

# Efficacy of sacral neuromodulation in treating chronic pain related to painful bladder syndrome/interstitial cystitis in adults

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## Abstract

**Objective:** The objective of this review is to evaluate the efficacy and safety of sacral neuromodulation in treating chronic pelvic pain related to Painful bladder syndrome/Interstitial-cystitis.

**Design:** The databases searched were MEDLINE and EMBASE [1950- Nov 2011]. Additional searches were performed on the Cochrane Database of Systematic reviews (CDSR), Scopus, CINAHL, BIOSIS, The Cochrane controlled trials register, the science citation index, TRIP DATABASE.

**Results:** Overall 70.8% or 170/244 patients were successful at the trial stage. The only randomized controlled trial reported a decrease in Visual analogue pain scores of 49% (7.9 to 4.0) for sacral nerve stimulation [SNS] and 29%(4.5 to 3.2) for pudendal nerve stimulation [PNS] at 6 months follow up. Nine observational studies reported a decrease in pain scores/decrease in pain medications at long term follow up following permanent sacral neuromodulation. One study showed an 80% improvement in Global response assessment score.

**Conclusion:** The results from the randomised controlled trial and case series/case reports demonstrate a reduction of pain symptoms of Painful bladder syndrome following sacral neuromodulation

**Key words:** Pain, chronic, neuromodulation, sacral, pelvic pain, painful bladder syndrome, interstitial cystitis

## Introduction

Painful bladder syndrome (also termed interstitial cystitis, bladder pain syndrome) is a clinical diagnosis based on symptoms of urgency, frequency, and pain in the bladder (related to filling/voiding) and/or pain in the pelvic region.<sup>[1]</sup> Patients often have a combination of voiding symptoms and pain, and usually one of the symptom complexes dominate. The quality of life is reported to be worse than those in patients with renal failure or hemodialysis.<sup>[2]</sup>

The treatment of painful bladder syndrome/interstitial cystitis (PBS/IC) is largely empiric and not well evaluated by large randomized control trials (RCTs).<sup>[3]</sup> Current pain

management techniques do not provide satisfactory pain relief and patients are either left in pain or have to choose to undergo major surgery of uncertain benefit.<sup>[1]</sup> The use of sacral neuromodulation (SNM) for pain relief specifically in PBS/IC was prompted by the observation that the use of SNM afforded collateral pain relief to patients with urological symptoms such as frequency and urgency.<sup>[4]</sup> Subsequent case series have backed up the pain-relieving efficacy of SNM in patients with chronic pain related to PBS/IC. SNM is recommended for the management of pain related to PBS/IC when all other treatment modalities have failed.<sup>[1]</sup>

A review of the efficacy of SNM for chronic pelvic pain was recently published.<sup>[5]</sup> However, the review included patients with non-specific pelvic pain in addition to those with PBS/IC. SNM therapy in clinical practice is offered mainly to patients with pain related to PBS/IC. To the best of my knowledge, no review has been undertaken to assess the efficacy and safety of SNM for chronic pain targeted exclusively on PBS/IC. The first step in offering a therapeutic modality to a patient group is to identify the patient population that is most likely to benefit. This review concentrates on evaluating the efficacy and safety of SNM techniques in the treatment of pain specifically related to PBS/IC.

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## Methodology

### Search strategy

A comprehensive search was undertaken to systematically identify literature concerning clinical effectiveness of SNM in adults for chronic pain related to PBS/IC. The databases searched were MEDLINE and EMBASE spanning from 1950 to 2011. Additional searches were performed on the Cochrane Database of Systematic reviews (CDSR), Scopus, CINAHL, BIOSIS, The Cochrane controlled trials register, the science citation index, TRIP DATABASE, and the NHS Centre for Reviews and Dissemination database (DARE). Other sources such as Google scholar, National Research Register (NRR), the Current Controlled Trials register, and the MRC Clinical Trials Register, and the table of contents of key journals were searched online.

SNM for PBS/IC pain is a recent therapy for pain and there is a paucity of literature on this special topic. Initially, critical review of literature was restricted to literature published within the last 5 years, but it was found to be too strict and restrictive. Thereafter, for the purposes of this literature review, research articles published in the last 10 years (2001–2011) were selected.

The reference list of the relevant journal articles identified was hand-searched for trials relating to SNM in pain related to PBS/IC. Back chaining of reference lists was undertaken.

The keywords searched were: Sacral neuromodulation, sacral nerve stimulation, neuromodulation and chronic pelvic pain, urogenital pain, painful bladder syndrome, and interstitial cystitis. The search was limited to humans and literature in the English language.

### Selection criteria

#### *Type of studies*

A single reviewer selected the studies after perusing the abstracts. For the purposes of this review, studies which have investigated the use of SNM in patients with PBS/IC were selected. Studies that included the use of SNM in chronic pelvic pain without PBS/IC were excluded. Studies that reported use of SNM in conditions like vulvodynia, endometriosis, clitoral pain, and anal pain were also excluded.

#### *Type of participants*

All adults with PBS/IC with inadequate response to medical and surgical treatments and who had undergone SNM were included.

#### *Type of intervention*

Studies with sacral nerve stimulation (SNS) by transforaminal, caudal and pudendal nerve stimulation (PNS) were included.

Clinical parameters for the selection of patients for SNM are still not very well defined and no predictive factors have been delineated. The present method of assessing and predicting success of a permanent implant is by means of a temporary trial of sacral stimulation.

SNM trial testing could be a temporary percutaneous nerve evaluation (PNE) or a two-staged procedure. PNE trial involves inserting a percutaneous electrode in the S3 sacral foramen and attaching to an external pulse generator. The trial usually lasts for 1 week and the outcomes of interest (urgency, frequency, and pain) are assessed. The two-staged lead procedure provides greater lead stability during the testing period. In this procedure, a quadripolar lead is inserted sacrally (S3) and tunneled subcutaneously to the anterior abdominal wall or buttock where it is attached to an external pulse generator. If the trial is successful, then the lead remains in place and a permanent implantable pulse generator (IPG) is implanted in the abdominal wall/buttock.

Transcutaneous electrical nerve stimulation (TENS) and tibial nerve stimulation were not considered in this review.

#### *Type of outcomes*

The following outcome measures were considered for the assessment of efficacy in treating pain:

1. Pain outcomes/pain medications usage
2. Quality of life measurements
3. Urological outcomes (along with pain outcomes)
  - Frequency of voiding
  - Bladder capacity
  - Number of leakage episodes per day

#### *Additional exclusion criteria*

Studies that involved stimulation of other parts of the nervous system spinal cord, deep brain, peripheral subcutaneous field stimulation, transcranial magnetic stimulation were excluded.

The following were also excluded:

- Use of SNM in urological indications other than chronic pelvic pain
- Pregnant women and children
- Publications in languages other than English

#### *Quality assessment of the studies*

Quality assessment of the studies was done utilizing the checklist provided by the STROBE website Strengthening the Reporting of Observational studies in Epidemiology This was done as most of the studies in this review fall under the category of observational studies. The lone [RCT] was quality assessed using the checklist for RCTs from the STROBE website mentioned above and checklist from the Oxford Centre for Evidence based Medicine.

A data extraction form was prepared using the recommendations of the IMMPACT group Initiative on Methods, Measurement and Pain Assessment in Clinical Trials available online at <http://www.immpact.org/> and the STROBE checklists mentioned above.

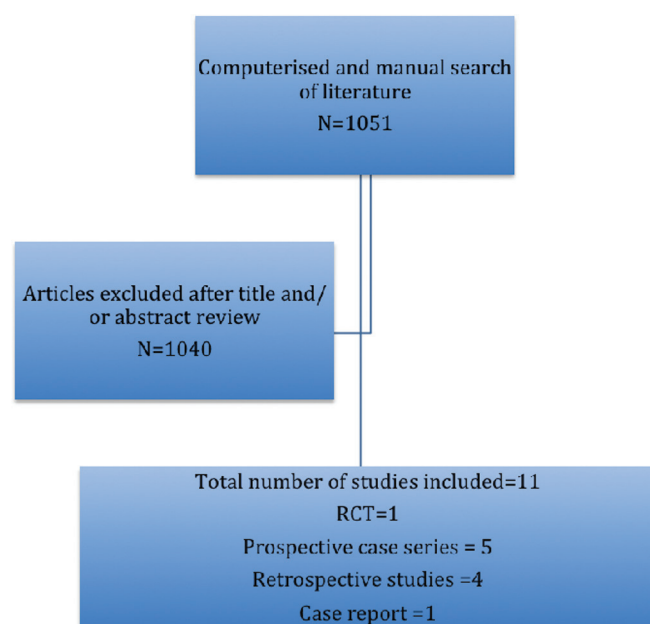
## Results

The flow diagram of the study selection process is shown in Figure 1.

The search strategy revealed 11 studies reporting the effectiveness of SNM for chronic pelvic pain related to PBS/IC. There was one RCT, five prospective case series studies, four retrospective studies, and one case report [Table 1]. Majority of the studies evaluated pain outcomes as a secondary measure.

The methodological quality of all 11 studies was assessed. Ten studies were graded as Level 4 evidence, whereas the study by Peters and Konsdant<sup>[6]</sup> could be graded as Level 3 evidence.

Seven of these studies were conducted in the United States of America, three in Europe, and one in Canada. Four of these studies<sup>[8-10,16]</sup> were either supported by Medtronic or the authors had a financial interest in Medtronic Inc., which manufactures the SNS kit (Inter Stim) used in these studies. The number of participants ranged from a solitary case report<sup>[7]</sup> to 209 participants in the Swiss registry study.<sup>[10]</sup> The average age of the participants ranged from 41 to 60 years in the included studies. Two of the studies<sup>[7,9]</sup> included only female patients, whereas all the other studies had a mixed male/female patient population.



**Figure 1:** Flow diagram of study selection process

There were 10 studies where the SNM technique used was transforaminal S3 nerve root stimulation, with one study<sup>[15]</sup> using caudal sacral root stimulation and another RCT comparing transforaminal sacral stimulation with PNS.<sup>[12]</sup> Seven studies used PNE for trial evaluation and the rest used staged lead testing. The methods of trial testing for SNM have been discussed earlier. The inclusion criteria used by the studies are shown in Table 2.

## Overview of efficacy findings

There are two steps in evaluating the efficacy of SNM. In the first step, patients undergo trial testing. If the trial testing is positive, then the patients proceed to permanent implantation. The efficacy is considered under two heads: (a) success at trial stimulation and (b) success at long-term follow-up following permanent implantation.

## Success at trial stimulation

Table 3 shows the success rate of trial stimulation. The success rate varied from 11.7 to 100%. Nine studies utilized improvement in baseline pain as the criterion for success during trial. Eight studies utilized greater than 50% pain relief as the criterion for proceeding to permanent implantation, whereas Siegel<sup>[8]</sup> used greater than 40% pain relief criterion

**Table 1: Studies reporting efficacy of SNM for pain related to PBS/IC**

Author	Year	Type of study	Total number of participants
Zermann <i>et al.</i> <sup>[7]</sup>	2000	Case report	1
Siegel <sup>[8]*</sup>	2001	Prospective observational case series	10
Whitmore <i>et al.</i> <sup>[9]</sup>	2003	Prospective observational case series	33
Peter and Konstandt <sup>[6]*</sup>	2003	Retrospective observational case series	21
Kessler <i>et al.</i> <sup>[10]</sup>	2007	Prospective observational case series	209
Lavano <i>et al.</i> <sup>[11]*</sup>	2007	Prospective observational case series	7
Peters <sup>[12]</sup>	2007	Randomized control trial	22
Zabihi and Mourtzinis <sup>[13]</sup>	2008	Prospective observational case series	30
Marinkovic <i>et al.</i> <sup>[14]</sup>	2010	Retrospective case control	30
Gajewski <i>et al.</i> <sup>[2]</sup>	2010	Retrospective case series	78
Powell and Kreder <sup>[15]</sup>	2010	Retrospective	39

\*Studies that evaluated pain outcomes as a primary measure

for proceeding to implantation. Three studies<sup>[2,10,12]</sup> used both improvement in pain and urological variables as the criteria for success during the trial.

### Efficacy of SNS permanent implant

A RCT by Peters *et al.*<sup>[12]</sup> reported a decrease in visual analog pain scores of 49% (from 7.9 to 4.0) for SNS and 29% (from 4.5 to 3.2) for PNS at 6 months follow-up [Table 4]. The decrease in pain of nearly 50% is a clinically significant decrease with the use of SNM, but was not commented upon for statistical significance.

#### Urological outcomes

Frequently, the urological issues associated with pain include increase in number of bladder voids per day, decrease in voided volume, and incontinence. These variables improved with SNM.

At 6 months, the number of voids decreased by 33% for the SNS group and by 41% for those on PNS. Mean voided volume increased by 95% and 17% for PNS and SNS, respectively. Incontinence decreased by 92% and 17%, respectively, for PNS and SNS.

The O'Leary/Sant IC symptom and problem index (ICSPI) and Pain Urgency and Frequency questionnaire (PUF) scales are commonly used by urologists to identify and monitor PBS/IC patients. The ICSPI improved by 44% and 38% for PNS and SNS, respectively. PUF improved by 35% and 29% for PNS and SNS, respectively.

#### Global outcome

100% of those with SNS said "yes" when asked if they would undergo implantation again as opposed to 90% of those with PNS.

### Efficacy of case series/retrospective studies/case report

#### Pain outcomes

The long-term pain outcomes of the 10 studies that were non-randomized trials are shown in Table 5. These outcomes reflect the patients who underwent permanent implantation. Eight studies showed a decrease in pain scores at long-term follow-up following permanent SNM. One study showed a significant decrease in narcotic consumption following SNM (Peter and Konsdant).<sup>[6]</sup>

Four studies reported pain scores using the visual analogue scale. Siegel<sup>[8]</sup> and Whitmore *et al.*<sup>[9]</sup> utilized non-standard 4/5-point pain scales as an outcome measure. The decrease in narcotic consumption was statistically significant in the study by Peter and Konsdant.<sup>[6]</sup>

**Table 2: Inclusion criteria for patients in the studies**

Author	Year	Inclusion criteria
Zerman <i>et al.</i>	2000	Clinical, cystoscopic
Siegel	2001	Clinical, cystoscopic; refractory to conventional Rx
Whitmore <i>et al.</i>	2003	NIDDK
Peter and Konstandt	2003	Clinical, cystoscopic with six previous failed treatments
Kessler <i>et al.</i>	2007	Refractory chronic pelvic pain and IC (clinical, cystoscopy)
Lavano <i>et al.</i>	2007	Clinical, cystoscopic; refractory to conventional Rx
Peters	2007	Clinical, cystoscopic; refractory to conventional Rx
Zabihi and Mourtzinos	2008	Refractory chronic pelvic pain and IC (clinical, cystoscopy)
Marinkovic <i>et al.</i>	2010	Clinical, cystoscopic; refractory to conventional Rx
Gajewski and Al-Zahrani	2010	ESSIC criteria
Powell and Kreder	2010	Clinical, cystoscopic; refractory to conventional Rx

**Table 3: Percentage success of trial stimulation**

Author	Year	Percentage permanent implantation after trial testing
Zermann <i>et al.</i>	2000	100
Siegel	2001	100
Whitmore <i>et al.</i>	2003	51.51
Peter and Konstandt	2003	-
Kessler <i>et al.</i>	2007	(11.7 for pain); overall 43.54
Lavano <i>et al.</i>	2007	100
Peters	2007	59
Zabihi and Mourtzinos	2008	77
Marinkovic <i>et al.</i>	2010	88.23
Gajewski and Al-Zahrani	2010	59
Powell and Kreder	2010	50

**Table 4: Pain outcomes at 6 months follow-up for sacral nerve stimulation versus pudendal nerve stimulation**

Author	Year	Pain outcome SNS	Pain outcome PNS
Peters <i>et al.</i>	2007	VAS decrease from 7.9 to 4.0 49% decrease	VAS decrease from 4.5 to 3.2 29% decrease

#### Urological outcomes

#### Global outcome measure

**GRA scale:** The study by Gajewski *et al.*<sup>[2]</sup> reported an 80% decrease in global response assessment scale (GRA) for those who underwent SNM.

**SF36 scale:** Siegel<sup>[8]</sup> reported 8/10 patients showed improvement in all 4 physical domains and 3/4 mental domains on the SF36 scale. Lavano *et al.*<sup>[11]</sup> reported a significant difference in all domains.

**BDI:** Siegel<sup>[8]</sup> reported 6/10 patients had an improved BDI score following SNM.

### Overview of safety findings

Adverse events related to the studies are shown in Table 6. One of the long-term problems is loss of efficacy/infection/pain that leads to removal of the device (termed explantation). Explantation rates were reported in eight studies. Four of these studies reported explantation/revision rates between 20 and 30%, whereas Kessler *et al.*<sup>[10]</sup> reported only 2/209 IPG that developed a malfunction. Powell and Kreder<sup>[15]</sup>

reported a 50% explantation rate. IPG site pain was reported in five studies. The incidence varied from 3.29% of IPG to 40%.

Revisions of lead/other lead issues were reported in four studies [Table 6]. The common issues reported were lead migration, broken leads, and lead fracture. The incidence of lead complications ranged from 3.29 to 28.57%.

**Table 5: Pain outcomes for case series/retrospective studies/case reports**

Author	Year	Study type	Number	Pain outcome
Zermann <i>et al.</i>	2000	Case report	1	VAS score decreased to 0 from 6.7
Siegel	2001	Prospective observational case series	10	5-point pain scale. Worst pain decreased to 2.2 from 4.7; least pain decreased to 1.2 from 2.4; average numbers of hours of least pain decreased to 6.9 from 13 h
Whitmore <i>et al.</i>	2003	Prospective observational case series	33	4-point pain scale. 2. (0.7) decreased to 1.6 (0.8); statistically significant
Peter and Konstandt	2003	Retrospective observational case series	21	Intake of narcotics. Statistically significant decrease from 81.6 to 52 mg/day (36%; $P = 0.015$ ); 20/21 patients reported marked decrease in pain
Kessler <i>et al.</i>	2007	Prospective observational case series	209	VAS statistically significant decrease from 8 to 2 median
Lavano <i>et al.</i>	2007	Prospective observational case series	7	Pain decreased in 5/7 patients
Zabihi and Mourtzinos	2008	Prospective observational case series	30	VAS improved by 40% ( $P = 0.04$ )
Marinkovic <i>et al.</i>	2010	Retrospective case control	30	VAS decreased from 6.5 to 2.4 ( $P < 0.01$ )
Gajewski, and Al-Zahrani	2010	Retrospective case series	78	GRA 80% improvement; no pain outcome mentioned
Powell and Kreder	2010	Retrospective	39	Dysuria or pelvic pain 64.7 (11/17) cured; 35.3% same

**Table 6: Overview of adverse events in all studies**

Study	Year	Explantation/implantation issues/revision	Implant site pain	Revision of lead/lead issues	Infection at implant site	Others
Zerman <i>et al.</i>	2000	0				
Siegel	2001	2/10 (20%)	4/10 (40%)	2/10 (20%)	1/10 (10%)	
Whitmore <i>et al.</i>	2003					Severe pain at PNE; unpleasant tapping
Peter and Konstandt	2003					
Kessler <i>et al.</i>	2007	1 = Implant migration; 1 = malfunction after MRI	3/91 (3.29%)	3/91 (3.29%); 2 migration/1broken	1/91 (1.098%)	
Lavano <i>et al.</i>	2007		1/7 (14.37%)	2/7 (28.57%); 1 lead fracture; 1 displaced		
Peters	2007					
Zabihi and Mourtzinos	2008	5/23 (22%); 1 revision			4/23 (17%)	
Marinkovic <i>et al.</i>	2010	3/30 (27% reimplantation due to erosion)	3/30 erosions	5/30 lead migration		
Gajewski and Al-Zahrani	2010	28% explantation; 9 poor outcome; 4 painful stimulation; revision 50% - loss of efficacy; 12/46; pain in area of implant; 115 painful stimulation	25%			
Powell and Kreder	2010	11/22 (50%) 4/11 depleted batteries; 3/11 loss of efficacy				Malfunction after shoplifting detector; destruction after DC cardioversion; troublesome foot movement responsible for 1 explant each



Three studies specifically reported infection at the IPG site. The other studies did not mention IPG site infection, but the rates of explantation/revision may be a clue to the infection rates. The rates of reported IPG site infection ranged from 8 to 17% [Table 6].

Powell and Kreder<sup>[15]</sup> reported an interesting problem with these IPGs. The sacral neuromodulator IPG malfunctioned after a shoplifting alarm went off, and in another case, the IPG was destroyed by DC cardioversion.

## Discussion

Chronic pelvic pain can arise from other pelvic organs (prostate, endometrium, anal canal) and from the pelvic floor apart from the urinary bladder.<sup>[8]</sup> However, majority of the efficacy studies of SNM available in literature have been done for chronic pain related to PBS/IC. This efficacy study was restricted to patients presenting with chronic pain related to PBS/IC.

Painful bladder syndrome/Interstitial cystitis is still a poorly defined condition. The definitions used in this literature review include the National Institute of Diabetes and Digestive and Kidney diseases (NIDDK) criteria,<sup>[16]</sup> clinical and cystoscopic diagnosis and the ESSIC criteria.<sup>[17]</sup> Common to all these definitions is the exclusion of urinary tract infection/cancer and pain attributable to any other pelvic organ such as prostate or endometriosis. As of present, no single case definition has high sensitivity and specificity to identify PBS/IC.<sup>[18]</sup> Some studies like Kessler's<sup>[10]</sup> also included urinary retention and other chronic pelvic pain patients, thus affecting the generalization of the results relating the efficacy of SNM for PBS/IC specifically.

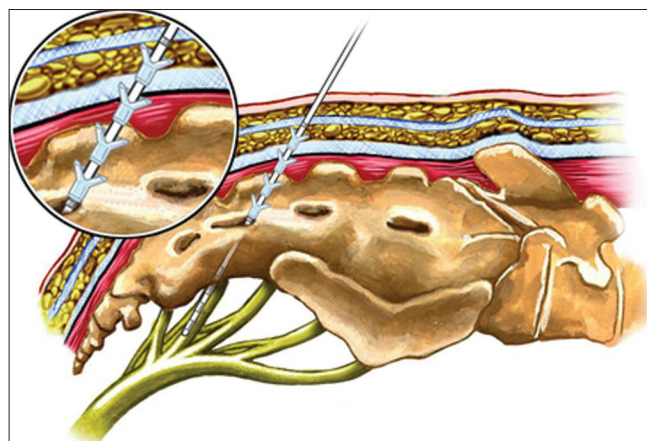
The etiology of PBS/IC is still unknown. Postulated causes include inflammation of the bladder wall,<sup>[19]</sup> mast cell activation in the bladder,<sup>[20]</sup> urothelial dysfunction,<sup>[21]</sup> urothelial glycosaminoglycan (GAG) defect,<sup>[22]</sup> autoimmune,<sup>[23]</sup> and neurogenic inflammation.<sup>[24]</sup> Elbadawi and Light<sup>[24]</sup> studied microscopic specimen from the bladder wall and reported the changes did not support a primary role for mast cells or deficient GAG layer in the pathogenesis of PBS/IC. The changes in nerves showed degenerative and regenerative features, with some showing plasticity. The electron microscopic changes suggested a neurogenic inflammation that resulted in a leaky epithelium and mast cell activation. This hypothesis is very important, as neuromodulation therapy has been shown to be successful for neuropathic pain.

SNS is the application of electrical impulses to the sacral nerves. The sacral nerve may be stimulated by commonly

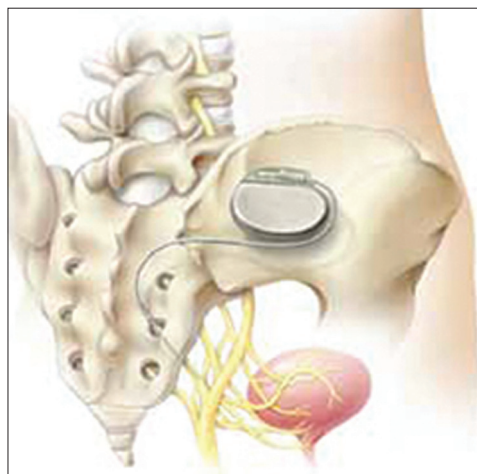
placing the electrode next to the sacral nerve via the sacral foramen or by placing the electrode next to the pudendal nerve which has sacral origins [Figures 2 and 3]. The electrical impulse improves the bladder activity and pain by possibly modulating sacral afferent nerve activity. A trial testing, usually for a week, is carried out to test the efficacy by attaching the lead to a pulse generator externally. If the trial is positive, then a pouch is usually created surgically in the buttock/abdomen and the pulse generator is implanted permanently.

Historically, SNM was first described for treating voiding dysfunction after experiments in paraplegic dogs (Tanagho and Schmidt).<sup>[25]</sup> Electrical stimulation via a sacral electrode resulted in good bladder voiding with minimal sphincter response. Tanagho reported the first human trials in the late 1980s,<sup>[26]</sup> followed by a larger case series of 35 patients suffering from voiding difficulties resulting from spinal cord lesions.<sup>[27]</sup>

The United States Food and Drug Administration (FDA)



**Figure 2:** Transforaminal sacral stimulation via S3 foramen. Note the tined lead in use. The tined lead provides a stable electrode position for sacral nerve stimulation



**Figure 3:** Line drawing of the whole SNM apparatus when implanted. This figure shows the external test stimulator that is eventually implanted as an implantable pulse generator (IPG) into the buttock in patients who are successful at trials

approved SNM in 1997 for urge incontinence, for urgency-frequency, and for non-obstructive urinary retention in 1999. The National Institute of Clinical Excellence (NICE) in the United Kingdom reviewed SNM for urinary urge incontinence and urgency-frequency and found that evidence from RCTs showed that 70% of patients achieved continence or exhibited an improvement of more than 50% showed improvement in their main incontinence symptoms after SNS. The technical evaluations by these bodies (especially NICE) have allowed an expansion of SNM services for urological conditions in the United Kingdom. The use of SNM for pain relief, specifically in PBS/IC, was prompted by the observation that the use of SNM also afforded pain relief to patients with urological symptoms. Shaker and Haussouna,<sup>[4]</sup> while studying the efficacy of SNM for 20 patients with idiopathic non-obstructive urinary retention, reported a substantial decrease in their pelvic pain scores along with improvement in the urinary parameters.

At present, SNM is recommended for treatment of chronic pain related to PBS/IC only after all conservative measures have been exhausted. However, there was great variability in the number and type of treatment the patients had received prior to being considered for SNM treatment. Most of the studies included patients who had failed conventional medications, pain management program, and had undergone hydrodistention. None of the studies included patients who had undergone surgery such as cystectomy or urinary diversions prior to entering the study.

The average age of the participants ranged from 41 to 60 years in the included studies. It is thus not known whether these results are applicable in older patients or in patients younger than 40 years. The majority of studies included both sexes, with two studies including only women. Even in the mixed population, majority of the included patients were females. This reflects a female preponderance of PBS/IC.

The best evidence for the efficacy of SNM for pain related to PBS/IC comes from the RCT by Peters *et al.*<sup>[12]</sup> However, this trial was a subset of a larger study whose primary objective was to evaluate urological outcomes, thus raising doubts that this RCT may not have been adequately powered for a pain outcome. The baseline characteristics of the SNS and PNS groups were not available, thus raising doubts about whether confounding variables had been eliminated prior to the intervention. This was a single-blind trial that does not eliminate observer bias. This study reports decrease of pain within each group (pre- and post-IPG), but there was no comparison of pain relief differences between the groups (SNS and PNS).

The rest of the evidence for SNM efficacy comes from case series/case reports and retrospective studies that are more prone

to bias than RCTs. In general, case reports and case series are prone to biased selection of subjects, and hence the conclusions are difficult to generalize. This introduces selection bias with regard to age, sex, duration of symptoms, and the referral pathway (whether patients are referred to the pain clinic by Urologist or Uro-gynecologists). The case series in this review had no control group, and hence it is difficult to determine the size of efficacy effect as compared to conventional treatment or placebo. The outcome measures for pain were mainly VAS scores, with one study reporting decrease in narcotic requirements and another evaluating efficacy by means of [GRA] scale. An interesting fact was that in all the studies, improvement in urinary variables mirrored improvement in pain that points to a possible common pathophysiological dysfunction for both pain and urinary dysfunction in patients with PBS/IC. However, the case series reported similar outcomes to the RCT in that SNM was efficacious in providing pain relief to patients with PBS/IC.

Patient's quality of life was studied in only three studies. One study utilized GRA scale to evaluate efficacy. All these studies showed improvement in patient's perception of improvement at long-term follow-up.

The more recent studies reported adverse events. The explantation/revision rates ranged between 20 and 30% in most studies, which is consistent with long-term use of SNM for urological conditions where the experience has been longer. The most common reported complications were IPG site pain, revision of lead, and infection at IPG site. The clinical experience of the clinician or the troubleshooting algorithm for these complications was not mentioned.

The prediction of successful SNM long term in all studies depended on a success at trial stimulation. The majority of studies utilized >50% pain improvement/urinary variables at the trial stage to proceed to the permanent implantation stage. The success rate varied from 11.7 to 100%. The lower rates of success have been skewed mainly by the Swiss study Kessler *et al.*<sup>[10]</sup> which had an 11.7% success rate for pain patients but 43.54% overall for both pain and urological patients. This could be attributed to using SNM for conditions other than PBS/IC, like chronic pelvic pain which is a conglomerate of ill-defined conditions under one roof and SNM may not be efficacious in all of them. If we exclude this study, then the success rate of trial stimulations has been upward of 50%. Apart from trial stimulation, no other feature predicted long-term success.

As SNM has evolved, the later trials have mainly used tined leads for trial testing and permanent implants because of their greater stability. Placement of permanent tined lead during the testing phase is the method of choice at present. The tined

lead is a lead with much improved anchoring properties.

The issue of bilateral versus unilateral stimulation for predicting long-term efficacy remains unanswered, and though buttock implantation of IPG has become the norm, there is insufficient evidence to recommend one over the other.

## Conclusions

The use of SNM for pain related to PBS/IC has generally been done for patients with pain related to painful bladder syndromes that have failed multiple previous treatments.

alone provides evidence of some benefit from SNM in terms of reduced pain scores along with improvements in frequency and bladder volume in patients with pain related to PBS/IC. The case series/case reports also report broadly similar findings to the RCT. Benefits of SNM for pain were reported at follow-up to 7 years after implantation. The impact of SNM on quality of life in the long term could not be established.

The explantation/revision rates ranged between 20 and 30% in most studies. The most common reported complications were IPG site pain, revision of lead, and infection at IPG site.

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