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# Treatment Strategies for Neurogenic Voiding Dysfunction

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**Abstract**

The main problems in neurogenic voiding dysfunction (NVD) are failure to store, failure to empty, and combined failure to store and empty. The management priorities in NVD should be as follows, in order: (1) preservation of renal function, (2) freedom from urinary tract infection, (3) efficient bladder emptying, (4) freedom from an indwelling catheter, (5) patient satisfaction with voiding management and (6) avoiding medication after proper management. Management of the urinary tract in patients with spinal cord injury must be based on urodynamic findings rather than inferences from a neurologic evaluation. Selecting high-risk patients is important to prevent renal function impairment in patients with chronic NVD. Patients with NVD should be regularly followed-up for lower urinary tract dysfunction using urodynamic study and any urological complication should be adequately treated. Avoiding a chronic indwelling catheter can reduce the incidence of developing a low compliant bladder. Intravesical instillation of vanilloids or injection of BOTOX provides an alternative treatment for refractory detrusor overactivity or low compliant bladder and can replace the need for bladder augmentation. When surgical intervention is necessary, a less invasive type of surgery and a reversible procedure should be considered first and unnecessary surgery in the lower urinary tract should be avoided. Keeping the bladder and urethra in good condition without interfering with neuromuscular continuity will give patients with NVD a chance to benefit from new technologies in the future. It is most important that the physician continues to try to improve the quality of life of patients with NVD. (*Tzu Chi Med J* 2008;20(1):35–39)

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## 1. Introduction

Neurogenic voiding dysfunction (NVD) includes dysfunction of the urinary bladder and urethra due to central nervous system or peripheral neurogenic lesions. Cerebrovascular accidents, Parkinson's disease, cerebral palsy, multiple sclerosis, transverse myelitis and spinal cord lesions can all result in NVD. Among all disorders resulting in NVD, spinal cord injury (SCI) remains the most difficult to manage. In patients with a single level SCI, a significant association between the level of injury and the type of voiding dysfunction has been noted. Management of the urinary tract in patients with SCI must be based on urodynamic findings rather than inferences from a neurologic evaluation [1].

The main problems in NVD are: (1) failure to store due to detrusor hyperreflexia (DH) or urethral incompetence, (2) failure to empty due to detrusor areflexia, bladder neck dysfunction (BND) or detrusor sphincter dyssynergia (DSD), and (3) combined failure to store and empty due to DSD or detrusor hyperactivity and impaired contractility.

The management priorities in NVD should be as follows, in order: (1) preservation of renal function, (2) freedom from urinary tract infection, (3) efficient bladder emptying, (4) freedom from an indwelling catheter, (5) patient satisfaction with voiding management and (6) avoiding medication after proper management.

## 2. Selecting high-risk patients

It is important to screen patients at high risk, such as those with a complete neurological lesion, cervical spinal cord paraplegia, a prolonged indwelling catheter, a high detrusor leak-point pressure, DSD and autonomic dysreflexia (AD), a large postvoid residual and vesicoureteral reflux. Correction of urological complications and improvement in the quality of life are the two main goals for management of NVD. In addition, individualized treatment strategies for each patient should be developed and carefully evaluated.

## 3. Conservative management of NVD

Conservative management is the mainstay of urological treatment for NVD if possible. Patients can be instructed to void by abdominal stimulation, the Crede maneuver or abdominal straining. If they cannot have a balanced bladder after training, clean intermittent catheterization (CIC), performed either by themselves or a caregiver, is necessary. Spontaneous voiding with and without triggered voiding and/or bladder expression has proven to be less safe except in well-defined patients with regular urological follow-up [2]. Long-term indwelling catheters should be avoided except for patients with tetraplegia and those who are bedbound, in whom an indwelling urethral Foley catheter or suprapubic cystostomy may be an alternative.

## 4. Intravesical treatment of DH

Medications to reduce DH by antimuscarinics [3], BND by alpha-blockers, and striated sphincter spasticity by skeletal muscle relaxants or nitric oxide donors [4] and to increase detrusor muscle tone by cholinergic agents (Urecholine) are commonly prescribed to achieve better bladder control or efficient emptying. However, patients with NVD might not be controlled without combined medication for detrusor dysfunction and bladder outlet resistance. A combination of alpha-adrenergic blockers and antimuscarinic agents would be expected to be more beneficial than the use of either one alone for the treatment of voiding dysfunction [5]. However, adverse effects increase in association with the number of medications used. Therefore, intravesical treatment of NVD will become the future treatment strategy for DH. Intravesical instillation of capsaicin or resiniferatoxin can successfully eradicate incontinence due to DH and can be considered a second line treatment for NVD [6–8]. In one study, DH decreased and urinary continence improved for 3–6 months after a single intravesical instillation of capsaicin. Patients treated with intravesical instillation of resiniferatoxin fared better than those treated with capsaicin, mainly because of less irritation and a longer duration of effects. For treatment of high level SCI and DSD, a dose of 10 μM was necessary to achieve better therapeutic results. However, the high concentration of intravesical vanilloid might induce AD during intravesical instillation and this has limited this treatment in the clinical trial stage [9].

## 5. Surgical management of NVD

For patients who do not receive any therapeutic effects from medical treatment or intravesical vanilloid instillation, surgical intervention is mandatory to treat urological complications and preserve renal function. A transurethral external sphincterotomy provides significant reduction of voiding pressure and AD in male SCI patients. The high systolic and diastolic blood pressure and postvoid residual decrease after sphincterotomy [10]. Transurethral incision of the bladder neck can also reduce AD and facilitate spontaneous voiding in incomplete cervical SCI patients [11]. In tetraplegic patients, a urethral stent implant can relieve urethral resistance and facilitate spontaneous voiding; however, patients should be monitored for

possible stent erosion or migration. In one study, the most common stent complication was displacement, followed by stenosis, lithiasis and intraprosthetic calcification. In all, 8.5% of patients required stent removal [12]. In another study, bladder augmentation either by a segment of intestine, or autoaugmentation using a myomectomy resulted in a large capacity, low intravesical pressure and a non-reflux condition. Most patients reported no significant change in bowel function and nearly all patients expressed extreme satisfaction with urological management [13]. However, long-term complications such as stone formation, loose stool, metabolic acidosis and chronic urinary tract infection remain to be solved [14]. In patients with cervical SCI or severe urethral sphincter deficiency, a continent lower urinary tract reconstruction (such as a Kock pouch) or closure of the bladder neck plus continent ileostomy and bladder augmentation might help the patient become continent by evacuation of the bladder by clean intermittent self-catheterization from an ileostoma [15].

## 6. Bladder and urethral neurotoxin injections

Future treatment strategies for NVD should include less invasive and reversible procedures such as neurotoxin injections into the detrusor or urethral sphincter for bladder control and emptying. Intravesical botulinum toxin-A (BOTOX or Dysport) injection has been demonstrated to be effective in restoration of urinary continence for up to 9 months [16–18]. This treatment is also effective in treating children with myelomeningocele with detrusor hyperreflexia and incontinence [19,20]. Repeated BOTOX detrusor injections seem to be as effective as the first injection [21]. In one study, BOTOX significantly reduced the maximum pressure of uninhibited detrusor contractions compared to resiniferatoxin at all follow-up time points [22]. Urethral BOTOX injection not only reduces urethral resistance in patients with DSD or AD [23], it also possibly aids the early return of detrusor contractility in patients with urethral sphincter pseudodyssynergia due to cerebrovascular accidents or Parkinson's disease [24].

## 7. Renal function preservation

Renal function is also an important issue in the management of NVD, especially in chronic SCI patients. Patients with DSD, low compliant bladder and high intravesical pressure at end-bladder filling may be at high risk of renal failure. The incidence of chronic renal disease in patients with paraplegia and neural tube defects is higher than in the general population [25]. Bladder management affects bladder compliance and changes in compliance with time. Patients using intermittent catheterization have a significantly higher incidence of normal compliance than those with Foley catheter management. Low bladder compliance is statistically associated with vesicoureteral reflux, radiographic upper tract abnormality, pyelonephritis and upper tract stones. CIC is the superior method for preserving bladder compliance and preventing upper tract complications associated with low compliance [26]. Patients with DSD who are currently using an indwelling catheter, performing CIC or spontaneously voiding should be monitored annually to prevent renal failure. Oral antimuscarinic agents or intravesical BOTOX injections might provide a low-pressure bladder and preserve renal function in the long-term management of NVD.

## 8. Quality of life issues

Quality of life (QoL) issues are also important in the treatment strategy for NVD. NVD patients' willingness to use a management modality, their hand function and self-care capability, socioeconomic support, and family support should be taken into consideration in management. Patients with neurogenic detrusor overactivity have reported a high rate of satisfaction with intravesical BOTOX injection [27]. However, more than 70% of patients need CIC to evacuate their bladder [28]. This treatment might not be accepted by patients in Asian countries as their environment and social support are not as good as those in Western countries [29]. When performing BOTOX injections for patients with DSD, injection into the detrusor or urethra should be carefully evaluated before treatment. In an unpublished study, SCI patients who received intravesical BOTOX had more improvement in QoL than those who received injections of BOTOX in the urethral sphincter. Reducing the dose of BOTOX or combined detrusor and urethral BOTOX injections might provide more therapeutic satisfaction in patients who wish to preserve spontaneous voiding and experience less incontinence.

## 9. Future technologies

Finally, many novel therapeutic trials of treatment for SCI and NVD have emerged in recent decades. Repair of spinal cord trauma with nerve grafts and stabilizing the grafted area with fibrin glue containing acid fibroblast growth factor have succeeded in treating chronic paraplegia [30]. Transplants of fibroblasts expressing BDNG and NT-3 were applied in an animal SCI model with improvement in both bladder and hind-limb function, which was associated with reorganization

of spinal circuitry (31). Using immortalized neural stem cells transplanted into the injured spinal cord promoted recovery of voiding function in the rat (32). Direct re-establishment of a somatoautonomic reflex pathway to re-innervate the neurogenic bladder has been successful in children with myelodysplasia (33). Nerve cross-over surgery for a neurogenic bladder, which is done by cutting the proximal portion of the S2-S3 roots and creating an end-to-end anastomosis to the intercostal nerves, can restore central connections to the bladder (34). Using intermittent electrical stimulation of the pudendal nerve or sacral anterior root stimulation are alternative treatments for detrusor areflexia or DSD (35–37). Using bladder acellular matrix grafts might be a choice for bladder augmentation to improve bladder capacity in spinal cord injury-induced neurogenic bladder (38,39). All these technical advancements show that neurogenic voiding dysfunction can be adequately treated in the future.

## 10. Rational treatment strategies for NVD

Patients with NVD should be regularly followed-up to evaluate lower urinary tract dysfunction, and any urological complication should be adequately treated. Avoiding a chronic indwelling catheter can reduce the incidence of a low compliant bladder. Intravesical instillation of vanilloids or BOTOX injection provides an alternative treatment for refractory detrusor overactivity or low compliant bladder, and can replace the need for bladder augmentation. When surgical intervention is necessary, a less invasive type of surgery and a reversible procedure should be considered first and unnecessary surgery of the lower urinary tract should be avoided. Keeping the bladder and urethra in good condition without interfering with neuromuscular continuity will give patients with NVD a chance to benefit from new technologies in the future. It is most important that the physician continues to try to improve the quality of life of patients with NVD.

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