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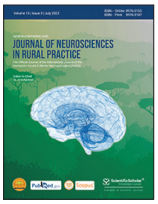

Original Article

Neuromodulation of spinal reflex pathway for the treatment of detrusor overactivity by medial plantar nerve stimulation at surface of sole of foot in patients with spinal cord injury

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ABSTRACT

Objectives: Suprasacral spinal cord lesions are prone to have neurogenic detrusor overactivity leading to urinary incontinence. Current medical management has known side-effects and often surgical managements are irreversible. Electrical stimulation to modulate spinal reflex pathway having same nerve root as urinary bladder is reported in the literature. This study aimed to reduce detrusor overactivity in patients with spinal cord injury (SCI) using surface electrical stimulation of medial plantar nerve at the sole of foot.

Materials and Methods: Twenty adults with SCI having episode of at least 1 leak/day due to detrusor overactivity as diagnosed by cystometrogram (CMG), were on clean intermittent catheterization and ankle jerk was present consented for the study. Participants were asked to maintain bladder diary a week before and during 2 weeks of treatment. CMG was done on day-0 and day-14. cmcUroModul@tor®, an inhouse developed electrical stimulator was used for ½ h daily for period of 2 weeks. Patient satisfaction feedback questionnaire was taken on completion of treatment. CMG data were analyzed using Wilcoxon signed-ranked test while bladder diary was analyzed using binomial distribution. $P < 0.05$ was considered as statistically significant. Institutional Review Board (IRB) and ethics committee of Christian Medical College, Vellore, approved the study (CMC/IRB/11061).

Results: Statistical significant improvement in maximum detrusor pressure ($P = 0.03$) and cystometric capacity ($P = 0.04$) was observed. Of 20 subjects, 18 showed improvement in bladder diary.

Conclusion: Neuromodulation of medial plantar nerve at sole of foot by surface electrical stimulation is non-invasive, cost-effective, and alternative simple treatment modality for urinary incontinence due to detrusor overactivity.

Keywords: Detrusor overactivity, Urinary incontinence, Spinal cord injury, Neuromodulation, Surface foot stimulation, Medial plantar nerve

INTRODUCTION

Neurogenic detrusor overactivity results in high bladder pressure which may lead to urinary incontinence.[1] Urinary bladder incontinence is a stressful and depressive event for an individual with spinal cord injury (SCI) which hampers daily living activities and leads to societal withdrawal.[2] Restoration of continence was the highest felt research priorities reported by individuals with SCI.[3-5] The current medical management of detrusor overactivity includes use of anticholinergic drugs along with clean intermittent catheterization (CIC) and often surgical managements are irreversible.[6,7] Long-term usage of anticholinergics is known to cause side-effects such as blurring of vision, dryness of mouth, cognitive impairment, and dementia.[8] Modulation of sacral reflex arc using electrical stimulation is an alternative approach. Several studies, including the one conducted at our center, have reported stimulation of sacral somatic nerves such as tibial nerve, pudendal nerve, or its branches, had improved continence after few weeks of treatment.[9-11]

Our previous work demonstrated that after 2 weeks of surface electrical stimulation of posterior tibial nerve, there was improvement in bladder capacity and reduction in number of leaks as reported in bladder diary.[1,9] This study is continuation of our research in this area. We report our findings on foot surface stimulation of medial plantar nerve for reducing detrusor overactivity by modulating of spinal reflex pathways.

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MATERIALS AND METHODS

This interventional trial was approved by Institutional Review Board (IRB) and ethics committee of Christian Medical College Vellore (CMC/IRB/11061). Twenty adults with SCI meeting inclusion criteria consented for the study. This study met the regulations of the Declaration of Helsinki.

Adults with SCI having at least one episode of leak/day, on CIC, presence of ankle jerk, and Cystometrogram (CMG) proven detrusor overactivity, were recruited. Ankle jerk confirmed spinal reflex loop arc's integrity to tibial nerve. The key exclusion criteria were patients with peripheral neuropathy, recurrent urinary tract infection (UTI), mental illness, stress-related incontinence, pregnant women, and presence of implantable devices.

Medications related to treatment of detrusor overactivity were withheld 1 week before and during stimulation period (i.e., total 21 days). Start and end of stimulation were considered day-1 and 14, respectively, while days before the treatment were considered from -7^{th} to 0^{th} day. Participants maintained bladder diary for all 21 days. Participants were advised for 4-hourly CIC. Bladder diary had columns for entering urine output, record of leaks, and fluid intake in a day. Demographic details were recorded on day-0.

CMG was performed using commercially available machine, on day-0 and day-15. Stimulation was given using a custom-built nerve stimulator, cmcUroModul@tor®. The parameters for stimulation were same as our earlier study.[1,9] The current strength was chosen based on plantarflexion of ankle and or maximum current tolerated by a person.

Electrical stimulation was given using self-adhesive gel electrodes (3.5×2 inch^2) wherein the cathode was positioned at the medial arch of foot over medial plantar nerve while placement of anode was at metatarsophalangeal joint approximately 2 cm apart from cathode [Figure 1]. The electrical stimulator was given for ½ h daily for period of 2 weeks.

Figure 1: Stimulation site with cmcUroModul@tor.

Analysis of data from bladder diary

The parameters obtained from the bladder diary were categorized into five categories: (1) Number of leaks in a day, (2) maximum urine output in a day, (3) total fluid intake in a day, (4) total volume of urine voided in a day, and (5) number of CIC. Trend lines were drawn for bladder diary parameters and were analyzed for -7^{th} to 14^{th} day for each patient. Reduction in frequency of leaks, increased volume of urine voided, increased fluid intake, and increased maximum urine voided in a day were marked as an improvement. Participants with no significant change in these parameters were put into no-change category. At the same-time, those with an increased tendency in frequency of leaks or a decrease in fluid intake or a decrease in maximum volume of urine passed or reduction in urine voided in a day were marked as deteriorated state of urinary bladder. The minimum number of CIC advised per day was six, that is, 4-hourly. Decrease in number of CIC was marked as an improvement, while an increase in CIC was marked as a deteriorated state of bladder. The bladder diary of a subject who developed UTI while undergoing study period was excluded from analysis for the days which he was clinically managed for UTI and was given additional 1 week of stimulation with no change in stimulation protocol. A binomial distribution test with 50% test proportion was used to compare between improved and not improved population.

Analysis of data from CMG

Pre- and post-parameters obtained from CMG procedure (maximum detrusor pressure, cystometric capacity, and reflex volume) were analyzed. The urodynamic procedure and reporting was in compliance with the International Continence Society guidelines.[12]

Post- and pre-CMG parameters were determined as percentage change for each patient [Equation 1].

$$\frac{(Post - Pre)}{Pre} \times 100 \quad [1]$$

Percentage change >10% was marked as an improvement, while percentage change <−10% was deemed to have worsened the bladder state. Percentage change falling between −10% and +10% was marked as no improvement.

Pre- and post-urodynamics parameters were analyzed for statistical significance using the Wilcoxon signed-rank test. At 95% of confidence interval, $P < 0.05$ was considered as significant.

Feedback questionnaire

Each participant filled a satisfaction questionnaire at the end of study.

RESULTS

Twenty SCI patients (3 female and 17 male) with mean age of 36 years, meeting the key inclusion criteria, were recruited. Participant's demographic details are shown in [Table 1].

Following treatment, 12 subjects showed an increase in reflex volume. Six participants showed a decrease in the reflex volume, and two had no significant change. Thirteen patients were seen to reduce maximum detrusor pressure from the baseline, while three had increased and four did not show any significant change. Fourteen subjects showed considerable improvement in bladder capacity, three did not show any improvement, while bladder capacity was reduced in three persons. Change in maximum pressure was −12.49 ± 35.69 (mean ± sd) cm H_2O, reflex volume was 45.75 ± 88.71 mL, and cystometric capacity was 69.88 ± 104.64 mL [Table 2]. The *P*-value, for pre- and post-change in detrusor pressure ($P = 0.03$) and cystometric capacity ($P = 0.04$), was significant. However, change in reflex volume ($P = 0.13$) was not significant.

[Figure 2] shows a trend in number of leaks (2a), fluid intake in a day (2b), urine output in a day (2c), maximum urine output of the day (2d), and similar number of CIC (2e) in bladder diary of a subject who had a noticeable improvement. Number of CIC reduced in three participants. During the study period, one subject developed UTI, which was managed with culture-specific antibiotics and stimulation period was extended to compensate for these days. Eighteen subjects showed improvement in bladder diary, while two participants did not show any noticeable change [Table 3]. Binomial distribution test on bladder diary data showed significant improvement ($P = 0.001$). All subjects reported satisfaction with treatment for the simplicity and ease in the stimulation procedure.

DISCUSSION

Management of neurogenic bladder focuses to protect upper urinary tract with a goal to provide low-pressure storage of urine in the bladder and continence. Detrusor overactivity leads to high bladder pressure, small bladder capacity, possible vesicoureteral reflux, and subsequently impairment of renal functions.[13] CIC and anticholinergic drugs are the gold standards in the management of detrusor overactivity. Intravesical agents such as Botulinum-A, Oxybutynin, and Capsaicin are commonly used for reduction of urinary incontinence due to detrusor overactivity. These medical management have side-effects and long-term efficacy is not certainty.[14]

Alternatively, sacral neuromodulation, pudendal nerve, and tibial nerve stimulation are novel approaches in management of urinary incontinence due to detrusor overactivity. These

Table 1: Demographic characteristics of the study population.

Subject	Age	Duration of injury (month)	Level of injury	Type of Injury	Cause of Injury	AIS Grade	Sex
S1	45	18	T5	I	N	-	F
S2	47	12	L3	I	N	-	M
S3	46	99	T5	C	T	A	M
S4	28	9	T5	C	T	A	M
S5	37	60	T5	C	T	A	M
S6	26	15	T7	I	N	-	M
S7	36	18	T4	C	T	A	M
S8	27	54	T5	C	T	A	M
S9	25	80	T6	C	T	A	M
S10	34	42	T4	I	T	B	M
S11	28	42	C5	I	N	-	F
S12	24	12	T4	C	T	A	M
S13	47	48	T10	I	T	B	M
S14	44	36	T8	I	N	-	M
S15	59	21	T9	C	T	A	M
S16	27	12	C5	I	T	C	M
S17	23	30	T4	C	N	-	F
S18	56	120	T5	C	T	A	M
S19	22	29	T8	I	N	-	M
S20	41	132	C8	I	N	-	M
Median	35	33		I=10	T=12	A=9	F=3
Min	22	9		C=10	N=8	B=2	M=17
Max	59	132				C=1	

I=Incomplete, C=Complete, N=Non-traumatic, T=Traumatic, M=Male, F=Female, AIS=American Spinal Injury Association Impairment Scale

Table 2: Pre and Post CMG data.

Subject	Reflex Volume			Max Detrusor Pressure			Cystometric Capacity		
	Pre	Post	% change	Pre	Post	%Change	Pre	Post	%Change
S1	202	171	-15.3	34	31	-8.8	205	177	-13.7
S2	342	275	-19.6	53	48	-9.4	397	357	-10.1
S3	206	347	68.4	64	88	37.5	265	820	209.4
S4	136	176	29.4	94	73	-22.3	152	273	79.6
S5	117	200	70.9	26	19	-26.9	117	207	76.9
S6	47	69	46.8	109	82	-24.8	53	97	83.0
S7	125	404	223.2	162	86	-46.9	128	439	243.0
S8	230	347	50.9	73	76	4.1	381	500	31.2
S9	168	221	31.5	56	41	-26.8	169	246	45.6
S10	340	337	-0.9	100	82	-18.0	343	355	3.5
S11	24	33	37.5	91	42	-53.8	24	47	95.8
S12	296	165	-44.3	53	47	-11.3	354	169	-52.3
S13	152	122	-19.7	101	87	-13.9	163	147	-9.8
S14	180	120	-33.3	44	84	90.9	270	171	-36.7
S15	196	143	-27.0	90	69	-23.3	200	196	-2.0
S16	130	219	68.5	61	58	-4.9	130	219	68.5
S17	64	84	31.3	77	49	-36.4	68	85	25.0
S18	76	83	9.2	93	132	41.9	81	83	2.5
S19	30	128	326.7	158	49	-69.0	30	130	333.3
S20	157	284	80.9	47	34	-27.7	157	510	224.8
Mean	160.9	196.4	45.75	79.3	63.85	-12.49	184.35	261.4	69.88
Std. Dev	92.79	105.77	88.71	36.41	26.72	35.69	116.19	189.14	104.64
Std. Err	20.75	23.65	19.87	8.14	5.98	7.98	25.98	42.29	23.40
		Improved 12 Worsen 6 Not improved 2			Improved 13 Worsen 3 Not improved 4			Improved 14 Worsen 3 Not improved 3	

approaches have varied success rates preventing them to replace standard medical practices.[10,11] Many researchers have used percutaneous tibial nerve (PTN) stimulation technique with a needle electrode, as anode, is inserted posterior to the medial malleolus and a surface electrode, as cathode, over the ipsilateral calcaneus with maximum current strength of 10 mA was used.[15,16] Our previous study was first to establish surface stimulation of tibial and dorsal penile nerve in modulating urinary bladder reflex pathway, a neuromodulation technique. Participants who had undergone treatment witnessed beneficial effects of this approach and found to be easy-to-implement non-invasive technique.[1,9]

The studies on use of electrical stimulation of the somatic afferent pathways for bladder reports effectiveness of neuromodulation technique.[17,18] Tai *et al*. have demonstrated usage of foot stimulation in suppression of bladder overactivity in the cat model.[17] Medial plantar nerve is a mixed sensory-motor nerve and is a branch of posterior tibial nerve. These have same spinal pathway targeted for sacral neuromodulation and are also involved in motor and sensory control of pelvic floor and bladder.[16] Urinary bladder activity is inhibited by electrical stimulation of these somatic afferent fibers leading to central inhibition of the micturition reflex pathway in the brain or spinal cord.[16]

This prospective study was conducted to observe effect of surface foot stimulation of medial plantar nerve in reducing the detrusor overactivity. Surface stimulation is preferred over percutaneous stimulation due to its non-invasive approach. Further, current strength is higher in surface stimulation than percutaneous stimulation to overcome skin impedance. We found that gel-based self-adhesive surface pad electrodes are cost-effective, convenient, and easy to use for home-based therapy. The bill of material for inhouse developed stimulator, that is, cmcUroModul@tor® is <Rs 2000.

To check the intact spinal reflex bladder, f-wave test from PTN was used in our previous study.[1,9] However, additional expenses and a visit to electrophysiology laboratory are required for f-wave test leading to delay in treatment. Hence, the presence of ankle jerk was used.

The parameters accessed from CMG were maximum detrusor pressure, cystometric capacity, and reflex-volume. There was statistical significant improvement in maximum detrusor pressure ($P = 0.03$) and cystometric capacity ($P = 0.04$) while

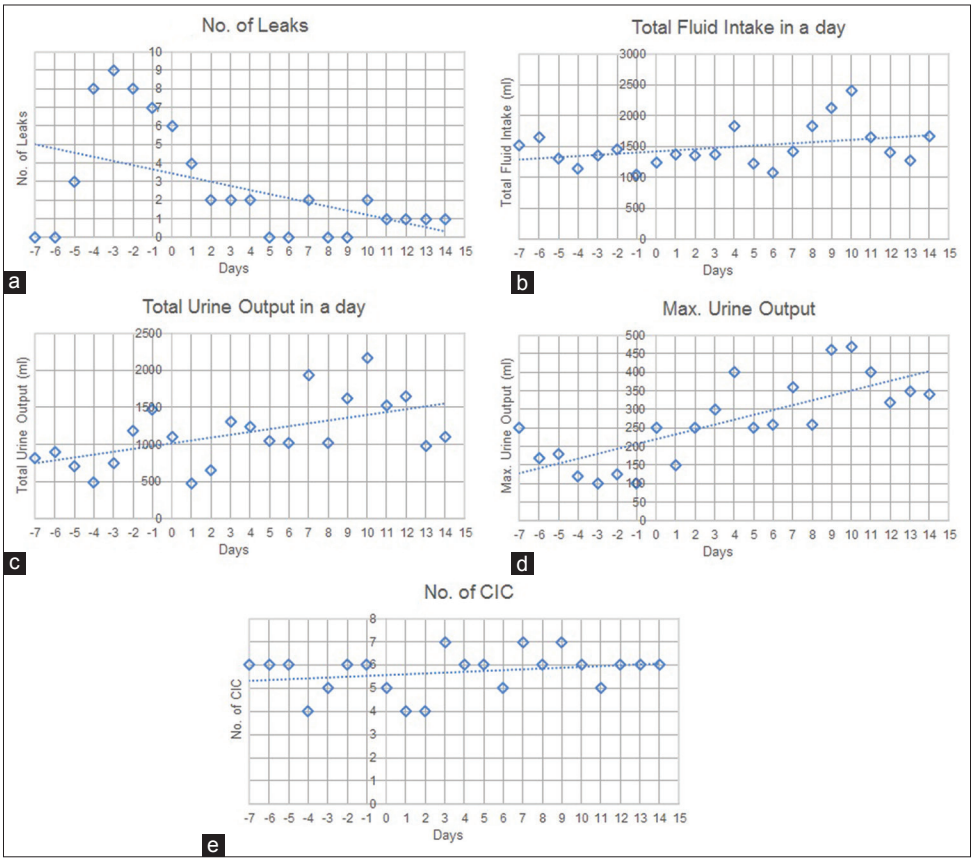

Figure 2: Bladder diary of a participant during the study period showing, (a) number of leaks, (b) total fluid intake in a day, (c) total urine output in a day, (d) maximum urine output in a day, and (e) number of clean intermittent catheterization.

Table 3: Binomial distribution test using voiding diary data.

Sample size (n)	Improved no. (%)	Not improved no. (%)	Test prop	*P*-value
20	18 (90%)	2 (10%)	0.5	0.001

reflex volume ($P = 0.13$) did not show statistical significant improvement. All participants were satisfied with ease of procedure and treatment methodology.

The bladder diary had record of urinary output and fluid intake of the day. After 2 weeks of electrical stimulation therapy, it was observed from the bladder diary that 18 participants had improvement in cystometric capacity, reduction in number of leaks, and increase in maximum urine output in a day. There was no significance difference in two participants while statistically significant improvement in the parameters from bladder diary was observed suggesting the effectiveness of electrical stimulation. There was an improvement in total urine voided throughout the day and maximum urine voided in a day in a subject (S1). However, in 2nd week of stimulation therapy, he had a rise in number of leaks. Clinical symptoms correlated to urinary infection and thus he was treated with culture-specific antibiotics, and therapeutic stimulation was extended for 1 week.

The bladder diary of a subject (S20) presented increased fluid consumption and improvement in urine voided without any statistical significant reduction in number of leaks. The subject's transrectal ultrasound imaging showed open bladder neck condition. Despite this, there was 224% of increase in cystometric capacity, 80% of increase in reflex volume, and 27% of decrease in maximum detrusor pressure. This case is an instance of mixed pathology with a combined open bladder neck and detrusor overactivity condition.

CONCLUSION

This pilot study on participants with detrusor overactivity due to SCI showed improvement in bladder function. Pre- and post-stimulation of medial plantar nerve at the sole of foot following 2 weeks of daily ½ h therapy showed improvement in bladder diary and CMG.

Our study reports statistically significant increase in cystometric capacity and reduction in maximum detrusor pressure. In contrast, reflex volume did not show any statistically significant results.

Of 20 subjects, 18 showed improvement in bladder diary while two participants did not improve. The results of this study indicates that the stimulation therapy given for the period of 2 weeks can modulate the bladder reflex pathways thereby it has potential for an alternative and safe treatment for urinary incontinence due to detrusor overactivity. None of the subjects reported any adverse effect of the treatment. This study will pave the way for larger studies for statistically conclusive results. Furthermore, studies involving standardization of stimulation parameters are warranted to set up treatment protocol as alternative approach for urinary bladder dysfunction due to bladder overactivity.

Results of our study show that neuromodulation therapy by surface foot stimulation of medial plantar nerve is non-invasive, cost-effective, safe and simple, and have potential substitute for management of urinary bladder incontinence due to overactive detrusor.

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Declaration of patient consent

The authors certify that they have obtained all appropriate consent.

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Conflicts of interest

There are no conflicts of interest.

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