

A Closed Loop Neuroprosthesis to Treat Neurogenic Detrusor Overactivity: A Clinical Study

John Hansen¹, Morten V. Fjorback¹, Asger L. Dalmose², Nico J. M. Rijkhoff^{1*}, Thomas Sinkjær¹

¹Center for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, Aalborg University, Denmark

²Institute of Experimental Clinical Research, Århus University Hospital Skejby, Århus N, Denmark

Introduction

Treating lower urinary tract dysfunction is a challenging task in patients with neurological disorders such as spinal cord injury (SCI), stroke, Parkinson's disease, and Multiple Sclerosis. Many of these patients suffer from detrusor overactivity which is a urodynamic observation characterized by involuntary detrusor contractions during the storage phase. Due to the neurological condition it is termed neurogenic detrusor overactivity (NDO). Often NDO is accompanied by detrusor sphincter dyssynergia (DSD), which is a detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated muscle [1]. These conditions leave the patient with problems during both the storage and the voiding phase of the micturition cycle (e.g. transient high bladder pressures, incontinence and large residual urine).

The first step in management of NDO is pharmacological treatment with anticholinergic agents. Some patients are however refractory to this treatment or they cannot tolerate the side effects which includes dry mouth, constipation, drowsiness and blurred vision. Other treatment options are ablative surgery like dorsal sacral rhizotomy and augmentation cystoplasty, or using intravesical capsaicin or resiniferatoxin, neurotoxins for c-fibers, but this treatment only has a temporary effect and need to be performed on a regular basis.

It has been shown that electrical stimulation of the dorsal penile nerve can inhibit bladder contractions in SCI patients and that bladder capacity can be increased by continuous [2] as well as conditional stimulation [3]. In normal subjects stimulation of the dorsal penile nerve have been shown to delay the desire to void and to suppress detrusor contractions [4]. This makes electrical stimulation a reversible alternative to the treatment methods mentioned above.

The primary clinical goal is to establish large volume, low-pressure urine storage in patients with NDO. Another goal is to preserve continence. It is believed that these goals can be obtained with functional electrical stimulation. The objective of this ongoing study is to evaluate the feasibility and clinical relevance of event driven electrical stimulation of the dorsal penile nerve in treatment of NDO. In order to evaluate the effect a treated as well as an untreated physiological bladder filling in SCI patients with NDO was monitored. A study of 10 patients was initiated.

Methods

Local ethics committee approval was obtained and an informed consent was obtained from all patients. At present a total of 4 SCI patients have been examined (see Table 1 for patient data). Inclusion criteria were occurrence of NDO at bladder capacities below 500 ml, male, age over 18 years and complete or incomplete suprasacral spinal cord injury. Exclusion criteria were urinary tract infection, lack of bulbocavernosus reflex, fever, general discomfort and recent episodes of autonomic dysreflexia. All patients managed their bladder by a combination of clean intermittent catheterization and medication except patient 1 who had not begun taking medication at the time of examination. The other participants were not asked to discontinue medication prior to participating in this experiment.

A custom made portable device was used to record intravesical, abdominal and urethral pressures [5]. The sample rate was 20 Hz for all 3 channels. Stimulation was applied with two round (diameter 32 mm) PALS PULS electrodes placed on the root of the penis and stimulation parameters were charge balanced biphasic pulses, 20 pulses/s, pulse width 200 μ s and amplitude two times threshold for elicitation of the bulbocavernosus reflex.

Experimental setup: A double lumen 8-F catheter with 6 cm between the openings was used to record vesicular pressure (Pves) and urethral pressure (Pura). The catheter was held in place by a self-adhesive condom, making it possible to measure pressure and simultaneously collect/record leakages without wetting the patient. Abdominal pressure (Pabd) was recorded with a 9-F balloon catheter placed in the rectum at 10 cm from the anal sphincter. A detrusor pressure (Pdet = Pves-Pabd) above 10 cmH₂O was used as a threshold for enabling electrical stimulation. In some cases the threshold was changed from 10 to 15 cmH₂O during the recording due to an initial detrusor pressure rising gradually from 0 to 10 cmH₂O without any spontaneous contractions occurring. Stimulation was automatically disabled when Pdet had remained under the threshold for a period of 10 s, or manually, when a leakage was detected (as a sudden increase in Pura and/or by visual inspection), or when stimulation had been on for several minutes but was unable to decrease pressure. The first patient however was part of a pilot study where stimulation was kept on for a fixed time and the urethral pressure was not recorded. In each patient two physiological fillings of the bladder (from empty to first leakage) were recorded: one with and one without stimulation enabled. The order of the 2 was randomized between patients (i.e. some had the treated filling in the morning and the untreated in the afternoon and some had it visa versa).

In all patients both treated and untreated physiological bladder fillings were monitored. In patient 4, however, the recording of the untreated filling was not completed due to technical problems.

Results

The stimulation had a positive effect in 3 out of the 4 patients. A positive effect was defined as at least one suppressed undesired bladder contraction not preceded by any unsuppressed contractions. Typical recordings with and without stimulation enabled are shown in Figs. 1 and 2 respectively. Fig. 1 shows the detrusor pressure during a treated bladder filling in the morning. Stimulation is indicated with a gray background color and the arrow marks the first leakage. In this patient stimulation was disabled due to a long time of stimulation without the pressure returning below threshold. Leakage occurred immediately after stimulation had stopped which in this case was 85 min. since bladder emptying. Fig. 2 shows the detrusor pressure from the untreated bladder filling in the afternoon. Bladder was emptied before starting the recording and leakage occurred after 157 min. Time from bladder empty to first leakage is almost twice as long in the afternoon as compared to the morning. Stimulation could not inhibit undesired contractions in patient 2 but during 6 out of 7 contractions, leakage occurred only when stimulation was disabled.

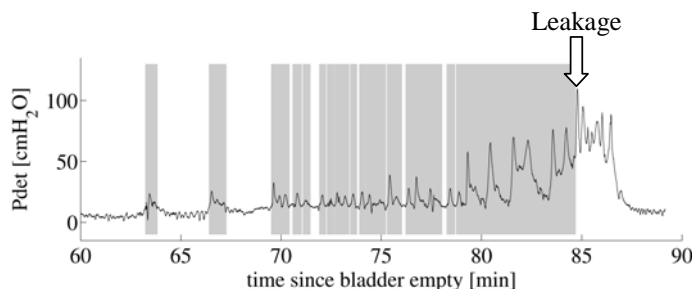


Figure 1: Detrusor pressure during treated bladder filling in the morning (Patient 3).

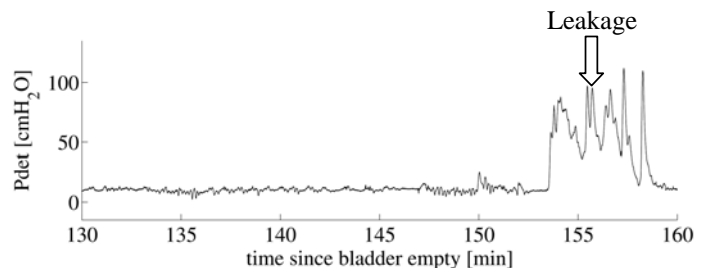


Figure 2: Detrusor pressure during untreated bladder filling in the afternoon (Patient 3).

Assuming linear urine production during the time of recording, the bladder volume at first inhibited contraction and at first leakage was estimated. From these estimates an increase in bladder capacity was calculated. During untreated filling leakage was observed shortly after an undesired bladder contraction in all patients. Based on this it is assumed that the first contraction in the treated filling would have produced a leakage too had it not been inhibited. Data from all patients can be seen in table 1.

Table 1: Patient data

Patient number	Level of injury	Estimated volume at first contraction *	Estimated volume at first leak *	Increase in bladder capacity
1	C5 incomplete	228 ml	450 ml	97 %
2	Th 4/5 complete	Failed to inhibit first undesired contractions		
3	Th 4 complete	345 ml	440 ml	28 %
4	Th 9/10 complete	290 ml	363 ml	25 %

(* from the treated filling)

Discussion

Results from the 4 subjects indicate that it is feasible to treat NDO by event driven electrical stimulation. The patient used for illustration in this abstract would have approximately 20 min. to find a toilet before incontinence emerges (if aware of or otherwise noticed about the first stimulation). Furthermore stimulation increased bladder capacity at a low pressure while preserving continence. The prolonged time from bladder emptying to first leakage in the afternoon as compared to the morning may be explained by the bladder being filled in the morning beyond its normal capacity due to the treated filling (i.e. treated filling can have a carry over effect on subsequent fillings [2]) or it could simply be due to variation in urine production. The fact that leakages only occurred when stimulation was disabled during 6 out of 7 contractions in patient 2 could indicate urethral sphincter activation. This treatment is however not recommended if continence is restored only by activation of the sphincter and not by a decrease in bladder pressure. The mean increase in bladder capacity is comparable to a similar study where artificial instead of physiological bladder filling was used [3]. If an event driven stimulation method is to be used in an implant the problem of elevated pressures during possible urethral sphincter activation has to be addressed. The need for a non-catheter based monitoring of bladder activity is essential if an event driven stimulation scheme is to be used in an implant.

References

- [1] Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, Van Kerrebroeck P, Victor A, Wein A, The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. *Urology*, 2003. 61(1): p. 37-49.
- [2] Wheeler JSJ, Walter JS, Zaszczurynski PJ, Bladder inhibition by penile nerve stimulation in spinal cord injury patients, *J Urol*, 1992. 147: p.100-103
- [3] Dalmose AL, Rijkhoff NJM, Kirkeby HJ, Nohr M, Sinkjaer T, Djurhuus JC. Conditional stimulation of the dorsal penile/clitoral nerve may increase cystometric capacity in patients with spinal cord injury, *Neurourology and Urodynamics*, 2003. 22(2): p. 130-137.
- [4] Craggs MD, Edhem I, Knight SL, McFarlane JP, Shah N, Suppression of normal human voiding reflexes by electrical stimulation of the dorsal penile nerve, *Journal of Physiology*, 1998. 507: p. 19
- [5] Fjorback MV, Hansen J, Dalmose AL, Rijkhoff NJM, Sinkjær T, A Portable Device for Experimental Treatment of Neurogenic Detrusor Overactivity, *Neuromodulation*, 2003 (accepted for publication)

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