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ORIGINAL ARTICLE

Sacral neuromodulation for multiple sclerosis patients with urinary retention and clean intermittent catheterization

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Abstract
Introduction and hypothesis Multiple sclerosis is a chronic, debilitating, neurological disease with numerous urological manifestations including urinary detrusor overactivity, detrusor sphincter dyssynergia, and urinary retention. Can sacral neuromodulation be successfully implemented for urinary retention in ambulatory women with multiple sclerosis?
Methods Between January 2002 and January 2008, we conducted an observational retrospective case–control study where 12 of 14 consecutive, ambulatory women with multiple sclerosis had stage 1/2 sacral neuromodulation performed under general anesthesia for urinary retention.
Results Twelve of 14 patients (86%) were successfully implanted, with a mean follow-up of 4.32±1.32 years and mean postvoid residual of 50.5±21.18 ml. The mean maximum uroflow was 17.7±7.9 ml/s. Two of the 12 patients (17%) required revisional surgeries for lead migration, and 40% needed battery replacement.
Conclusion Urinary retention in multiple sclerosis female patients can be successfully and safely managed with sacral neuromodulation with few complications with a mean of 4 years follow-up.

Keywords Sacral neuromodulation · Urinary retention · Multiple sclerosis · Demyelination · Remyelination

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Introduction

Multiple sclerosis is the most commonly acquired central demyelinating disease of the nervous system, afflicting over 400,000 Americans each year [1]. Multiple sclerosis is a distinct inflammatory disorder of the spinal cord and brain, defined by focal lymphocytic infiltrates leading to damage of the myelin coats of neural axons [1, 2]. Its inflammation is transitory, and remyelination occurs but is short-lived. In the early stages of the disease, multiple sclerosis is characterized by episodic neurological dysfunction with a degree of recoverability [1, 2]. As time passes, however, pathological changes are widespread with microglial activation and prominent long-term neurodegeneration. This correlates with progressive physical and mental disability. Two distinct physical symptoms may occur: Lhermitte's sign (an electrical sensation running down the spine or limbs with neck flexion) or Uhthoff phenomenon (transient worsening of symptoms when the core body temperature increases after bathing or exercise).

Multiple sclerosis is defined by typical symptoms and disease progression with an annual incidence of one to 11 patients per 100,000 [1, 2]. The age of onset peaks between 20 and 30 years with almost 70% of patients manifesting symptoms somewhere between 21 and 40 years of age. The disease rarely occurs prior to age 10 or after 60, but patients as young as 3 and as old as 67 have been reported. Like other immuno-mediated disease entities, females are more commonly affected than males (1.4–3.1 times more frequently). Multiple sclerosis has a familial recurrence rate of 20%, showing a higher monozygotic than dizygotic twin occurrence of 25% versus 5% [1]. Recurrence is higher for a child of conjugally rather than singly affected parents. This most likely undermines genetic factors in determining familial clustering and individual susceptibility. Individual

episodes of inflammatory demyelination are accompanied by symptoms and are referred to as relapses, usually followed by an improvement in symptoms. A characteristic of demyelinating disease is the formation of sclerotic plaque, which is the end stage of inflammation, demyelination, and remyelination. The waxing and waning of the disease may be typical. There are six subtypes of multiple sclerosis [1]: benign multiple sclerosis, relapsing/remitting, secondary progressive, primary progressive, malignant, and chronic progressive. The cause of multiple sclerosis involves environmental exposure and genetic susceptibility [1]. Arguing the merits of one faction versus the other is unproductive. Each is clearly implicated, together with the cultural condition of age at which the interplay between genes and the environment occurs. The initiating cause of this disease entity is unknown, but autoimmune-mediated demyelination with its corresponding axonal injury has been well noted [1]. Diagnosis is confirmed with intermittent or progressive central nervous system symptoms, supported by evidence of two or more central nervous system white matter lesions occurring in the absence of alternative explanations (i.e., cerebrovascular stroke or systemic lupus erythematosus; Fig. 1a, b) [1]. Treatment of exacerbations usually includes corticosteroids and either of two forms of recombinant interferon-β or interferon-β1a [1, 2]

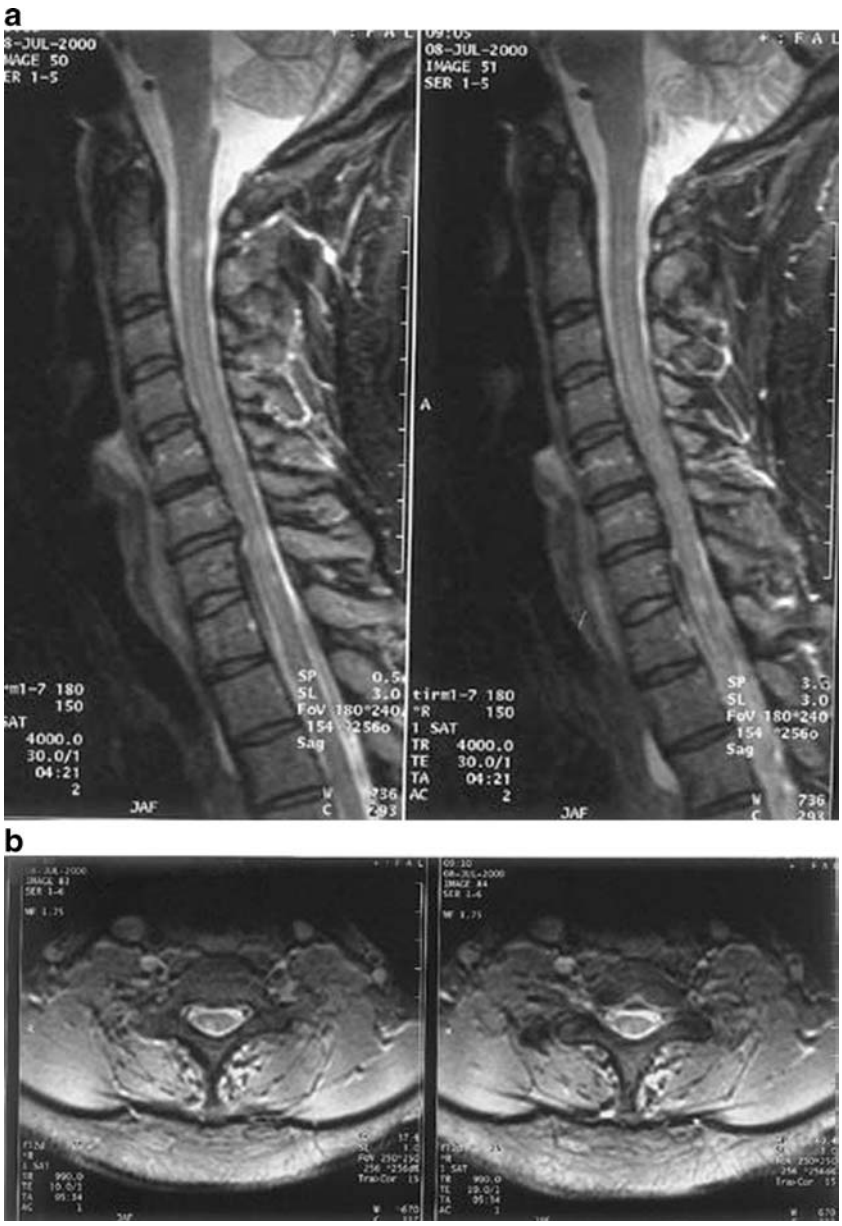

Fig. 1 **a** Magnetic resonance imaging scans of the spinal cord in a patient with multiple sclerosis. Sagittal images using the short tau inversion recovery protocol reveal multiple high-signal lesions within the spinal cord (*left*), consistent with demyelination. **b** These lesions, which can also be seen on the transverse cuts, are often situated dorsolaterally and are usually less than one vertebral body in length. The lesions rarely cause cord swelling

The majority of patients with multiple sclerosis have diversified genitourinary complaints including urgency, urge incontinence, frequency, and urinary retention [2, 3]. Symptoms do not accurately reflect the underlying genitourinary pathology but do have certain congruence with their spinal cord pyramidal tract utility. Sophisticated videourodynamics studies play an important role in defining appropriate bladder care management. Some of the most common urodynamic study results include detrusor hyperreflexia (62%), detrusor sphincter dyssynergia (25%), and hypocontractility (20%) [3]. Less than 1% of patients have renal function deterioration, and most may be treated with conservative measures including anticholinergic medications and/or clean intermittent catheterization [3]. Urinary retention is an important genitourinary corollary of multiple sclerosis [3]. While rarely life-threatening, urinary retention can interfere in patients' lives with noteworthy morbidity, patient frustration, and decreased quality of life measurements. The condition can be readily treated with a closely followed regimen of clean intermittent catheterization but may, for many patients, decrease quality of life. Sacral neuromodulation was approved by the Food and Drug Administration for refractory urge incontinence in 1997 and for non-obstructive urinary retention and refractory urgency and frequency in 1999 [4]. Recently, the use of sacral neuromodulation for neurologically impaired patients with voiding complaints that are resistant to conservative measures has gained attention and utilization, with suitable clinical results in cerebral palsy [5]. Short-term (<1 year) to medium-term (1–5 years) effects of sacral neuromodulation in female patients with multiple sclerosis with urinary retention have not been well documented. Minimal discussion has been noted in studies with very few study participants [6, 7].

Materials and methods

Our evaluation was an observational, retrospective case–control study of 14 consecutive patients with neurologist-confirmed multiple sclerosis and multichannel videourodynamics-assessed urinary retention. Three patients had benign multiple sclerosis, seven had relapsing remitting multiple sclerosis, and four had secondary progressive multiple sclerosis. Patients had urodynamics-proven urinary retention and underwent sacral neuromodulation (Interstim, Medtronic, Minneapolis, MN, USA; implantable pulse generator [IPG] model number 3023 and tined lead with larger lead number 1 model number 3093) stage 1 and 2 (only those with a >50% reduction in postvoid residual urine via straight catheter were candidates for stage 2 implantation) under general anesthetic between January 2002 and January 2008. This study received Internal Review Board approval. Workup included complete history and physical examination, urine analysis with microscopic evaluation and culture, preoperative and at time of last follow-up Expanded Disability Status Score for multiple sclerosis (EDSS, 0=no apparent disease to 10=death resulting from multiple sclerosis) videourodynamics with electromyography, office cystoscopy, preoperative catheterization diary, and postoperative 72-h micturition log, as well as technical data on implantation and operative revisions. All patients had attempted maximal conservative therapies (intermittent catheterization, pelvic floor rehabilitation, alpha blockers, and bethanechol therapy) before undergoing staged sacral neuromodulation. All patients had preoperative catheterizations greater than 250 ml and were managing their bladder with clean intermittent catheterization four to six times a day because of their inability to void preoperatively. No videourodynamics were performed postoperatively to ascertain their detrusor pressure improvement. At the onset of this study and at the time of writing, there were no standardized and verified questionnaires for urinary retention. Urodynamic information prior to urinary retention and after the return of voiding was not performed. The Urinary Distress Inventory (UDI-6) and Incontinence Impact Questionnaire (IIQ7) are primarily applicable to urgency and stress incontinence but not urinary retention, so these were not included in our evaluation. All patients were asked the question whether they were satisfied with their operative result—"Yes" or "No". Program settings for all patients were not recorded.

Urinary retention was defined as the failure of the detrusor muscle to contract and generate a detrusor pressure even though the bladder had reached and/or exceeded its bladder capacity. Bladder filling was performed with room temperature, sterile water at a filling rate of 25 ml/min. Failure was defined as the recurrence of urinary retention not allowing progression from stage 1 to stage 2, IPG placement, or retention recurring after stage 2 implantation. Lead displacement was not considered a failure if revisional surgery returned the patient to voiding. Battery replacement was also not considered a therapy revision or failure if due to battery quiescence. Statistical analysis was performed using the Statistical Package for Social Sciences, version 11.0 (SPSS, Chicago, IL, USA). Analysis included simple means, medians, and standard deviations (Tables 1 and 2). Comparisons of preoperative catheterized and postoperative postvoid residual urines were performed with an analysis of covariance. There were no pharmaceutical, university, local, state, or federal government funds requested or received.

Results

With a median age of 46±9.36 years (Table 1) and a mean duration of multiple sclerosis of 9.28±4.59 years, the following results were obtained. Overall, 12 of 14 (86%) women were voiding spontaneously, with a mean preoper-

Table 1 Patient demographics and results

Category	Result	Range
Median age (years)	46±9.36	30–60
Mean body mass index	31.45±4.42	25.5–39.0
Duration of multiple sclerosis (years)	9.28±4.59	4–17
Preoperative EDSS	4.03±1.14	2.5–7.0
Follow-up EDSS (p=0.22)	4.22±1.21	3.0–7.5
Mean preoperative clean intermittent catheterization (ml)	308±53.60	225–380
Mean postoperative postvoid residual (ml; p<0.001)	50.5±21.18	0–350
Duration of preoperative clean intermittent catheterization (years)	0.95±0.74	0.25–7
Mean postoperative maximum uroflow (ml/s)	17.7±7.9	8.6–26.9
Reoperation rate for battery wear (%)	40	
Mean follow-up (years)	4.32±1.32	1.0–7.0

ative catheterization of 308.2±53.6 ml compared to a mean postoperative postvoid residual urine of 50.5±21.18 ml (p< 0.001) via straight catheterization and mean follow-up of 4.32±1.32 years. The mean postoperative maximum flow rate was 17.7±7.9 ml/s. Two study participants (14%) continued to utilize clean intermittent catheterization for bladder management and were considered failures. The reoperation rate was 40% for battery wear and 25% for lead migration. Twelve of the 14 who were voiding successfully without the utilization of clean intermittent catheterization were fully ambulatory, while the two patients who did not proceed to stage 2 implantation were non-ambulatory, wheelchair-bound, and continued to successfully manage their bladders with clean intermittent catheterization. Patient satisfaction with treatment and follow-up was 86% (all spontaneously voiding patients were happy with their surgery, while the two failures were dissatisfied with clean intermittent catheterization). Mean EDSS scores preoperatively and at the time of last follow-up were essentially unchanged from 4.03±1.14 (range 2.5–7.0) to 4.22±1.21 (range 3.0–7.5; p=0.22). Intraoperative lead power levels for both good bellows and ipsilateral plantar flexion were comparable among all four parts of the partitioned tine lead (p<0.19). The mean number of office reprogramming sessions per patient during follow-up was 3.67±2.22. There was no correlation between type of multiple sclerosis and videourodynamics diagnosis. There is no proven method for determining sacral neuromodulation method of function, and we do not offer any other objective opinion other than intraoperative lead function (Table 2).

Table 2 Intraoperative lead function and other information

Category		Result
Intraoperative power level for good bellows/plantar flexion lead	0	3±3.49
	1	4.58±2.47
	2	4.01±1.41
	3	4.41±1.56
Mean number of reprograms per patients during follow-up		3.67±2.22
Side of tine probe placement (%)		75% right
		25% left

Discussion

The major urinary complaints for multiple sclerosis patients are centered on neurogenic detrusor overactivity and potentially neurologically mediated urinary obstruction with detrusor sphincter dyssynergia [3]. Urinary retention is less frequently experienced, but until recently, very few effective treatment alternatives existed, especially those leading to the resumption of normal voiding [8]. Chronic catheterization consistently empties the bladder but leads to a decreased quality of life and the potential for symptomatic urinary tract infection and calculus formation [8]. Sacral neuromodulation applications for urinary retention in female patients are diverse: following kidney transplant [9], tension-free vaginal tape surgery [10], Fowler's syndrome [11], cerebral palsy [5], and in studies delineating the urodynamic changes after sacral neuromodulation [12]. We do recommend that all patients follow Medtronics precautions for not allowing magnetic resonance imaging (MRI) after lead and/or IPG placement. The necessities of MRI follow-up studies for these patients should be reviewed and discussed with the consulting neurologist and request their advice into the placement of this titanium device.

Two medium-range to long-range studies with sacral neuromodulation for non-neurologically impaired patients serve as good juxtapositioning guides to reaffirm acceptable results with our smaller multiple sclerosis study cohort. Dasgupta et al. [13] studied 20 patients (mean age 35 years) with a 6-year follow-up in presumed neurologically intact

patients with 17 of 25 (68%) still voiding without the use of a catheter at follow-up. Three were encouraged to use clean intermittent catheterization for their consistent residuals greater than 200 ml with another three reporting loss of efficacy. Mean postoperative residual urine was 75 ml with a mean maximum uroflow of 20.8 ml/s. Fifty-four percent experienced revisional surgery. Another review of charts conducted by Datta et al. [6] (mean age 37.6 years) with 1 year follow-up with a two-staged approach revealed 73% voiding spontaneously without the need for a Foley catheter and with noticeably higher mean residual urines of 113.6 ml. Maximum flow rate was not recorded. Forty-five percent required revisional surgery. Mean battery life was 7.31 years. Our study data with 12 of 14 (86%) participants with complete, spontaneous voiding unassisted with catheters revealed a smaller postoperative postvoid residual urine of 50.5±21.18 ml/s and a slower mean maximum flow rate of 17.7±7.9 ml/s. Revisional surgery rates were 25%. Mean battery life was 6.1 years, which may indicate greater current utilization with a neurologically impaired population (although both are within the recommended duration of 5–8 years). Another two understudied parameters that were defined in our study group were number of reprogramming sessions and percent ambulatory. Our study group had a rate of 3.67±2.22 reprogramming episodes with 4.35±1.33 years of follow-up. None of these three study groups related episodes of severe debilitation from any surgery or revisional surgeries. In addition, our group with multiple sclerosis impairment who were ambulatory preoperatively have remained ambulatory and without the assistance of walking aids at time of writing. Although revisional surgery secondary to an improperly working apparatus (lead migration) was high in each study group (54%, 53%, and 25%), it does not seem to affect overall voiding function since all three studies had volitional voiding after implantation approaching 70% or more. The two studies reviewed did not discuss intraoperative lead function, which may be defined as the power needed at each of the four lead terminals (Table 2) to attain strong bellows and ipsilateral plantar flexion of the big toe. I have ascertained with formal review of over 30 stage 1 cases for female retention that it is most useful to have an IPG power rating of 6 or less (range 0–10) for each positive bellows and/or plantar flexion producing lead. Patients with two or more leads fulfilling these criteria have a 76% chance of or better voiding. Additionally, the ability to self-ambulate may be pivotal to the success of implantation for retention. Although all patients had an Anesthetic Assessment Score (ANAS) of 2 (seven patients) or 3 (five patients) out of 5, comorbidities did not appear to influence outcomes. The two non-ambulatory patients had been non-ambulatory for at least 12 months prior to the procedure, and both scored an ANAS of 4. Five other patients underwent successful stage 2 with an ANAS of 3. None of our patients was rated higher than a minimal to moderate cardiac risk for surgery. Non-ambulatory status may be a higher risk factor for failure of sacral neuromodulation for the treatment of female urinary retention with multiple sclerosis. We believe that our success is attributable to our multiteam approach and close periodic re-evaluation (no less than every 6 months) of all successfully implanted patients. With more experience, non-ambulatory status may become an exclusionary criterion for this surgical intervention in multiple sclerosis and potentially in other neurologically impaired patients after more study.

Each patient's neurologist informed us of their interval EDSS from both their preoperative time frame and at the time of the study assessment to give us an appreciation of their multiple sclerosis condition. Mean EDSS scores preoperatively and, at the time of last follow-up, were essentially unchanged from 4.03±1.14 (range 2.5–7.0) to 4.22±1.21 (range 3.0–7.5; $p=0.22$), which demonstrated no statistically significant difference ($p=0.22$). Four of 14 (29%) had a marginal worsening of their multiple sclerosis as determined by their neurologist and was not considered clinically significant while not appreciably affecting their postvoid residual urines. In the 4.32 years of follow-up, only these four patients had a worsening of their EDSS listed as: 3 to 3.5, 4 to 4.5, 4 to 4.5, and 7 to 7.5, respectively. Of these four patients, the one with a score of 7.5 did not succeed to stage 2 implantation while the other three did and, at the time of the follow-up study, were voiding without the necessity of clean intermittent catheterization for consistent residual urine's greater than 100 ml. No patient had an improvement in EDSS, which would entail a numerical reduction in EDSS.

Conclusion

Sacral neuromodulation may be successful for urinary retention in ambulatory women with multiple sclerosis, with short-term to medium-term follow-up, good efficacy and patient satisfaction, minimal morbidities, and few revisional surgeries. Additional studies with well-defined clinical, long-term outcomes (including complications, cost, pain, return to normal activity, and quality of life) are needed to fully assess the value of sacral neuromodulation in neurologically impaired patients.

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