Techniques in Coloproctology (2020) 24:215–220
https://doi.org/10.1007/s10151-020-02148-2

ORIGINAL ARTICLE

Outcomes of sacral neuromodulation for chronic pelvic pain: a Finnish national multicenter study

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Received: 30 July 2019 / Accepted: 6 January 2020 / Published online: 21 January 2020

Abstract

Background The aim of this study was to report the outcomes of sacral neuromodulation (SNM) in chronic pelvic pain (CPP) patients in the Finnish national cohort.

Methods This was a register-based retrospective study, involving all the centers that provide SNM treatment in Finland. The data of all patients treated with SNM for CPP were gathered from Oulu-, Turku-, Tampere- and Helsinki University Hospitals, as well as Jyväskylä and Seinäjoki Central Hospitals. All patients who had been tested for SNM implantation prior to April 2017 were included in the study.

Results A total of 51 patients were selected for SNM treatment due to CPP from 2004 until 2017. The mean follow-up time was 13.8 months (SD 22.9 months). A total of 28 patients (57%) advanced from testing to permanent stimulator implantation. There were 21 patients (41%) who had a working modulator implanted at the end of follow-up. Patients with endometriosis-related pain had a significantly higher permanent implantation rate than the overall implantation rate (88% vs. 57%; $p=0.01$). The endometriosis patients also had a higher overall success rate by the end of the follow-up (75% vs. 41%; $p=0.026$)

Conclusions SNM may be a viable treatment option for patients with CPP due to endometriosis. Further research on SNM treatment for endometriosis patients with refractory CPP is needed.

Keywords Sacral neuromodulation · Chronic pelvic pain · Endometriosis · Finnish national study

Introduction

Sacral neuromodulation (SNM) is a treatment based on an implanted electrode that stimulates the S3 or the S4 nerve root. SNM was first used in urology for treatment of overactive bladder symptoms, urge urinary incontinence with or without confirmed detrusor overactivity, and chronic urinary retention [1]. SNM has been increasingly used in other pelvic disorders, such as fecal incontinence, chronic pelvic pain (CPP), and also in the treatment of chronic constipation [2]. SNM has been used to treat CPP with success rates ranging from 60 to 98% in small studies [3, 4] and more studies have been called for [5, 6].

CPP is associated with a variety of gastrointestinal disorders (irritable bowel syndrome, inflammatory bowel disease, diverticulosis, polyposis), urological disorders (interstitial cystitis, complications after urological surgery), gynecological disorders (pain after surgery, PID, endometriosis and adenomyosis), neurological disorders (musculoskeletal nerve-related disorders), vascular diseases (pelvic congestion syndrome), and psychiatric disorders [7]. The prevalence of chronic pelvic pain amongst women of reproductive age is between 2.1 and 24% of the female population worldwide [8]. Up to 20% of the visits to gynecologists, 40% of laparoscopies and 15% of hysterectomies are linked to CPP [9]. In about one third of the laparoscopies performed for CPP, endometriosis lesions are found.

The aim of this study was to report the outcomes of SNM in CPP patients using a national database.

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Materials and methods

This was a register-based retrospective study, involving all the centers that provide SNM treatment in Finland. The study was part of a bigger project, in which we gathered all the Finnish patients that were treated by SNM for any indications between 2004 and 2017 (701 in total). From this cohort we selected all the patients ($n = 51$) whose most significant symptom was CPP (Fig. 1) Six centers performed SNM for CPP: Oulu-, Turku-, Tampere- and Helsinki University Hospitals, as well as Jyväskylä and Seinäjoki Central Hospitals, the indication usually failure of conservative treatment. Patients who could not cooperate, those with cognitive disorders or with a condition that might require magnetic resonance imaging were not offered SNM. The etiology of CPP in the study population is shown in Table 1

The following data were collected from the patient records: age, sex, etiology of pain, degree of pain as indicated by the patient on the visual analogue scale (VAS:scale of 1–10, 10 = worst pain), placement of the electrodes, test phase characteristics (pulse amplitude, frequency and duration), complications during testing, complications after placement of permanent stimulator. Data input took place in 2017.

The SNM implantation procedure was carried out in two stages. Stage 1 was performed with the patient in the prone Jack-knife position under either local or general anesthesia. The electrodes were implanted unilaterally in the S3 or S4 foramina. Stage 1 evaluation was conducted 3–4 weeks after the implantation. Patients with over 50% reduction in VAS, reduction in use of pain medication or self-reported pain relief advanced to Stage 2. Stage 1 of SNM treatment was defined as successful, when patients progressed to stage 2. This is similar to the International Continence Society best practice statement for use of SNM [2]. In Stage 2, patients were implanted with a permanent pacemaker. The success of SNM stage 2 was defined by patients having a working electrode in place with self-reported pain relief at the time of data collection. This method of evaluating success was chosen because Finnish centers lack a common practice of evaluating treatment success.

Table 1 Etiology of chronic pelvic pain in the patient cohort ($n = 51$)

Etiology	Frequency	Percent
Obstetric injury	1	2
Postoperative pain	15	29
Endometriosis	16	31
Idiopathic pain	16	31
Unknown	3	2

Statistical analysis

Microsoft® Excel® for MAC version 15.13.1 was used for data collection. IBM® SPSS® software Version 25 was used for statistical analysis. The Shapiro–Wilk test was used to check for normality, where $p > 0.05$ indicated a normal distribution. For continuous values, the Kruskal–Wallis independent samples test was utilised, where a p-value of < 0.05 indicated a significant difference in means. When

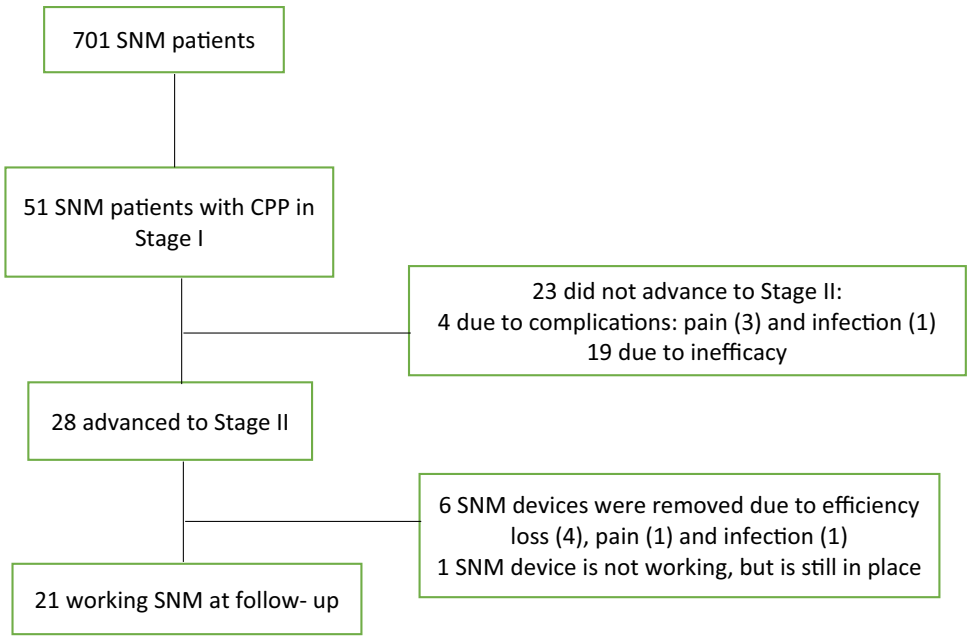

Fig. 1 STROBE flow chart

a significant difference was noted, the groups were further analysed with the Mann–Whitney *U* test to determine the differences between groups. Either Pearson's Chi-squared test or the Fisher's exact test was used to compare nominal values. The overall change in pre- and post-testing VAS was tested using the single sample *t*-test. A *p*-value of < 0.05 was set as statistically significant.

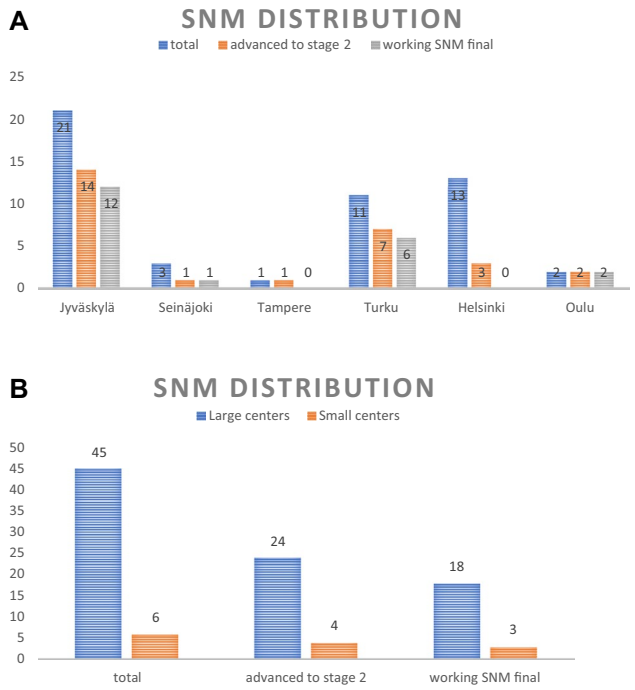

Fig. 2 SNM distribution: **a** by hospital; **b** by large vs small centers

This study was conducted in accordance with Finnish Medical Research Act 488/199, 295/2004 and approved by the Ethics Committee of the Hospital District of Southwest Finland (ETMK: 163/1801/2015).

Results

There were a total of 51 patients selected for SNM treatment due to CPP in Finland from 2004 until 2017. Most of the patients (82.4%; $n = 42$) were female, and the median age of patients was 43 years (range 20–83 years) SD 17.0. The etiology of CPP is presented in Table 1. The VAS were available for 20 patients, the median VAS before testing was 7.4, and dropped to 2.2 during SNM testing. The median follow-up time was 3.2 months range (0.3–98.9 months SD 22.9 months). A total of 28 patients (57%) advanced from testing to permanent stimulator implantation. There were 21 patients (41%) who had a working modulator implanted at the end of the follow-up. The results for each centre can be seen in Figs. 2 and 3. Three of the centers had completed > 10 implantations during the period and were classified as large, and 3 had done ≤ 4 and were classified as small. In large centers, 53% of the SNM patients advanced to stage 2 and 40% of the patients had a working SNM by the end of the follow-up. In small centers, there was a slightly higher percentage of SNM patients advancing to stage 2 (67%) and also of patients having a working device at the time of the data collection (50%).

Patients who advanced to permanent stimulator implantation were significantly younger (median age 42 years, range 20–60 years) than patients who did not advance to permanent stimulator implantation (median age 60 years, range

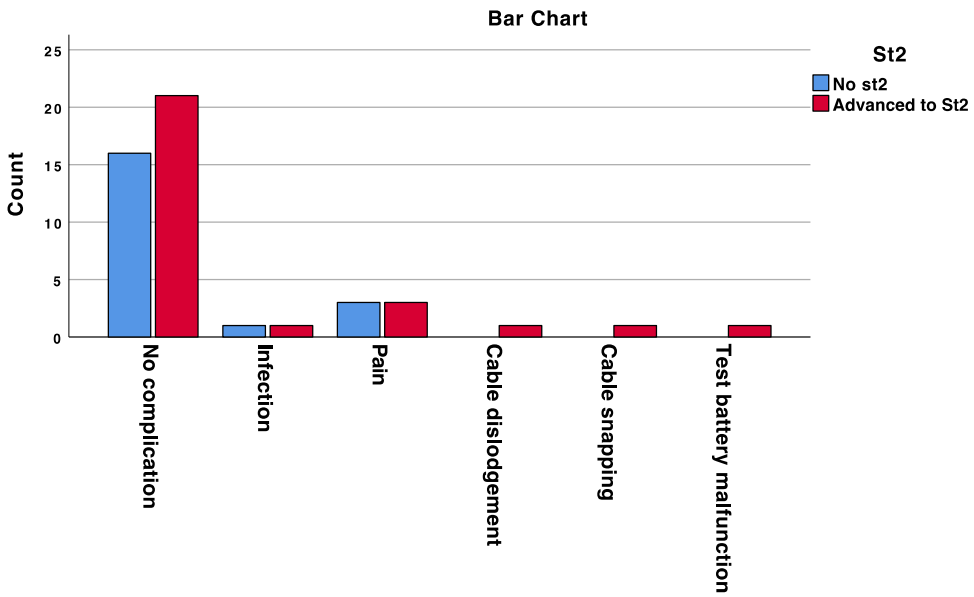

Fig. 3 Frequencies of the complications occurring during testing

24–83 years) ($p=0.01$). However, the age of the patients did not significantly affect the final outcome: the median age was 41 years for patients who had a working SNM by the end of the follow-up, and 52 years for those that did not have a working SNM, but this age difference was not statistically significant ($p=0.054$).

The leads were placed in the S3 foramen in 49% and in the S4 foramen in 51% of the cases. The placement of the leads did not influence the advancement to permanent modulator implantation, which was 54% [10] for S3 placement and 60% [11] for S4 placement of the electrodes ($p=0.776$), nor had it any effect on the overall outcome, with good results for 48% [12] for S3 placement and 44% [12] for S4 placement ($p=1.000$). Technical data regarding SNM parameters were found for 34 patients. The number of electrodes provoking a motor response during testing did influence the advancement to permanent stimulator implantation ($p=0.009$). Only 18% of the patients with two electrodes provoking a motor response advanced to permanent stimulator implantation. Moreover, 67% with three electrodes provoking a response and 75% of those with four electrodes provoking a motor response advanced to permanent stimulator implantation.

The number of electrodes provoking a motor response during the test phase clearly had an effect on the overall success rate of treatment ($p=0.014$), as can be seen in Table 2.

Patients who advanced to permanent modulator implantation had an average VAS of 2.1 (SD = 1.63) during testing (documented for 15 patients). This was significantly lower than the average VAS 6.3 (SD = 2.15) of patients who did not advance to permanent modulator implantation (documented for 5 patients) ($p=0.004$).

The etiology of the pelvic pain was primarily endometriosis or idiopathic pain. There were clear differences between patients with different etiologies in advancing to permanent modulator implantation and overall success rates, as can be seen in Table 3.

The complication rate did not have any effect on the advancement to permanent stimulator implantation ($p=0.200$), nor on the overall outcome ($p=0.211$). The total number of complications during the test phase was 11 (22%).

Table 2 Relationship between number of electrodes provoking a motor response during the test phase and overall success rate of treatment

	2 working electrodes (%)	3 working electrodes (%)	4 working electrodes (%)
Advanced to stage 2	2 (18)	2 (67)	15 (75)
No stage 2	9 (82)	1 (33)	5 (25)
Good result	2 (18)	1 (33)	14 (70)
Bad result	9 (82)	2 (67)	6 (30)
Total	11 (100)	3 (100)	30 (100)

Table 3 Permanent stimulator implantation and overall results

Etiology	Total	Advanced to permanent stimulator implantation (%)	Good overall result (%)
Endometriosis pain	16	14 (88)	12 (75)
Idiopathic pain	16	6 (38)	5 (31)
Post operative pain	15	7 (47)	5 (33)
Obstetric injury	1	1 (100)	–
Data missing	3	3	5
		$p=0.010$	$p=0.026$

The frequencies of the complications occurring during testing are presented in Fig. 3: 6 had pain, 2 had infection, 1 had cable dislodgement, 1 cable snapped, and test battery malfunction was reported in 1. A total of 6 patients (12%) required additional procedures during the test phase: the test cable was removed in 4 patients, in 3 cases due to operation site pain, and in 1 case an infection led to a further procedure. The test electrode was replaced in two patients, 1 case after cable dislodgement and 1 due to operation site pain.

The permanent modulator was removed from six patients (12%). The reasons for removal were loss of effect in 4 cases, pain in 1 case, and infection in 1 case.

Discussion

This is the first national study in Finland to assess the results of SNM for CPP. Our study confirms the results of other studies and shows that SNM may be efficient in the treatment of CPP, with a relatively low rate of complications. The success rate of SNM for CPP after stage 1 based on implantation rate was 57%, dropping to 41% by the end of the follow-up. This is lower than the pooled success rate of 84% (ranging from 60 to 98%) reported in a global systematic review and meta-analysis of SNM for refractory bladder pain and interstitial cystitis [3]. However, it is similar to the implantation rate of 59% reported by Martellucci et al. [13] in a prospective multicenter study with 27 patients suffering from multietiological medication resistant pelvic pain. Interestingly, in their study, Martellucci and colleagues reported that all the patients with pelvic pain following a hysterectomy received permanent implantation. The total complication rate was 21.5%, and the explantation rate 11.8%. This is lower than the explantation rate reported by other studies of 14–17% [14]. The implant site pain rate of 11.8% was also lower than the rate of 15% reported in the most recent prospective, controlled data with 5-year follow-up [15]. The infection rate of 3.9% is similar to the 2–11% reported by other studies [2].

The most important finding in our study was that patients with endometriosis related pain had a significantly higher permanent implantation rate (88%), compared to the overall implantation rate of 57%. The endometriosis patients also had a higher overall success rate of 75% by the end of the follow-up.

There are only a few studies investigating the role of SNM in the treatment of endometriosis. A review [16] of neuromodulation for treatment of endometriosis-related symptoms that suggests that SNM may be effective in the treatment of endometriosis patients with CPP. There is only one study [17] in which SNM was found to be effective during the testing period in three out of four patients, with all three patients having a functioning device at the end of the follow-up of 2.5 years.

It is not completely clear why SNM is more effective in endometriosis related CPP. The etiology of endometriosis pain is complex, with neurogenic inflammation, pelvic floor muscle hypertonicity and central sensitization being potentially involved [16]. The prevalence of muscle spasms and hypertonicity is three times higher in women with endometriosis than in controls [18]. Four mechanisms of actions of neuromodulation have been demonstrated in vitro: afferent modulation, synaptic facilitation, direct stimulation and increased neuroplasticity, the first one possibly explaining the modulation of abnormal fibres in neuropathic pain or the reduction of pelvic floor hyperactivity in myofascial pain, thus explaining why SNM was more efficient in the treatment of endometriosis-related CPP [19].

Endometriosis is common [20] and has a significant cost of illness burden, with the majority of the costs being related to productivity costs [21]. Studies indicate that as little as a 10% reduction on a pain scale is needed to improve productivity [22], while the more generally accepted figure for chronic pain is 30% [23].

Our study does not encourage the use of SNM for CPP with idiopathic etiology or after surgery. There is only 1 study that specifically investigates and underlines the role SNM may play for chronic idiopathic anal pain [24].

This is a retrospective study that has its limitations: patients' recorded data were different from center to center, the scarce documentation of VAS scale and the absence of a common pain evaluation method between the different centers, long-term results relying on data saved in patient records, with no specific questionnaires or phone interviews.

Conclusions

Our results facilitate further research on SNM treatment for endometriosis patients with refractory CPP. Long- term results are needed, as well as prospective studies.

Funding No grants or funding have been received for this study.

Compliance with ethical standards

Conflict of interest Adrian Zegrea has received financial support for attending symposia from Medtronic, Olympus, Johnson & Johnson. The other authors declare that they have no conflict of interest.

Ethical approval This study was conducted in accordance with Finnish Medical Research Act 488/199, 295/2004 and approved by the Ethics Committee of the Hospital District of Southwest Finland (ETMK:163/1801/2015).

Informed consent Formal consent was not required for this retrospective study.

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