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Conservative Treatment of Patients with Neurogenic Bladder

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Abstract

Objectives: To review the up-to-date literature of the mostly used conservative treatment modalities in patients with neurogenic bladder.
Methods: material from literature on conservative management in patients with neurogenic bladder was reviewed. Pubmed search results and recent books were consulted.
Results: The conservative treatment is in almost all cases the first and will remain the primary choice in the majority of patients with neurogenic bladder. Treatment will depend on the type of underlying disease, on the bladder dysfunction, its natural evolution but also on the patients' general condition, and the available resources. Behavioural training, catheters, external appliances, drugs and electrical stimulation are presented, their indications and limitations.
Conclusions: Conservative treatment is the mainstay in neurogenic bladder management. It offers different methods which permit to successfully treat most symptoms and conditions in this prevalent LUT pathology.

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1. Introduction

Neurologic lower urinary tract (LUT) dysfunction is prevalent in many neurological diseases [1–5]. The condition is known to be life threatening if not properly managed. The conservative treatment is in almost all cases the first to give and will remain the primary choice in the majority of patients with neurogenic bladder. A good review and listing of conservative treatment for neurogenic incontinence can be found in the report of ICI 2004 [1]. More actual data have been included here.

Treatment will depend on the type of underlying disease, on the bladder dysfunction, its natural evolution but also on the patient's general condition, and the available resources. Urodynamic testing will be necessary in many patients to gain more complete diagnosis of how the neurogenic dysfunction has changed the function of different componenets in the lower urinary tract and their interaction.

This manuscript will not deal specifically with the period of spinal shock or cerebral shock in acute neurological lesions when the urologic treatment consists of proper bladder drainage.

For the post shock period or for slowly developing dysfunctions several conservative treatments exist which will be discussed (Table 1):

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Table 1 – Actual principles of conservative management of the neurogenic bladder

- Stress incontinence due to sphincter incompetence: behavioral/timed voiding and external appliances.
- Detrusor overactivity with detrusor sphincter dyssynergia: intermittent catheterization ± bladder relaxing drugs; indwelling catheter + bladder relaxing drugs.
- Detrusor overactivity with negligible post void residual and no detrusor sphincter dyssynergia: depending on cooperation and mobility: behavioral, bladder relaxant drugs, intermittent catheterization; triggered voiding (if urodynamically safe); external appliances, indwelling catheter + bladder relaxing drugs.
- Detrusor underactivity with post void residual: intermittent catheterization; alpha blockers; intravesical electrical stimulation; bladder expression (if urodynamically safe).

No surgical treatment in this table.

a. Behavioral therapy: Triggered reflex voiding, bladder expression (Crede and Valsalva maneuver), toileting assistance.
b. Catheters: Intermittent catheterization, indwelling catheterization,
c. Condom catheter and external appliances
d. Pharmacotherapy
e. Electro stimulation: Electrical neuromodulation, electrical stimulation of the pelvic floor musculature, intravesical electrical stimulation (IVES)

2. Behavioural therapy

2.1. *Triggered reflex voiding*

Triggering the bladder reflex comprises various manoeuvres performed by patients in order to elicit reflex detrusor contractions by exteroceptive stimuli. Integrity of the sacral reflex arc is mandatory. The most commonly used are suprapubic tapping, thigh scratching and anal/rectal manipulation. Frequency of use, intervals and duration have to be specified for each patient. Today, triggered voiding should not be done without taking care of bladder outlet obstruction. Also continence, easy to use appliances, gender, level and type (complete or incomplete lesions, para- vs quadriplegic patients) of the lesion are important.

It is necessary to check if the bladder is functioning in a urodynamic safe way (not too high pressure development). Regular follow-up between every 6 months and every 2 years should be guaranteed. To improve emptying, control autonomic dysreflexia, and avoid renal damage, alpha-blockers [6] or botulinum toxin sphincter injections can be tried before sphincterotomy and/or bladder neck incision is performed.

Triggered voiding should not be recommended as first line management.

2.2. *Bladder expression (Credé and Valsalva)*

Bladder expression has been recommended for patients with a combination of an areflexic detrusor with an areflexic or anatomic incompetent sphincter (e.g. after sphincterotomy). Difficulties in emptying may be due to inability to open the bladder neck and/or functional obstruction at the level of the striated external sphincter by the downward movement.

The most commonly used are the Valsalva (abdominal straining) and the Crédé (manual compression of the lower abdomen) manoeuvre.

During follow up, more than 50% of patients developed influx into the prostate and the seminal vesicles and other complications, e.g. epididymo-orchitis. Other complications are reflux into the upper urinary tract, genital-rectal prolapse and haemorrhoides.

Adjunctive therapy to decrease outflow resistance includes alpha-blockers, sphincterotomy or botulinum toxin injections in the sphincter. If effective they usually cause or increase urinary stress incontinence. The indication is thus limited and the technique should only be done in patients where it has been shown to be urodynamically safe.

2.3. *Behavioural training*

Behavioural training is often part of the urological management in neurologic patients. It consists of different approaches [7]: correcting habit patterns of frequent urination, improving ability to control bladder urgency, prolonging voiding intervals, increasing bladder capacity, reducing incontinent episodes, and building patient's confidence. Keeping a voiding diary is important in many aspects and can have a direct therapeutic effect [8].

Behavioural measures are most valuable in brain diseases as cerebro vascular disease, Parkinson disease, multiple system atrophy, dementia, and cerebral palsy. Other diseases as multiple sclerosis, incomplete spinal cord injury, transverse myelitis, diabetes mellitus can also be good indications. Frail elderly neurologic patients who need assistance can also benefit.

- *Timed voiding* is characterized by a fixed interval between toiletting. It is initiated and maintained by caregivers and therefore the interval will depend both on bladder function and the working schedules of the caregivers. The latter will depend on staffing, number of patients under care and facilities available. In our practice it means mostly every 3 hours during daytime and no toileting

during the night. Its aim is more to avoid incontinence than to restore a normal bladder function. During the night this is often more difficult to achieve. Timed voiding has also been used as an adjunct therapy to tapping and/or Crédé manoeuvre and/or intermittent catheterisation. Timed voiding is one of the first steps of treating too high bladder volumes as in diabetes patients with loss of bladder filling sensation.

- *Habit retraining* has to be inititated and maintained by caregivers. It is more indicated for patients with brain diseases than with spinal cord lesions and for patients with cognitive and/or motor deficits. The aim is to avoid incontinence and/or involuntary bladder contractions by decreasing voiding intervals. Such program can be very useful for institutionalised patients.
- *Prompted voiding* is used to teach people to initiate toileting through request for help and with positive reinforcement from caregivers when they do this.
- *Keeping a voiding diary*: has been shown to be very beneficial in early and institutional care.

Most of behavioural treatment has not been well documented in patients with neurological problems but they are used as routine in many rehabilitation settings. Studying them on clinical value would be worthwhile.

3. Catheters

3.1. *Intermittent catheterization [IC]*

Intermittent catheterization (IC) and self-catheterization (ISC) have become properly introduced during the last 40 years [9]. In general, the purpose of catheterization is to empty the bladder and of IC is to resume normal bladder storage and regularly complete urine evacuation. With IC and ISC there is no need to leave the catheter in the LUT all the time, thus avoiding complications of indwelling catheterization (ID).

It is clear that IC can improve or make patients with neurologic bladder continent if bladder capacity is sufficient, bladder pressure kept low, urethral resistance high enough, and if care is taken to balance between fluid intake, residual urine and frequency of catheterization.

The optimal post-void residual indicating the need to start bladder catheterization remains to be clarified, though Dromerick et al [10] demonstrated in a series of stroke patients that a post-void residual greater that 150 ml is an independent risk factor for development of urinay tract infection (UTI). There exists not one best technique or one best material as both depend greatly on patients' individual anatomic, including the possible handling, social and economic possibilities [11].

Two main techniques have been adopted, a sterile IC (SIC), and a clean IC (CIC). The sterile non-touch technique implicates the use of sterile materials handled with sterile gloves and forceps. In an intensive care unit, some advocate wearing a mask and a sterile gown as well. Mostly used is the clean technique which can be done almost everywhere. For aseptic handling, the catheter is moved out of a sterile sheath into the urethra without touching the catheter itself. Frequency of catheterization will depend on bladder volume, fluid intake, postvoid residual, urodynamic parameters (compliance, detrusor pressure). Usually it is recommended to catheterize 4–6 times a day during the acute stage after spinal cord lesion. Some will need to keep this frequency if IC is the only bladder emptying. Others will catheterize 1–3 times a day to check and evacuate residual urine after voiding or on a weekly basis during bladder retraining. To overcome high detrusor pressure, bladder relaxing drugs can be indicated. For those who develop a low compliance bladder, upper tract deterioration or severe incontinence, injection of Botulinum toxin in the bladder wall or surgery as with bladder augmentation may be necessary.

If catheterization is begun by patients with recurrent or chronic UTI and urinary retention, the incidence of infection decreases and patients may become totally free of infection. If symptomatic infections occur, improper CIC or misuse often can be found. Chronic infection persists if the cause remains. Treatment of UTI is necessary if the infection become symptomatic. The incidence of urethral strictures increases with a longer follow-up as is stone formation [12,13]. Epididymo-orchitis is rare but can occur [14]. The safety in longterm remains acceptable [15].

Nocturnal bladder emptying has emerged as a specific treatment for nighttime overdistension of the neurogenic bladder, and can reverse or prevent bladder and upper tract deterioration [16].

Proper education and teaching are absolute requirements to guarantee success with IC.

3.2. *Indwelling urethral catheters – transurethrally (ID)/ suprapubically (SC)*

Long term indwelling catheterization has got very negative comments for the last decades due to the high complication rate: urethral trauma and

bleeding, urethritis, fistula due to pressure caused by improper size of the catheter and improper technique, bladder and renal stones, cystitis, acute and chronic urinary tract infection (UTI), bladder neck incompetence, meatus and urethral sphincter erosion, bladder stones and bladder carcinoma. The complication rate has been shown to be higher than with IC also in recent articles [17]. But ID is still used in many patients due to difficulty in performing IC or persistent leakage between catheterisations. In developing countries ID is still the method of choice for those with urinary retention or incontinence. Nowadays the complications of ID seem less due to better materials, the use of smaller size catheters and a proper technique of securing the catheter. The frequency of catheter change is not well studied but change weekly or every two weeks has been shown to be of benefit in patients with recurrent symptomatic UTI [18]. Recent studies showed that the incidence of bladder cancer in a group of spinal cord injured with ID was similar to that observed in the general population, but more than 60% of these initially presented with muscle-infiltrating bladder cancer [19]. Hamid however did not find bladder cancer on bladder biopsies in patients with a suprapubic catheter for mean 12.1 years [20]. For prevention of UTI, general cleanliness and local hygiene should be encouraged. If the patient has a symptomatic UTI, it is important to check for catheter blockade and complications as urinary stones. Encrustation of a catheter is highly predictive of the presence of bladder stones [21]. Encrustation and blockage of indwelling urethral catheters is primarily brought about by infection of the urinary tract by Proteus mirabilis or other urease-producing species. To prevent encrustation, urease inhibitors [22] high fluid intake [23] valve regulated release of urine from the bladder [24], inflating the retention balloons with triclosan [25] and regular catheter change do seem to have an effect. Cranberry juice [23], and catheter type [26] offer little help, Routine antibiotic prophylaxis for patients with SC or ID is not recommended [27]. Symptomatic urinary infections have to be treated with the most specific, narrowest spectrum antibiotics available for the shortest possible time [28].

A suprapubic catheter minimises the risk of urethral trauma in men and women, of urethral destruction in neurologically impaired women with even relatively short-term indwelling urethral catheters, and of urethral pain. The key disadvantage is that it requires a minor 'surgical' act to insert the suprapubic catheter with potential to injury adjacent structures as the intestine or paravesical blood vessels. The preferred insertion technique varies by region and country. There is no evidence that there is one best way to insert the SC though the basic principles are universal.

Long-term management of the neurogenic bladder with a SC remains a controversial topic in neurourology. Some favor it as a safe and effective treatment, while a large number of experts has personal experience with suprapubic tube complications during its long-term use.

The literature on suprapubic catheterization is however still limited and most publications are 20 years or older. Also here there is room for much more research.

4. Condom catheter (CC) and external appliances

Male patients with neurogenic bladder and chronic urinary incontinence can be candidates for a condom catheter connected to a urine or leg bag to collect the urine. Some have difficulty in applying CC due to overweight and/or some degree of penile atrophy or retraction. Long-term use may cause bacteriuria but it does not increase the risk of UTI when compared to other methods of bladder management. Complications may be less with good hygiene, frequent change and maintenance of low bladder pressures.

5. Drugs

Drugs are often used in patients with neurogenic bladder. They aim at decreasing detrusor activity, increasing bladder capacity and/or increasing/decreasing bladder outlet resistance. The effectiveness of drugs for the treatment of detrusor/sphincter dyssynergia is not well documented.

Pharmacologic therapy alone has been most helpful in patients with relatively mild degrees of neurologic bladder dysfunction. When more severe bladder disturbances are present drugs will mostly support other forms of management such as intermittent catheterization (IC).

5.1. *Drugs for neurogenic detrusor over activity (NDO) and/or low compliant detrusor*

5.1.1. *Bladder relaxant drugs*

Antimuscarinic agents are by far the most used pharmacologic agents in the symptomatic management NDO. The doses have to be chosen individually in every patient.

5.1.1.1. *Oxybutynin.* Oxybutynin hydrochloride is a moderately potent antimuscarinic agent with a pronounced muscle relaxant activity and local anesthetic activity as well.

Oral administration effectivity has been shown in many publications [29]. Side effects as dry mouth proved significantly lower with oxybutynin XL than with immediate-release oxybutynin [30]. Transdermal oxybutynin is another therapeutic option avoiding most of the side effects, but no clinical studies are as yet available in neurologic patients. Intravesical application prolongs the systemic effect of oxybutynin [31]. But oxybutynin can produce central nervous system side effects [32]. Intravesical electromotive administration of oxybutynine solution is believed to increase bioavability and tolerance [33]. Intrarectal administration of oxybutynin has been found clinically valuable but has not been evaluated in neurologic patients yet [34].

5.1.1.2. *Propiverine.* Propiverine hydrochloride is a benzylic acid derivative with musculotropic (calcium antagonistic) activity and moderate antimuscarinic effects.

It has a well documented effectiveness and a favourable tolerability and safety profile [35].

5.1.1.3. *Trospium.* Trospium is a quaternary ammonium derivative with mainly antimuscarinic actions, its effectiveness and safety was confirmed by meta-analysis [36]. It does not break the blood–brain barrier. Central nervous system side effects are therefore not expected.

5.1.1.4. *Tolterodine.* Tolterodine is a competitive muscarinic receptor antagonist with a better tolerability and comparable efficacy than oxybutynine. Published reports on the specific effect on NDO have shown the therapeutic effects of increased dosage [37].

5.1.1.5. *Propantheline.* Propantheline bromide was the classically described oral antimuscarinic drug. Despite its success in uncontrolled case series, no recent controlled study of this drug for NDO are available.

5.1.1.6. *Oxyphencyclimine.* Oxyphencyclimine is a cheap antimuscarinic that was used originally for treatment of peptic ulcer.

Due to its availability and very low cost, oxyphencyclimine may be an alternative bladder relaxant for SCI patients in developing countries where other potent bladder relaxant drugs are not available or too expensive [38].

Solifenacin and Darifenacin must be mentioned, although there are no specific studies on neurogenic detrusor overactivity so far available with them.

5.1.1.7. *Flavoxate.* Flavoxate hydrochloride has a direct inhibitory action on detrusor smooth muscle in vitro. The ICI report states that several randomized controlled studies have shown that the drug has essentially no effects on detrusor overactivity therefore it is not recommended in the treatment of NDO [1].

5.1.1.8. *Tricyclic Antidepressants.* Many clinicians have found tricyclic antidepressants, particularly imipramine hydrochloride, to be useful agents for facilitating urine storage, both by decreasing bladder contractility and by increasing outlet resistance. However, no controlled trials of tricyclic antidepressants in NDO have been reported. Nevertheless in some developing countries tricyclic antidepressants are the only bladder relaxant substances which people can afford. But caution is warranted [39].

5.2. *Drugs for blocking nerves innervating the bladder*

5.2.1. *Vanilloids*

The vanilloids, capsaicin and resiniferatoxin, activate nociceptive sensory nerve fibers through an ion channel, known as vanilloid receptor subtype 1 (VR1). Activation of VR1 results in spike-like currents, and selectively excites and subsequently desensitizes C-fibers. Capsaicin-desensitization is defined as a long lasting, reversible suppression of sensory neuron activity [40]. Resiniferatoxin (RTX) is approximately 1,000 times more potent than capsaicin, based on the Scoville Heat Scale. Like capsaicin, it possesses vanilloid receptor agonist activity, resulting in desensitization [41]. However, RTX acts without the potent neuronal excitatory effect of capsaicin, and therefore elicits less discomfort. RTX has been found superior to capsaicin, causes less inflammatory side effects [42,43]. But again more data are needed.

5.2.2. *Botulinum toxin*

Botulinum toxin A (BTX) has taken a substantial place in the treatment of neurogenic bladder. Though invasive it is still discussed here as it is being used in ambulatory setting and as adjunctive treatment in many conservative techniques. The toxin acts by inhibiting acetylcholine release at the presynaptic cholinergic junction. It can also modulate abnormal sensory function [44]. Inhibited acetylcholine release results in regionally decreased muscle contractility and muscle atrophy at the site

of injection though such atrophy has not been seen in the smooth bladder muscle [45]. The chemical denervation results in a reversible process as axons resprout in approximately 3–6 months.

The drug is used for detrusor overactivity [46] and for sphincter overactivity [47,48]. Many studies are published and experience grows on the long term effect of repeated injections. Overall the results are satisfactory and the safety is good [49]. There have been publications so far showing that BTX injections in sphincter /or detrusor can cause transient general muscle weakness [50,51]. Some caution is warranted about these and other side effects and it is recommended to evaluate these further as more patients get treated this way. Today these rare side effects do not change the clinical value of the treatment. Botulinum B does seem to have insufficient effect [52].

- *new suggested treatments* promising results are given with intravesical atropine [53] and 1 mg of the endogenous peptide nociceptin/orphanin FQ [54].

5.3. *Drugs for neurologic sphincter deficiency*

Alpha-adrenergic agonists, estrogens, beta-adrenergic agonists and tricyclic antidepressants have been used to increase outlet resistance but no studies on their use in neurogenic sphincter deficiency have been published. The information remains so far anecdotal.

5.4. *Drugs for facilitating bladder emptying*

Alpha adrenergic antagonists as have been reported to be possibly useful in neurogenic bladder in the facilitation of storage and emptying, and in the prevention of autonomic dysreflexia. [6,55].

Cholinergics as bethanechol chloride seems to be of limited benefit for detrusor a/hypocontractility.

6. Electrostimulation (ES)

6.1. *Electrical neuromodulation*

The current techniques of neuromodulation used mainly for treating detrusor overactivity are (a) anogenital ES, (b) transcutaneous electrical nerve stimulation (TENS), (c) sacral nerve neuromodulation, (d) percutaneous posterior tibial nerve stimulation (Stoller afferent nerve stimulation, SANS) and (e) magnetic stimulation. It is suggested that neuromodulation works at a spinal and at a supraspinal level. Neuromodulation in its different forms would either activate the striated urethral sphincter causing reflexively detrusor relaxation either activate afferent fibers causing inhibition at a spinal and a supraspinal level [56].

Publications have described effects in patients with Parkinson's disease, spinal cord lesion, multiple sclerosis, cerebral palsy and other [57–61].

There are no significant data available so far on the clinical value of magnetic stimulation.

Electrical stimulation of the pelvic floor musculature aims in patients with neurologic urinary stress incontinence to improve strength and timing of the pelvic floor muscle contraction. It has been used with different wave forms, frequencies, intensities, electrode placements etc.

In patients with incomplete denervation of the pelvic floor muscle and of the striated sphincter, electrostimulation may improve pelvic floor function, and may thus improve incontinence [62,63].

6.2. *Intravesical electrical stimulation (IVES)*

Intravesical electrical stimulation of the bladder (IVES) is still a controversial therapy for patients with neurologic detrusor dysfunction despite its application for several decades.

The mechanisms involved in eliciting bladder contraction with IVES are still uncertain though the technique has been used in clinical practice for several decades. Some authors consider IVES induced contractions as neurological reflex responses [64] while others think they are a direct bladder muscle effect [65]. IVES is an option to induce/improve bladder sensation and to enhance the micturition reflex in incomplete central or peripheral nerve damage [66].

7. Announcement

Work is under way both from the Neurourology Guidelines Committee of EAU and from the Neurourology working group of the International Consultation on Incontinence (ICI) 2008 that will present full reports this year with level of evidence and grade of recommendations for all treatments mentioned here.

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CME questions

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1. Triggered reflex voiding comprises various manoeuvres performed by patients in order to elicit reflex detrusor contractions by exteroceptive stimuli:
   A. The most commonly used technique is straining.
   B. Integrity of the sacral reflex arc is not mandatory.
   C. Triggered voiding should not be recommended as first line management.
   D. Alpha adrenergic stimulators can facilitate the technique.

2. Bladder expression has been recommended for patients with a combination of an areflexic detrusor with an areflexic or anatomic incompetent sphincter (e.g. after sphincterotomy):
   A. Integrity of the sacral reflex arc is not mandatory.
   B. The most commonly used technique is gently tapping on the bladder.
   C. The technique has a wide indication after spinal cord injury.
   D. The technique is very safe.

3. Behavioural training is often part of the urological management in neurologic patients. It consists of different techniques as correcting habit patterns of frequent urination, improving ability to control bladder urgency, prolonging voiding intervals, increasing bladder capacity, reducing incontinent episodes, et al. Timed voiding:
   A. Is characterized by a flexible interval between toileting.
   B. Needs very little effort from caregivers.
   C. Is not to be used in patients with brain diseases.
   D. Aims more to avoid incontinence than to restore a normal bladder function.

4. Intermittent catheterization (IC) and self-catheterization (ISC) are nowadays used very frequently. To guarantee success:
   A. Catheterization should be done less than 3 times a day.
   B. Balance must be made between fluid intake, residual urine and frequency of catheterization.
   C. Control for UTI on a regular basis is unnecessary.
   D. Urodynamic investigation is unnecessary.

5. Indwelling catheter (ID) use is considered negative as the complication rate is high. But ID is still used in many patients due to difficulty in performing IC or persistent leakage between catheterisations. In developing countries ID is still often the method of choice:
   A. Incidence of bladder cancer in spinal cord injured treated with ID is higher than in the general population.
   B. 60% of bladder cancers found in patients with chronic ID is muscle-infiltrating.
   C. UTI can be avoided in most neurogenic patients with chronic ID.
   D. With symptomatic UTI antibiotics are prohibited to avoid resistance.

6. Botulinum toxin A (BTX) has taken a substantial place in the treatment of neurogenic bladder. The drug is used for detrusor overactivity and for sphincter overactivity:
   A. The substantial literature shows low efficacy.
   B. BTX B is as effective as BTX A.
   C. Repeating the treatment is seldom needed.
   D. Transient general muscle weakness can happen.