

ORIGINAL ARTICLE

The effect of semiconditional dorsal penile nerve electrical stimulation on capacity and compliance of the bladder with deformity in spinal cord injury patients: a pilot study

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Study design: Bladder capacity, bladder compliance, the volume of the first overactive contraction, maximal volume during cystometry (CMG) and the vesicoureteral reflux, bladder wall deformity before and after semiconditional stimulation on DPN.

Objectives: To evaluate the effect of the semiconditional electrical stimulation on dorsal penile nerve (DPN) to improve the complicated bladder function in male with spinal cord injury (SCI).

Setting: Semiconditional stimulation system and urodynamic laboratory in a university hospital.

Participants: Six men (age, 33–59 years) with SCI incurred from 38 to 156 months before this study.

Intervention: semiconditional stimulation parameters were set during CMG and semiconditional stimulation on DPN by surface electrodes via Empi Focus stimulator was applied from 14 to 28 days, at home. Parameters about bladder function were measured before and after stimulation applied.

Result: All parameters for bladder after semiconditional stimulation were increased. Also, the vesicoureteral reflux and bladder wall deformity was improved in five of six patients.

Conclusion: Semiconditional electrical stimulation on DPN effectively suppresses neurogenic detrusor overactivity and distend the bladder physiologically in the SCI patient with a complicated bladder. The bladder capacity and compliance as well as the bladder wall deformity were improved as a result of this treatment.

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Keywords: spinal cord injuries; electric stimulation therapy/methods; neurogenic detrusor overactivity; neurogenic lower urinary tract symptom; urodynamic studies

INTRODUCTION

The goal of neurogenic bladder management in patients with spinal cord injury (SCI) is to achieve low-pressure urinary storage in bladders with continence, efficient and complete emptying with normal pressures, and preservation of kidney function, as well as preventing urinary tract infections. A poorly compliant bladder distends with high intravesical pressure at relatively low volumes and may lead to vesicoureteral reflux. These problems put the upper urinary tract at an even greater risk for deterioration.¹ Following the suprasacral SCI, the pontine micturition center cannot control bladder function and sphincter activity. Thus, after suprasacral SCI, detrusor overactivity, urethral smooth muscle synergia, and striated urethral muscle dyssynergia can occur.² The neurogenic detrusor overactivity correlates closely with low compliance and bladder wall deformity.³ Neurologic injury and denervation could increase the collagen content in the bladder wall. The increasing collagen content decreases the bladder wall's viscoelasticity and results in lower bladder compliance.⁴

Several methods for the control of the neurogenic detrusor overactivity have been recommended. Medications such as detrusor muscle relaxant are prescribed for patients with neurogenic detrusor overactivity in order to increase bladder capacity and compliance.⁵ Intravesical administration of capsaicin or resiniferatoxin achieves similar results. However, these above-mentioned methods may be

restricted in use for side effects such as the thirsty and hematuria. BoNT-A injection on bladder wall also use and did not make systemic effect that could occur with medication.

Another management option for the control of neurogenic detrusor overactivity is electrical stimulation. Electrical stimulation of pudendal afferent nerves has frequently been shown to inhibit neurogenic detrusor overactivity contraction in SCI patient.⁶ This stimulation suppresses pelvic nerve activity to detrusor muscle by inhibiting the sacral micturition reflex at either the afferent input or the parasympathetic pre-ganglionic motor neurons. Activation of the sympathetic neurons that run in the hypogastric nerves causes inhibition of the parasympathetic efferent motor neurons at the level of the pelvic ganglia.⁷ A study reported that electrical stimulation of dorsal penile nerve (DPN) effectively inhibited the overactive detrusor contractions in 12 out of 13 patients with suprasacral SCI.⁸ This method showed favorable result not only in the laboratory but also after discharge to home.⁹

Two different stimulation methods are introduced to inhibit the neurogenic detrusor overactivity contraction by electrical stimulation on pudendal afferent nerve: a continuous method and a conditional method. Continuous method applies the electrical stimulation throughout the process of bladder filling and conditional method starts the electrical stimulation as the intravesical pressure begins to rise at the beginning of an overactive contraction.^{10,11} Both contin-

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uous and conditional DPN stimulations reliably increased bladder capacity in patients with spinal injuries, and continuous stimulation significantly increased compliance.¹¹ However, both of these techniques have some disadvantages. The continuous stimulation might damage the tissue or induce neural habituation due to long-term electrical stimulation. It also results in high energy consumption.

The conditional stimulation, which is applied only at the onset of each bladder contraction during filling phase, might reduce such unwanted effects. However, it requires a method for detecting intravesical pressure or continuous patient alertness.

To improve such shortcomings, we attempted a semiconditional stimulation that starts with the first bladder contraction, and continues in cyclic pattern with preset on-off duration of burst of electric current. The purpose of this study was to evaluate the effect of the semiconditional stimulation on DPN to improve the storage function of the bladder with complications such as wall deformity and/or vesicoureteral reflux in male with SCI.

SUBJECTS AND METHODS

Patients

All procedures were in accordance with the standards of the local ethics committee. Six male patients with SCI participated in this study. They had symptoms of low-capacity bladder, such as frequency and incontinence. They all had radiologic findings of complication of bladder, such as vesicoureteral reflux and/or bladder wall deformity. Four patients showed grade II–III vesicoureteral reflux.¹² All of the patients managed their bladder with intermittent catheterisation every 4–6 h with or without reflex voiding. They could feel bladder contraction with normal sensation or autonomic dysreflexia (AD), such as sweating, increasing the blood pressure or flushing. The mean age of the patients was 44.50 ± 9.01 -year-old. The neurologic level of injury was between C₅ and T₁₀. The mean duration after injury was 76.83 ± 57.03 months. Five patients took some medication for controlling the neurogenic detrusor overactivity (Table 1).

Urodynamic study

Standard water cystometry (CMG) was performed in supine position. 3-way transurethral catheter was inserted in the bladder for pressure measurement, fluid infusion and ballooning. Pressure line were fluid filled and connected to transducer in water CMG (Menuet, Dantec, Denmark). Balloon of the Foley catheter was inflated to prevent leakage during the study. The initial fluid infusion rate was 30 ml min^{-1} , and from the time of the onset of the first overactive contraction of the bladder, it was infused slowly at a rate of 10 ml min^{-1} .

In the CMG test protocol using the electrical stimulation, CMG was stopped if

- (1) the electrical stimulation to pudendal nerve did not suppress the overactive contraction;
- (2) the infusion volume was over 450 ml;
- (3) the subject could not tolerate the test.

Table 1 Subject characteristics

Subject	Age (years)	Sex	NLOI	ASIA scale	Duration (month)	Voiding method	Medication	Duration of treatment (day)
A	46	Male	T8	A	38	P & C, CIC	Toterodine (detrusitol) 4 mg per day	26
B	59	Male	T8	A	35	P & C, CIC	Oxybutynin (ditropan) 30 mg per day	21
C	49	Male	T10	C	114	CIC	Oxybutynin (ditropan) 30 mg per day	28
D	40	Male	C6	A	50	P & C, CIC	Oxybutynin (ditropan) 30 mg and terazosin (hytrine) 4 mg per day	21
E	33	Male	C6	C	38	CIC	Oxybutynin (ditropan) 15 mg per day	28
F	40	Male	C5	B	156	P & C	No medication	14
Mean	44.50				76.83			23
s.d.	9.01				50.96			5.44

Abbreviations: ASIA scale, American Spinal Injury Association scale; CIC, clean intermittent catheterization; NLOI, neurological level of injury; P & C, percussion and Crede.

DPN stimulation

Electrical stimulation was applied using a portable neuromuscular stimulator, Empi FOCUS equipped with a remote switch, with which the parameters could be programmed. The DPN was stimulated using surface electrodes with 1 cm diameters. The cathode and anode were placed, proximally and distally, respectively, on the dorsum of the penile shaft. The stimulation parameters used were biphasic rectangular pulses of 25 Hz frequency, with 250 μs pulse width. The intensity of the stimulation used was twice that of the pudendo-anal reflex threshold.

Programming for semiconditional electrical stimulation

Semiconditional stimulation is the programmed current delivery, which starts with the first bladder contraction, and continues in cyclic pattern with preset on-off duration (Figure 1). A stimulation on the DPN of 50 s was repeated on every overactive contraction (C_n) during the CMG, which was sufficient to lower the detrusor pressure to pre-contraction level.¹³ The stimulation (S_n) was applied after the detrusor contraction was identified, by observing 2 or more typical oscillations in the detrusor pressure curve and detrusor pressure reached at 20 cm H₂O.

To determine the efficient 'off' duration, the period of suppression (T_n) by 50 s pudendal nerve stimulation was identified by measuring interval from the end of stimulation to the occurrence of following overactive contraction.

Switch-on duration of cyclic stimulation was 50 s, and switch-off duration was determined as 5 s shorter than the shortest duration of suppression (T_3) by 50 s stimulation. Establishing an adequate program usually required admission to the rehabilitation unit for 2–3 days.

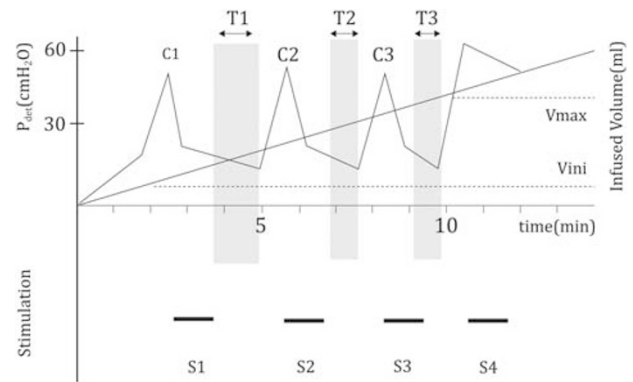


Figure 1 Electrical stimulator setting for Semiconditional electrical stimulation. T_1 , T_2 : duration of suppression after stimulation for inhibition of the first and next overactive contraction, respectively. V_{ini} : infused volume at first contraction (C_1). V_{max} : infused volume at last contraction, which was suppressed effectively by semiconditional stimulation on the DPN.

Treatment and evaluation

At home, the patient waited for bladder contraction with the preparations to apply the semiconditional electrical stimulation (ES), and when they felt the bladder contraction, stimulation was started. The patient used semiconditional ES at home, 1–3 times daily for 14–28 days. Mean duration of treatment was 23 ± 10.90 days. Standard water CMG with semiconditional ES was performed before and after the 2–4 weeks of treatment. The infusion volume at the first contraction (V_{ini}) and maximal volume that could be attained by semiconditional stimulation (V_{max}) were compared (Figure 1). Clinical bladder capacity, measured as the voiding volume by reflex voiding and/or clean intermittent catheterization (CIC), was recorded using a voiding diary. The severities of the vesicoureteral reflux and bladder wall deformity were evaluated upon cystography.

RESULTS

Figure 2 shows the result of treatment in patient C, a 49-year-old male who had a T₁₀ incomplete SCI and had a sense of bladder fullness and bladder contraction. He had managed his voiding dysfunction using CIC with Oxybutynin, and complained of increasing incontinence and decreasing voiding volume. According to radiological and water CMG findings, before treatment, the first overactive contraction occurred at 40 ml of infusion (V_{ini}). The bladder wall compliance was 3.08 ml per cm H₂O and GIII vesicoureteral reflux was presented (Figure 2a).

Neurogenic detrusor overactivity were well inhibited by the stimulation on the DPN and the duration of suppression after 50 s stimulation was longer than 20 s. We set the on and off duration of semiconditional stimulation at 50 s on, 10 s off. After 28 days of treatment with this semiconditional on dorsal penile stimulation at home, the infused volume at the 1st overactive contraction (V_{ini}) increased to 450 ml. His bladder wall compliance was increased to 26.47 ml per cm H₂O, and left-side vesicoureteral reflux disappeared (Figure 2b).

The capacity of the bladder increased in all patients after 2–4 weeks of treatment. V_{ini} increased from 45.17 ± 23.84 to 165.5 ± 156.5 ml after treatment (Figure 3a). V_{max} also increased from 203.67 ± 77.55 to

359.50 ± 70.43 ml after treatment (Figure 3b). Clinical bladder capacity measured by the voiding volume upon reflex voiding, and CIC increased from 201.67 ± 106.10 ml to 383.33 ± 51.64 ml after treatment (Figure 3c). Bladder compliance improved from 3.30 ± 1.89 ml per cm H₂O before treatment to 11.26 ± 9.18 ml per cm H₂O after treatment (Figure 4).

The vesicoureteral reflux present in four cases before the treatment disappeared, and the severity of bladder wall deformity improved in five cases after the treatment (Table 2).

DISCUSSION

Several methods for the control of neurogenic detrusor overactivity have been recommended. Medications, such as a detrusor muscle relaxant and an alpha-antagonist, are used in the neurogenic detrusor overactivity. These medications increase bladder capacity and compliance, while lowering bladder outlet pressure.⁵ However, these medications cause unwanted systemic effect.¹⁴ Intravesical administration of capsaicin or resiniferatoxin might result in unwanted side effects such as suprapubic burning sensation, hematuria, urine leakage, a hot flush, and/or signs of AD.¹⁵ BoNT-A injection into bladder detrusor muscle could use but it is expensive and it need the another procedure, cystoscopy. And sacral rhizotomy could also be used, but these methods are invasive and could incur complications.

Electrical stimulation of pudendal nerve afferents has been shown to produce acute inhibition of the neurogenic detrusor overactivity by stimulating the pudendal-pelvic spinal reflex pathways.^{9,11}

Although continuous DPN stimulation is an effective and simple way to increase bladder capacity in patients with SCI, in many situations it is not ideal. These constant current applications would shorten the battery and electrode life. If the patient can feel the sensation of bladder contraction, then conditional DPN stimulation of the DPN could be useful as an easy and safe technique to improve the

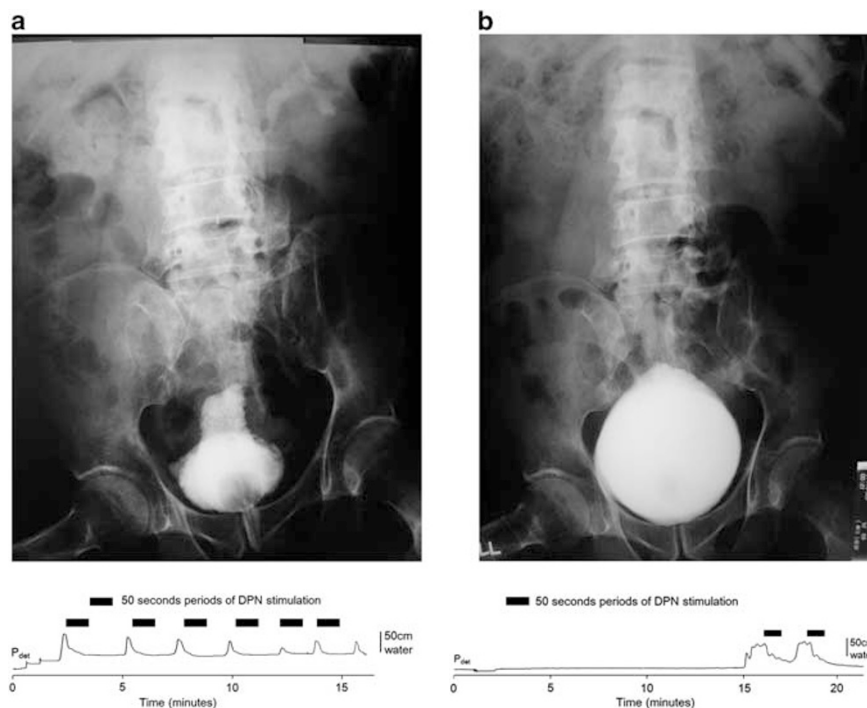


Figure 2 The effect of management using semiconditional stimulation on the DPN in Patient C who had neurogenic overactive bladder with deformity. (a) Before starting ES management, V_{ini} was 60 ml and compliance was 3.08 ml per cm H₂O. There was a grade III VU reflux on left side and level 4 deformity of bladder by X-ray. (b) After 4 weeks of management using semiconditional ES to DPN, V_{ini} and compliance was increased to 450 ml and 26.47 ml per cm H₂O, respectively. Also the VU reflux was disappeared and bladder wall deformity was improved to level 1.

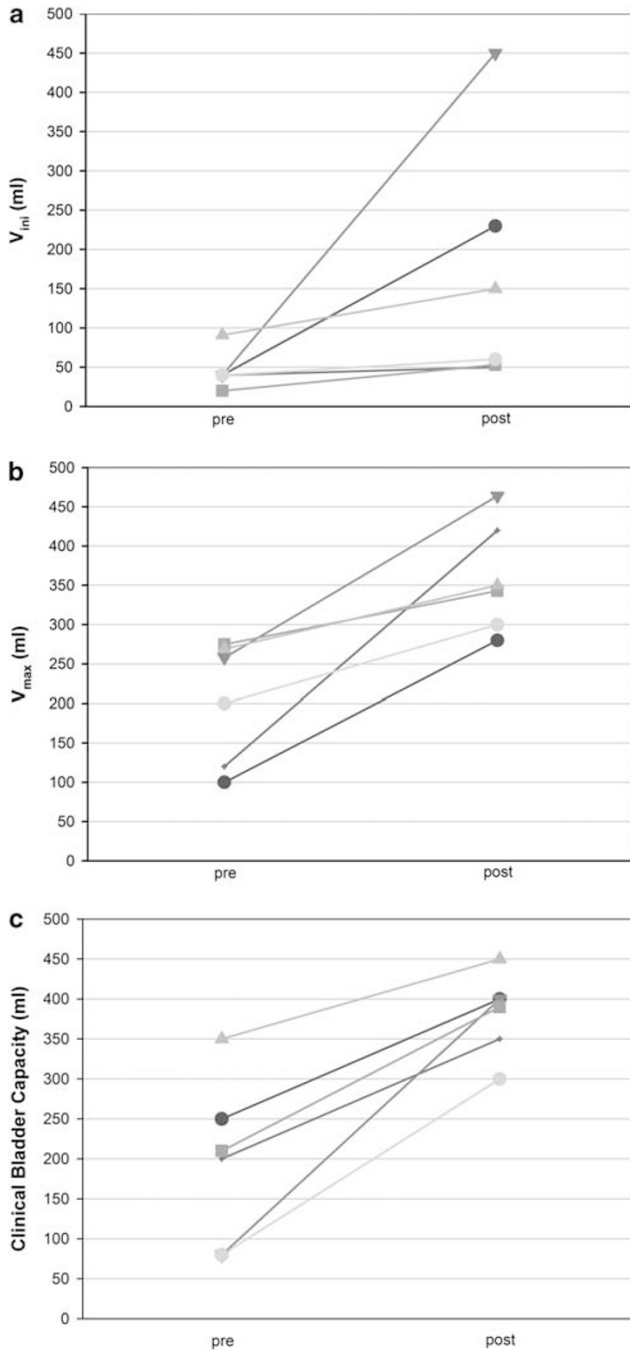


Figure 3 The effect of Semiconditional electrical stimulation on Volume. (a) The effect on volume of the first overactive contraction (V_{ni}). (b) The effect on the maximal volume attainable by semiconditional stimulation (V_{max}). (c) The effect on clinical bladder capacity (volume by reflex voiding and/or CIC).

condition.⁹ However, conditional stimulation requires that the patient concentrates on the sensation of bladder contraction in order to know when to switch on the stimulation each time.

Self-controlled semiconditional stimulation could be more efficient and convenient. This type of stimulation involves electrical stimulation at the first sensation of bladder contraction according to a preset program. Therefore, there is no need for the patient's continued concentration on incontinence or the voiding sensation.

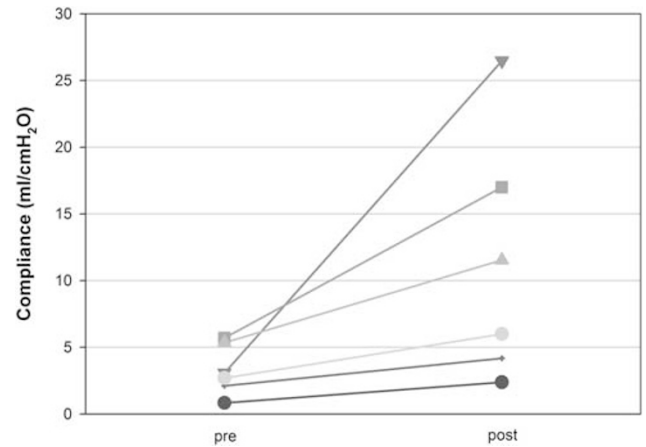


Figure 4 The effect of Semiconditional electrical stimulation on bladder compliance.

In the SCI patient, upper urinary tract damage and bladder deformity are secondary conditions, which are associated with low bladder compliance and low bladder capacity. Bladder compliance refers to the viscoelastic behavior of the urinary bladder that is dependent upon the viscoelastic properties of bladder components, including smooth muscle, collagen, and elastin.⁴ Chronic inflammation or chronic infection from cystitis secondary to CIC causes lower urinary tract complications. These complications include diverticula and trabeculation of the bladder, low bladder compliance, and low bladder capacity. Neurovascular injury, like SCI, increases the collagen content in the bladder wall. This decreases bladder compliance. These structural complications are difficult to treat.⁴

Surgical treatment, such as ureteral reimplantation, external sphincterotomy, open intravesical excision, direct removal of the wall deformity, or augmentation cystoplasty, is used to manage the complicated bladder. Finally, many of these patients who had taken the surgical treatment were found to suffer from early and late complications.¹⁶ Moreover, the surgical intervention requires invasive procedures and works only to increase the capacity of bladder, not to increase bladder compliance.

Another management option for low compliance and low-capacity bladder is bladder distension therapy. This treatment increases the bladder capacity by serially increasing the infusion volume of saline.¹⁷ Although bladder distension therapy was effective if it started from an early stage of SCI, before bladder compliance decreases. The risk of extraperitoneal rupture after bladder distension therapy should be considered.¹⁸

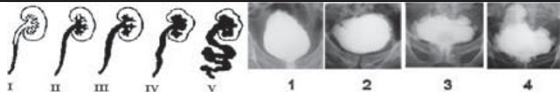
Semiconditional ES on the DPN in clinical situation is more advantageous compared with the distension therapy mentioned above. The semiconditional stimulation on the DPN could suppress unwanted detrusor overactivity during the filling phase and the bladder distension is much more physiologic because it is done by filling of urine.

If the semiconditional stimulation on the DPN showed favorable result during CMG with 30–50 ml min⁻¹ bladder-filling rate, the better outcome of semiconditional stimulation on the DPN stimulation could be expected in the clinical situation.

In this study, we investigated the transcutaneous semiconditional stimulation on the DPN in SCI patients who had urinary tract complications, including low bladder compliance and low bladder capacity. The suppression of neurogenic detrusor overactivity using semiconditional stimulation on the DPN, along with the

Table 2 Changes in the severity of the vesicoureteral reflux and bladder wall deformation

Subject	VU reflux ^a		Trabeculation/Diverticulum	
	Pre	Post	Pre	Post
A	GIII,Right	0	2	2
B	0	0	4	3
C	GIII,Left	0	4	1
D	GII, Left	0	2	1
E	0	0	3	1
F	GII, Left	0	4	1



^aVesicoureteral reflux is according to the International Classification of Vesicoureteral reflux.

physiologic distension of the bladder, improved not only the capacity of the bladder but also structural bladder deformity and the vesicoureteral reflux.

This clinical trial had some limitations. Firstly, we enrolled a small group of volunteers with complicated bladders in this study. Then, we recruited six patients who showed a positive response to conditional DPN stimulation. This procedure was not applied to women because there was difficulty in applying the electrical stimulator on the clitoris, as the surface electrode easily detached from the moist skin.

Secondly, the long-term effect of this therapy should be studied, as the mean duration time of therapy was 23 days. Thus, we should need further study on the long-term effects of therapy and the effect of cessation of therapy.

Thirdly, we did not check the bladder diary or questionnaire. Symptom of the patients improved but we checked the precise volume only.

We need additional investigation about methods and possible complications. Transcutaneous semiconditional stimulation on the DPN requires attaching the surface electrode on the patient's penis. Those patients who had SCI above C₇ were unable to place the surface electrode by themselves. At home, caregivers should help them to apply the electrode. Urine and sweat makes the surface electrode detach easily. Specialized design of surface electrode, or implantable electrode, is required in order to make attachment easier for patients with high cervical SCI. Possible development of AD should be considered, although we identified that hypertension induced by bladder distension reduced effectively by dorsal penile electrical stimulation in the previous study.¹⁹ A study warned that electrical stimulation of the pudendal nerve could decrease the heart rate by aggravating AD in patients with SCI above T₆. These pain sensations induced by electrical stimulation increased the sympathetic outflow.²⁰ In this study, AD during semiconditional stimulation on the DPN was not observed in the six subjects.

CONCLUSION

Semiconditional stimulation on the DPN effectively suppresses neurogenic detrusor overactivity and distends the bladder physiologically

in the SCI patient with a complicated bladder. The capacity and compliance of the bladder as well as the bladder wall deformity was improved as a result of this treatment.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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