Original article

Sacral neuromodulation treatment for refractory interstitial cystitis: long-term experience at one center

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Abstract: The objective of this study is to examine the long term efficacy of sacral neuromodulation for the treatment of refractory interstitial cystitis. All patients diagnosed with interstitial cystitis who received sacral neuromodulation from 1998 to 2002 were approached for participation in this study. After informed consent was obtained subjects were mailed questionnaires consisting of a global response scale and several questions regarding the average number of voids per day and night. Fifty-six patients were identified and were mailed questionnaires. Twenty-eight patients (50%) responded to the questionnaire packet. The mean length of time of sacral neuromodulation was 4.3 years. The mean voiding interval for the subjects improved from voiding every 1.22 hours to every 2.57 hours after implantation (p=.001). Nocturia rates improved from 3.43 voids per night to 2.20 voids per night (p<.001). 89% of subjects reported an improvement of symptoms over time. This study indicated that there may be a long term benefit of sacral neuromodulation for the treatment of refractory interstitial cystitis.

Key words: Sacral neuromodulation; Interstitial cystitis.

INTRODUCTION

Interstitial Cystitis (IC), characterized by pelvic pain, nocturia, urinary urgency, and urinary frequency is a chronic condition with unknown etiology and no available cure.[1-3] It is estimated to affect 60 per 100,000 to 200 per 100,000 people worldwide.[2,4] The goal of therapy is to reduce symptoms and improve the quality of life of people with this disease. Conservative therapies include a low acid diet, physical therapy and behavioral therapy. Medical therapy includes the use of pentosan polysulfate sodium (FDA approved for the treatment of IC), anti-cholinergic medications, oral bladder analgesics, and bladder instillations with analgesic medications.[5-11] If a patient fails to obtain relief from the above therapies then at this center we offer sacral neromodulation.

The InterStim® System (Medtronic Corporation, Minneapolis, MN) is a sacral neuromodulation system FDA approved to treat urinary urge incontinence, urinary urgency and frequency, and non-obstructive urinary retention. Its mechanism of action is not completely established, however it is hypothesized to stimulate the somatic afferent nerve at the third sacral nerve root, which will inhibit the activity of the pontine micturition center.[12-15] Long-term efficacy has been demonstrated in the treatment of these conditions for up to 13 years.[16, 17] Several studies have demonstrated that this therapy can be effective in the treatment of IC; [18-25] however, available long-term data is minimal. We sought to evaluate the long-term efficacy of sacral neuromodulation for the treatment of IC.

MATERIALS AND METHODS

A retrospective chart review was performed on all patients from 1998 to 2002 who underwent a permanent implantation of the InterStim® device for the symptoms of IC following a successful Stage 1 test period. All patients had attempted and failed at least two conservative or medical therapies before being offered sacral neuromodulation. All patients were diagnosed with IC using the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) criteria.[26] The patients were mailed questionnaires consisting of a global response assessment scale (GRA) and several questions regarding the frequency of voiding.[27,28] Follow up phone calls were performed to ascertain receipt of the questionnaire and encourage completion. Paired t-test and Wilcoxon signed-rank tests were used for statistical analysis. The Institutional Review Board at Graduate Hospital approved this study.

RESULTS

Fifty-six patients, all female, were identified and mailed the questionnaires. Twenty-eight patients (50%) responded. Mean age at the time of implant was 57 years old (range 28-93). Mean length of time of sacral neuromodulation was 4.3 years (range 3.2-6.3 years). The mean number of reprogramming visits after implantation was 2.2 visits per year over the lifetime of the implant. The majority of reprogramming visits occurred during the first year with a mean of 4.5 visits over the first year and then decreased each year thereafter with an average of 0.9 reprogramming visits at the fourth year, post implant.

Patient's voiding interval significantly improved from baseline. Prior to the placement of the implantable pulse generator (IPG), the patients were voiding on average, every 1.22 hours. After the IPG was implanted this improved to voiding every 2.57 hours (p=.001) (Tab. 1). The patient's nocturia rates improved 64%, decreasing from 3.43 voids *per night* to 2.20 voids *per night* (p<.001) (Tab. 1). Fifteen (54%) patients indicated marked improvement, six (21%) patients indicated moderate improvement, four (14%) patients indicated mild improvement, two (7%) patients indicated no change, and one (4%) indicated moderately worse symptoms from the global response assessment. (Fig. 1). Overall, 24 patients (89%) reported an improvement in their symptoms, and three patients (11%) reported either no change or worsening of symptoms.

Twenty-eight out of fifty-six (50%) patients did not respond to the questionnaires. Of those that did not respond, nine (16% of the total) were lost to follow up, ten (18% of the total) had the device explanted and three (5% of the total) had turned the device off. The remaining six (11% of the total) were incapable of responding secondary to a terminal illness or death (Tab. 2).

The research project was conducted at The Pelvic and Sexual Health Institute, Philadelphia, PA

TABLE 1. – *Long-term follow-up statistics. Nocturia rate pre- and post-implant and voiding interval pre- and post-implant. Statistical difference was seen pre- and post-implant.*

	n.	*Pre-implant Mean (SD)*	*Post implant Mean (SD)*	*Difference Mean (SD)*	*P-value*
Nocturia	28	3.43 (1.4) voids	2.20 (1.2) voids	1.21 (1.6) voids	<.001
Voiding Interval (hours)	28	1.22 (0.8)	2.57 (1.5)	1.38 (1.8)	.001

TABLE 2. – *Non-responders. Reasons for non-responders: lost to follow up, device explanted, device turned off, or unable to respond.*

	Number of non-responders	*Percentage of the total sample*
Lost to Follow Up	17	16
Device Explanted	10	18
Device turned off	3	5
Unable to respond	6	11

DISCUSSION

Prospective trials have shown that sacral neuromodulation can have short term improvement in the symptoms of IC.[19, 21, 24, 25] These studies followed patients an average of 14-15 months after implantation. This current study indicates that there is a potential long term (average 4.3 years) efficacy for the symptomatic treatment of IC. The need for reprogramming decreased every year to just under one reprogramming visit per year after four years of use.

Of those that responded, 89% reported improvement in symptoms. Of those that completed the questionnaires, the patients reported an improvement in voiding interval by 1.38 hours and a decrease in nocturia by 1.21 voids per night. If all of the non-responders were considered treatment failures, then the success rate of this therapy would decrease to 45%. This response rate is still superior to long term results of pentosan polysulfate sodium, an FDA approved medication for interstitial cystitis. In a long term analysis of pentosan polysulfate sodium for the treatment of IC, Jepsen et al. found that only 6.2% to 18.7% of patients reported improvement from the therapy.[29] In a meta-analysis of the efficacy of pentosan polysulfate sodium for the treatment of IC over a three month period, Hwang et al. found that 37% of subjects reported improvement of pain, 28% reported improvement in urgency, 54% reported improvement in frequency, and 48% reported improvement in nocturia.[30] In the context of these studies, it would appear that sacral neuromodulation may be a valid therapy for IC.

Due to the nature of the study design these results can be affected by recall bias. The treatment of IC often uses a multi-modal approach combining both medical and conservative therapies simultaneously. Due to the nature of combining multiple therapies, it is difficult to state that improvement of symptoms is solely due to one of their treatments and not others. In order to better understand the effect of sacral neuromodulation on IC, a prospective trial has begun by the principal author that is designed to remove these possible confounding variables.

Only 10 of the 56 patients (18%) had their devices explanted. This corresponds to other published explant rates for patients with interstitial cystitis.[31] The rate of explant in non-IC patients has been reported to be approximately 10%.[15, 16] This is not well understood, however, a theory for this could be that the therapy does not appear to control the pain as much as it controls the urinary urgency and frequency. If patients expect the InterStim therapy to control their pain substantially, they may become disappointed and request the device be removed.

Patients suffering from refractory IC may benefit from sacral neuromodulation therapy with the InterStim device. This therapy appears to maintain high efficacy rates over an average of 4.3 years. This therapy has shown to significantly decrease nocturia rates and improve voiding intervals. The majority of patients in this study found their IC symptoms improved over several years.

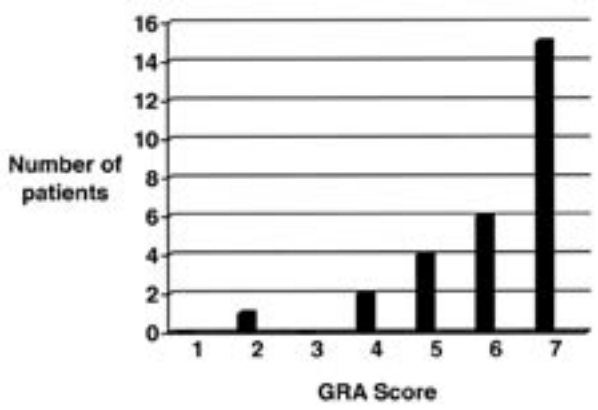

Fig. 1. – *Global Response Assessment.* Global response scores for those that had the device implanted, 7 being the best score and 1 being the worst score. Most patients found this device helped their symptoms compared to those who thought it made their symptoms worse. *Legend:* Global Response Scale: 1 - Markedly Worse; 2 - Moderately Worse; 3 - Slightly Worse; 4 - No Change; 5 - Mild Improvement; 6 - Moderate Improvement; 7 - Marked Improvement.

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5 – RETENTIONS

Oral mucosal grafts urethroplasty for the treatment of long segmented anterior urethral strictures. *Xu YM, Sa YL, Fu Q et al. World J Urol. EPUB: 2009-02-14.* Combined two oral mucosal grafts substitution urethroplasty is an effective technique for the treatment of long, complex segmented urethral strictures. In 25 patients followed-up for 6-72 months, urethrocutaneous fistulas developed in 2, and urethral stricture in 1 who needed urethral dilations, after which he voided well with a urinary peak flow of 26.4 ml/s.

Decreased colonic transit time after transcutaneous interferential electrical stimulation in children with slow transit constipation. *Clarke MC, Chase JW, Gibb S. et al. Journal of Pediatric Surgery EPUB: 2009-02-24* Idiopathic slow transit constipation is diagnosed by demonstrating delayed colonic transit on nuclear transit studies and describes a clinical syndrome characterised by intractable constipation. A possible new treatment is interferential therapy, which is a form of electrical stimulation that involves the transcutaneous application of electrical current and in children can speed up colonic transit significantly compared to placebo.

6 – INCONTINENCES

Sacral Nerve Modulation and other treatments in patients with faecal incontinence after unsuccessful pelvic floor rehabilitation: a prospective study. *Koch SM, Melenhorst J, Uluda_ O, Baeten CG et al. Colorectal Dis. EPUB: 2009-02-18.* Patients whith faecal incontinence were included in a multicentre study and treated with standardized pelvic floor rehabilitation. Those with an unsuccessful result who were eligible for sacral nerve modulation were included in the present study while failures at test stimulation received another treatment. Clinical outcome, Vaizey scores and quality of life (EQ-5D and HAQL) indicated a 49% overall success rate in patients with SNM with a significant improvement disease specific quality of life compared to other treatment.

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