Original Article

Effectiveness of sacral neuromodulation in the management of refractory bladder pain syndrome

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Abstract: INTRODUCTION AND AIM OF THE STUDY. Bladder Pain Syndrome (BPS) is a complex pathology, with a prevalence ranging from 0.06% to 30%. In patients refractory to first line treatment, sacral neuromodulation (SNM) can reduce BPS symptoms and improve patients' lower urinary tract symptoms (LUTS) associated. The aim of this study was to evaluate the effectiveness of SNM for the treatment of symptoms in patients with refractory BPS. *Materials and methods:* The data regarding patients undergoing SNM refractory to medical/conservative therapy, who underwent InterStim® SNM 2012 and 2014 in a single Italian centre, were retrospectively evaluated. Bladder pain was assessed with a 0-10 Visual Analogue Scale (VAS) before and one year after the treatment and at the last follow-up visit, whereas LUTS were evaluated using a three-day bladder diary. *Results:* Twenty-three patients underwent first stage unilateral S3 stimulation; median age was 56 years and mean follow-up was 32 months; 78% of the patients showed a significant improvement and underwent a definitive implant. Patients' reported pain score decreased from a mean of 8 at baseline to 3 at one-year follow-up ($p < 0.001$). Urgency decreased from 4.6 ± 2.4 up to 1.3 ± 1.9 ($p < 0.001$). Daily urinary frequency improved from 12.7 ± 4.8 times up to 8.7 ± 2.8 ($p < 0.001$) and nocturia decreased from 2.5 ± 1.9 up to 0.7 ± 1 ($p < 0.001$). Mean voided volume increased from 145.4 ± 70.5 ml to 208.2 ± 73.4 ml ($p < 0.001$). Clinical effectiveness was maintained in the last follow-up visit. Conclusions: SNM appears to be effective and safe in treating refractory BPS with associated LUTS.

Keywords: Sacral neuromodulation; Bladder pain syndrome; Pelvic pain; Interstitial cystitis; Effectiveness.

INTRODUCTION

Bladder Pain Syndrome (BPS), formerly known as interstitial cystitis (IC) and painful bladder syndrome, was defined in 2008 by The European Society for the Study of Bladder Pain Syndrome (ESSIC) as the presence of chronic (more than 6 months) pelvic pain, pressure or discomfort perceived to be related to bladder, accompanied by at least one urinary symptom such as persistent urgency to the emptying or frequency. [1] At the moment, there is no agreement how this complex syndrome should be referred to.This disease is a multidimensional and invalidating pathology; it is difficult to evaluate BPS prevalence, because this condition is underestimated. Reports of BPS prevalence have varied greatly, along with the diagnostic criteria and populations studied. Prevalence of BPS ranges from 0.06% to 30%,[2] whereas a survey conducted in USA in 2004 on the female members of the University of California (San Diego) identified a probable IC in 30.6% of the young women and a documented IC in a minimum of 10% of the female medical students.[3] A review conducted by Buffington in 2004 supposed, moreover, that this pathology is not a single disease, but a member of large clinical conditions, due to a stress response pattern of increased sympathetic nervous system function.[4] IC/BPS patients are, moreover, more frequent affected by irritable bowel syndrome (38.6% versus 5.2%), fibromyalgia (17.7% versus 2.6%) and chronic fatigue syndrome (9.5% versus 1.7%; all $p < 0.001$), in comparison with asymptomatic control subjects.[5] Management of BPS symptoms is a therapeutic challenge and needs a multi-disciplinary management; unfortunately, available studies, due to the great heterogeneity of methodology, give only limited evidence on several options proposed for the treatment of PBS/IC. [6]

First-line treatments of BPS/IC are conservative and includes: education and patient support, dietary and behavioural changes, stress reduction, dietary changes, relaxation techniques and pelvic floor muscle training.[2]

Second line treatments include both oral (antidepressant, pentosanpolysulphate sodium, and anti-convulsivants) and intravesical therapies (pentosanpolysulphate sodium, heparin, hyaluronic acid). When intravesical instillation therapies have failed, it is possible to consider intravesical bladder wall and trigonal injection of botulinum toxin A. Actually, in refractory patients sacral neuromodulation (SNM) may be a further option, as well. SNM can reduce BPS symptoms and improves voids and over 90% of patients treated with neuromodulation would undergo the implant again.[7]

Moreover, SNM decreases Interstitial Cystitis Symptom and Problem Index scores decreased from 16.5 to 6.8 and 14.5 to 5.4, respectively ($p < 0.01$), showing safety and efficacy of this treatment.[8]

The aim of this study was to evaluate safety and effectiveness of SNM for the treatment of patients with refractory BPS.

MATERIALS AND METHODS

We retrospectively collected and analysed the data regarding a cohort of patients undergone SNM with InterStim® for refractory bladder pain syndrome (BPS) between March 2012 and July 2014.

All patients fulfilled the diagnostic criteria for BPS:

- chronic presence (more than six months) of pelvic pain, pressure or discomfort perceived to the bladder
- association with at least one lower urinary tract symptom, such as urgency or frequency)
- not results responsive to oral and intravesical therapy.

All patients were older than 18 years and organic causes of BPS were ruled out.

All patients affected by neurological diseases, stress urinary incontinence or pelvic organ prolapse, were excluded from the study. Each patient was evaluated by medical history, urologic physical examination and bladder diary. Both

the first stage and the definitive implant of SNM were conducted by the same surgeon (FC).

The first stage of the procedure was conducted using the tined lead[9] of InterStim (Medtronic, Inc., Minneapolis, MN, USA).

All responders patients, that showed an improvement of pain and urinary symptoms > 50%, underwent a definitive implant. Bladder pain was evaluated with a a 0-10 point scale visual analogue scale (VAS) and all patients completed preoperatively a 3-day voiding diary, with the aim to evaluated frequency of micturition, episodes of urgency or incontinence and voided volume.

Moreover, all patients were evaluated at 12 months after the procedure with history, physical examination and voiding diary.

After a minimum follow up of 12 months a global evaluation was conducted and patients filled VAS score and voiding diary. All complications were recorded and evaluated. Statistical analysis was performed using the Statistical Package for Social Science (SPSS Inc, Chicago, IL) version 18.0. Continuous variables with normal distribution were reported as means and standard deviations; non-normally distributed continuous variables were reported as medians and interquartilic range (IQR) or range; the t-test and the Wilcoxon tests were used to compare the continuous variables, as appropriate. A $p \leq 0,05$ was considered statistically significant.

RESULTS

The data regarding 23 patients (18 females and 5 males), diagnosed with refractory BPS and treated with SNM were collected and retrospectively evaluated. A uro-gynaecological physical examination excluded organic diseases in all patients.

After the first stage procedure, 18/23 patients (78.3%), all females, showed an improvement of at least 50% in pain relief and LUTS. Therefore, these patients were candidates for definitive implant with InterStim® (Medtronic, Inc., Minneapolis, MN, USA).

Median age of the patients was 56 years (range 43-75 years), with a median time from diagnosis of 2.5 years (range 1 to 6.5 years).

Median follow up was 32 months (range 12-38 months). In 85% of cases the electrode was placed at the S3 nerve root, on the right side, in the standard manner. VAS score decreased significantly from a median value of 8 at the baseline (range: 8-10) to 3 (range: 2-5) at one-year-follow up ($p < 0.001$) (Figure 1). The pain reduction was, therefore, statistically significant.

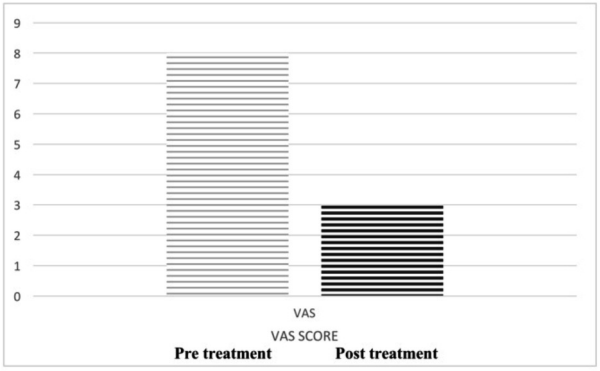

Figure 1. – Median pain reduction from baseline to one-year follow-up after SNM.

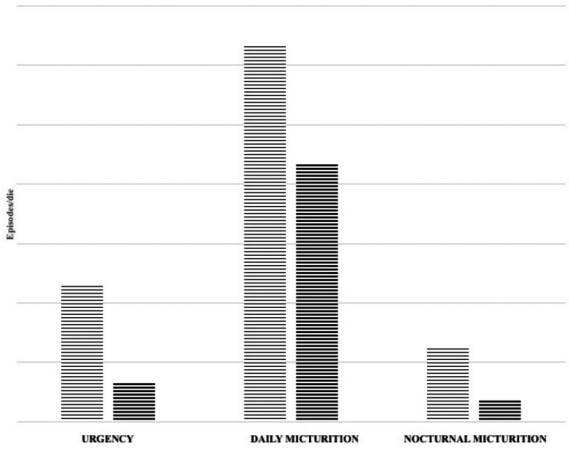

Figure 2. – LUTS reduction from baseline to one-year-follow-up after SNM.

With regard to the associated LUTS, urgency episodes decreased from 4.6 ± 2.4 to 1.3 ± 1.9 ($p < 0.001$) (Figure 2), daily micturitions improved from 12.7 ± 4.8 to 8.7 ± 2.8 ($p < 0.001$) (Figure 2) and nocturnal micturitions from 2.5 ± 1.9 to 0.7 ± 1 ($p < 0.001$) (Figure 2).

The mean voided volume, moreover, increased after SNM from 145.4 ± 70.5 ml to 208.2 ± 73.4 ml ($p < 0.001$) (Figure 3).

Overall, SNM showed a statistically significant improvement in both VAS score and LUTS.

During the analysed follow-up, no patient has replaced the impulse generator because of battery depletion or developed pain or infection at the site of the definitive implant. No complications led to the extraction of either the electrode or the impulse generator.

DISCUSSION

The aim of our study was to evaluate safety and effectiveness of SNM in a cohort of patients affected by refractory BPS at a mid term follow up; SNM demonstrated a statistically significant improvement in reducing both bladder pain and LUTS.

Median VAS score was reduced from 8 (range: 3-10) to 3 (2-5) (62%) at one year follow up after treatment; moreover, daily frequency reduced from 12.7 ± 4.8 to 8.7 ± 2.8 (31%), whereas nocturnal micturition from 2.5 ± 1.9 to 0.7 ± 1 (72%), urgency episodes from 4.6 ± 2.4 to 1.3 ± 1.9 (71%) and voided volume increased from 145.4 ± 70.5 ml

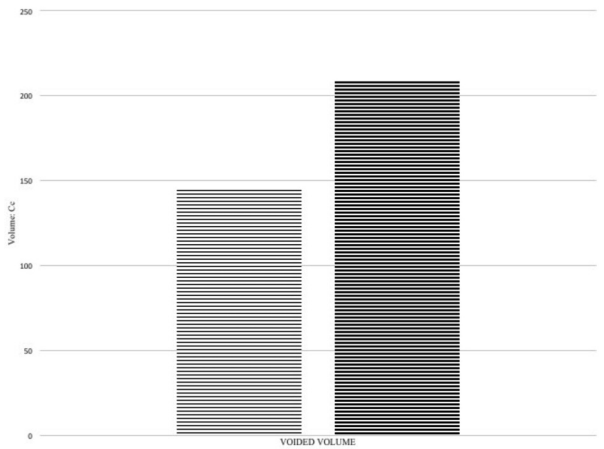

Figure 3. – Voided volume improvement from baseline to one-year-follow-up after SNM.

to 208.2 ± 73.4 (50%). Our results seem to be at least overlapping to those from the most recent literature.

Marinkovic *et al* conducted a observational, retrospective, case controlled review on a small series of 34 female patients undergone SNM for IC and documented a reduction of the visual analogue pain scale from 6.5 ± 2.9 at the baseline to 2.4 ± 1.1 ($p < 0.01$) at 86 months of follow up.[10]

Patients from Marinkovic's series were younger than our patients (median age 41 versus 56 years) with a significantly longer follow up (86 months versus 32 months); moreover, SNM confirmed its effectiveness also on LUTS, showing a reduction of urgency/frequency scores from 21.61 ± 8.6 to 9.22 ± 6.6 ($p < 0.01$), thus confirming the effectiveness of this technique also in a long term follow up.[10]

In 2010 Gajewski et al carried out a larger study on 78 patients treated with SNM for BPS; at a mean follow up of 61.5 months, they showed an improvement at the Global Response Assessment (GRA) and a good long term success in 72% of patients, confirming the good effectiveness of this technique.[11] The Authors supposed that the presence of urgency was a positive predictor of the long term successful effects of the SNM.[11]

The only randomized trial that evaluated SNM and pudendal neurodulation (PNS) in the treatment of IC was conducted by Peters et al in 2007.[7] This study was a prospective randomized, single blind, crossover trial, conducted on 22 patients (19 women and 3 men), with a mean age of 46 years; 77% of them experienced a significant symptoms improvement after tined leads placement and underwent a definite implant. Bladder pain was evaluated with a 10-cm VA and decreased by 49% in the SNM group (from 7.9 to 4.0) and by 29% in the PNS group (from 4.5 to 3.2), whereas in our series bladder pain decreased of 62% (8 to 3).[7] Patients' satisfaction was high, because all patients treated with SNM and 90% of those treated with PNS answered "yes" when asked if they would undergo the implantation again.[7]

Both SNM and PNS were effective also in the management of LUTS, showing a reduction of micturition frequency by 41% for PNS and 33% for SNM, whereas mean voided volume increased by 95% and 21%, and incontinence decreased by 92% and 17%, respectively.[7]

In our series, with a longer follow up (32 versus 6 months), daily frequency reduced by 31%, nocturnal micturition by 72%, urgency episodes by 71% and voided volume by 50%, confirming the results from Peters et al.

Bladder pain evaluation is, unfortunately, heterogeneous; Whitmore showed a bladder pain reduction from 2.2 + 0.7 to 1.6 + 0.8 (0: none; 3: severe pain),[12] whereas Steinberg showed a UDI-6 mean change between the preoperative and postoperative values of 5 ($p = 0.001$).[13]

Despite the heterogeneity in BPS evaluation and the low number of patients treated in the present series, our data are at least overlapping to those from the literature, and confirmed the effectiveness of SNM in the treatment of BPS at a mid term follow up.

CONCLUSION

SNM is a safe and effective treatment in patients affected by refractory BPS, improving both bladder pain and LUTS. Larger randomized study are needed to confirm the long term effectiveness of this technique.

DISCLOSURE STATEMENTS

There was no conflict of interest, informed patient consent was obtained, and the study was approved by the local ethical committee

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