SUMMARY

Neurological control of micturition is undertaken by central and peripheral nerve systems through complex neuronal interconnections that are mediated by the action of several neurotransmitters, finally controlling the function of detrusor muscle and external urethral sphincter. In normal circumstances, both muscles must have co-ordinated contractions in such a way that when the detrusor contracts, the external urethral sphincter relaxes. The loss of this co-ordinated action leads to the so-called syndrome of detrusor-sphincter dyssynergia. Without adequate treatment, more than 50% of men with this condition will develop severe complications. There are several neurological diseases that might lead to this condition where a common physiopathology consists of a distortion of the complex neural mechanism innervating the lower urinary tract. Because of this complexity, it is difficult to find a curative treatment providing a definitive solution for a majority of patients. Although most of the currently available therapies only provide partial or temporary solutions, some modalities offer a promising perspective.

Keywords: Detrusor-sphincter dyssynergia; external urethral sphincter; pontine micturition centre; electromyography; pseudodyssynergia; botulinum toxin; sphincterotomy

INTRODUCTION

Normal micturition is the result of a synergic action between the bladder smooth muscle (detrusor muscle) and the striated smooth muscle of the urethral sphincter. This process consists of relaxation of the urethral sphincter followed by a detrusor contraction, which expels the urine stored in the bladder.

This synergy between the detrusor muscle and the external urethral sphincter is controlled by a specific area in the caudal brainstem named the pontine micturition centre. Disruption of the pathways between this area and the caudal part of the spinal cord often results in detrusor-sphincter dyssynergia (DSD) (1).

Detrusor-sphincter dyssynergia has been defined as a detrusor contraction concurrent with an involuntary contraction of the external sphincter (2). DSD typically occurs in patients with a supra-sacral lesion (e.g. after a high spinal cord injury) and is uncommon in lesions of the lower cord. Although the intra- and peri-urethral striated muscles are usually held responsible, the smooth muscle of the bladder neck or urethra may also be responsible (2). Dyssynergia between detrusor muscle and bladder neck refers to a condition characterised by a detrusor contraction, which is coincident with a failure in the opening of the bladder neck demonstrated objectively. Both conditions should be clearly distinguished from the so-called dysfunctional voiding, which consists of striated sphincter hyperactivity in the absence of a detrusor contraction preventing adequate voiding, usually occurring in the absence of a demonstrable neurological condition.

Detrusor-sphincter dyssynergia implies an involuntary detrusor contraction accompanied by an involuntary contraction of the external sphincter, which prevents adequate voiding and which might lead to a low compliant and thick-walled bladder, elevated retrograde pressures in the ureter and pelvis, hydrenephrosis, renal scarring and terminal kidney failure. Without adequate treatment more than 50% of men with DSD will develop severe complications (3). In women, maybe due to lower detrusor pressures, these complications are less common. Most available therapies for DSD are focused on decreasing or even eliminating abnormal activity of the external sphincter.

PHYSIOPATHOLOGY OF DSD

The pontine micturition centre is connected to the sacral spinal cord through ascendant and descendant neural pathways. When there is an abnormality (i.e. disruption) in these pathways, the synergic action between the detrusor...
and the external sphincter is lost. A few weeks after signalling breakdown, detrusor muscle contraction becomes synchronised with external sphincter contractions instead of relaxation. This condition is known as ‘DSD’ (4).

Diagnostic confirmation of this condition must be performed with electromyography (EMG) of the external sphincter. DSD must be suspected in any patient having a suprasacral lesion. The most common causes of DSD are: spinal cord injury, multiple sclerosis, acute transverse myelitis and myelomeningocele (3,5–10). In patients with different diagnosis, DSD must be suspected.

Stimulation of the pontine micturition centre in adults promotes relaxation of the external urethral sphincter followed by a co-ordinated detrusor contraction. After a spinal cord disruption (complete or incomplete), there is a spinal shock phase with an acontractile detrusor and urinary retention, which lasts a few weeks until low volume reflex detrusor contractions with hyperactive voiding develops (11).

**CLASSIFICATION AND DIFFERENTIAL DIAGNOSIS**

Three types of DSD have been identified depending on EMG findings (12).

Type 1. Characterised by a simultaneous increase of detrusor pressure and external sphincter EMG activity that reaches its maximum at the peak of detrusor contraction. As the detrusor pressure begins to decline, sudden complete external relaxation occurs.

Type 2. Characterised by clonic contractions of the external urethral sphincter interspersed throughout the detrusor contraction. Patients usually void with an interrupted stream.

Type 3. In type 3 DSD, the external sphincter contraction persists throughout the entire detrusor contraction. These patients void with an obstructive stream or cannot void at all.

Types 2 and 3 DSD are considered to have a greater risk of urological complication, as bladder outflow obstruction is continuous throughout the detrusor contraction (13). It has been shown that DSD tends to worsen over time and there is a correlation between the neurological status and the neurological examination. Patients with complete sensory and/or motor deficit have either type 2 or 3 DSD whereas patients with incomplete sensory and motor deficits have type 1 DSD (13).

Pelvic floor hyperactivity or dysfunctional voiding are terms used to describe the external sphincter urodynamic abnormality when it occurs in the absence of neurological disease. Bladder neck dyssynergia (BND) refers to incomplete opening of the bladder neck during voiding. BND has also been referred to as detrusor-internal sphincter dyssynergia, smooth sphincter dyssynergia, and proximal sphincter dyssynergia when it is due to a neurological lesion.

Diagnosis of DSD has traditionally been made by needle EMG or voiding cystourethrogram (VCUG). In a recent study comparing needle EMG with VCUG, only a 60% agreement between needle EMG and VCUG was found for the diagnosis of DSD. This discordance seems to be due to the fact that BND prevents visualisation of the external sphincter (14). Videourodynamics will show a detrusor contraction with opening of the bladder neck without concurrent relaxation of the external sphincter in patients of DSD, and a failure of bladder neck opening in patients of BND.

**TREATMENT**

Type 1 DSD is usually managed conservatively by means of watchful waiting, with the exception of those patients having vesicoureteric reflux, hydronephrosis or autonomic dysreflexia. Types 2 and 3 DSD should be treated in order to avoid complications. The aim of DSD treatment is to significantly decrease or eliminate the abnormal activity of the external urethral sphincter.

For the most part, pharmacological therapy for DSD has not provided acceptable outcomes. Alpha-blocking agents and those that might relax the striated sphincter should, at least theoretically, decrease urethral resistance during micturition. This approach can be beneficial in the neurologically normal patient, but their use in the patient with neurological disease is not very effective. So far, no randomised, double-blind study has confirmed a role for these substances in patients with DSD.

Benzodiazepines seem to potentiate the action of gamma-aminobutyric acid (GABA) at both presynaptic and postsynaptic sites in the brain and spinal cord; however, there is no evidence of any benefit of these compounds in DSD patients (15).

Baclofen, a glycine and GABA agonist, depresses excitation of motor neurons and interneurons in the spinal cord. It has been found useful in the treatment of skeletal spasticity attributable to a variety of causes, especially multiple sclerosis and traumatic spinal cord lesions (15). However, its utility for the treatment of DSD has not been thoroughly proven. Intravenous, but not oral, baclofen was found effective for patients with DSD, but the side effects of weakness and dizziness were common. High oral doses might decrease intravesical pressure in some patients, but because of its potential side effects this drug cannot be readily recommended for the treatment of DSD (16). Baclofen has also been used through an intrathecal implanted pump, showing promising results in some patients with DSD (17).

Botulinum toxin A (BoNT-A) has also been used for the treatment of DSD. The toxin acts at the neuromuscular junction of the external sphincter to block vesicle transport of acetylcholine, thus producing chemical denervation. The clinical effects begin within 2–3 days and are reversible as...
terminal nerve sprouting occurs within 3–6 months (18). Dykstra et al. (19) first reported BoNT-A injection into the external urethral sphincter in 11 patients with DSD. Endoscopic injection of the toxin into the sphincter as an alternative to conventional sphincterotomy has also been shown to be effective (20,21). Schurch et al. (21) reported that, in 21 of 24 patients with DSD, urethral pressures were significantly reduced with a concomitant decrease in postvoid residual volumes in 38% of patients who received BoNT-A injections. The durability of effect was increased from 2 to 3 months to over 9 months when a single injection of 100 U of BoNT-A (Botox®; Allergan Inc., Irvine, CA, USA) was compared with three repeated monthly injections. De Seze et al. (38) carried out a double-blind lidocaine-controlled study in 13 spinal cord injury patients, demonstrating the superiority of BoNT-A (again, Botox®) in improving the urethral hypertension associated with DSD (22–24). In multiple sclerosis patients, a placebo-controlled, randomised, double-blind study showed that a single injection of 100 BoNT-A units may not decrease postvoid residual urine (25). However, there are no large randomised trials comparing this treatment to placebo. It is suggested that Botox® injected into the sphincter may be used as a temporary solution for patients who may be considering surgical sphincterotomy.

Transurethral incision of the external urinary sphincter (TURS) has been used to promote bladder emptying and prevent urological complications in male spinal cord injured patients for nearly 50 years (26). This procedure helps decrease urinary outflow resistance because of DSD. The goal is to reduce the intravesical voiding pressure mediated by bladder contractions against a dysynergically contracted external urethral sphincter. The primary indication for sphincterotomy is in those individuals who have elevated residual urine volumes in the presence of good but involuntary detrusor contractions and in those who have failed conservative management. Other indications are: repeated episodes of autonomic dysreflexia (27), typically in a tetraplegic patient with poor hand function whose bladder drainage through intermittent catheterisation is cumbersome and difficult to maintain 24 h/day; repeated urinary tract infections; difficult catheterisations because of urethral false passages (28); and/or secondary bladder neck obstruction because of ‘ledge’ formation (29). Patients with inadequate bladder drainage resulting in upper tract changes, decreased renal function, vesico-ureteral reflux, stone disease and prostatic-ejaculatory reflux, with associated epididymo-orchitis, may also be considered for TURS.

The goals of sphincterotomy are: stabilisation or improvement in renal function, prevention of urosepsis, lowering detrusor leak point pressure, stabilisation or elimination of vesicoureteral reflux and eliminating the need for chronic indwelling catheterisation. Following the successful sphincterotomy, improvement in bladder emptying and stabilisation of upper urinary tract function can be reasonably expected in 70–90% of patients (30).

Transurethral external sphincterotomy can be performed with either a knife electrode or using a resection loop at the 12 o’clock position (30). Following electrosurgical TURS, significant intraoperative and postoperative bleeding may occur, with subsequent clot retention requiring prolonged drainage using a large-diameter catheter. In addition, urethral strictures, impotence and need for re-operation have been reported in 30–60% of patients (31). In some initial TURS failures, an additional bladder neck incision or a transurethral resection of the prostate is required (31,32). Other failures are due to inadequate surgery, post-TURS bulbous urethral strictures and poor detrusor contractility. In order to improve these results both contact and beam lasers have been applied through standard cystoscopes. The laser energy is delivered fibre-optically either through a reusable contact laser probe screwed on to the tip of a rigid fibre or through the direct contact of fibre for the delivery of the Holmium laser. Free beam laser leads to coagulative necrosis, and is therefore not suitable for TURS. TURS with a contact laser requires repeated passes to cut and vaporise all urethral tissue just short of the spongiosum to prevent perforation of the urethra (33). Results following the use of a contact laser have been encouraging with a significantly reduced incidence of operative and perioperative bleeding and reduced need for repeat sphincterotomy: 7–15% vs. over 30% in reported series following the conventional electrocautery TURS (33). Bladder leak point pressure below 40 cm H2O seems to be a useful urodynamic parameter for the successful outcome of TURS (34).

External sphincter stents have the potential to reduce dysynergic external sphincter activity and reduce the incidence of recurrent obstruction. In addition, some stents may be truly reversible. The UroLume prosthesis is made of a superalloy mesh that expands and shortens (similar to a Chinese finger toy) when deployed from the insertion tool. The geometry, elastic property and the radial force of the stent material allow it to maintain its position to continuously prevent obstruction by the external sphincter. The large lumen (42 Fr) created by the prosthesis permits catheterisation and cystoscopy after epithelialisation. In 153 patients at 15 centres, sphincter stent placement has achieved clinical success with up to 2 years of follow-up. The simplicity of placement and minimal associated morbidity make the sphincter prosthesis an attractive modality to treat external sphincter dyssynergia. A prospective randomised study comparing the UroLume stent with sphincterotomy at three model spinal cord injury centres has been reported. Decrease in voiding pressure was significant for both sphincterotomy and stent patients. No significant change in bladder capacity occurred after either sphincterotomy or stent placement. Residual urine decreased in both sphincterotomy and stent
patients. The mean length of hospitalisation and operation times were significantly shorter for stent patients vs. sphincterotony patients (35). Long-term results confirming the initial results have also been reported, but it should be noted that out of 160 patients, only 42 were evaluable after 5 years, throwing some doubt on the positive conclusions of this study (36). A smaller long-term study on seven patients who were 12 years out from stent placement has also been reported. Again the positive conclusions are tempered by the fact that all needed some further surgical intervention during follow-up (37). There have been several nonrandomised studies on the use of different stents, which had disappointing results. The main reported complications are migration of the stent, persisting urinary tract and prostatic infection leading to autonomic dysreflexia, calculus formation, encrustation and tissue growth, in addition to pain and irritative symptoms (38, 39).

**CONCLUSION**

Detrusor-sphincter dyssynergia is a dangerous condition, which might lead to severe upper urinary tract complications. The aim of therapy is to significantly decrease or eliminate abnormal activity of the external urethral sphincter.

**DISCLOSURE**

The authors have confirmed no conflicts of interest.

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