# Electrical Stimulation for Lower Urinary Tract Dysfunction in People with Multiple Sclerosis: A Systematic Review

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## Abstract

**Introduction:** Lower urinary tract dysfunction (LUTD) is highly prevalent in patients with multiple sclerosis (MS) who suffer from some degrees of voiding dysfunction and/or urinary incontinence (UI), six to eight years after the initial diagnosis of MS. Electrostimulation is an established therapeutic option for neurogenic LUTD. This study aimed to investigate the efficacy of various types of electrical stimulation (ES) used for LUTD in MS patients. **Materials and Methods:** A systematic review of English-language articles was carried out in PEDro, PubMed, Science Direct, and Google Scholar databases between 1980 and 2017 using the following keywords: multiple sclerosis, electrical stimulation, LUTD, and neurogenic bladder. All the titles and abstracts were checked. Thereafter, full-text copies were obtained in cases where the studies had possible relevance. We carried out a background search by examining reference lists of all obtained articles. Ten treatment studies were identified in the search process. **Results:** Out of 10 articles, four were about the effects of percutaneous tibial nerve stimulation (PTNS) on LUTD. In three studies, neuromuscular ES, and in one study, interferential current was used. One study surveyed the effect of ES on the dorsal penile or clitoral nerve, and another studied the effect of ES on sacral dermatomes with regard to urinary symptoms. Also, three studies surveyed the effect of ES and its combination with pelvic floor muscle (PFM) training. **Conclusion:** This review showed that various types of non-invasive ES used for neurogenic LUTD in patients with MS for suppressing detrusor overactivity have also improved bladder compliance. Patients with MS require daily home stimulation treatments. Also, a combination of ES with PFM training is effective in reducing the symptoms of LUTD in MS patients.

**Keywords:** Electrical Neuromodulation, Lower Urinary Tract Dysfunction, Multiple Sclerosis, Neurogenic Bladder

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## Introduction

MS is a unique, inflammatory central nervous system (CNS) disease with a broad spectrum of clinical presentations that are related to time and disease progressing factors. It usually affects young adults and has a female predominance of 3:1(1).

Lower urinary tract symptoms (LUTS) are highly prevalent among the MS patient population, with approximately 90% showing some degree of voiding dysfunction and/or UI at six to eight years after the initial diagnosis (2). Neurogenic voiding patterns range from bladder atony to neurogenic detrusor overactivity (NDO). The most common urological disorder in MS is NDO, which develops in 60–80% of all MS patients. NDO is characterized by involuntary bladder contractions at low bladder volume; the main symptoms include urgency, frequency, nocturia, urge incontinence, hesitancy, and retention. These symptoms affect the patient's quality of life (QoL) because of both social and hygienic complications (3).

Due to the wide divergence of clinical symptoms and disease courses, evaluation and treatment differ among patients. Thus, treatment must be customized for each patient. MS-related LUTS treatment focuses on improving QoL by reducing UI, and ameliorating storage symptoms and bladder emptying, while avoiding urological complications like urinary tract infections (UTIs). Antimuscarinic drugs, alone or in combination with intermittent self-catheterization, botulinum toxin injection, indwelling catheters, neuromodulation, behavioral and/or physical treatment, and surgery are the various treatment options for different MS-related urinary symptoms (4).

Various electrostimulation techniques have been widely used to manage LUTS (5-8). This study aimed to investigate the efficacy of different non-invasive ES techniques used for neurogenic LUTS in patients with MS.

## Materials and Methods

We conducted a systematic review of English-language articles obtained from PEDro, PubMed, Science Direct, and Google Scholar databases between 1980 and 2017 using a set of keywords including multiple sclerosis, electrical stimulation, lower urinary tract dysfunction, and neurogenic bladder. We included studies that assessed different non-invasive ES techniques for neurogenic urinary disorders in patients with MS; studies that incorporated sacral neuromodulation treatment were excluded. We checked all titles and abstracts. Full-text copies were obtained where the studies had possible relevance. A background search was carried out by examining reference lists of all obtained articles. Ten clinical trials were identified in the search process.

## Results

Out of 10 articles, four were about the effects of PTNS on LUTD (9-12). In three studies, neuromuscular ES (13-15), and in one study, interferential current was used (16). One study surveyed the effect of ES on the dorsal penile or clitoral nerve (17) and another study investigated the effect of ES on sacral dermatomes with regard to urinary symptoms (18). Also, three studies investigated the effect of ES along with PFM training (14-16).

***Percutaneous Tibial Nerve Stimulation (PTNS)***

The tibial nerve is a mixed nerve containing L4-S3 fibers. It originates from the same spinal segments as the innervations of the bladder and pelvic floor. The idea of stimulating these nerves was based on the traditional Chinese practice of using acupuncture points over the common peroneal nerve to affect bladder activity, the ankle region of stimulation used along with PTNS being close to the Sanyinjiao (SP6) employed in Chinese acupuncture (19).

Amarenco *et al.* verified urodynamic changes during acute PTNS on 13 patients with MS. Left PTNS was carried out using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode with a frequency of 10 Hz and pulse width 200 milliseconds. Routine cystometry was done before PTNS and was repeated immediately after the first study during PTNS. Volume comparison was carried out during the first involuntary detrusor contraction at maximum cystometric capacity. The results of the study showed that PTNS was associated with significant improvements in the first involuntary detrusor contraction volume or $1^{st}$ IDCV (p=0.0001) and at the maximum cystometric capacity or MCC (p=0.0001) (9).

Kabay *et al.* investigated acute urodynamic effects of PTNS in MS patients. A total of 29 patients with NDO enrolled in the study. Urodynamic studies were performed before and during PTNS. PTNS was applied unilaterally using 26-gauge stainless steel needles inserted 5-cm cephalad from the medial malleolus and posterior to the edge of the tibia, placing the ground electrode on the ipsilateral extremity. ES was applied using charge-compensated 200 microsecond pulses with a pulse rate of 20 Hz. The mean $1^{st}$ IDCV and the mean MCC before and during PTNS were compared. Improvements in the $1^{st}$ IDCV and the MCC were found to be statistically significant during stimulation ($P$=0.001). The difference between the mean $1^{st}$ IDCV and the mean MCC at baseline and after PTNS was also observed to be statistically significant ($P$=0.001) (10).

In another study, Kabay *et al.* investigated the effect of 12 weeks of PTNS on urodynamic findings in MS patients with NDO. A total of 19 patients enrolled in the study. Urodynamic studies were performed before and after the 12-week period. PTNS was applied in a similar manner to the previous study. The mean $1^{st}$ IDCV and the mean MCC before and during PTNS were compared. Improvements in the $1^{st}$ IDCV and MCC were statistically significant after stimulation (11).

Additionally, de Seze *et al.* performed a three-month PTNS on 70 MS patients suffering from overactive bladder (OAB). Daily sessions consisting of 20 minutes of PTNS were provided. PTNS was applied unilaterally with two adhesive electrodes placed above and behind the medial malleolus at the right ankle. ES was applied using charge-compensated 200 microsecond pulses with a pulse rate of 10 Hz. The intensity level was just above the perception threshold but lower than the intensity that caused pain. The primary outcome measurements were urgency and frequency as reported by the bladder diary; symptom scores were performed before the treatment (Day 0 or D0), and on D30 and D90. Secondary outcome measures were included: a 3-day bladder diary, the French validated urinary symptom score, and QoL, with psychosocial burden at D0, D30, and D90, and cystometry at baseline with and without PTNS and on D90. Clinical improvement of OAB was shown in 82.6% and 83.3% of patients on D30 and D90, respectively, with significant improvement of primary and secondary outcomes as compared with the baseline (12).

***Table 1.*** Published English-language Studies (PUBMED) of ES for LUTD in People with MS

| Author | Intervention | Patients (number) | Age (mean or range) | Outcomes and Assessment Instruments | Length of Follow-up | Results |
|---|---|---|---|---|---|---|
| **Primus *et al.* (13)** | Maximal ES by intravaginal or intra-anal electrodes 15 sessions of 20 minutes duration | 75 patients (51 women and 24 men) 30 women with MS and 45 patients with idiopathic diseases | 11–82 | Urodynamic improvement was assessed by cystometry Subjective improvement | 2 years | Of the 30 patients with MS, 40% improved both urodynamically and subjectively, 56% only subjectively, and one patient experienced no benefit at all. In the MS group, relapse occurred within 2 months approximately |
| **Vahtera *et al.* (16)** | ES by interferential current using intravaginal or intra-anal electrodes in 6 sessions and then PFM exercises for at least 6 months | 50 women and 30 men, randomized to treatment group (A) and control group (B) | 25–57 | Surface EMG for testing PFM activity Subjective improvement was assessed using a questionnaire | 6 months | The maximal contraction power and endurance of PFM increased after 6 sessions of ES. Symptoms of urinary urgency, frequency, and incontinence were significantly less frequent in the treated group |
| **Amarenco *et al.* (9)** | Transcutaneous PTNS | 13 patients with MS | 53.3±18.2 | Urodynamic changes using cystometry | Immediately after intervention | Significant improvement in 1st IDCV (*P*<0.0001) and significant improvement in MCC (*P*<0.0001) |
| **McClurg *et al.* (14)** | Pelvic floor training and advice (PFTA) Electromyography (EMG) biofeedback Intravaginal neuromuscular ES (NMES) Treatment was for 9 weeks | 30 women Group 1: PFTA Group 2: PFTA and EMG biofeedback Group 3: PFTA, EMG biofeedback, and NMES | 33–67 | 3-day voiding diary; 24 hr Pad Tests; uroflowmetry; pelvic floor muscle assessment; Incontinence Impact Questionnaire (IIQ) | 24 weeks | Group 3 demonstrated superior benefits as measured by the number of leaks and Pad Tests as compared to Group 2, with Group 1 showing less improvement when compared to Week 0 |
| **Fjorback *et al.* (17)** | Event-driven ES of the dorsal penile or clitoral nerve | 10 patients (6 men and 4 women) | 35–55 | Urodynamic improvement | --- | Undesired detrusor contractions could be suppressed by stimulation. Increase in bladder capacity and reduction in the number of incontinence episodes |
| **Fjorback *et al.* (18)** | ES of sacral dermatomes | 14 patients (8 men and 6 women) | --- | Urodynamic improvement | --- | ES of sacral dermatomes failed to suppress detrusor contractions in all patients |
| **McClurg *et al.* (15)** | NMES Pelvic floor muscle training (PFMT) EMG biofeedback 9 weeks | 74 patients Group 1: PFMT, EMG biofeedback, and placebo NMES (n=37) Group 2: PFMT, EMG biofeedback, and active NMES (n=37) | 27–72 | Leakage episodes per 24 hours 24-hour Pad Tests Uroflowmetry Digital assessment of pelvic floor muscles EMG biofeedback Contraction (work), relaxation (rest), and endurance Visual analogue scale | 24 months | PFMT and EMG biofeedback significantly reduced symptoms of LUTD. Addition of NMES significantly increased the gained benefits. Benefits appeared to be relatively long-lasting. |
| **Kabay *et al.* (10)** | Posterior tibial nerve stimulation (PTNS) | 29 patients (12 men and 17 women) | 29–55 | Urodynamic improvement | Immediately after intervention | Improvements in the 1st IDCV and MCC were statistically significant during stimulation (*P*<0.001) |
| **Kabay *et al.* (11)** | PTNS 12 weeks | 19 patients (6 men and 13 women) | 29–56 | Urodynamic improvement | 12 weeks | Urodynamic results demonstrated that PTNS is effective in suppressing NDO in MS patients |
| **de Seze *et al.* (12)** | Transcutaneous PTNS 3 months | 10 patients (6 men and 4 women) | 48.3±10.2 | Urodynamic improvement was assessed by cystometry Subjective improvement | 3 months | Clinical improvement of OAB was shown in 82.6% and 83.3% of the patients on D30 and D90, respectively |

### *Neuromuscular ES*

Anal or vaginal ES may inhibit spontaneous detrusor contractions and thus appear as an alternative in UI therapy caused by detrusor overactivity. Primus *et al.* used maximal ES by intravaginal or intra-anal electrodes for the treatment of 30 MS patients with complaints of urgency and/or urge incontinence. All patients underwent 15 sessions of 20 minutes each during the three-week treatment period. Stimulation parameters (except for amplitude) were fixed at 1-millisecond monophasic square waves with frequency of 20 Hz, intermittently on for 1.5 seconds and off for three seconds. The maximum tolerable amplitude (maximum 95 mA) was chosen by slowly increasing the current intensity. Cystometry was performed before and after three weeks of neuromuscular ES (NMES). Also, lower urinary tract function and frequency/volume charts were filled out by patients at home within 48 hours. Among the 30 patients with MS, 40% improved both urodynamically and subjectively, 56% only subjectively, and one patient experienced no benefit at all. In MS patients, relapse occurred within approximately two months (13).

In a randomized pilot study, McClurg *et al.* investigated the effectiveness of a combined program of pelvic floor training and advice (PFTA), electromyography (EMG) biofeedback, and NMES for bladder dysfunction in MS. Thirty female patients were randomly allocated according to a computer-generated randomization list to one of three groups (10 patients in each group): PFTA (Group 1), PFTA and EMG biofeedback (Group 2), and PFTA, EMG biofeedback, and NMES (Group 3). There was a nine-week intervention period for all groups with participants attending on a weekly basis for monitoring and progression. Weekly intravaginal NMES was performed in Group 3 (initially for five minutes and then increasing to a maximum of 30 minutes). Two parameter settings were used. The first was a biphasic constant current with a pulse rate of 40 Hz and a pulse width of 250 $m_{sec}$, with 5 seconds on and 10 seconds off; this was at the maximum-tolerated intensity with active assisted exercises. The second setting was 10 Hz and 450 $m_{sec}$, with 10 seconds on and three seconds off; this was at the maximum-tolerated intensity. Outcome measures (at Weeks 0, 9, 16, and 24) included three-day voiding diary, 24-hour Pad Test, uroflowmetry, pelvic floor muscle assessment, Incontinence Impact Questionnaire (IIQ), Urogenital Distress Inventory (UDI), King's Health Questionnaire (KHQ), and the Multiple Sclerosis Quality of Life-54 (MSQoL-54) instrument. At Week 9, Group 3 demonstrated superior benefits (measured by the number of leaks and Pad Tests) as compared to Group 2, with Group 1 showing less improvement when compared to Week 0. The differences were statistically significant between Group 1 and Group 3 for the number of leaks (p=0.014) and Pad Tests (*P*=0.001), and between Group 1 and Group 2 for Pad Tests (*P*=0.001). A similar pattern was evident for all other outcome measures (14).

In another study, McClurg *et al.* conducted a double-blind, placebo-controlled, randomized clinical trial to evaluate the efficacy of NMES, and to establish the benefit of NMES above and beyond that of EMG biofeedback and PFM training. A total of 74 MS patients with LUTS were randomly allocated to two groups. Group 1 received PFM training, EMG biofeedback, and placebo neuromuscular ES (n=37). Group 2 received PFM training, EMG biofeedback, and active neuromuscular ES (n=37). Treatment was conducted for 9 weeks with outcome measures recorded at Weeks 0, 9, 16, and 24. Outcome measures and NMES parameters were similar to the previous study. The results showed that the mean number of incontinence episodes reduced in Group 2 by 85% (*P*=0.001), whereas in Group 1, a lesser reduction of 47% (*P*=0.001) was observed. There was a statistically superior benefit in Group 2 as compared to Group 1 (*P*=0.0028). This superior benefit was evident in all other outcome measures (15).

### *Interferential Current*

In a randomized controlled study, Vahtera *et al.* investigated the effect of interferential current combined with PFM exercises on LUTD in 80 MS patients randomly assigned to treatment group (A) and control group (B). The outcome measures included muscle activity of the PFM with maximal contraction power and endurance, which was tested using surface EMG. ES was performed via interferential current using intravaginal or intra-anal electrodes with a carrier frequency of 2000 Hz and treatment frequencies of 5–10 Hz, 10–50 Hz, and 50 Hz (7 seconds pulse/25 seconds pause). A treatment session consisted of 10 minutes of each frequency followed by three minutes of rest. All currents, at maximal tolerated intensity, were executed in six sessions; then patients were taught to exercise their PFM and advised to continue these exercises regularly for at least six months. The control group was not treated. Maximal contraction power and endurance of the PFM increased after six sessions of ES with interferential currents. Symptoms of urinary urgency, frequency, and UI were found to be significantly less frequent in the treated group than in untreated individuals (16).

***ES of Dorsal Penile or Clitoral Nerve***

Fjorback *et al.* studied the effect of automatic event-driven ES on the dorsal penile or clitoral nerve for management of NDO in 10 patients suffering from MS. Detrusor pressure was recorded during physiological filling of the bladder and ES of dorsal penile or clitoral nerve was automatically applied whenever the detrusor pressure exceeded 10 cm H2O. Charge-compensated 200 microsecond pulses with a frequency of 20 Hz were used. The results indicated that involuntary detrusor contractions in patients with MS can be effectively inhibited with event-driven stimulation of the dorsal penile or clitoral nerve, thereby improving bladder capacity (17).

***ES of Sacral Dermatomes***

Transcutaneous ES of the dorsal penile or clitoral nerve (DPN) has been shown to suppress detrusor contractions in patients with NDO. However, long-term use of surface electrodes in the genital region may not be well-tolerated and may introduce hygienic challenges. In another study, Fjorback *et al.* evaluated the effect of automatic event-driven ES of sacral dermatomes to suppress detrusor contractions in 14 MS patients with NDO. Detrusor pressure was recorded during physiological filling of the bladder and ES of sacral dermatomes was automatically applied whenever the detrusor pressure exceeded 10 cm H2O. Charge-compensated 500 microsecond pulses with a frequency of 20 Hz were used. The results showed that ES of sacral dermatomes failed to suppress detrusor contractions in all patients (18).

## Discussion

LUTD is highly prevalent in patients with MS and its symptoms, including urinary frequency, urgency, and UI, may affect the QoL. These symptoms are also often compounded with immobility. Standard treatment with anticholinergic and clean intermittent self-catheterization may be highly effective in the early stages, but increasing disability often requires an intervention with significant morbidity. Additional therapies for refractory urinary symptoms in patients with advanced MS are needed to prevent or postpone the need for long-term indwelling catheterization.

The results of this review showed that both acute and chronic PTNS are effective for suppressing detrusor overactivity in MS patients, and also for improving bladder capacity without any side effects. Safety of transcutaneous PTNS (TPTNS) is of particular interest to disabled patients who may be more susceptible to deleterious adverse effects of anticholinergic agents. McGuire *et al.* first reported the efficacy of direct ES of the tibial nerve in patients with urge incontinence. The tibial nerve is a mixed nerve containing L4-S3 fibers, and originates from the same spinal segments as the innervations to the bladder and pelvic floor (20). PTNS inhibits bladder activity by depolarizing somatic sacral and lumbar afferent fibers. Afferent stimulation provides central inhibition of the preganglionic bladder motor neurons through a direct route in the sacral cord (21). The feasibility of TPTNS, which can be easily used at home by patients or their caregivers, represents a real advantage as compared to PTNS, which requires the insertion of a needle close to the tibial nerve. However, the continuation of the effect after three months remains unknown and further studies should be carried out to evaluate the optimal timing of TPTNS administration (12).

According to the results of these studies, anal or vaginal ES may inhibit spontaneous detrusor contractions, and thus, appears as an alternative to the therapy of UI caused by detrusor overactivity, leading to both subjective and urodynamic improvement. Also, findings have indicated that a combination of PFTA, EMG biofeedback, and NMES is more effective in reducing episodes of incontinence and the amount of leakage as compared to PFTA alone or combined only with EMG biofeedback. These findings have also demonstrated that the addition of NMES significantly increases gained benefits. Furthermore, the benefits appear to be relatively long-lasting.

## Conclusion

This study shows that ES along with interferential currents activates PFM in MS patients and that such therapy, in combination with regular PFM exercises, improves the symptoms of urinary dysfunction.

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