

EFFECTS OF PENILE VIBRATORY STIMULATION IN SPINAL CORD LESIONED MEN

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PREFACE

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INTRODUCTION

Background:

A spinal cord lesion may be congenital or caused by trauma or disease. In Denmark there are approximately 3000 persons with a spinal cord lesion, with a gender distribution of the traumatic lesions of about 75 % men and 25 % women. The majority of those with a traumatic lesion are younger, and the lesions are most frequently caused by traffic accidents ¹. Spinal cord lesioned (SCL) individuals suffer from a number of disabilities, of which the most common according to a Swedish study were pain (67%), sexual dysfunction (45%), urinary bladder and bowel problems (40%), and problematic spasticity and spasms in the lower extremities (30%) ². How severe these challenges are depends on the level and completeness of the spinal cord lesion.

Spasticity is clinically characterised by increased muscle tone and hyperactive tendon reflexes. Spasms are sudden, involuntary muscle contractions. These symptoms and signs are often seen at the same time in SCL individuals. Spasticity and spasms in the legs may limit activities of daily life and are usually treated with physiotherapy and spasmolytic agents ³. Spasmolytic agents are often ineffective and have many potential side effects including drowsiness.

Urinary bladder dysfunction, including filling and emptying failure, is a common consequence of SCL. In the majority of SCL subjects, dysfunction is manifest by neurogenic detrusor overactivity ⁴ and detrusor sphincter dyssynergia which may lead to urinary incontinence as well as upper urinary tract deterioration ^{5:6}. Bladder dysfunction may be treated with anticholinergic or other pharmacological agents as well as electrical nerve stimulation or surgery, but the effect is not always satisfactory, and there are several potential side effects of these treatments ⁷.

More optimal means of reducing bladder dysfunction and spasticity/spasms would therefore be of great value.

Penile vibratory stimulation (PVS) has been practiced for about 20 years as a method to obtain ejaculation in SCL men with the purpose of fertilisation ⁸. Since 1994, the method has been the standard treatment for SCL men with a wish of fertilisation at Rigshospitalet, Copenhagen, and a specifically designed vibrator has been developed for that purpose ⁹.

Through these years of use, a reduction in the frequency of spasms in the lower extremities, and in particular spasticity, has been reported by the SCL men following reflex ejaculation induced by PVS. Furthermore, clinical observations have indicated that ejaculation induced by PVS might increase bladder capacity due to suppression of urinary detrusor reflex activity.

It was the aim of the present study to pursue these observations in a systematic investigation.

Spasticity in SCL individuals:

Definition: It is difficult to find an exact definition of spasticity. Spasticity has been defined to include increased muscle tone, increased tendon reflexes, increased flexion reflex and clonus ¹⁰. It may be defined as a motor disorder characterised by a velocity-dependent increase in tonic stretch reflexes that results from abnormal intraspinal processing of primary afferent input ¹¹. Spasms, defined as sudden involuntary contractions of the muscles, are a component of the spasticity syndrome.

Physiology: Spasticity is caused by disturbed transmission in the spinal networks distal to a lesion of descending motor pathways ¹². A selective lesion of the pyramidal tract does not lead to spasticity, whereas a lesion of descending pathways from the brainstem, as well as the cortical

control of these pathways, does lead to development of spasticity. In SCL individuals, impaired transmission has been found in different spinal inhibitory pathways, such as reciprocal inhibition and presynaptic inhibition. This leads to increased excitability of spinal motor neurons, exaggeration of reflex activity and increased muscle tone. It is assumed that physiological changes in the signalling properties of the spinal neurons as well as more structural changes such as sprouting are involved. Changes in the mechanical properties of muscles in SCL individuals have also been found, and this may clinically be mistaken as signs of spasticity.

Spasticity tends to be less severe in SCL individuals with either complete spinal cord lesions or incomplete with functional voluntary movements, and is more severe in those with incomplete lesions and only minimal sparing of voluntary movement ³.

Clinical characteristics of spasticity in SCL individuals: Spasticity is one of the most common and potentially disabling complications affecting SCL individuals. The clinical characteristics of spasticity can be described as follows ¹³:

- Spasticity shows large between individuals variation.
- The tendency to elicit spasticity varies within individuals.
- Spasticity varies in extent during the day.
- When spasticity has been elicited by an activity such as transfer or movement provocation, the tendency to elicit a new muscle contraction is decreased immediately thereafter for a short while.
- After physical exercise the tendency to elicit spasticity decreases for hours.
- Both physical and psychological stress e.g. urinary tract infection; pain and frustration may increase the tendency to elicit spasticity.

Methods of spasticity measurements:

Biomechanical methods: Isokinetic dynamometers are of great value for objective biomechanical measurements when a precise objective and reproducible measure of spasticity is necessary, but play no role in the daily clinical evaluation of spasticity. These techniques are based on the application of well-defined passive movements of specific joints, mostly knee and ankle joint, and measurement of the resistance to these movements. This makes it possible to determine the velocity-dependency of the muscle resistance, which is central to the definition of spasticity ¹⁴.

Other objective methods for measuring the spasm component of the spasticity syndrome, are neurophysiological recordings such as electromyography (EMG) using surface electrodes, as used in the present project ¹⁵.

Clinical methods: Spasticity can be registered objectively and subjectively. The most commonly used objective clinical spasticity rating scale is the Modified Ashworth Scale (Table 1). The original Ashworth scale from 1964 ¹⁶ was modified and tested for interrater reliability in 1987 by Bohannon and Smith ¹⁷. Since the raters agreed on 86.7% of the ratings, the relationship between the raters' judgments was significant and the reliability was good. Although the results were limited to the elbow flexor muscle group, they were positive enough to encourage further trials of the modified Ashworth scale for grading spasticity after an additional grade was added to the scale along with the description of where in the range of motion (ROM) the resistance was experienced.

The subjective methods are clinical self-rating scales e.g. a Visual Analogue Scale, (VAS). A subjective method to measure the frequency of spasms during the day is the Penn Spasm Frequency Scale ¹⁸ (Table 2).

Table 1.

The Modified Ashworth Scale (MAS) ¹⁷ 0-5.

0	No increase in muscle tone.
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part is moved in flexion or extension.
2	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of motion.
3	More marked increase in muscle tone through most of the range of motion, but affected part easily moved.
4	Considerable increase in muscle tone, passive movement difficult.
5	Affected part rigid in flexion or extension.

Table 2.

The Penn Spasm Frequency Scale ^{18;19} 0-4.

0	No spasms
1	Mild spasms at stimulation
2	Irregular strong spasms less than 1/hour
3	Spasms between 1-10/hour
4	Spasms more than 10/hour

Treatment of spasticity:

Spasticity is a problem in the SCL population, and treatment is frequently needed. Before treatment, underlying factors should be excluded such as infection, pressure sore, deep vein thrombosis and fracture, which may aggravate the symptoms of spasticity. Also, emotional or physical stress may have an impact on the degree of spasticity present and some drugs may affect spasticity adversely. When treating spasticity, it should be considered that it is sometimes difficult to treat spasticity without also affecting the functional ability of the SCL person by increasing muscle weakness.

The treatment today is physiotherapy, physical treatment or spasmolytic drugs ^{3;11}.

Physiotherapy: This includes exercise with stretching of the muscles and proper positioning to prevent contractures.

Physical treatment: Physical treatment could be electrical stimulation, which may vary according to different stimulation techniques particularly such as amperage, duration, frequency and location, which make it difficult to compare results from different studies. Also, the methods of evaluation, such as EMG, Ashworth scale or changes in reflexes, may differ from study to study. A side effect may be that the stimulated muscles become stronger, and this may cause even stronger spasms.

Electroejaculation, as well as vibration induced ejaculation may reduce spasticity and spasms ^{11;20}.

Pharmacological treatment: There are insufficient guidelines to assist clinicians in implementing a rational approach to antispastic treatment for SCL persons, since there is very little evidence for the effectiveness of spasmolytic drugs ²¹, and in each patient the treatment more or less depends on a “trial and error” approach. The most commonly used spasmolytics are baclofen, tizanidine, diazepam, dantrolene and clonidine ³. All these drugs are not always effective and may cause

serious unwanted side effects such as drowsiness and lethargy of the senses. Therefore they should only be continued if there is a clear beneficial effect.

The only drug with significant evidence of effectiveness and without the side effects of the oral spasmolytics is baclofen when administered intrathecally¹⁸. This is indicated for SCL persons who do not respond or have intolerable side effects from oral spasmolytics. Before the administration of intrathecal baclofen, a trial dose of baclofen is given and if the effect is satisfactory, a reservoir pump is surgically positioned in a subcutaneous pocket at the abdomen and connected with an intrathecal catheter. The pump then releases baclofen continuously at a preset amount.

Botulinum toxin A: This is effective for treating local spasticity with minimal systemic side effects¹¹. The botulinum toxin A is injected into motorpoints and reduces the release of acetylcholine from presynaptic motor axons, thereby weakening the muscle. This chemical denervation develops over a few days and lasts for months.

Surgical methods: Surgical interventions for spasticity can be classified into peripheral ablative procedures, such as rhizotomy or peripheral neurectomy, and central ablative procedures, such as cordectomy, myelotomy, or stereotactic procedures. These methods were used earlier but are presently considered obsolete²².

Urinary Bladder and Urethra:

Anatomy: The bladder wall is formed by bundles of smooth muscle cells, which form a complex meshwork. The innervation consists of both sympathetic and parasympathetic components. The parasympathetic fibers arise from S2-S4 of the spinal cord (nn. erigentes). The sympathetic fibers are derived from T10-L2 of the spinal cord. Small autonomic ganglia occur throughout all regions of the bladder wall and the majority of these nerve terminals correspond morphologically to

presumptive cholinergic fibers. The detrusor smooth muscle cells are supplied with nerves containing acetylcholine and possess only a sparse supply of sympathetic noradrenergic nerves²³.

The male bladder neck may be considered as a separate functional unit where the smooth muscle cells form a complete circular collar and possess rich sympathetic, noradrenergic innervation. The male urethra consists of four parts: preprostatic, prostatic, membranous and spongiosae. Distally, the prostatic urethra is encircled by a layer of circular striated muscle cells which are continuous with a collar of striated muscle (m. sphincter urethrae, the rhabdosphincter) within the wall of the membranous urethra²⁴. The first part of the pars spongiosa, running through the bulbus penis, is also termed pars bulbosa.

The pelvic floor is innervated by the pudendal nerve, which arise from the S2 –S4 roots. It is a mixed nerve carrying both motor and sensory fibers. The sensory dorsal penile nerve is a branch of the pudendal nerve.

Physiology: The micturition function is coordinated from both the central and the peripheral autonomic and somatic nervous system. According to one theory about this regulation,²⁵ the nerve-coordination of the micturition process can be described by 4 reflexes/loops:

Reflex 1: Neural connections between the frontal area of the cerebrum and the micturition center in the pons and mesencephalon, responsible for the voluntary control of the micturition process.

Reflex 2: Afferent and efferent nerves between the brainstem and the detrusor motor neurons in the sacral spinal cord, responsible for a coordinated detrusor function.

Reflex 3: Peripheral detrusor afferent fibers inhibiting the pudendal motor neurons, which innervate the periurethral striated muscle.

Reflex 4: Supraspinal and segmental fibers influencing on the pudendal motor neurons to ensure a normal coordination of the detrusor- and sphincter function.

Bladder dysfunction in SCL persons: In spinal cord lesioned individuals, the bladder dysfunction depends on both the level and extent of the lesion. It is important to distinguish between the suprasacral lesions, confirmed by the presence of the bulbocavernosus reflex (test S3 and S4 root) and the anal skin reflex (test S5 root), and the lesions of the sacral spinal cord or the conus/cauda equina.

In complete suprasacral lesions the sacral micturition center is left intact but separated from the higher centers, and reflex bladder activity returns after the spinal shock phase. Reflex bladder activity is characterized by neurogenic detrusor overactivity and detrusor-sphincter dyssynergia. This frequently results in incomplete bladder emptying with high residual urine volumes and a risk of developing a high pressure voiding system with upper urinary tract deterioration. To prevent this condition, almost all SCL persons are now instructed to use clean intermittent catheterisation (CIC), but nevertheless they may still experience many daily episodes of urinary incontinence. The SCL men can use a condom sheath, and the SCL women a pad or permanent catheter. For bladder overactivity due to uninhibited detrusor contractions an anticholinergic agent such as Tolterodin (Detrusitol®) may be the first choice of oral treatment, however, with varying effects depending on the concentration. Botulinum Toxin A (Botox®) can be injected with more convincing results and may be the best treatment of this condition in the future²⁶.

In complete lesions of the sacral spinal cord or the conus/cauda equina, all detrusor contractions are lost and the bladder becomes an acontractile sac. The bladder fills to a point where the bladder neck becomes incompetent and leakage occurs²⁴. In these SCL men there may be an inability to open the external sphincter, and this condition also incurs a risk of developing a high pressure voiding system with upper urinary tract deterioration²⁴.

Ejaculatory function:

The ejaculatory reflex is complex, and involves the brain, spinal cord, sympathetic and parasympathetic nerves and somatic motor and sensory peripheral nerves²⁷. The two major afferent stimuli for the ejaculatory reflex are the tactile stimulation of the genitals and the input from the cerebral cortex. Physical manipulation of the penis results in neural transmission via the dorsal penile nerve and the pudendal nerve. From there, the transmission into the sacral spinal cord (S2-S4) ascends to the ejaculatory center in the thoracolumbar spinal cord (T11-L2). Input from the cerebral cortex arises from psychogenic, visual, auditory and olfactory stimuli, but the exact location of an ejaculatory center in the brain is unknown. The afferent stimuli from the cerebral cortex are transmitted to T11-L2 where they are coordinated with input from the genital afferents giving rise to sympathetic efferent nerve fibers and, consequently, initiating the ejaculatory reflex. The sympathetic efferent nerve fibers continue into the sympathetic chain ganglia and merge into the hypogastric plexus. The hypogastric nerves carry impulses into the pelvis towards the ejaculatory organs; the epididymis, vasa deferentia, ampullary glands, seminal vesicles, ejaculatory ducts, prostate and the urinary bladder neck/internal urinary sphincter, where they synapse with adrenergic neurons near or in the walls of these organs. The ejaculatory organs also include the external urinary sphincter, urethra, m. bulbocavernosus and the bulbourethral glands.

During the ejaculatory reflex, semen is expelled from the ejaculatory ducts into the posterior part of the urethra, which is termed “seminal emission”. The function of the bladder neck during seminal emission is to close tightly to prevent retrograde ejaculation into the bladder. The predominant innervation of the seminal emission is sympathetic.

After seminal emission, rhythmic contractions of the bulbocavernosus and ischiocavernosus muscles and external urinary sphincter lead to expulsion of semen from the

posterior urethra termed “projectile ejaculation”. The predominant innervation of the projectile ejaculation is from somatic fibers arising from the pudendal nerve (S2-S4).

Penile vibratory stimulation (PVS):

It seems that during PVS a “normal” ejaculatory reflex is induced²⁸. Successful ejaculation by PVS in SCL men requires an intact ejaculatory reflex arc to allow transmission of afferent stimuli to the sacral spinal cord, communication between the sacral and thoracolumbar regions, and efferents from these spinal cord segments. It should be noted, that ejaculation induced by PVS in SCL men with complete lesions is not accompanied by any somatic sensation of orgasm.

To obtain reflex-ejaculation by penile vibration, it is necessary in the majority of SCL men to use a sufficient vibration amplitude (amplitude ≥ 2.5 mm)⁹. Vibration induced afferent nerve stimulation is transmitted via n. dorsalis penis, a branch of the pudendal nerve, to the sacral spinal cord (S2-S4) and from there to the T11-L2 segments. The efferent innervation of the ejaculatory organs is via the hypogastric and pudendal nerves²⁸. Since the afferent input from PVS depends on an intact sacral spinal cord, the procedure is only an option in SCL men with a suprasacral lesion.

Observations following ejaculation induced by penile vibration:

In previous studies^{9;29} a reduction in lower extremity spasms and, in particular, spasticity has been reported in SCL subjects following reflex ejaculation induced by PVS. In a recent study an increased bladder capacity was incidentally observed during video-urodynamics³⁰. Furthermore, in a recent report³¹ a significant increase in bladder capacity due to suppression of urinary detrusor reflex activity was observed in one SCL man following vibration induced

ejaculation. These observations indicate that vibration induced ejaculation may have an effect of relaxation in the smooth detrusor muscle of the bladder and the striated muscles of the lower extremities.

AIMS OF THE STUDY

The study was divided into two separate parts:

- 1) *The Spasticity study:*** To evaluate the possible antispastic effect of penile vibratory stimulation (PVS) in the lower extremities of spinal cord lesioned (SCL) men.
- 2) *The Bladder study:*** To evaluate the effects of ejaculation induced by PVS on bladder capacity and neurogenic detrusor overactivity in SCL men.

MATERIAL

In both studies the SCL men were recruited as a convenience sample from the Clinic for Para- and Tetraplegia and the Urological Outpatient Clinic, Rigshospitalet, Copenhagen, Denmark.

Spinal cord lesions:

To grade the lesions the ASIA Impairment Scale³² was developed as a neurological classification, and all participants in the study were classified according to this. The level of the spinal cord lesion was defined as the most caudal normally functioning spinal cord segment.

Spasticity:

Nine SCL men with self-reported spasticity and/or leg spasms participated in the Spasticity study. Their age ranged from 27 to 67 years (median 34). Time since spinal cord lesion ranged from 4 months to 50 years. Their level of lesions ranged from C2 to T8. Six had motor complete lesions and three were motor incomplete (Table 3).

Table 3.

Characteristics of the spinal cord lesioned men participating in the project, including use of spasmolytic agents, prophylactic nifedipine during the penile vibratory stimulation and whether antegrade ejaculation was obtained during the stimulation.

SCL Person Characteristics – Spasticity Study							
Person	Age (years)	Years since lesion	Level of spinal cord lesion/ ASIA* impairment scale	Type of lesion traumatic/ non-traumatic	Spasmolytic agents	Prophylactic nifedipine	Antegrade ejaculation
1	27	1	C4/A	traumatic	yes	yes	yes
2	28	4/12	T6/A	traumatic	yes	no	no
3	50	5/12	T6/D	non-traumatic	yes	yes	no
4	34	16	C5/A	traumatic	yes	yes	yes
5	67	50	C2/C	non-traumatic	yes	no	no
6	35	8	T2/A	traumatic	yes	yes	yes
7	46	28	T6/D	traumatic	yes	no	yes
8	34	14	C6/A	traumatic	no	no	no
9	29	24	T8 + cerebral contusion/A	traumatic	yes	yes †	no

*ASIA impairment scale³² classification:

A = Complete: No motor or sensory function is preserved in the sacral segments S4-S5.

B = Incomplete: Sensory but no motor function is preserved below the neurological level and includes the sacral segments S4-S5.

C = Incomplete: Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3.

D = Incomplete: Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more.

†) Person number 9 stated that his level of lesion was C6 and therefore received prophylactic nifedipine. Afterwards the neurological level was found to be T8 according to his medical record.

Urinary bladder:

Fourteen SCL men with urodynamically documented neurogenic detrusor overactivity participated in the Bladder study. There were no specific criteria concerning bladder capacity or detrusor pressure. Their age ranged from 24 to 62 years (median 32). Time since spinal cord lesion ranged from 1.5 to 24 years. Their level of the lesions ranged from C4 to T7. Twelve had motor complete lesions and two were motor incomplete (Table 4).

Table 4.

Person characteristics.

SCL Person Characteristics – Bladder Study								
Person	Age (years)	Years since lesion	Level of spinal cord lesion/ ASIA	Type of lesion traumatic/ non-traumatic	Anti-cholinergic agents	Prophylactic nifedipine	Antegrade ejaculation	Urinary bladder management
1	27	1.5	C5/B	traumatic	yes	yes	yes	Intermittent catheterization
2	34	16	C4/A	traumatic	no	yes	yes	Suprapubic tapping
3	29	11	T6/B	traumatic	no	no	yes	Intermittent catheterization
4	62	4	C5/C	traumatic	no	yes	yes	Intermittent catheterization
5	35	17	C6/A	traumatic	no	yes	yes	Intermittent catheterization
6	52	24	C5/B	traumatic	yes	yes	yes	Intermittent catheterization
7	33	11	C5/B	traumatic	no	yes	yes	Intermittent catheterization
8	26	22	C8/C	non-traumatic	yes	yes	yes	Suprapubic tapping
9	37	18	T3/A	traumatic	no	yes	yes	Suprapubic tapping
10	31	11	C5/A	traumatic	no	yes	yes	Suprapubic tapping
11	28	8	T6/B	traumatic	no	no	yes	Intermittent catheterization
12	24	9	T4/A	traumatic	no	yes	yes	Suprapubic tapping
13	51	13	T5/A	traumatic	no	yes	yes	Intermittent catheterization
14	25	22	T3/A	traumatic	no	yes	yes	Intermittent catheterization

METHODS

Design:

The project was divided in two totally separate studies, a Spasticity study and a Bladder study. Both studies were designed as prospective unblinded Before-After Trials and each person served as his own control.

Penile vibratory stimulation (PVS):

A vibrator (Ferti Care[®] *personal*, Multicept A/S, Gørløse, Denmark) developed specifically to induce ejaculation in SCL men was used⁹. The stimulation was performed with a vibrating disc with a diameter of 3.5 cm made of hard plastic and placed against the frenulum of the penis (Fig. 1). An amplitude of 3.0 mm with a frequency on 100 Hz was used. The vibration was performed for a maximum of 3 minutes followed by a pause of 1 minute before the cycle was repeated, maximally 4 times.

Figure 1.



The PVS procedure.

Spasticity measurements:

Electromyography (EMG) measurements were carried out in order to determine the spasm frequency. All participants were allocated randomly into two study groups. In both groups, 24 hours of EMG recording from the lower extremities were performed initially, followed by either one session of PVS or “no treatment”. Subsequently, a new period of 24 hours EMG recording was performed. After at least one week, those men who had PVS performed now received “no treatment” and those men who had “no treatment” previously now received PVS, and again they had 24 hours of EMG recording before and after.

The SCL men were all encouraged to maintain their daily life with a normal level of physical activity including physiotherapy. Also, they were told to write a diary with all incidents differing from their normal programme, such as extraordinary physical activity or hours spent at rest in their bed. No changes were made in antispastic medication during the study period.

Electromyographic recording (EMG) from surface electrodes was used as the objective method to measure the frequency of spasms in the lower extremities. The Modified Ashworth Scale was used for clinical assessment of spasticity in the legs and the Penn Spasm Frequency Scale was used for subjective evaluation of the frequency of spasms in the legs.

Electromyography (EMG): Electromyographic activity (EMG) was recorded by monopolar surface electrodes (Blue sensor, Disposable electrodes, type NF-50-K, Medicotest A/S, Ølstykke, Denmark) placed over the muscle bellies of the quadriceps femoris and tibialis anterior muscles bilaterally. The reference electrode was placed over the major trochanter on the left side. The signals were sampled and amplified (1000-5000x) by a Biosaca[®] (Biosys, Stockholm, Sweden) ambulatory 8 channel EMG-recorder. The sampling frequency rate was 128 Hz. A 10 Hz high-pass filter was applied before subsequent data analysis. All wires from the electrodes to the amplifier were taped with plaster (Mefix, SCA Mölnlycke Clinical Products AB, S-435 35 Mölnlycke, Sweden.) to the

skin to minimize movement artifacts. The surface electrodes remained in the same position during each of the 48 hours recording sessions. The EMG recorder was placed in a small bag, which was hanging on the wheelchair or lying on a table near the bed.

To analyse the EMG recordings, software built for that purpose, programmed in Matlab³³, was used to automatically detect the occurrence of EMG activity in any of the four leg muscles from which measurements were made. The chosen criteria for a spasm were EMG with activity exceeding 4 times the baseline and with duration longer than 5s, and this was called an “event”. It was subsequently checked visually that the identified EMG activity reflected genuine electrical activity from the muscles rather than artifacts due to movement of the electrodes or connecting wires.

Modified Ashworth Scale (MAS): A clinical assessment of the spasticity was made by the same physician according to the Modified Ashworth Scale (MAS) at study entry (baseline), immediately after and 24 hours after PVS or “no treatment”. The assessment was a total evaluation of the muscle tone in the flexors and extensors of the knee and ankle.

Penn Spasm Frequency Scale: In addition, the SCL persons gave their subjective evaluation of the effects of the treatment by using the Penn Spasm Frequency Scale to grade the spasm-frequency during a 24 hours period. This evaluation was made for the 24 hours before PVS or “no treatment” and then again 24 hours after this.

Urodynamic investigations:

In the Bladder study each SCL man went through four urodynamic investigations over a period of approximately one month. All of the SCL men had tried PVS before and were instructed not to do so for at least two weeks before entering the study in order to minimize any possible effect of PVS on baseline urinary bladder function. All participants had the first cystometry done to

establish baseline conditions. Two days later, the second cystometry was performed immediately after ejaculation induced by PVS in order to examine the acute effect of PVS treatment on the urinary bladder. The third cystometry was conducted following one month of ejaculation by PVS every third day at home in order to examine any long-term effects of the treatment. This cystometry was carried out after an interval of 72 hours after the last ejaculation in order to exclude any acute effects of ejaculation by PVS on the neurogenic detrusor overactivity. At the final visit, one to three days later, ejaculation was induced by PVS and immediately followed by the fourth cystometry in order to examine if it was possible to achieve any further acute effect in addition to a potential chronic effect.

A Windows-based MMS® urodynamic system (Medical Measurements Systems, Enschede, Holland) was used. Cystometry was carried out with an 8F double-tip pressure-transducer (DTPT) catheter (Gaeltec Pressure-Transducer Catheter Type C70, Gaeltec®LTD, Dunvegan, Isle of Skye, Scotland). Initially, the distal tip of the catheter was placed in the bladder. The catheter was fixed in this position by a cotton thread taped to the shaft of the penis, with the distal tip measuring the bladder pressure. An 8F perfusion-catheter was placed in the rectum to measure abdominal pressure. Surface-electrodes were placed near the anus for electromyographic recording (EMG) of the external urethral sphincter.

Saline with a temperature of 37 degree Celsius was infused into the bladder at a rate of 50 mL/min until maximum bladder capacity or a volume of 700 mL was reached. If any signs of autonomic dysreflexia were observed, the filling of the bladder was stopped immediately. During the filling phase recordings of EMG, abdominal pressure, intravesical pressure, the subtracted detrusor pressure (intravesical pressure – abdominal pressure) and bladder volume, were made. Bladder capacity was registered at leak point (V_{leak}) defined by the observed presence of leakage

of urine from the meatus. Furthermore, the bladder volume tolerance (Vp40), defined as the maximum volume instilled with detrusor pressures remaining below 40 cm H₂O, was determined.

All persons had a dipstick urine test and a urine culture before the urodynamic investigation. If the dipstick was positive to nitrite, the investigation was cancelled until the result of the urine culture. Bacteriuria ($\geq 10^3$ CFU per mL) was treated according to the sensitivity test and the investigation was then postponed until after the sufficient treatment period. A control urine culture was made at the next investigation, and the procedure was repeated if bacteriuria was found again. In two cases the dipstick was negative to nitrite and the investigation was carried out, but bacteriuria was found later by the urine culture, and the investigations were then repeated after sufficient treatment. At every urodynamic investigation prophylactic antibiotic treatment using ciprofloxacin 500 mg was given orally immediately before the investigation, in the evening the same day and the next morning. Prior to urodynamics the bladder was emptied by a hydrophilic, coated transurethral catheter (Lofric®, AstraTec AB, Göteborg, Sweden).

No changes were made in anticholinergic medication and urinary drainage method during the study period.

Autonomic dysreflexia:

The only major complication known to occur with PVS is autonomic dysreflexia in persons with spinal cord lesions above T6. The symptoms may be a sudden pounding headache due to rapid increase in the blood pressure, flushing, sweating and cardiac arrhythmias. This condition was prevented by the prophylactic use of a calcium-antagonist (nifedipine 10-20 mg)³⁴, applied sublingually 15-20 minutes before the vibration procedure in all SCL men with a high level lesion unless they had tried the PVS procedure before without any signs of autonomic dysreflexia. Blood pressure was monitored at every occasion before, during and after PVS, and if any of the mentioned

signs or symptoms occurred, they were placed in an upright position and the procedure was stopped at once.

Statistics:

Since the results were not expected to fit a normal distribution, and since the studies were generating paired data, non-parametric statistics for paired data was used. The Wilcoxon matched pairs signed rank sum test data was used³⁵. Fisher's exact test was used for finding the correlation between results and person characteristics in pairs. The EMG analysis software generated a parametric descriptive analysis of the EMG data, but the Wilcoxon matched pairs signed rank sum test was used for comparison of the data.

A p value of < 0.05 was considered statistically significant. The p value is the probability of having observed our data when the null hypothesis, that there is no difference between the treatments, is true.

Role of the funding source:

This study was a PhD project funded by an unrestricted grant from Multicept A/S, Gørløse, Denmark.

RESULTS

Spasticity/spasms:

In five of the males from the spasticity study antegrade ejaculation did not occur by penile vibratory stimulation after five minutes of stimulation and no investigations were made to confirm whether retrograde ejaculation had occurred or not. In these cases the point of stimulation leading to an antegrade ejaculation was not reached.

All EMG recordings were of a technically satisfactory quality except the EMG-recordings from person number 8, which failed due to a technical problem.

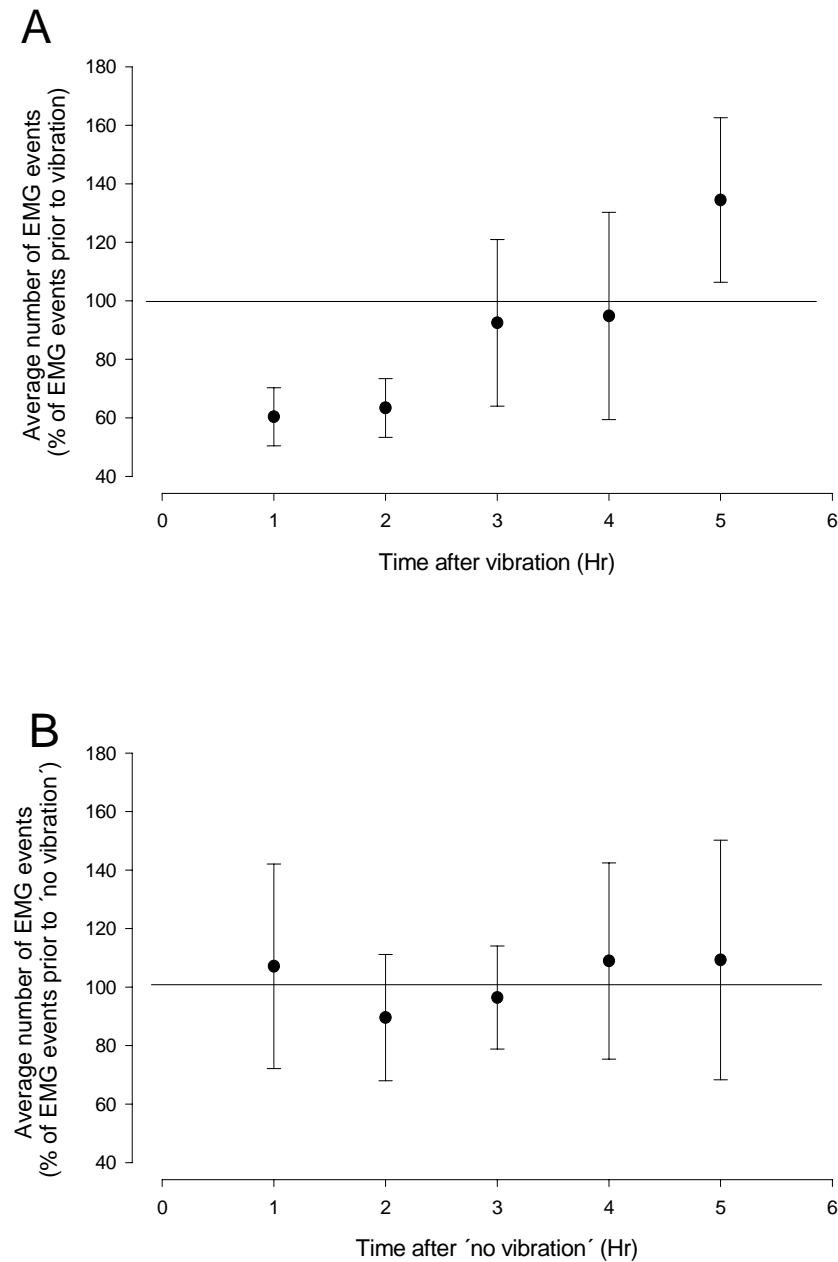
Since initial analysis revealed that the effect of treatment was only seen within 3 hours after the treatment, the statistical analysis was restricted to 5 hours before and after the treatment. The EMG analysis software detected on average (mean \pm SD) 30 \pm 21 EMG events per hour in the 8 SCL subjects in the 5 hours prior to vibration. The number of EMG events varied significantly from one hour to the next in the same individual (mean variability 10 EMG events per hour) as well as between subjects (mean variability 28 EMG events per hour). Nevertheless, there was a reduction in the number of EMG events during the first 3 hours after vibration (mean events per hour = 20) as compared to the number of EMG events in the 3 hours prior to vibration (mean events per hour = 30).

When analysing the total number of EMG events from all the 8 SCL subjects in the 3 hours before and after vibration a statistically significant reduction was found by the Wilcoxon matched pairs signed rank sum test ($p < 0.05$).

In Fig. 2 the mean number of EMG events per hour in the 8 subjects in the first 5 hours after vibration has been expressed as a percentage of the mean number of EMG events per hour prior to vibration (A). It is seen that the largest reduction occurred in the first hour after

vibration after which it gradually decreased until no significant effect was observed in the third hour after vibration. A similar reduction was not observed following “no vibration” (B).

Figure 2.



Decrease in the number of Electromyography (EMG) events following vibration in spinal cord lesioned (SCL) men.

The graphs show the average number of EMG events (defined as EMG activity exceeding 4 times the baseline activity and lasting more than 5 s) as a percentage of the control number of events following either vibration (A) or “no vibration” (B) in the 8 SCL men. The number of EMG events per hour was calculated for each of the SCL men in a control period prior to either vibration or “no vibration”. The number of EMG events for each hour following vibration or “no vibration” was then expressed as a percentage of this control number of EMG events. Finally, the data from all subjects was pooled to obtain the graphs. The vertical bars signify one standard error of the population mean.

The clinical evaluation revealed a significant decrease in muscle tone after PVS as evaluated by MAS ($p < 0.01$) (Table 5). When the subjects were clinically evaluated again 24 hours later this reduction in muscle tone had vanished.

Table 5.

Clinical assessment of the spasticity made by using the Modified Ashworth Scale (MAS)¹⁷ before penile vibratory stimulation (PVS)/"no treatment", immediately after, and 24 hours after PVS/"no treatment". The assessment was a total evaluation of the muscle tone in the flexors and extensors of the knee and ankle.

Modified Ashworth Scale						
Person	Before vibration	Immediately after vibration	24 hours after vibration	Before "no treatment"	Immediately after "no treatment"	24 hours after "no treatment"
1	3	0	2	3	3	4
2	3	2	3	1	1	1
3	4	1	3	3	4	4
4	3	2	2	5	4	4
5	1	0	2	3	3	2
6	1	0	1	1	1	1
7 †	0	0	0	0	0	0
8	4	3	3	3	3	3
9	4	1	4	4	4	4
Mean	2.6	1.0 ‡	2.2	2.6	2.6	2.6

†) Person number 7 clinically was graded 0 at all occasions, but was suffering from self-reported spasticity nevertheless.

‡) $p = 0.009$

The subjects spontaneously reported that they experienced a relaxation in the legs and a reduction in the spasm frequency following vibration and there was a tendency towards a decrease of the number of spasms according to the Penn Spasm Frequency Scale (Table 6). However, this did not reach a statistically significant level at 24 hours ($p=0.26$).

Table 6.

The spinal cord lesioned men`s subjective evaluation of the effects of the treatment by using the Penn Spasm Frequency Scale to grade the spasm-frequency^{18;19}.

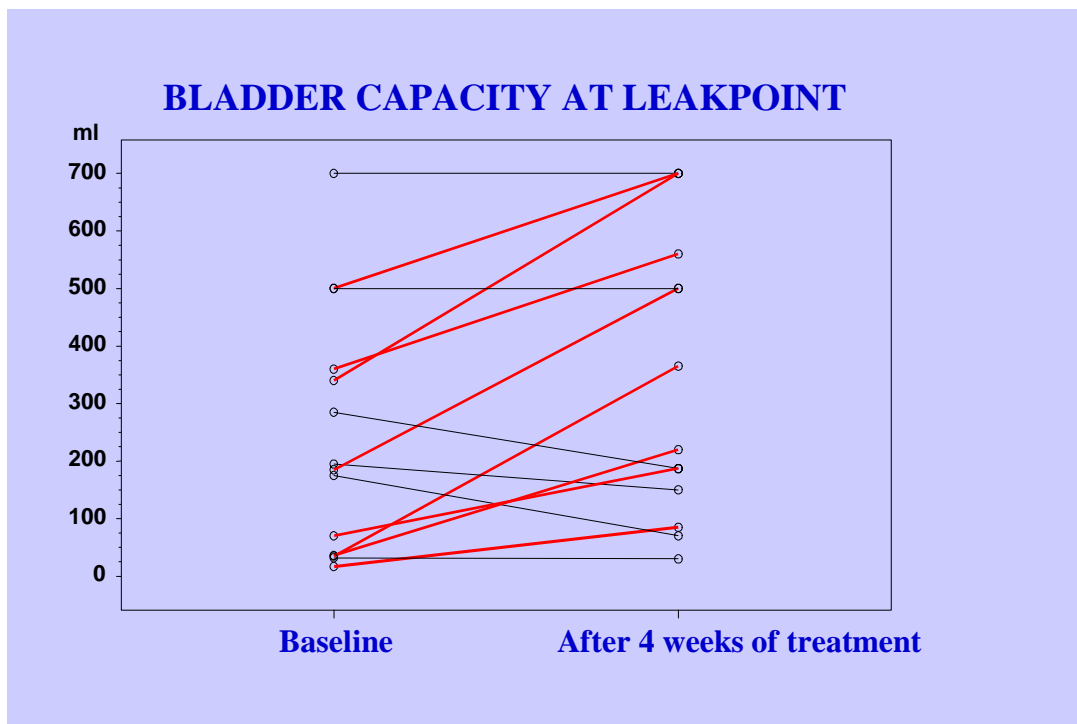
Penn Spasm Frequency Scale				
Person	Before vibration	24 hours after vibration	Before “no treatment”	24 hours after “no treatment”
1	3	3	3	3
2	4	3	3	4
3	3	3	3	4
4	4	2	4	4
5	3	3	3	3
6	3	3	3	3
7	3	3	3	3
8	2	3	4	4
9	3	2	4	3
Mean	3.1	2.8	3.3	3.4

Urinary Bladder:

In the bladder study six SCL men had the baseline investigation done, but since it was not possible to obtain antegrade ejaculation by PVS, they were not included in the study.

There was no statistically significant change in Vleak at baseline (median 190 mL) compared to immediately after ejaculation by PVS (median 189 mL). Vleak increased significantly from a median of 190 mL (17-700 mL) at baseline to 293 mL (30-700 mL) after 4 weeks of frequent PVS treatment ($p=0.03$, Wilcoxon matched pairs signed rank sum test). These results are illustrated in Fig. 3.

Figure 3.



The changes in bladder capacity at leakpoint, at baseline, and after 4 weeks of treatment.

Red lines: Illustrate an increase in bladder capacity (8 persons).

Black lines: Illustrate no change (3 persons) or a decrease (3 persons) in bladder capacity.

In addition, no further significant acute effect in Vleak was seen following four weeks of stimulation (median 293 mL) compared to the fourth cystometry (median 233 mL) (Table 7).

Table 7.

Bladder capacity at leakpoint. All parameters are measured in mL.
PVS = penile vibratory stimulation.

Bladder capacity at leakpoint				
Person	Baseline	Immediately after PVS	After 4 weeks of treatment	Immediately after PVS
1	340	700	700	310
2	35	160	365	265
3	700	700	700	700
4	195	230	150	190
5	185	345	500	500
6	500	700	700	700
7	17	110	85	200
8	175	50	70	95
9	36	57	220	195
10	285	217	187	355
11	70	47	187	48
12	32	95	30	56
13	360	600	560	118
14	500	110	500	600
Median	190*	189	293*	233
Range	17 - 700	47 - 700	30 - 700	48 - 700
95% c.i.	35 - 500	57 - 700	85 - 700	95 - 600

The bladder capacity before involuntary leaking or at maximum filling (700 mL or until signs of autonomic dysreflexia).

*) $p = 0.03$, Wilcoxon signed rank test.

There was a trend towards an increasing bladder capacity with detrusor pressures remaining below 40 cm H₂O, expressed by Vp40, through the entire investigation period but it did not reach statistically significant levels (Table 8).

Table 8.

Bladder volume tolerance. All parameters are measured in mL.
PVS = penile vibratory stimulation.

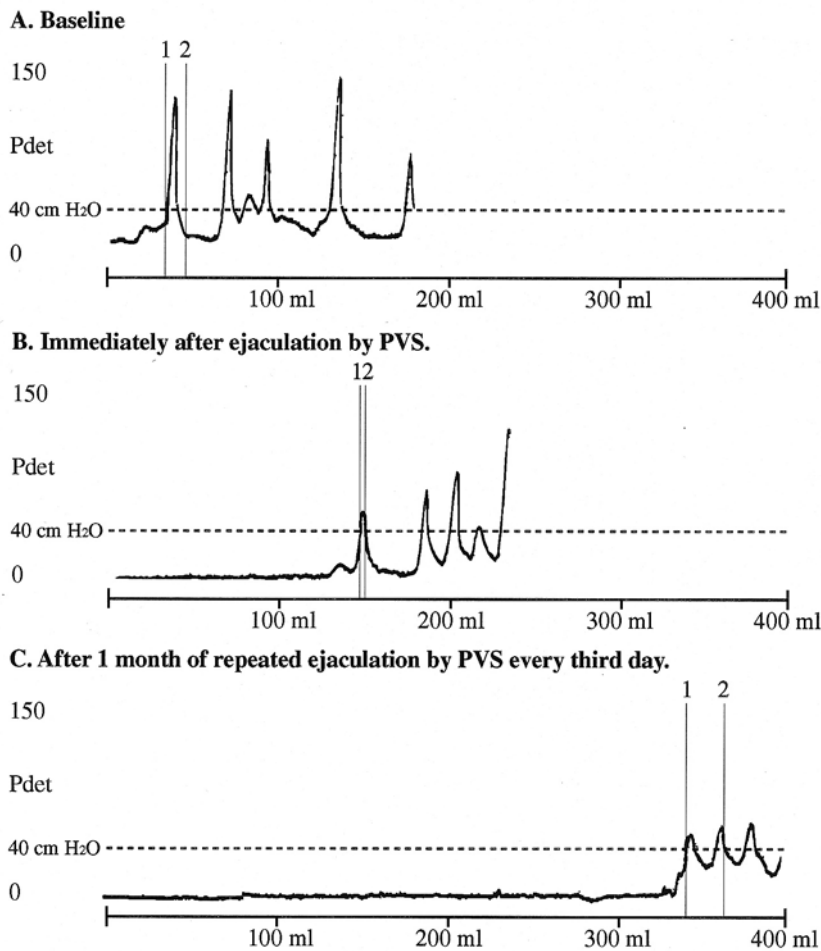
Bladder volume tolerance				
Person	Baseline	Immediately after PVS	After 4 weeks of treatment	Immediately after PVS
1	170	480	90	283
2	27	155	335	245
3	125	190	185	170
4	70	110	50	110
5	60	50	165	123
6	370	80	80	235
7	15	100	80	185
8	70	42	50	70
9	27	40	125	120
10	210	140	125	265
11	62	41	172	45
12	28	85	28	47
13	240	285	447	> 700*
14	318	30	90	158
Median	70	93	108	158
Range	15 - 370	30 - 480	28 - 447	45 - 280
95% c.i.	27 - 240	41 - 190	50 - 185	70 - 245

The bladder volume tolerance defined as the maximum volume instilled with detrusor pressures remaining below 40 cm H₂O.

*: The detrusor pressure remained below 40 cm H₂O during the entire investigation.

The bladder volume tolerance increased from a median of 60 mL (15-240 mL) at baseline to 172 mL (80-447 mL) after 4 weeks of frequent PVS treatment in 7 out of 14 persons (Subject numbers 2, 3, 5, 7, 9, 11 and 13 in Table 8). No positive effect on the bladder volume tolerance was found in the other persons. An example of the changes in the detrusor pressure curves in person number 2 is shown in Fig. 4³¹.

Figure 4.



Example of the standard cystometry from patient number 2 showing the relation between the detrusor pressure (Pdet) and the volume instilled in the bladder (velocity 50 mL/min).

1: The bladder volume tolerance defined as the maximum volume instilled with detrusor pressures remaining below 40 cm H₂O.

2: The bladder capacity before involuntary leaking.

No statistically significant relationships were found between age, time since lesion, level of the lesion, urinary bladder management, the number of urinary tract infections per year, use of anticholinergic medication and use of prophylactic nifedipine compared to Vleak and Vp40. Furthermore, there was no significant differences between the group of men responding to treatment and the group of non-responders in relation to the person characteristics as listed above (Table 4). Since only two persons had incomplete lesions, it was not possible to conclude on the relation between completeness of the lesion and the other parameters.

Drop-outs: Three SCL men dropped out after entering the study. In two, it was not possible to obtain antegrade ejaculation by PVS at home during the 4 weeks investigation period. One developed a pressure sore in the gluteal region during the four weeks investigation period, unrelated to the investigation, and was not able to complete the study.

DISCUSSION

SCL persons:

Since the project was considered to be a basic study, the inclusion criteria were made very wide and there was a large inter-subject variation concerning the person characteristics in both studies. In spite of that, an effect was demonstrated on spasticity as well as bladder capacity.

Spasticity and Spasms:

Electromyography (EMG): There is no validated and standardized method of EMG using surface-electrodes to measure spasticity and spasms. Many factors may influence the quality of the EMG measurements by surface electrodes such as the size of the electrodes, the contact to the skin, the position of the electrodes in relation to the muscles and the recording sampling rate and filtration. In each person the skin was cleaned with alcohol before the electrodes were placed. They were fixed by non-conductive paper tape (Mefix) to be in the same position for 48 hours.

Measuring the number of involuntary EMG events provides an alternative, objective source of information regarding the spasm frequency. However, this method is not without problems.

First, it is unclear to what extent the EMG activity reflects the clinically perceived spasms. Most likely, in many cases the EMG activity was not sufficient to reflect an actual movement of the leg or the muscle and thereby produce a clinical spasm. The fact that most SCL men indicated 3 on the Penn scale (spasms between 1-10/hour), whereas the programme detected on average 30 EMG events per hour, confirms this. Furthermore, it was only possible to record from 4 muscles and it may be that the clinically perceived spasms did not involve activation of these

specific muscles. Although the EMG events do provide information about involuntary muscle activity, it must be kept in mind that they do not fully reflect the clinically perceived spasm activity.

A second problem with the EMG method is, that we have no standardization to control the factors that may have provoked the EMG activity in the SCL men. They were instructed to maintain the same daily activities on each of the 4 days during which recordings were made and they were asked to keep a diary to document this, but otherwise no surveillance of the subjects was made during the EMG measurements. Some of the EMG activity was probably provoked by external factors such as toilet visits, movement from wheelchair to bed, handling by health care personnel, etc. The diaries of the SCL persons did provide some information about this, but it was not possible to establish a clear correlation between such factors and the occurrence of the EMG events. What is important in relation to this study is that there was no difference in the number of these “external stimuli” on the 4 days of the study, and although we cannot fully exclude this possibility, we find it unlikely that a change in the number and/or nature of “external stimuli” should be responsible for the observed reduction in the number of EMG events following PVS. Also, the persons were randomised to have the vibration treatment done in either the first or the second period of measurements to minimize changes in activity as confounding factor.

A third problem with the EMG method is the very large variability. It was not surprising to find a large inter-individual variability, since it is well known that the spasm frequency may vary significantly between SCL persons. It was, however, more surprising that the number of EMG events varied markedly from hour to hour in the same individual without any evident change in the number of “external stimuli” recorded in the diary. This variability makes it difficult to use the method to evaluate the effect of therapeutically interventions and it may explain why a significant reduction in the spasm frequency was not found in the individual person, but only when pooling the data from all 8 individuals. At the same time, the fact that we did observe a statistically

significant reduction despite the large variability within and between the individuals, emphasizes that the reduction in the number of the EMG events, induced by PVS, was indeed of a very significant magnitude (40 % average reduction in the 8 subjects).

Modified Ashworth Scale (MAS): The reduction in muscle tone as evaluated by the MAS scale was also very remarkable, typically resulting in a normalization of the muscle tone from a state of clearly pathologically increased muscle resistance. Although the MAS scale is widely accepted as the most optimal scale for evaluation of the extent of muscle tone, it is not without problems^{17;19}. In relation to the present study the main problem is that the evaluation of muscle tone is based on the examining physician's evaluation of the response to passive manipulation of the person's legs. A precise estimate based on this evaluation requires a very experienced examiner and expectations of the outcome may easily influence the evaluation. More optimally, the evaluation should therefore have been performed by a physician who was blinded as to whether the person had been vibrated or not, or alternatively by evaluating the muscle tone objectively by biomechanical measurements, but this was not possible in the present study. Nevertheless, the very significant reduction in the MAS score and the agreement with the changes in the EMG events and the subjective perception of the person, suggest that the change in the MAS score reflects a reduction in spasticity.

Penn Spasm Frequency Scale: In this study we have shown that PVS produces a significant reduction in the number of involuntary bursts of EMG activity and muscle tone in leg muscles. The subjects also reported that their leg muscles were more relaxed immediately after vibration and that the number of spasms was reduced, but using the Penn spasm frequency scale at 24 hours this reduction did not reach a statistically significant level.

Since many of the SCL subjects indicated 3 on the Penn scale (corresponding to more than 1 spasm and less than 10 spasms per hour) both before and after vibration, and at the same time experienced a reduction in the number of spasms, it is possible that the methodology of the Penn

scale may allow exposure of a marked reduction in the number of spasms (for instance, a reduction from 10 to 6 spasms pr hour, corresponding to the 40 % reduction observed in the number of EMG events). We therefore believe that the most likely reason why no significant reduction was found in the number of spasms when using the Penn scale is, that it provides a too crude measure of the number of spasms and does not precisely reflect the experience of the individuals to be a useful tool.

Urinary Bladder:

Urodynamic procedures: In the bladder study there was a large variability in the bladder capacity at baseline between-subjects. All the participants had documented neurogenic detrusor overactivity, but there were no limits of maximum bladder capacity or detrusor pressure, which made it difficult to make a marked improvement in the men with a large bladder capacity or low detrusor pressure when entering the study. The changes in bladder capacity are illustrated in Figure 3.

There was also a large intra-subject variability in the bladder capacity between the cystometries that could be due to the effect of PVS and/or the repeated cystometry investigations itself. Therefore, it could be argued that a control group should have been included in the study. However, the reproducibility of repeated cystometry is considered to be acceptable as long as the interval between the investigations exceeds several hours³⁶. In this study the interval was several days, so the reliability of the cystometry results was considered to be satisfactory.

Cystometry was carried out using a double-tip pressure-transducer catheter made of very smooth and flexible plastic material. This kind of microtip catheter estimates urethral pressure by measuring the direct force in the system on the surface of the transducer. Saline was infused at a rate of 50 mL/min. This is a very fast, non-physiological filling rate that may lead to an increased neurogenic detrusor overactivity but a standard rate in urodynamic studies. For practical reasons, it

was considered impossible to accomplish the investigations with a physiological filling rate in view of the time required and SCL person compliance. Since the used infusion rate probably would influence on the results by making the significance of the effects of the treatment even more difficult to demonstrate, it was considered acceptable.

Autonomic dysreflexia:

Severe symptoms of autonomic dysreflexia did not occur in any occasion during the PVS procedure. During the filling phase of the urodynamic investigation procedure, symptoms of mild dysreflexia occurred in subject number 5, 13 and 14 at all cystometries. This was manifest by sweating, flushing and general discomfort, and the filling of the bladder was stopped before 700 mL (at 500 mL, 600 mL and 500 mL, respectively). Neither headache nor increasing blood pressure was observed in any case. No other adverse events were noted.

Neuromodulation:

Neuromodulation may be defined as a way to restore reflex mechanisms or compensate for disturbed functions by utilizing the plasticity of the nervous system itself²⁴.

Peripheral electrical stimulation is a method to induce sacral neuromodulation²⁴. PVS may be considered as another but similar method to induce sacral neuromodulation. In peripheral electrical stimulation of the dorsal penile nerve, which is a branch of the pudendal nerve, surface electrodes are placed over the nerve at the dorsum of the penis shaft in order to inhibit bladder activity³⁷⁻³⁹. In a recent Danish study ten SCL persons with suprasacral lesions were included. During cystometry, conditional short duration electrical stimulation of the penile/clitoral nerve was performed as treatment for one or more detrusor hyperreflexic contractions³⁷. This stimulation

significantly increased cystometric capacity by an inhibition of detrusor contractions. In another study of six SCL persons with suprasacral lesions, it was not possible to demonstrate the efficacy of maximal electrical stimulation of the dorsal penile nerve in inhibiting neurogenic detrusor overactivity³⁸. Another recent study of eight SCL men with cervical lesions concluded that dorsal penile nerve stimulation could significantly decrease the detrusor pressure and inhibit neurogenic detrusor overactivity³⁹.

A different kind of peripheral electrical stimulation is functional electrical stimulation (FES) of the peroneal nerve⁴⁰ and transcutaneous electrical stimulation of the posterior tibial nerve⁴¹. The reported reduction in spasticity and bladder overactivity induced by this type of stimulation is probably also a way of inducing sacral neuromodulation.

During peripheral electrical stimulation, several parameters can be adjusted, including current intensity (mA), frequency (Hz) and pulse duration (ms). This kind of stimulation may be the one most similar to vibratory stimulation since the afferent stimulus goes through the pudendal nerve to the S2-S4 of the spinal cord resulting in sympathetic thoracolumbar (T11-L2) and somatic sacral (S2-S4) efferent outflow. Nevertheless, when electrical stimulation is used the nerves are stimulated directly, whereas vibration is considered as a method of indirect nerve stimulation, possible initiated through the pacinian corpuscles resulting in a more “natural” reflex⁴². Another large difference is the fact, that peripheral electrical stimulation does not induce ejaculation, and most likely the ejaculation itself is the key to the effects from PVS. This may lead to differences in detrusor response to the two procedures, but it remains to be studied further.

The underlying mechanism of the effects of PVS on both bladder and spasticity remains unknown and demands further neurophysiological investigations. As mentioned earlier, it is also uncertain whether it is the vibratory stimulation or the ejaculation itself, or both, that generates the effect. However, when analysing the spasticity results evaluated by MAS, it was not

possible to demonstrate any significant difference in the reduction of spasticity between the SCL men who obtained antegrade ejaculation compared to the men who did not obtain antegrade ejaculation. This indicates that antegrade ejaculation is not an essential prerequisite of inducing a significant reduction in spasticity by PVS.

The neurogenic mechanism activated by PVS and its influence on urinary bladder reflex activity in SCL subjects is not known, but may be similar to peripheral electrical stimulation which is related to reflex inhibition of the detrusor and contraction of the sphincteric and/or pelvic floor muscles. In general, the basic mechanism of electrical stimulation in the urogenital area, is believed to be an artificial activation of normal inhibitory reflexes²⁴. The afferent nerve impulses travel through the pudendal nerve into the sacral spinal cord (S2-S4) and from here to the spinal cord segments of T11-L2. The inhibitory effect on the urinary bladder is mediated through efferent sympathetic fibers of the hypogastric nerve originating from the thoracolumbar spinal cord (T11-L2)⁴³. The contraction of the pelvic floor muscles is mediated through somatic efferent nerve fibers of the pudendal nerve originating from the sacral spinal cord (S2-S4)⁴⁴.

Furthermore, when using PVS a strong contraction in the external sphincter is seen before ejaculation, and the bladder inhibition could be a response to this contraction⁴⁵. It is known that closing of the urethra may inhibit detrusor contraction reflexogenically by afferent impulses through the pudendal nerve and efferent outflow through sympathetic pelvic nerves and lead to bladder relaxation⁴⁶.

Female SCL:

When both studies were designed, they were planned to include the same number of female and male SCL persons, since the mechanism of the treatment was supposed to be the same for both genders.

Technically, the vibratory stimulation is carried out the same way as in men, but the vibrating disc is placed directly on the clitoris in women. Since there is no objective sign in women such as an antegrade ejaculation, it may be rather difficult to know if you have reached the maximum point of stimulation similar to the ejaculation in men, but the observed end-point was a reaction indicating an orgasm. Signs of this were contractions of the abdominal muscles, flushing, gooseflesh and limb movements induced by vibration on clitoris. As in the SCL men, the orgasm induced by vibration on the clitoris, in SCL women with complete lesions, is not usually accompanied by any somatic sensation of orgasm.

It was a challenge to recruit SCL women to participate in the studies. In the end, only two SCL women (person characteristics, Table 9) participated and accomplished the spasticity study. Another two SCL women (person characteristics, Table 10) were included in the bladder study, but dropped out during the investigation period with vibration at home. As explanations, one reported pain in the legs after the vibration, and the other felt pain in the abdomen.

Table 9.

Characteristics of the spinal cord lesioned women participating in the project, including use of spasmolytic agents, prophylactic nifedipine during the clitoral vibratory stimulation and whether signs of orgasm were obtained during the stimulation.

SCL person characteristics – Spasticity Study							
PERSON	Age (years)	Years since lesion	Level of spinal cord lesion/ ASIA* impairment scale	Type of lesion traumatic/ non-traumatic	Spasmolytic agents	Prophylactic nifedipine	Signs of orgasm
10 Female	55	1	T11/D	non-traumatic	yes	no	yes
11 Female	76	2	T10/C	non-traumatic	yes	no	yes

*ASIA impairment scale classification.

Table 10.

Female SCL person characteristics.

SCL person characteristics – Bladder Study								
PERSON	Age (years)	Years since lesion	Level of spinal cord lesion/ ASIA	Type of lesion traumatic/ non-traumatic	Anti-cholinergic agents	Prophylactic nifedipine	Signs of orgasm	Urinary bladder management
15 Female	37	5	T11/A	traumatic	yes	no	yes	Permanent catheter
16 Female	43	5	T7/C	non-traumatic	no	no	yes	Intermittent catheterization

The results for the SCL women are listed in Table 11, 12, 13 and 14 but it should be noted that the EMG data were not analysed. It was not possible to make any statistical calculations due to the small number of SCL women. However, when looking at the individual results, the tendency was the same as in the men. In the bladder study, the bladder capacity increased in one of

the women, and the bladder volume tolerance increased in both, immediately after vibration. In the spasticity study, a reduction in the spasticity measured by MAS was seen in both SCL women after vibration but not after “no treatment”. No changes were found according to the Penn Spasm Frequency Scale.

Table 11.

Clinical assessment of the spasticity made by using the Modified Ashworth Scale (MAS) before clitoral vibratory stimulation/”no treatment”, immediately after, and 24 hours after vibration/”no treatment”. The assessment was a total evaluation of the muscle tone in the flexors and extensors of the knee and ankle.

Modified Ashworth Scale						
Person	Before vibration	Immediately after vibration	24 hours after vibration	Before “no treatment”	Immediately after “no treatment”	24 hours after “no treatment”
10 Female	3	0	3	2	2	2
11 Female	3	1	2	4	3	3

Table 12.

The spinal cord lesioned women`s subjective evaluation of the effects of the treatment by using the Penn Spasm Frequency Scale to grade the spasm-frequency^{18;19}.

Penn Spasm Frequency Scale				
Person	Before vibration	24 hours after vibration	Before “no treatment”	24 hours after “no treatment”
10 Female	3	3	2	2
11 Female	2	2	3	3

Table 13.

Bladder capacity at leakpoint. All parameters are measured in mL.
CVS = clitoral vibratory stimulation.

Bladder capacity at leakpoint		
Person	Baseline	Immediately after CVS
15, Female	700	700
16, Female	90	140

The bladder capacity before involuntary leaking or at maximum filling (700 mL or until signs of autonomic dysreflexia).

Table 14.

Bladder volume tolerance. All parameters are measured in mL.
CVS = clitoral vibratory stimulation.

Bladder volume tolerance		
Person	Baseline	Immediately after CVS
15, Female	255	335
16, Female	87	130

The bladder volume tolerance defined as the maximum volume instilled with detrusor pressures remaining below 40 cm H₂O.

Since the compliance of the SCL women was so poor, a meeting was arranged to debate the treatment with participation of approximately 20 SCL women and the responsible persons of the project. The general attitude towards vibration on the clitoris was that it was not an acceptable method to use as a treatment of physical problems, in spite the fact that it could be an alternative to spasmolytic drugs. The SCL women expressed that vibration on the clitoris would involve and activate both psychological and sexual trauma and feelings, and without any offer of

therapy to take care of this, they did not feel comfortable with the project. Certainly, these statements should be taken into consideration in the design and planning of future studies of this kind involving SCL women.

In a recent pilot-study the vibration treatment has been used in a group of women without spinal cord lesions suffering from urge and/or stress incontinence, but it should be noted that the vibration in this group was performed on the perineum and not on the clitoris. In this group, we did not meet the same barriers as in the group of SCL women. We also did not note this in the group of SCL men of whom several had relationships with able-bodied women. This corresponds very well with previous observations⁴⁷. There is no obvious explanation for these differences, but a possible reason could be that SCL women experience a great loss of sexual identity and physical relation to their own body⁴⁸, so that any physical treatment of the genital region, such as vibration or a gynaecological investigation, will be perceived as a very unpleasant experience and activate unhappy feelings.

Future studies concerning SCL women and their sexuality are necessary.

CONCLUSION

In consideration of the aims of the studies the following conclusions were reached.

- 1) Spasticity/Spasms:** This study demonstrated a significant antispastic effect of PVS on the spasm frequency in the lower extremities evaluated by EMG-measurements before and after vibration. Furthermore, a clinical effect was found by MAS, reflecting a reduced spasticity in the lower extremities, immediately after PVS. This suggests that PVS may be useful as an antispastic therapy, at least in some SCL men and in distinctive to electroejaculation, penile vibration has the advantage of being easily applied by the SCL person himself at home.
- 2) Urinary Bladder:** Ejaculation by PVS induced a significant increase in bladder capacity at leakpoint following 4 weeks of frequent treatment. Furthermore, there was a trend towards a decrease in intravesical pressure during the filling phase. These findings reflect a reduction in the neurogenic detrusor overactivity and may have implications in the management of incontinence in some SCL men with low bladder capacity and in SCL men at risk for upper urinary tract deterioration from high storage pressure. Since, it is not possible to predict in each individual case who will benefit from using PVS, it can easily be tried because the treatment seems rather harmless and without adverse effects.

FUTURE ASPECTS

Many ideas for future projects were created during this study. It would be interesting to investigate the effects of PVS in SCL men without ejaculation. It is still an important question whether or not it is necessary to induce ejaculation to obtain the effects. If you do not have to induce ejaculation to have the effect, more SCL men could use it, since SCL men with all levels of lesion above T10 could be included, and possibly it would be considered more comfortable and easy to perform vibration without ejaculation. In such a study, it should also be investigated whether retrograde ejaculation did occur or not.

Although SCL women were not included in this study, we would still like to investigate the effects of clitoral vibratory stimulation in SCL women in another study designed to be acceptable for that group of patients.

To investigate the antispastic effect of PVS it would be desirable to use a more objective method of measuring spasms, such as the Kin-Com machine. This machine is able to create a standardised movement of a joint and measure the force/resistance developed by muscle rigidity. It can be used as a standardised method of measurement, which could be more objective than a clinical evaluation by the MAS. Problems with the Kin-Com method are at present the lack of evaluation and standardization and probably a risk of inducing fractures.

Since PVS leads to a contraction of the pelvic floor, it seems logical to use it for training of the muscles of the pelvic floor in women suffering from stress incontinence. In a private incontinence clinic, vibratory stimulation of the perineum was tried in women with stress and/or urgeincontinence as a kind of “physiotherapy” of the bladder and pelvic floor may seem to have an effect. A pilot study is now carried out in the Urological department in collaboration with the Gynaecological department, Rigshospitalet, Copenhagen, including women with stress and/or urge incontinence. They are instructed to use perineal vibratory stimulation every third day, and 24-hours

pad test, voiding scheme and cystometry are performed before and after 6 weeks of treatment. The results of this study are not fully analysed yet, but early results seem very promising, and the subjective evaluations of the treatment are positive. Other studies are planned with this group of patients comparing perineal vibratory stimulation with the common treatments of this condition.

Another project is planned including healthy women to investigate the relation between the increment in the urethral pressure induced by vibratory stimulation on the clitoris/perineum and the magnitude of the vibratory amplitude. This study would give a good basis for the future possibilities of using vibratory stimulation as a treatment of urinary incontinence.

Since the mechanism behind the effects of vibratory stimulation is still unknown, a basic neurophysiological study will have to be done probably using a suitable animal model.

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ENGLISH SUMMARY

This PhD thesis is based on two original articles. The project was carried out in the Urological department, Rigshospitalet, University of Copenhagen, Denmark from 1999 to 2003.

The aim of this study was to investigate the effects of penile vibratory stimulation (PVS) on the spasticity in the lower extremities and the bladder capacity in spinal cord lesioned (SCL) men. PVS has been known for about 20 years and used for the last 10 years at Rigshospitalet to obtain ejaculation in SCL men with the purpose of fertilization. Throughout this period there have been occasional reports of reduced spasticity and spasms in the lower extremities, and clinical observations of an increased bladder capacity, but this have never been investigated systematically. Both spasticity/spasms as well as reduced bladder capacity with consequently urinary incontinence are limiting factors in the daily life of SCL persons. The usual medical treatment of these problems is often ineffective and has several serious side effects.

In the spasticity study, 9 SCL men were included with lesions ranging from C2 to T8. Electromyographic (EMG) recordings using surface electrodes on the quadriceps and tibialis muscles of the legs, were carried out before and after PVS or “no treatment” with an ambulatory EMG recorder. The number of spasms per hour was calculated, and the spasticity was evaluated by the Modified Ashworth Scale (MAS).

A statistically significant reduction in the number of spasms/hour was found by EMG in the first 3 hours after PVS. A significant reduction in the spasticity was found by MAS immediately after PVS.

In the bladder study, 14 SCL men were included with lesions ranging from C4 to T7 and documented neurogenic detrusor overactivity. Cystometry was carried out before (baseline) and immediately after ejaculation induced by PVS. After one month with ejaculation every third day at

home by PVS performed by the SCL person himself, another cystometry was done to investigate the long-term effect of the treatment.

In all persons, neurogenic detrusor overactivity and detrusor sphincter dyssynergia were found at the baseline investigation. After 4 weeks of ejaculation by PVS every third day, a statistically significant increment of the bladder capacity was found from a median of 190 mL at baseline to 293 mL ($p=0.03$, Wilcoxon matched pairs signed rank sum test). Furthermore, a trend towards a reduction in the detrusor pressure in the filling phase was found.

We conclude that PVS may have implications in the management of spasticity/spasms and decreased bladder capacity in some SCL men. Since, it is not possible to predict in each individual case who will benefit from using PVS, it can easily be tried because the treatment seems rather harmless and without adverse effects. Also, PVS has the advantage of being easily applied by the SCL person himself at home.

Future neurophysiological studies have to be carried out probably in a suitable animal model to document the mechanism behind the effects of PVS.

DANSKSPROGET RESUMÉ

Ph.d.-afhandlingen består af to originale artikler. Projektet er gennemført på Urologisk afdeling, Rigshospitalet, København i perioden 1999 - 2003.

Formålet med Ph.d.-projektet var at undersøge effekten af penil vibratorisk stimulation på henholdsvis spasticiteten i benene og blærekapaciteten hos rygmavsskadede mænd. Penil vibratorisk stimulation har været anvendt i ca. 20 år på Rigshospitalet til frembringelse af ejakulation hos rygmavsskadede mænd i fertilitetsøjemed. I denne forbindelse har der været tilbagemeldinger om reduceret spasticitet/spasmer i benene, samt kliniske observationer af en øget blærekapacitet, men dette har ikke tidligere været undersøgt systematisk. Både spasticitet/spasmer og nedsat blærekapacitet med deraf følgende urininkontinens er store gener i dagligdagen for rygmavsskadede personer. De eksisterende medicinske behandlinger af disse tilstande er ofte ineffektive og med mange uønskede bivirkninger.

I Spasticitets-studiet indgik 9 rygmavsskadede mænd med læsioner fra C2 – T8. Der blev foretaget elektromyografisk måling (EMG) med overfladeelektroder på quadriceps/tibialis anterior musklerne før og efter penil vibratorisk stimulation eller ”ingen behandling” med et transportabelt EMG-apparat. Antallet af spasmer/time blev beregnet. Spasticiteten blev bedømt ud fra den Modificerede Ashworth Skala.

EMG-målingerne viste en signifikant reduktion i antallet af spasmer i de første 3 timer efter penil vibratorisk stimulation. Undersøgelserne fra den modificerede Ashworth Skala viste en signifikant reduktion i spasticiteten umiddelbart efter penil vibratorisk stimulation.

I Blære-studiet indgik 14 rygmavsskadede mænd med læsioner fra C4 – T7 og dokumenteret detrusor hyperrefleksi. Der blev foretaget cystometri før og umiddelbart efter ejakulation fremkaldt med penil vibratorisk stimulation. Efter en måned, hvor personen selv havde

foretaget penil vibratorisk stimulation hver 3. dag i hjemmet, blev der atter foretaget cystometri for at undersøge langtidseffekten af behandlingen.

Hos alle deltagere fandtes detrusor hyperrefleksi og detrusor-sphinter dyssynergi ved den første undersøgelse. Efter 4 ugers behandling fandtes en signifikant øgning af blærekapaciteten fra en median på 190 mL ved baseline til 293 mL ($p=0.03$, Wilcoxon signed rank sum test for parrede data). Desuden fandtes en tendens til et reduceret blæretryk i fyldningsfasen.

Konklusionen var, at penil vibratorisk stimulation kan få en mulig betydning med hensyn til behandling af spasticitet og nedsat blærekapacitet hos nogle rygmarvsskadede mænd. Da det ikke er muligt på baggrund af dette studie på forhånd at udpege de personer, som vil have gavn af behandlingen, kan det nemt afprøves i det enkelte tilfælde. PVS kan anvendes i hjemmet af den rygmarvsskadede person selv, og er desuden uden kendte væsentlige bivirkninger.

Der mangler fortsat undersøgelser, evt. på en egnet dyremodel, som kan dokumentere virkningsmekanismen bag PVS.

STATUS OF PUBLICATION

Article I:

Læssøe L, Sønksen J, Bagi P, Biering-Sørensen F, Ohl DA, McGuire EJ and Kristensen JK. Effects of ejaculation by penile vibratory stimulation on bladder capacity in men with spinal cord lesions. *J.Urol.* 2003;**169**:2216-9.

Article II:

Læssøe L, Nielsen JB, Biering-Sørensen F, Sønksen J. Antispastic effect of penile vibration in spinal cord lesioned men. *Arch.Phys.Med.Rehabil.* 2004. In press.

ARTICLE I

ARTICLE II