

The most common adverse events associated with intravesical BoNT injection are incomplete bladder emptying and urinary tract infections.72 Contraindications to onabotulinumtoxinA are active infection and known hypersensitivity to agents; relative contraindications include preexisting neuromuscular disorders and concomitant use of agents interfering with neuromuscular transmission; pregnancy (Class C) and nursing mothers; and bladder outlet obstruction. Incidence of autonomic dysreflexia may occur in patients treated for detrusor overactivity associated with a neurologic condition that requires prompt medical therapy.75

**Surgical treatments**

Surgical options include transurethral sphincterotomy, endourethral stents, urethral and bladder neck procedures, bladder augmentation, and urinary diversion (Table 3).

**Barriers to care**

Barriers to care include patient embarrassment about their condition, lack of awareness that serious complications can result from mismanagement of inconti-
nence, the perception that bladder issues are not life-threatening, fear of needing invasive surgical intervention, a lack of awareness that effective treatment options are available, and a lack of access to treatment options covered under insurance-plan benefits. Patients and clinicians need to be aware of the potentially detrimental effects of poorly managed or unmanaged NDO on disease outcomes.

**Patient satisfaction with treatment**

Patient expectations, perception, and satisfaction with treatment can affect adherence, as can costs and reimbursement issues. To ensure treatment adherence and a successful outcome, patients and clinicians need to be informed of available options and any training as well as the day-to-day requirements and long-term expectations for treatment. Ideally, bladder management strategy should be adapted to the underlying disease.

Patient satisfaction with treatment in the NGB population has been inadequately studied, using tools developed for idiopathic overactive bladder. The Actionable MS Urinary Function Screening Tool is a new measurement instrument developed to assess the impact of NGB dysfunction on quality of life in patients with MS. Until study results are available, clinicians cannot accurately assess patient satisfaction with treatment.

**Conclusion**

Successful treatment of the patient with NGB dysfunction encompasses satisfactory treatment with therapy as well as meaningful improvement in symptoms. Optimal management can result in improved patient outcomes, and a consistent effect on bladder control can result in sustained improvement in quality of life.

**Table 3: Types of Surgical Treatments for the Patient with NGB**

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Patient Selection</th>
<th>Advantages/Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transurethral spincterotomy</td>
<td>• Detrusor external sphincter disynkera</td>
<td>• May need to be repeated</td>
</tr>
<tr>
<td>• Endoscopic</td>
<td>• Beneficial in long-term management in patients with SCI</td>
<td>• May need to be repeated</td>
</tr>
<tr>
<td>Endourethral by-passes</td>
<td>• potentially reversible procedure</td>
<td>• Upper tracts not endangered</td>
</tr>
<tr>
<td>Endoscopic</td>
<td>• Reduced hospital stay</td>
<td></td>
</tr>
<tr>
<td>Stents</td>
<td>• Second stent can be placed after first stent is epithelialized</td>
<td></td>
</tr>
</tbody>
</table>

**Bladder augmentation**

- Generally reserved for patients refractory to more conservative therapy
- Complications include bacteria, metabolic disorders, absorption disorders, stones, risk of malignancy, and long recovery period
- Excellent continence rates with high patient satisfaction
- Simple procedure, relatively low adverse-effect profile

**Other options**

- Detrusor myectomy (auto-augmentation) in selected patients is an extraperitoneal procedure wherein the detrusor muscle over the dome of the bladder is removed and the compliance and capacity of the bladder can be increased much like a diverticulum

**Urethral or bladder neck procedures**

- Bladder neck incision indicated in secondary changes of the bladder neck caused by scar- ring and fibrosis
- Autologous fascial slings effective in increasing the Valsalva or stress leak point pressures without increasing leak point pressures
- Generally reserved for patients refractory to more conservative therapy
- Complications include bacteria, metabolic disorders, absorption disorders, stones, risk of malignancy, and long recovery period
- Excellent continence rates with high patient satisfaction
- Simple procedure, relatively low adverse-effect profile

**References**


4. Rosenblum N. Will the evolution of overactive bladder management result in sustained improvement in quality of life.


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1. Which of the following is generally used in conjunction with clean intermittent catheterization to treat neurogenic bladder dysfunction?
   a. Bladder augmentation
   b. Intravesical instillation
   c. Antimuscarinic agents
   d. Sacral neuromodulation

2. The most commonly used class of agents for neurogenic bladder dysfunction is:
   a. Tricyclic antidepressant
   b. Anticholinergics
   c. Capsaicin
   d. Botulinum toxin

3. Patients may discontinue oral pharmacotherapy primarily due to what well-known adverse effect?
   a. Facial flushing
   b. Dizziness
   c. Hypotension
   d. Dry mouth

4. Which of the following statements is true regarding various botulinum toxin serotypes?
   a. They are interchangeable
   b. The dosing units are not equivalent
   c. All have the same generic name
   d. They are all approved to treat neurogenic detrusor overactivity

5. One of the most common adverse events of intravesical injection of BoNT is:
   a. Urinary tract infection
   b. Stones
   c. Autonomic dysreflexia
   d. Urinary leak

6. Which of the following statements about endourethral stents is false?
   a. Patients with spinal cord injury can have long-term benefit
   b. Hospital stay can be reduced
   c. Procedure is generally irreversible
   d. Patients who have difficulty catheterizing can benefit

7. Which of the following is among the most commonly used methods for patients with normal hand function and neurogenic bladder that fails to empty?
   a. Crede
   b. Valsalva
   c. Indwelling catheter
   d. Clean intermittent catheterization

8. A surgical treatment with excellent continence rates and high patient satisfaction is:
   a. Bladder augmentation
   b. Transurethral sphincterotomy
   c. Detrusor myectomy
   d. Urinary diversion

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