Spinal Cord (2015) 53, 204–208

www.nature.com/sc

ORIGINAL ARTICLE

Sacral neuromodulation for neurogenic bladder and bowel dysfunction with multiple symptoms secondary to spinal cord disease

G Chen[1,2,3] and L Liao[1,2,3]

Study design: Retrospective case series.
Objectives: The primary aim was to assess the clinical effects of sacral neuromodulation (SNM) for neurogenic bladder and/or bowel dysfunction with multiple symptoms secondary to spinal cord disease or injury.
Setting: Beijing, China.
Methods: Between 2011 and 2013, 23 patients with multiple bladder and/or bowel problems secondary to spinal cord disease or injury were treated with a preliminary test SNM. If at least 50% clinical improvement occurred, then the patient underwent a permanent SNM procedure. We evaluated the patients using a bladder diary, post-void residual volume measurement and the Wexner questionnaire score for constipation before the test phase, during the test phase and after the permanent SNM.
Results: In the test phase, the rate of improvement in dysuria (29.4%) was significantly lower than urgency frequency (64.7%), urinary incontinence (69.2%) and constipation (75.0%). An implant was performed in 13 (56.5%) patients, including 4 patients who still used intermittent catheterization to exclude urine after permanent SNM because the symptom of dysuria could not be improved significantly and 1 patient who achieved $\geqslant$50% improvement in lower urinary tract dysfunction but not in constipation. During follow-up (17.5 ± 2.0 months), 1 patient (7.7%) failed and 1 patient had bilateral vesicoureteral reflux.
Conclusion: Chronic SNM cannot always resolve all the bladder and bowel symptoms secondary to spinal cord disease or injury, but combined with other treatments may help improve multiple symptoms.
Spinal Cord (2015) **53,** 204–208; doi:10.1038/sc.2014.157; published online 16 September 2014

INTRODUCTION

Control of the lower urinary tract is a complex, multilevel process that involves the peripheral and central nervous systems.[1] Thus, patients with spinal cord diseases or injuries often have multiple bladder problems, such as urinary urgency, frequency, incontinence and retention, and/or bowel disorders.[2,3]

In patients who fail conservative therapy, sacral neuromodulation (SNM), a minimally invasive and reversible procedure, is an alternative treatment option to surgical intervention. SNM has become a well-established treatment modality in recent years for patients with refractory non-obstructive chronic urinary retention, urgency-frequency syndrome and urgency incontinence.[4–6] Many patients have achieved significant improvement in lower urinary tract symptoms and bowel disorders, such as fecal incontinence and constipation.[5,7–9] Originally, SNM was not considered as an option for neurogenic lower urinary tract dysfunction (LUTD); however, some studies now suggest that SNM is also effective in this group of patients.[10,11] The aim of this retrospective study was to assess the clinical effects of SNM on patients with neurogenic bladder and/or bowel dysfunction who had multiple symptoms secondary to spinal cord disease or injury.

MATERIALS AND METHODS

Between 2011 and 2013, 23 patients (6 women and 17 men) with a mean age of 37.3 ± 2.9 years, underwent a preliminary test SMN for the treatment of neurogenic LUTD and/or bowel dysfunction secondary to spinal cord disease or injury.

All subjects previously underwent a detailed clinical evaluation, including a complete history, physical examination, urinary tract ultrasound and video-urodynamic examination. The technical procedure of the video-urodynamic examination was according to ICS Guidelines for Good Urodynamic Practice.[12] Nature of injury or disease was evaluated according to ASIA standards.[13] Detrusor overactivity (DO) was defined as a urodynamic observation characterized by involuntary detrusor contractions during the filling phase, which were spontaneous or provoked. Detrusor underactivity (DU) is defined as a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span. Detrusor sphincter dyssynergia (DSD) is defined as a detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated muscle, then occasionally flow may be prevented altogether.[14]

All the patients had more than one symptom of urinary urgency, frequency, incontinence and constipation. The distribution of the spinal cord diseases, symptoms and urodynamic findings are shown in Table 1. The mean time between the onset of the underlying spinal cord disease or injury and the

[1]Department of Urology, China Rehabilitation Research Center, Beijing, China and [2]Department of Urology, Capital Medical University, Beijing, China
[3]Co-first authors.
Correspondence: Professor L Liao, Department of Urology, China Rehabilitation Research Center, No. 10 Jiaomen Beilu, Beijing 100068, China.
E-mail: lmliao@263.net
Received 10 May 2014; revised 24 July 2014; accepted 5 August 2015; published online 16 September 2014

preliminary test was 15.5 ± 3.6 years. No patients had upper urinary tract damage, such as hydronephrosis and vesicoureteral reflux, or impairment of renal function. All eligible patients gave informed consent before starting the treatment program.

Before the test SMN was performed, all of the patients recorded voiding diaries and a post-void residual volume for ⩾ 3 days, and were evaluated using the Wexner questionnaire.[15] On the basis of the report from International Continence Society[14] and Wexner score system,[15] we categorized patient symptoms as urgency frequency, urinary incontinence, dysuria and constipation.

The specific steps of the SNM procedure have been described previously.[16,17] For the test SNM, the lead implantation (InterStim Model 3889; Medtronic, Inc., Minneapolis, MN, USA) was placed under local anesthesia. The left S3 root was systematically stimulated. Other roots were tested in patients who had no motor response. The lead was positioned by the left S3 root in 14 patients, the right S3 root in 8 patients and the right S4 root in 1 patient. According to the recommended parameters,[4] the neuromodulation device settings were as follows: frequency, 14 Hz; pulse width, 210 msec; continuous stimulation. The mean amplitude was 1.9 ± 0.8 V in our group.

The test results were evaluated based on a bladder diary, a post-void residual volume measurement using suprapubic ultrasonography, and the Wexner questionnaire score for constipation. The test was considered as positive if at least 50% clinical improvement was achieved and the symptoms reappeared after stopping SNM stimulation.

If the test was positive and the patients agreed to a permanent SNM implant, then an implant (InterStim Model 3023; Medtronic, Inc.) was connected to the tined lead inserted during the test (13 of 23 patients). The stimulator was then activated and continuous stimulation was begun the day after the implant procedure.

For quantitative values, data are presented as the mean ± standard error. Quantitative values were compared using a repeated-measures ANOVA and Tukey's multiple comparison test. Qualitative values were compared using a chi-square test. $P<0.05$ was considered as significant.

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

Table 1 Distribution of spinal cord diseases, symptoms and urodynamic analysis

Neurologic pathology	n = *23*
Myelomeningocele	9
Incomplete spinal cord injury	7
Spina bifida	3
Complete spinal cord injury	2
Post-resection of spinal cord tumor	1
Intravertebral anesthesia complication	1
Nature of injury or disease	n = *23*
Incomplete	21
Complete	2
Voiding diary	n = *23*
Urgency frequency	
Yes	17
No	6
Urinary incontinence	
Yes	13
No	10
Dysuria	
Yes	17
No	6
Constipation	
Yes	16
No	7
Urodynamic findings	n = *23*
DO + DSD	12
DO	6
DU	5

Abbreviations: DO, detrusor overactivity; DSD, detrusor-sphincter dyssynergia; DU, detrusor underactivity.

RESULTS

Overall, 23 patients underwent SNM testing, with a mean duration of the test phase between 7 and 28 days. The pooled success rate of the test phase based on the symptoms is shown in Table 2. The rate of improvement for dysuria (29.4%) was significantly lower than the rate of improvement for urgency frequency (64.7%), urinary incontinence (69.2%) and constipation (75.0%). No complications were reported in this initial phase.

An implant was performed in 13 patients (56.5%; 3 women and 10 men; Table 3) whose mean age was 34.1 ± 3.2 years and the mean time between the onset of the underlying spinal cord disease or injury and the test was 14.4 ± 4.8years. In eight patients (patient 1, 2, 4, 5, 6, 8, 10 and 13), all symptoms were improved ⩾50%. For three patients (patient 3, 7 and 12) symptoms of urgency frequency, urinary incontinence and constipation all achieved ⩾50% improvement, but the residual urine volume did not decrease significantly. Patient 9 only achieved a positive result for constipation but no improvement on dysuria, and patient 11 only achieved a positive result for LUTD. However, these patients still accepted the permanent SNM including four patients (patient 3, 7, 9 and 12) who still used intermittent catheterization to exclude urine.

The mean duration of follow-up was 17.5 ± 2.0 months. SNM was successful (⩾50% improvement) in 12 of 13 patients (92.3%). Figures 1–4 show the variation in clinic data and Wexner scores during the entire test phase, and during the last follow-up visit compared with baseline.

One patient with an incomplete spinal cord injury and symptoms of dysuria and constipation did not achieve long-term improvement. In the test phase, the patient only achieved a positive result in constipation with 100% improvement, but the effect was lost 3 months after permanent SNM.

One patient with a myelomeningocele had ⩾50% improvement in urge incontinence, frequency urgency, dysuria and constipation during the test phase, and experienced bilateral vesicoureteral reflux 1-year post-second phase (SNM procedure). The reflux resolved after insertion of an indwelling catheterization for 6 months. The patient continued using intermittent catheterization and no other complications were reported.

Table 2 Results of the test stimulation based on symptoms

	Positive (%)	*Negative (%)*	P-*value*
Urgency frequency	11 (64.7)	6 (35.3)	0.0348
Urinary incontinence	9 (69.2)	4 (30.8)	
Dysuria	5 (29.4)	12 (70.6)	
Constipation	12 (75)	4 (25)	

Positive: ⩾50% improvement; Negative: <50% improvement. $P<0.05$ was considered as significant.

Table 3 Results of symptom improvements in patients who underwent permanent SNM

Patient	*Neurologic pathology*	*Urodynamic findings*	*Urgency frequency*	*Urinary incontinence*	*Dysuria*	*Constipation*
1	Myelomeningocele	DO + DSD	Y[a]	Y[a]	Y[a]	Y[a]
2	Spina bifida	DO	Y[a]	Y[a]	N	N
3	Incomplete spinal cord injury	DO + DSD	Y[a]	Y[a]	Y	Y[a]
4	Incomplete spinal cord injury	DO	Y[a]	Y[a]	N	Y[a]
5	Myelomeningocele	DO + DSD	Y[a]	N	Y	N
6	Incomplete spinal cord injury	DU	N	N	Y[a]	Y[a]
7	Post resection of spinal cord tumor	DO + DSD	Y[a]	Y[a]	Y	Y[a]
8	Myelomeningocele	DO + DSD	Y[a]	Y[a]	Y[a]	Y[a]
9	Incomplete spinal cord injury	DU	N	N	Y	Y[a]
10	Myelomeningocele	DO	Y[a]	N	N	Y[a]
11	Myelomeningocele	DO + DSD	Y[a]	Y[a]	Y[a]	Y
12	Myelomeningocele	DO + DSD	Y[a]	Y[a]	Y	Y[a]
13	Incomplete spinal cord injury	DO + DSD	Y[a]	Y[a]	Y[a]	Y[a]

Abbreviations: DO, detrusor overactivity; DSD, detrusor-sphincter dyssynergia; DU, detrusor underactivity; N, no; Y, yes.
[a]$\geqslant$50% improvement.

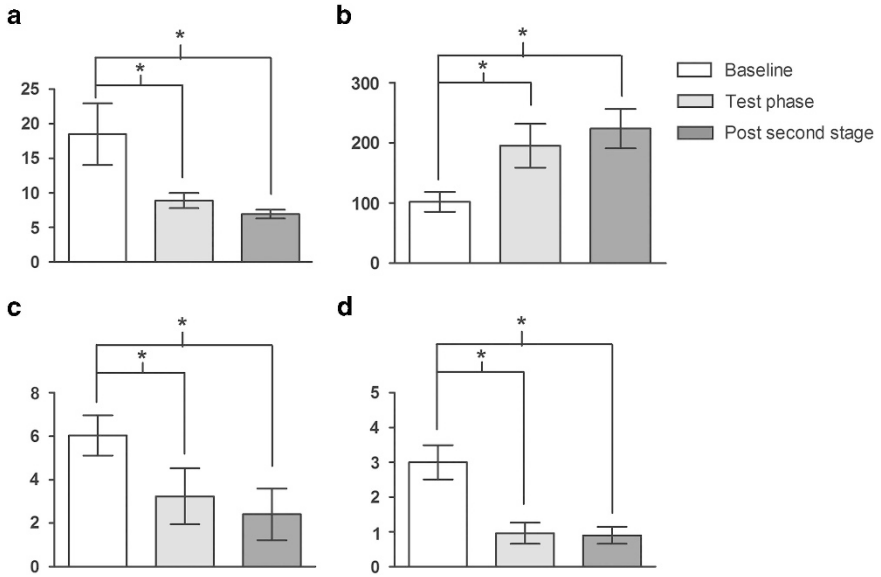

Figure 1 Clinic data for patients with urgency frequency at baseline, test phase and post-second stage. (**a**) Number of voids/24 h; (**b**) volume per void (ml); (**c**) number of episodes of urgency/24 h; (**d**) degree of urgency (0–5, 0: no urgency, 5: maximum urgency with maximum disturbance of lifestyle). *$P<0.05$, $n=11$.

DISCUSSION

SNM is an established, minimally invasive and reversible surgical procedure for LUTD and bowel dysfunction.[4–9] The mechanism of action is not entirely clear; however, inhibition of afferent signals presumably interrupts inappropriate detrusor contractions.[18,19] Although originally not thought to be a promising treatment option for patients with neurogenic bladder disorders, more recent studies suggest that these patients can benefit from SNM and up to 68% of patients in the test phase and 92% of patients in the permanent SNM phase can be successfully treated;[10,11] we report similar success rates (56.5 and 92.3%, respectively).

Patients with spinal cord disease or injury often suffer not only from LUTD, but also from bowel dysfunction. Because SNM may be beneficial for both conditions, patients with combined dysfunction are good candidates for SNM, which can have a high impact on the associated quality of life.[10,11] In our group, all the patients had multiple symptoms. In these patients, SNM may only have had an effect on one or two symptoms, but if quality of life could be improved, an implant may be indicated, even if not all symptoms are improved. In our study, 13 patients who underwent permanent SNM had multiple symptoms before the procedure, including 3 patients whose symptoms of urgency-frequency, urinary incontinence and constipation achieved $\geqslant$50% improvement, although the residual urine volume did not decrease significantly; one patient achieved positive results with respect to constipation only but no improvement on dysuria, and one patient achieved positive results with respect to LUTD only. However, these patients still accepted the permanent SNM including four patients who still used intermittent catheterization to exclude urine.

In this study, only two patients with complete loss of spinal cord function (two patients with complete spinal cord injury) underwent SNM testing as in Table 1. However, the two patients all had no

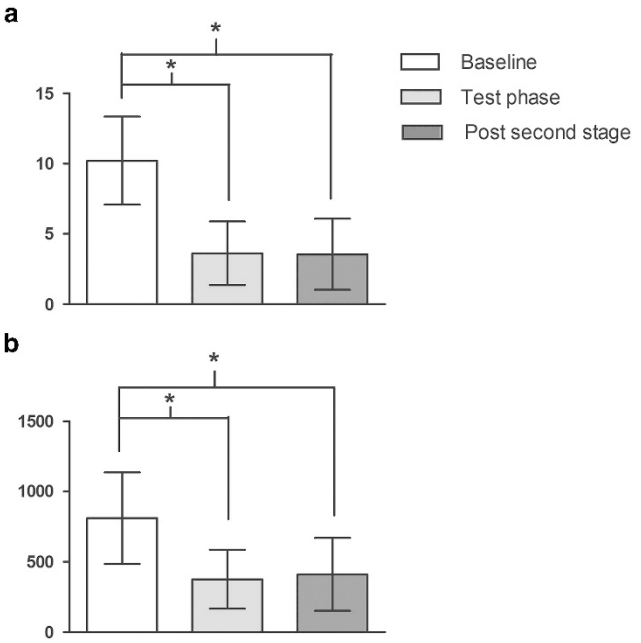

Figure 2 Clinic data for patients with urinary incontinence at baseline, test phase and post-second stage. (**a**) Number of leakage episodes/24 h; (**b**) volume of leakage/24 h (ml). *$P<0.05$, $n=9$.

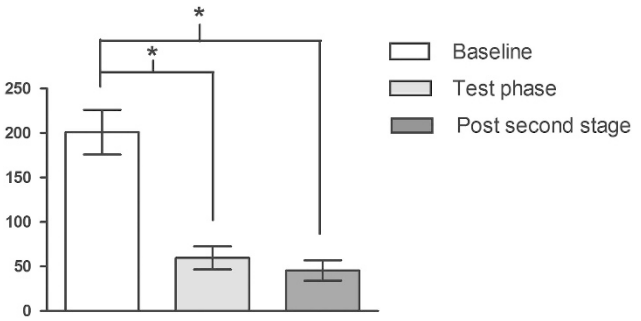

Figure 3 Residual volume for patients with dysuria (ml) at baseline, test phase and post-second stage. *$P<0.05$, $n=5$.

improvements for clinical symptoms, and did not go into the permanent implantation phase finally (see Table 3). But the results of the recent literature showed that early SNM can prevent urinary incontinence after complete spinal cord injury.[20] They indicated acute SCI initially leads to detrusor acontractility and complete urinary retention, which is followed by slow overactivity development and urinary incontinence caused by C-fiber-mediated spinal reflex pathways, probably related to the interrupted regulatory mechanism between the end organ (bladder and urethral sphincter and midbrain for the two separated pathways of micturition and continence). Early SNM bilateral implantation during the bladder-areflexia phase might preserve nerve plasticity, such that C-fibers remain silent, DO is avoided, and sympathetic preganglionic neuron activation in the thoracolumbar cord is suppressed. So we should carry on SNM implantation before detrusor status change from acontractility to overactivity in complete spinal cord damage patients in future.

During follow-up, one patient who had dysuria before the test phase had bilateral vesicoureteral reflux 1-year post implantation,

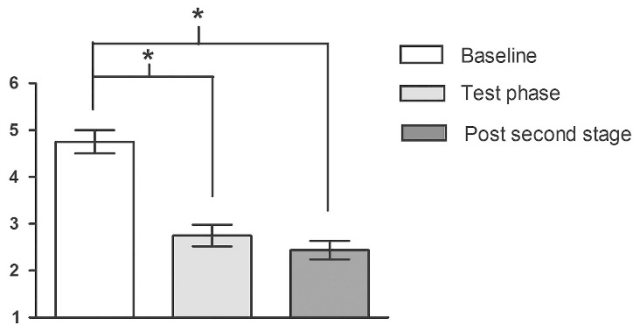

Figure 4 The Wexner scores for patients with constipation (scale 0–30, 0: normal, 30: maximum constipation with maximum disturbance of lifestyle) at baseline, test phase and post-second stage. *$P<0.05$, $n=9$.

although the residual urine volume decreased significantly (>50%) after permanent SNM. The patients with dysuria may have also used Valsalva maneuvers to empty their bladders after implantation, which has not been documented by urodynamic testing to be safe. Wyndaele *et al.*[21] reported that with increasing time, >40% of patients using Valsalva maneuvers had influx into the prostate and seminal vesicles, which suggests that bladder expression may generate reflux to the upper urinary tract. We suggest those patients with multiple bladder problems, such as urge incontinence, urgency frequency and dysuria, consider permanent SNM combined with intermittent catheterization if Valsalva maneuvers are documented to be dangerous by urodynamic testing.

Currently, there are no good measures to predict which patients will achieve sufficient benefit to warrant permanent SNM implantation. In our study, we found that the rate of improvement for dysuria (29.4.0%) was significantly lower than urgency frequency (62.5%), urinary incontinence (66.7%) and constipation (73.3%) during the test phase, which is different from what has been reported in the non-neurogenic population. In non-neurogenic bladder patients, 70–83% of urinary retention patients achieve improvement >50%.[4] The recent literature also showed a 42.5% success rate for neurogenic non-obstructive urinary retention in incomplete spinal cord patients.[22] We thought that the reason for dysuria in patients with neurogenic bladder was different with it in non-neurogenic population. Non-neurogenic urinary retention was thought to be psychogenic, but several findings such as hyperactivity of the pelvic floor and lack of pelvic floor control in many patients with urinary retention have suggested an organic origin. SNM may function by directing the patient to relocalize the pelvic floor and inhibit the urethral activation caused by exaggerated guarding reflex and allow bladder emptying.[18] However, the dysuria was resulted from DSD (12 patients) and DU (5 patients) in this study. We hypothesized that SNM was difficult to restore the coordination between detrusor and sphincter when micturition. Ongoing investigations should focus on those factors increasing the success rate of first stage of SNM; for example, adopting bilateral SNM and the time/duration of efficacy during testing SNM.

In our study, patients with neurogenic bladder and bowel dysfunction secondary to spinal cord disease or injury seem to benefit and maintain improvement during follow-up. These improvements may depend on the type of underlying spinal cord disease, and in particular, whether or not there is progression. Future studies may identify some conditions that are more amendable to treatment with SNM in patients with spinal cord disease or injury.

In conclusion, chronic SNM is an effective and safe treatment alternative for neurogenic lower urinary tract and bowel dysfunction with multiple symptoms secondary to spinal cord disease or injury. SMN may not resolve all of the symptoms in every patient, but combined with other treatments, SNM may be a good option for those patients with multiple symptoms.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

This study was supported by China National Technology R&G Program (No. 2012BAI34B02).

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