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REVIEW ARTICLE

Sacral neuromodulation: an effective treatment for lower urinary tract symptoms in multiple sclerosis

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Abstract
Introduction and hypothesis Most subjects with multiple sclerosis (MS) suffer from lower urinary tract symptoms (LUTS). Detrusor overactivity, detrusor hypocontractility and detrusor–sphincter dyssynergia are the most common bladder dysfunctions. Management is not straightforward due to the progressive course of the disease. Sacral neuromodulation (SNM) has received increasing attention among new effective treatments for bladder disorders associated with MS. The aim of this study was to review the published literature on the role of SNM in the treatment of LUTS in patients with MS.
Methods A literature search was carried out up to December 2014, using relevant search terms in MEDLINE and EMBASE databases. The ClinicalTrials.gov and Controlled-trials.com online trial registries and the abstracts from international scientific meetings were searched for English-language studies containing relevant search terms. Relevant reviews and trials and prospective studies were analysed by two independent reviewers.
Results Two prospective studies and four retrospective studies were included. Overall, MS patients represented small series (4 to 25 subjects). The longest follow-up was 7 years and the evaluation of the treatment outcomes was not homogeneous among the studies. The definition of objective cure was often unclear. The subjective cure rate was 45 %, patients' reported satisfaction was 85 % and all the results were stable over time.
Conclusions SNM seems to be a safe and effective treatment for LUTS in MS patients. Further and larger studies as well as randomized controlled trials are needed to confirm its clinical role in patients with MS.

Keywords Multiple sclerosis · Sacral neuromodulation · Lower urinary tract symptoms · Neurogenic detrusor overactivity · Voiding disorders · Detrusor sphincter dyssynergia · Detrusor underactivity

Introduction

Multiple sclerosis (MS) is a chronic and progressive inflammatory disease in which the fatty myelin sheaths around the axons of the brain and spinal cord are damaged, leading to demyelination and scarring. These inflammatory episodes are transitory and remyelination usually occurs. However, remyelination is not long-lasting, and thus subsequent multiple physical disabilities are likely. Despite significant advances in immunomodulatory therapy, repair of existing nerve injuries is still not possible [1]. Clinical findings of the disease include fatigue, muscle spasticity, general body pain, cognitive dysfunction, depression, bladder, bowel and sexual dysfunction with a great impact on quality of life (QoL) [1–3]. Lower urinary tract symptoms (LUTS) are common disorders occurring in about 80 % of patients with MS [4, 5]. Overactive bladder (OAB) symptoms due to neurogenic detrusor overactivity (NDO) is the most common LUTS, occurring in 60 – 80 % of MS patients [6]. However, voiding dysfunction such as obstructed, slow, interrupted or prolonged flow,

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incomplete emptying and/or urinary retention are often reported by MS patients.

These voiding difficulties have been shown to be related to a hypotonic and/or atonic detrusor, as well as a lack of coordination between the detrusor and urethral sphincter during voiding, also termed detrusor–sphincter dyssynergia (DSD) which often coexists with detrusor overactivity (DO) [4]. In view of the high intravesical pressure, chronic urinary retention and recurrent urinary tract infections (UTIs) are experienced by these patients, and upper urinary tract complications such as renal failure, pyelonephritis, hydronephrosis, and bladder and kidney stones have been described in 5 – 10 % of patients with MS [3, 7]. Further results have shown that if the DSD and chronic urinary retention are not treated, up to 50 % of patients with MS might develop the above complications [8, 9]. Therefore, a detailed assessment of bowel, bladder and sexual function in MS patients is mandatory in order to prevent complications and subsequent morbidities as well as to improve their QoL [1, 3].

Current management of OAB symptoms and NDO includes conservative therapies such as individualized bladder rehabilitation programmes and/or pharmacological treatment with oral anticholinergic or beta-3 agonist drugs with or without clean intermittent self-catheterization (CISC) or insertion of a suprapubic catheter [1, 2, 4]. Short-term efficacy of these agents has been reported, more so with the established anticholinergics [10] and recently with the beta-3 agonist mirabegron [11]. However, side effects of anticholinergics, such as constipation and central nervous system (CNS) effects such as cognitive impairment, can restrict their long-term use and suitability in MS patients. In addition incomplete voiding experienced by MS patients may worsen with the use of anticholinergics.

A review of the role of botulinum toxin (BTX) in the management of MS concluded that in MS patients with DO intravesical BTX injections are effective in reducing incontinence episodes and urinary urgency, day-time frequency and nocturia, as well as in improving QoL [12]. In addition, although BTX injection of the bladder has proven to be an effective treatment for urinary frequency and urgency as well as for urinary incontinence [13], paralysing the detrusor muscle leads to further deterioration in bladder contractility that is already present in MS patients. The limited duration of action, the need for repeated injections, the increased risk of UTIs and the need for CISC are the major limitations of BTX [14].

Electrostimulation has been used to treat both the overactive and hypocontractile bladder in the past. Electrical stimulation of the dorsal penile/clitoral nerve with surface electrodes has been shown to suppress detrusor contractions and increase bladder capacity in MS patients [6]. However, its long-term use may be limited by tolerance of the electrostimulation in the genital area in addition to hygiene concerns. Posterior tibial nerve stimulation (PTNS) is another noninvasive method of electrical stimulation. The precise mechanism of action is unknown, but it has been proposed that PTNS inhibits bladder activity by depolarizing somatic sacral and lumbar afferent fibres. Initial studies of the use of PTNS using either percutaneous or transcutaneous electrodes in MS neurogenic DO have shown it to be an effective, safe and well-tolerated treatment [5, 15–17].

Sacral neuromodulation (SNM) for the treatment of detrusor disorders has been used since the 1960s and it has been approved by the Food and Drug Administration (FDA) since the 1990s for refractory voiding dysfunction, urgency incontinence, urgency-frequency syndrome and non-obstructive urinary retention [18, 19]. SNM has gained popularity as an approach in NDO since the 1980s and in 2005 it was included in treatment recommendations for idiopathic and NDO as a second-line treatment [18–20]. The mechanism of action of SNM is not fully understood, but it has been shown to be effective in treating apparently opposite bladder disorders such as refractory OAB, voiding dysfunctions and chronic urinary retention, all of which are very common in MS patients [19].

In the 1980s, Tanagho et al. [21] demonstrated that electrical stimulation of efferent fibres to the external urethral sphincter, which may be triggered through the third sacral nerve (S3), is effective in suppressing bladder contractions. In 2000, Chartier-Kastler et al. [22] suggested that stimulation of somatic afferent axons in the spinal roots would modulate voiding and continence reflexes in the CNS. The mechanism is thought to be somatic afferent inhibition of sensory processing in the spinal cord [18, 22, 23]. Hohenfellner et al. [24] described the effects on bladder sensitivity of excitation of the pudendal somatomotor neurons combined with modulation of efferent sympathetic and parasympathetic activity. Other authors have confirmed the mechanism of action as inhibition of sacral afferent signals and interruption of inappropriate bladder contractions most likely targeting unmyelinated C-fibres and sparing A-delta fibres [19, 22, 25].

Less is known about the mechanisms of enhancing detrusor–sphincter coordination. Bosch [26] and Elneil [27] have reported that SNM may interfere with the increasing afferent activity arising from the urethral sphincter, restoring the sensation of bladder fullness and reducing the inhibition of detrusor muscle contraction. Two mechanisms have been postulated: a “pro-continence reflex” characterized by activation of efferent fibres to the urethral sphincter resulting in negative feedback to the bladder activity, and activation of afferent sacral spinal fibres resulting in an inhibitory efferent signal to the bladder [27]. Mapping of the pudendal afferents has shown that S1, S2 and S3 sacral roots contribute, respectively, 4 %, 60.5 % and 35.5 % to its overall activity and that in 18 % of people, the afferents are confined to a single level, most likely S2. This finding may explain the failure of

S3 stimulation in some subjects who could benefit from direct pudendal nerve stimulation [25, 26].

Insertion of the SNM implant can be done as either a one-stage or two-stage procedure. The one-stage procedure involves an initial test stage using a percutaneous nerve evaluation (PNE) test by implanting a temporary stimulating electrode through the S3 foramen, positioned to produce the sensation of vaginal or rectal tingling or contraction. The electrode is kept in place for 4 – 7 days and voiding diaries kept to record any improvement in voiding function. If voiding is shown to improve (test positive), patients are offered a permanent stimulator. A different electrode is inserted using an open sacral procedure, and connected to a permanent implantable pulse generator (IPG) placed either within the buttock or within the subcutaneous fat of the anterior abdominal wall. In 2000 the two-stage percutaneous technique was introduced, with a tined electrode. The permanent tined lead is inserted and a prolonged external stimulation period is assessed. If successful, the permanent IPG is implanted [27].

The aim of this review was to evaluate the evidence on the use of SNM in MS patients with LUTS.

Methods

All English-language articles describing the use of SNM in MS were included in this review. A systematic literature search was carried out up to December 2014 using relevant search terms ("multiple sclerosis", "sacral neuromodulation", "neurogenic detrusor overactivity", "lower urinary tract symptoms", "voiding disorders", "detrusor sphincter dyssynergia" and "detrusor underactivity") in the MEDLINE and the EMBASE databases, the ClinicalTrials.gov and Controlled-trials.com online trial registries, and abstracts from international scientific meetings. Hand searches of reference lists of all relevant articles were also carried out. Relevant trials and prospective studies as well as relevant reviews were selected and analysed by two independent reviewers. No ethical approval was sought for this study, as it was a systematic review.

Study selection. We identified 68 references by electronic and hand searches. Screening of titles or abstracts or unavailability of full texts led to the exclusion of 22 papers, and 34 more papers were considered not suitable for the purpose of this review. We initially included seven papers, three prospective studies and four retrospective studies. One of the papers described a five-patient case series and the same group later reported a 25-patient retrospective case series on the same subject [28, 29]. We therefore excluded the smaller study, and thus in this review included six studies in total. Unfortunately, the majority of studies includes heterogeneous groups of patients including those with MS, Parkinson's disease, spina bifida and neurological disorders following trauma. Overall, there were small numbers of MS patients, ranging from 6 to 25 subjects.

Results

A total of six studies were included in this review. Three studies involved MS patients only and the remaining three studies included patients with other neurological diseases in addition to MS patients. A summary of the included studies is presented in Table 1.

Ruud Bosch et al. [23] carried out a prospective study involving six MS patients. Patients were included if they had urodynamic evidence of DO (termed detrusor hyperreflexia in this paper), a functional bladder capacity of at least 150 ml, a diagnosis of MS and stable or slowly progressive disease. All patients underwent baseline video-urodynamics and completed two 4-day bladder diaries. The initial test stimulation was done by PNE for 5 days, and patients were instructed to keep a bladder diary for this time. Patients with a greater that 50 % reduction in pad use and/or number of leakages were considered for permanent electrode implantation. Follow-up tests included regular bladder diaries and urodynamic studies 6 months after implantation. Of the six patients (all women), five completed the test period and four responded with >50 % improvement and went on to have a permanent IPG implanted. Symptomatically there was a reduction in the mean number of leakage episodes from 4 to 0.3 per 24 h. Two patients were completely dry. The urodynamic data at 6 months follow-up showed disappearance of the hyperreflexia in one patient, improvement in two patients and worsening in one patient. The worsening in the fourth patient may be explained by progression or even a relapse of MS.

A further prospective study looked at the use of SNM in nine patients with neurological disease, of whom five had MS [22]. Patients were included if they had a history of refractory neurogenic DO and severe alteration in QoL. The initial test stimulation was done by PNE for more than 3 days. Assessments included bladder diaries, urodynamics and patient satisfaction using a visual analogue scale (VAS). If there was more than a 75 % improvement in the number of leakage episodes per day and pad use, a decrease in the number of voids per day and/or improvement in urgency symptom in addition to a greater than 75 % satisfaction on VAS, then patients were selected for unilateral surgical implantation of the IPG. Follow-up included bladder diaries, urodynamics at 6 months and last follow-up. All of the MS patients had had the disease for more than 3 years. Three of the six MS patients were completely dry at 6 months. At 6 months follow-up the mean frequency for the MS group improved from 15 to 9.16 voids per day, and the mean volume per void increased from 124 to 208 ml. However, in two of the MS patients the

Table 1 Summary of included studies

Reference	Type of study	Patients included (*n*)		Patients implanted (*n*)		Mean follow-up (months)	Assessments used	Assessments done	Outcomes after implantation
		With neurological disease	With MS	With neurological disease	With MS				
[23]	Prospective	6	6	4	4	34	Voiding diary (no. of pads used per 24 h, no. of leakage episodes per 24 h, voiding frequency per 24 h, mean voided volume per micturition) UDS (bladder volume at first hyperreflexic contraction, amplitude at first hyperreflexic contraction, bladder volume at maximum hyperreflexic contraction, amplitude of maximum hyperreflexic contraction, bladder capacity)	Preimplantation Subchronic test stimulation 6 months after implantation with stimulation on	More than 50 % reduction in in pad use and/or leakage episodes in four patients Hyperreflexia disappeared in one patient, volume at first and maximum hyperreflexic contraction and bladder capacity increased in one patient, amplitude of the hyperreflexic contractions decreased in one patient
[22]	Prospective	9	5	9	5	43.6	Voiding diary (no. of pads used per 24 h, no. of leakage episodes per 24 h, voiding frequency/clean intermittent self-catheterizations per 24 h, mean voided volume per micturition in millilitres) UDS (bladder volume at first uninhibited contraction, maximum bladder capacity before leakage, detrusor pressure at maximum unstable contraction) VAS (subjective improvement)	Preimplantation 6 months after implantation with stimulation on and off Last follow-up	Subjective improvement on VAS of at least 75 % in all patients Improvement in maximum bladder capacity and volume at first uninhibited contraction with neurostimulator on Frequency improved from 16.1 to 8 voids per day, mean volume per void increased from 115 to 249 ml, no. of leakage episodes improved from 7.3 to 0.3 per 24 h Six patients completely dry at 6 months
[19]	Retrospective	33	16	28	13	12.4	Voiding diary (no. of pads used per 24 h, no. of leakage episodes per 24 h, voiding frequency/clean intermittent self-catheterizations per 24 h)	Preimplantation 6 months after implantation with stimulation on and off Last follow-up	More than 50 % reduction in leakage episodes, nocturia or pad usage in all patients More than 50 % reduction in number of self-catheterizations in eight patients
[30]	Observational retrospective case-control	14	14	12	12	51.2±15.2	Preimplantation catheterization diary Preimplantation video-UDS with electromyography Uroflow and PVR measurements with suprapubic ultrasonography after implantation EDSS before implantation and at last follow-up	Preimplantation Postimplantation (not specified)	86 % of patients had spontaneous voiding Decrease in PVR Mean postoperative maximum flow rate of 17.7±7.9 ml/s
[20]	Retrospective	62	13	37	7	51±43	Voiding diary (frequency, urgency, urinary incontinence) UDS (bladder contractility, compliance, detrusor–sphincter dyssynergia, PVR) PVR measurement with suprapubic ultrasonography	Preimplantation Subchronic test stimulation 1 and 6 months after implantation and then every 12 months with stimulation on	More than 50 % clinical improvement in 75.7 % of patients (decreases in day-time frequency, nocturia, no. of incontinence episodes and urgency) Increase in mean first uninhibited detrusor contraction volume and mean maximum cystometric capacity, loss of detrusor–

Table 1 (continued)

Reference	Type of study	Patients included (*n*)		Patients implanted (*n*)		Mean follow-up (months)	Assessments used	Assessments done	Outcomes after implantation
		With neurological disease	With MS	With neurological disease	With MS				sphincter dyssynergia and decrease in maximum intravesical pressure
[29]	Observational retrospective case series	25	25	15	15	49.4	Voiding diary (number of daily voidings, voided volumes, number of episodes of incontinence, number of clean self-intermittent catheterizations) Preimplantation UDS PVR measurement with suprapubic ultrasonography I-QOL questionnaire	Preimplantation Postimplantation (not specified)	Increase in voiding volumes Decrease in frequency, urgency, PVR, no. of incontinence episodes and mean number of self catheterizations Increase in QoL scores

UDS urodynamics, *PVR* postvoid residual, *EDSS* Expanded Disability Status score, *VAS* visual analogue scale

symptomatic improvement had declined at the last follow-up. Overall urodynamic parameters (maximum bladder capacity and volume at first uninhibited contraction) had improved at 6 months from baseline. All patients reported improved VAS results by at least 75 % at the last follow-up.

A retrospective case series looked at 33 patients with neurological disease who had undergone SNM, of whom 16 had MS [19]. The test stimulation period was between 1 and 3 weeks (tined lead). At baseline, urodynamics and bladder diaries were completed. During the test phase, 4-day bladder diaries were completed and those who experienced greater than a 50 % improvement in symptoms (frequency, nocturia, incontinence episodes per 24 h and number of pads per 24 h) were offered placement of an IPG. For those with urinary retention, a greater than 50 % reduction in the number of catheterizations and a greater than 50 % increase in voided volumes were criteria for implantation. Of the 16 patients with MS, 13 went on to have implantation of the IPG, but results were presented for the group as a whole and not broken down into disease-specific outcomes. In this cohort of patients with neurological disease (including Parkinson's disease, spina bifida, cerebrovascular accident, spinal stenosis, autoimmune polyneuropathy and neurofibromatosis, in addition to MS), the mean number of incontinence episodes per 24 h decreased from 4 to 1.3 (SD 2.4; $p<0.0001$). The mean number of pads per 24 h decreased from 3.5 to 1.0 (SD 1.9; $p<0.002$). Of patients with urinary retention, 50 % had a 58 % reduction in the number of self-catheterizations per 24 h. The mean follow-up period was 12.4 months (range 4 – 32 months). This study lacked any QoL data for before and after implantation, so subjective assessment was not possible.

Another smaller retrospective case-control study specifically assessed SNM in MS patients with urinary retention [30]. A group of 14 patients with neurologist-confirmed MS (three with benign MS, seven with relapsing–remitting MS and four with secondary progressing MS) were evaluated. All patients had urodynamics-proven urinary retention and had a two-stage SNM procedure (tined lead). Assessments before and after implantation included completion of the Expanded Disability Status score (EDSS; *0* no apparent disease to *10* death resulting from MS) and 3-day bladder diaries. Video-urodynamics were done only before implantation and not after implantation to ascertain detrusor pressure improvement. All patients were asked whether they were satisfied with the operative result ('yes' or 'no'). The IPG was successfully implanted in 12 of the 14 MS patients (two did not void successfully during the stage 1 test phase). The mean follow-up was 4.32±1.32 years. All 12 of these patients were voiding spontaneously after implantation. The mean preoperative CISC volume was 308±53.60 ml compared to a mean postoperative residual urine of 50.5±21.18 ml. There was no significant change in the EDSS score.

Chaabane et al. carried out a retrospective study to assess the clinical and urodynamic effects of SNM in 62 patients with neurogenic lower urinary tract dysfunction [20]. Patients either had PNE and then placement of the IPG or a two-stage procedure. Of the 62 patients, 13 had MS. Preoperative evaluation included a 3-day bladder diary and urodynamics. The IPG was implanted if there was a 50 % improvement in the clinical and urodynamic findings during the test phase (which lasted a mean of 17 days). Patients were followed up at 1 month, 6 months and then yearly, with a bladder diary at each visit and repeat urodynamics if symptoms had recurred. Of the 13 patients with MS, 7 received the IPG after a positive test phase. Again in this study, the results were presented for the group as a whole. Mean follow-up was 4.3±3.7 years. There was a significant decrease in the mean number of voids per 24 h (10.90 to 6.07), the mean number of incontinence episodes per 24 h (3.08 to 0.14), the mean number of urgency episodes per 24 h (7.57 to 1.53) and the mean number of nocturia episodes per 24 h (2.63 to 0.15). Urodynamic evaluation showed a significant increase in maximum cystometric capacity and mean volume of first uninhibited detrusor contraction. SNM was considered to have failed in six patients, of whom three had MS. In the patients with MS the failure occurred on average 12 months after implantation and in each patient followed a new relapse of disease.

In 2012 a retrospective observational case series included 25 patients with MS and refractory neurogenic lower urinary tract dysfunction [29]. The first five patients had the test stimulation by PNE and the subsequent 20 had the test stimulation with the percutaneous tined lead described above. Preoperative assessments included a 4-day bladder diary, urodynamics and postvoid residual assessment and a QoL questionnaire (I-QOL). Patients with greater than 50 % improvement in symptoms of frequency and incontinence episodes and/or a greater than 50 % decrease in the number of catheterizations and a greater than 50 % increase in voided volumes were offered placement of the IPG. Of the 25 patients, 15 (ten women and five men) reported clinically significant improvement after the test stimulation procedure and were considered suitable for implantation. All 15 of these patients had urodynamic evidence of DO with DSD. The ten not implanted had detrusor underactivity. The mean follow-up was 49.4 months. Assessments carried out at follow-up included a 4-day bladder diary and the I-QOL questionnaire. Patients with urinary retention secondary to DSD (nine patients) were all performing CISC before the procedure (mean residual urine 300±55.7 ml (range 180 – 350 ml). There was a significant increase in the mean voiding volume (from 84.4± 36.8 ml to 237.8±31.5 ml) and a significant decrease in the mean residual volume (81.1±27.7 ml, range 35 – 120 ml). The mean number of catheterizations per day significantly decreased from 3.3±1.3 (range 2 – 6) to 1.2±0.7 (range 0 – 2). Incontinence episodes before implantation in patients who also had frequency in addition to retention significantly decreased from 6.7±4.1 (range 0 – 12) to 2.2±2.2 (range 0 – 6). Six patients had urinary incontinence due to DO. Three patients had frequency and high residual volumes. At follow-up, in these patients, mean frequency was reduced from 17.7±3.5 (range 14 – 21) to 9±0 times per day; mean residual urine decreased from 126.7±20.8 ml (range 110 – 150 ml) to 33.3 ±15.3 ml (range 20 – 50 ml). Incontinence episodes per day decreased from 13±2.6 (range 10 – 15) to 3.3±3.1 (range 0 – 6). In the three patients in whom frequency was not associated with high residual volume (mean 56.7±11.5 ml, range 50 – 70 ml), frequency was reduced from 18.3±1.5 (range 17 – 20) to 9.6±2.1 (range 8 – 12) times per day and incontinence episodes decreased from 15±0 to 6±1.7 (range 5 – 8) per day. All the above differences between before and after implantation were statistically significant. There was also a significant improvement in QoL scores in all 15 patients.

General considerations

It has reported that the initial test stimulation is the only constant factor in predicting success [31]. However, an accurate and comprehensive evaluation is mandatory to improve the chance of successful response to treatment. Age is not a limitation, but its role is still controversial, as patients older than 65 years seem less likely to be eligible for SNM [26, 32]; motivation, ability to handle the remote control and realistic expectations are other important factors to consider [32, 33]. Psychiatric disorders and psychological factors had been advocated as predictors of failure, but recently this relationship has not been confirmed [26, 31]. A longer duration of symptoms, detrusor underactivity and neurogenic bladder dysfunction seem predictive of a poorer outcome [22, 26, 29, 34], while the urodynamic diagnosis of DO has little relevance even if urodynamics is recommended to provide additional information about other possible diagnoses such as stress incontinence and bladder pain [25]. It has also been suggested that overall women respond better than men [22, 26].

The prognostic value of sensory and motor response is still uncertain [32]. Patients suffering from neurological diseases such as MS, should be carefully evaluated and, although there is a lack of randomized controlled trials, SNM is usually offered if the course of the underlying neurological disorder can be considered stable or slowly progressive and patients are not likely to require repeated magnetic resonance scans [32, 33]. In fact, it has been reported that loss of efficacy over time is a result of a new relapse [20, 22, 23]. One study found that patients with relapsing disease require adjustment of the stimulation parameters [29]. In two patients the IPG was removed because of progressive disease and symptom relapse and it was not possible to further adjust the stimulation parameters to obtain a significant clinical improvement. It has been suggested that bilateral stimulation could be more effective in

some patients, but extensive studies are still needed [25, 26, 31, 32]. Patients were offered the peripheral nerve evaluation (PNE) with temporary electrodes in the past and now more commonly a staged implantation with the definitive quadripolar tined-lead electrode, irrespective of the clinical indication. Evaluation and treatment algorithms, recommendations, procedures and implantation success rates are described elsewhere [25, 27, 32, 33].

Adverse events

Reports of complication rates include data on failure of the procedure (25 %), perceived pain and discomfort at the site of the implant (25 – 56 % and 40 %, respectively) [27, 35], lead migration over time (11 – 20 %) [26, 27, 36], revisional surgery (6 – 50 %) [25, 26, 30], neuropathic pain, hypersensitivity to stimulation, failure of the device and infections (6 – 15 %) [19, 25, 30, 36]. Amend et al. [32] have reported that the introduction of the tined lead and improvement in surgical technique have reduced the revision rate from 50 % to 31 %. Regarding the infection rate, it is not clear yet if differences in antibiotic use may explain the different infection rates reported by different authors [36], and it has been reported that the tined lead is associated with a high rate of infections (57 %) probably due to the longer test duration [20]. However, 16 % of complications can be treated conservatively [26].

Discussion

SNM has gained popularity in the treatment of neurological bladder disorders over the last few decades. However, the exact mechanism of action is not fully elucidated and predictive parameters are not yet available. Moreover, only small series of MS patients have been studied and the majority of studies have included heterogeneous groups of patients. Thus we have extrapolated predictive factors, complications rates and outcomes of SNM from data obtained in neurogenic and non-neurogenic populations. Although the maximum duration of follow-up is 7 years, which might be a limitation, the data analysed show a reasonably promising outlook.

A limitation of SNM in MS is the unpredictable course of the disease which may jeopardize the long-term results, or the potential need for magnetic resonance scans. Chaabane et al. [20] found loss of efficacy following disease relapse. Based on their experience, their recommendation is to propose SNM only in patients with relapsing–remitting disease who have not had a relapse for 2 years, but preferably longer. Despite these limitations, there is general agreement about safety and efficacy over time of SNM, and patients consider it a satisfactory option. SNM is also considered an attractive treatment for refractory neurological bladder disorders because it is minimally invasive and does not imply irreversible changes to the bladder or nerves, and does not bear the risk of late malignancy associated with bladder augmentation or urinary diversions. This may have particular relevance in patients with urinary retention for which there are few effective treatments, especially treatments resulting in the return of normal voiding. Long-term catheterization can lead to a decrease in QoL and there is the risk of UTI and urinary calculus formation [37]. In addition, SNM does not compromise the potential for future treatments. Further and larger studies are still needed to confirm its clinical role in MS patients, as well as randomized controlled trials.

Conflicts of interest F. Puccini: none.
A. Bhide: travel expenses – Astellas, Promega.
S. Elneil: travel expenses – Uroplasty, Medtronic.
G.A. Digesu: travel expenses – AMS, Astellas, Pfeizer, Uroplasty, Medtronic.

References

1. Crayton HJ, Rossman HS (2006) Managing the symptoms of multiple sclerosis: a multimodal approach. Clin Ther 28(4):445–460
2. Cohen BA (2008) Identification, causation, alleviation, and prevention of complications (ICAP): an approach to symptom and disability management in multiple sclerosis. Neurology 71(24 Suppl 3): S14–S20
3. Courtney AM, Castro-Borrero W, Davis SL, Frohman TC, Frohman EM (2011) Functional treatments in multiple sclerosis. Curr Opin Neurol 24(3):250–254
4. Crayton H, Heyman RA, Rossman HS (2004) A multimodal approach to managing the symptoms of multiple sclerosis. Neurology 63(11 Suppl 5):S12–S18
5. Gobbi C, Digesu GA, Khullar V, El NS, Caccia G, Zecca C (2011) Percutaneous posterior tibial nerve stimulation as an effective treatment of refractory lower urinary tract symptoms in patients with multiple sclerosis: preliminary data from a multicentre, prospective, open label trial. Mult Scler 17(12):1514–9
6. Fjorback MV, Van Rey FS, Rijkhoff NJ, Nohr M, Petersen T, Heesakkers JP (2007) Electrical stimulation of sacral dermatomes in multiple sclerosis patients with neurogenic detrusor overactivity. Neurourol Urodyn 26(4):525–30
7. Onal B, Siva A, Buldu I, Demirkesen O, Cetinel B (2009) Voiding dysfunction due to multiple sclerosis: a large scale retrospective analysis. Int Braz J Urol 35(3):326–333
8. Mahfouz W, Corcos J (2011) Management of detrusor external sphincter dyssynergia in neurogenic bladder. Eur J Phys Rehabil Med 47(4):639–650
9. Bacsu CD, Chan L, Tse V (2012) Diagnosing detrusor sphincter dyssynergia in the neurological patient. BJU Int 109(Suppl 3):31–34
10. Chapple CR, Khullar V, Gabriel Z, Muston D, Bitoun CE, Weinstein D (2008) The effects of antimuscarinic treatments in overactive bladder: an update of a systematic review and meta-analysis. Eur Urol 54(3):543–62
11. Nitti VW, Khullar V, van Kerrebroeck P, Herschorn S, Cambronero J, Angulo JC et al (2013) Mirabegron for the treatment of overactive bladder: a prespecified pooled efficacy analysis and pooled safety analysis of three randomised, double-blind, placebo-controlled, phase III studies. Int J Clin Pract 67(7):619–632

12. Habek M, Karni A, Balash Y, Gurevich T (2010) The place of the botulinum toxin in the management of multiple sclerosis. Clin Neurol Neurosurg 112(7):592–596
13. Khan S, Game X, Kalsi V, Gonzales G, Panicker J, Elneil S et al (2011) Long-term effect on quality of life of repeat detrusor injections of botulinum neurotoxin-A for detrusor overactivity in patients with multiple sclerosis. J Urol 185(4):1344–1349
14. Yokoyama T, Chancellor MB, Oguma K, Yamamoto Y, Suzuki T, Kumon H et al (2012) Botulinum toxin type A for the treatment of lower urinary tract disorders. Int J Urol 19(3):202–215
15. de Sèze M, Raibaut P, Gallien P, Even-Schneider A, Denys P, Bonniaud V et al. (2011) Transcutaneous posterior tibial nerve stimulation for treatment of the overactive bladder syndrome in multiple sclerosis: results of a multicenter prospective study. Neurourol Urodyn 30(3):306–311
16. Kabay SC, Yucel M, Kabay S (2008) Acute effect of posterior tibial nerve stimulation on neurogenic detrusor overactivity in patients with multiple sclerosis: urodynamic study. Urology 71(4):641–645
17. Kabay S, Kabay SC, Yucel M, Ozden H, Yilmaz Z, Aras O et al (2009) The clinical and urodynamic results of a 3-month percutaneous posterior tibial nerve stimulation treatment in patients with multiple sclerosis-related neurogenic bladder dysfunction. Neurourol Urodyn 28(8):964–968
18. Van Rey FS, Heesakkers JP (2008) Applications of neurostimulation for urinary storage and voiding dysfunction in neurological patients. Urol Int 81(4):373–378
19. Wallace PA, Lane FL, Noblett KL (2007) Sacral nerve neuromodulation in patients with underlying neurologic disease. Am J Obstet Gynecol 197(1):96–95
20. Chaabane W, Guillotreau J, Castel-Lacanal E, Abu-Anz S, De Boissezon X, Malavaud B et al (2011) Sacral neuromodulation for treating neurogenic bladder dysfunction: clinical and urodynamic study. Neurourol Urodyn 30(4):547–550
21. Tanagho EA, Schmidt RA, Orvis BR (1989) Neural stimulation for control of voiding dysfunction: a preliminary report in 22 patients with serious neuropathic voiding disorders. J Urol 142(2 Pt 1):340–345
22. Chartier-Kastler EJ, Ruud Bosch JL, Perrigot M, Chancellor MB, Richard F, Denys P (2000) Long-term results of sacral nerve stimulation (S3) for the treatment of neurogenic refractory urge incontinence related to detrusor hyperreflexia. J Urol 164(5):1476–1480
23. Ruud Bosch JL, Groen J (1996) Treatment of refractory urge urinary incontinence with sacral spinal nerve stimulation in multiple sclerosis patients. Lancet 348(9029):717–719
24. Hohenfellner M, Humke J, Hampel C, Dahms S, Matzel K, Roth S et al (2001) Chronic sacral neuromodulation for treatment of neurogenic bladder dysfunction: long-term results with unilateral implants. Urology 58(6):887–892
25. Bolton JF, Harrison SC (2009) Neuromodulation 10 years on: how widely should we use this technique in bladder dysfunction? Curr Opin Urol 19(4):375–379
26. Bosch JL (2010) An update on sacral neuromodulation: where do we stand with this in the management of lower urinary tract dysfunction in 2010? BJU Int 106(10):1432–1442
27. Elneil S (2010) Urinary retention in women and sacral neuromodulation. Int Urogynecol J 21(Suppl 2):S475–S483
28. Minardi D, Muzzonigro G (2005) Lower urinary tract and bowel disorders and multiple sclerosis: role of sacral neuromodulation: a preliminary report. Neuromodulation 8(3):176–181
29. Minardi D, Muzzonigro G (2012) Sacral neuromodulation in patients with multiple sclerosis. World J Urol 30(1):123–128
30. Marinkovic SP, Gillen LM (2010) Sacral neuromodulation for multiple sclerosis patients with urinary retention and clean intermittent catheterization. Int Urogynecol J 21(2):223–228
31. Marcelissen TA, Leong RK, Nieman FH, van Lankveld JJ, Van Kerrebroeck PE, De Wachter SG (2011) Psychological and psychiatric factors as predictors for success in sacral neuromodulation treatment. BJU Int 108(11):1834–1838
32. Amend B, Khalil M, Kessler TM, Sievert KD (2011) How does sacral modulation work best? Placement and programming techniques to maximize efficacy. Curr Urol Rep 12(5):327–335
33. Norderval S, Rydningen M, Lindsetmo RO, Lein D, Vonen B (2011) Sacral nerve stimulation. Tidsskr Nor Laegeforen 131(12): 1190–1193
34. Scheepens WA, Jongen MM, Nieman FH, de Bie RA, Weil EH, Van Kerrebroeck PE (2002) Predictive factors for sacral neuromodulation in chronic lower urinary tract dysfunction. Urology 60(4):598–602
35. Leong RK, Marcelissen TA, Nieman FH, de Bie RA, Van Kerrebroeck PE, De Wachter SG (2011) Satisfaction and patient experience with sacral neuromodulation: results of a single center sample survey. J Urol 185(2):588–592
36. Siddiqui NY, Wu JM, Amundsen CL (2010) Efficacy and adverse events of sacral nerve stimulation for overactive bladder: a systematic review. Neurourol Urodyn 29(Suppl 1):S18–S23
37. Comiter CV (2008) Sacral nerve stimulation to treat nonobstructive urinary retention in women. Curr Urol Rep 9(5):405–411