DISEASES OF THE COLON & RECTUM

Temporary Sacral Nerve Stimulation for Treatment of Irritable Bowel Syndrome: A Pilot Study

ORIGINAL CONTRIBUTION

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PURPOSE: This study was designed to evaluate the effect of temporary sacral nerve stimulation in patients with diarrhea-predominant irritable bowel syndrome.

METHODS: Symptoms of diarrhea-predominant irritable bowel syndrome and disease-specific quality of life was evaluated in six patients before and during percutaneous sacral nerve evaluation test. Primary end points were differences between total irritable bowel syndrome symptom score and total quality of life score before and during stimulation. Secondary end points were differences between the variable domains.

RESULTS: Percutaneous sacral nerve evaluation test was performed in five women and one man (median age, 33 (range, 26–54) years). The irritable bowel syndrome symptom score decreased from 48.9 to 28.3 ($P=0.004$). Pain, bloating, and diarrhea were significantly reduced from 7.9, 13.5, and 17.3 to 4.4, 7.2, and 10.6, respectively ($P=0.02$, $P=0.01$, $P=0.03$). The irritable bowel syndrome quality of life score decreased from 99.3 to 59.6 ($P=0.009$). Daily activities, emotional distress, eating habits, and fatigue were significantly reduced from 26.9, 22.2, 15.2, and 23.2 to 16.9, 13.3, 8, and 14.4, respectively ($P=0.02$, $P=0.02$, $P=0.02$, $P=0.007$). Two weeks after cessation of stimulation, the patients had symptoms as before stimulation.

CONCLUSIONS: Temporary sacral nerve stimulation provides a significant reduction in diarrhea-predominant irritable bowel symptoms and improves quality of life. Further studies with permanent implantation and double-blind crossover ON-and-OFF-stimulation to evaluate the impact of placebo effect are needed.

KEY WORDS: Sacral nerve stimulation; Irritable bowel syndrome; Quality of Life.

Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by abdominal pain, cramping, bloating, and changes in bowl habit. The pain and discomfort is commonly relieved by defecating. It affects approximately 10 to 20 percent of the general population, and it is the most common disease diagnosed by gastroenterologists and one of the most common disorders seen by primary care physicians.[1,2] For most patients the symptoms are inconvenient and can be relieved with dietary advice, but for some patients the symptoms are outright debilitating and disabling. They may be unable to work, attend social events, or even travel short distances. These patients typically have a health-related quality of life that is considerably worse than patients with diabetes mellitus or end-stage renal disease.[3]

The pathophysiology of IBS is unclear and several mechanisms have been hypothesized, including genetic factors, psychosocial factors, abnormal gastrointestinal motility, visceral hypersensitivity, infection and inflammation, neurotransmitter imbalance, and dysregulation of the brain-gut axis.[1,4] Based on these assumptions, a number of different treatments have been suggested, but so far no single treatment option is effective to relieve the symptoms in the majority of patients.[2]

Sacral nerve stimulation (SNS) is a well-established treatment, since 1995, for patients with fecal incontinence.[5,6] Treatment with SNS was primarily restricted to patients with an intact external sphincter; however, indications for SNS have gradually developed to include patients with partial spinal cord injury,[7] scleroderma,[8] rectal prolapse repair,[9] low anterior resection,[10,11] and constipation.[12] The mechanism of action of SNS is still unclear, but recent studies show that the motility during stimulation is modulated throughout the colon.[13,14] This modulation of gastrointestinal motility could be a potential mechanism of action to relieve the symptoms in patients with IBS. This study was undertaken to assess the therapeutic efficacy and effect on quality of life of sacral nerve stimulation in patients with diarrhea-predominant irritable bowel syndrome.

PATIENTS AND METHODS

Between October 2006 and May 2007, percutaneous nerve evaluation test (PNE) was performed in six patients (5 women; median age, 33 (range, 26–54) years. All patients

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met the Rome III criteria for diarrhea-predominant irritable bowel syndrome (IBS-D). Patients were recruited from the gastroenterology department where any history of celiac disease, lactose intolerance, inflammatory bowel disease, and any other significant bowel disorder were excluded. All patients have been suffering from their symptoms for more than one year and have previously had colonoscopy, including biopsy that was negative. Endoanal ultrasonography did not reveal any lesions in the internal or external anal sphincter in any of the patients. The inclusion criteria consisted of a more than 12-week history of bloating and/or excessive flatulence and any of the following: chronic abdominal pain or discomfort, disturbances in bowel movements, including feeling of incomplete evacuation, or abnormal stool consistency. Exclusion criteria were: younger than aged 18 years, any evidence of organic or psychiatric disease that may have an impact on compliance to the study protocol. All patients were evaluated according to the regimen described below.

Anorectal Manometry, Questionnaire, and Diary

Patients were assessed by colonoscopy, anorectal physiology tests consisting of resting pressure, squeeze pressure, and rectal sensation, including threshold, desire to defecate, and maximum tolerable volume, electrophysiology, including pudendal nerve terminal motor latencies, endoanal ultrasonography, general questionnaire, including Wexner incontinence and constipation scoring system. The patients completed an IBS symptom score (Gastrointestinal Syndrome Rating Scale (GSRS) Irritable Bowel Syndrome (IBS) version) and an IBS quality of life score (Irritable Bowel Syndrome Impact Scale (IBS-IS)) for three consecutive weeks before stimulation and during stimulation. Daily bowel movements, episodes of fecal incontinence, and urge to defecate were recorded. Two weeks after the electrodes were removed, the patients were contacted by telephone and asked to signify status of current symptoms.

Gastrointestinal Symptom Rating Scale (GSRS-IBS)

The GSRS-IBS is a symptom scale that includes 13 items in 5 symptom clusters: abdominal pain, bloating, diarrhea, constipation, and satiety. It records symptoms during the past seven days using a 7-point Likert scale ranging from "no discomfort" to "very severe discomfort." Patients measured three consecutive weeks, and a mean item score was used to provide a score from 1 to 7 for each dimension. The symptom scale is a valid and reliable disease-specific symptom score.[15]

Irritable Bowel Syndrome Impact Scale (IBS-IS)

The IBS-IS is a disease-specific questionnaire to measure the impact of irritable bowel syndrome on patients' quality of life.[16] Twenty-six items represents five domains: fatigue, impact on daily activities, sleep disturbance, emotional distress, and eating habits. A 7-point Likert scale was used to assess how often ("none of the time" to "all of the time") each item was present during the past seven days in three consecutive weeks, and a mean item score was used to provide a score from 1 to 7 for each dimension.

Sacral Nerve Stimulation

Informed consent was obtained from the six patients included in this study. Stimulation of the sacral nerves was performed as a percutaneous nerve evaluation test (PNE) for three weeks. The procedure was performed by using general anesthesia. Temporary percutaneous electrodes (Medtronic Interstim® model 3057, Minneapolis, MN) were placed at the sacral foramina (S3 or S4) based on the best motor response with contraction of the pelvic floor muscle. Stimulation parameters used were: pulse width 210 μs, frequency 14 Hz, and continuous stimulation. The level of stimulation ranged from 1/2 to 4 V, just above what the patient could feel. The patients were subsequently tested by sacral nerve stimulation for a three-week period, and during the stimulation they completed the questionnaires on a weekly basis. After the three-week test period, a rectal sensation test, including threshold, desire to defecate, and maximum tolerable volume, was performed and the temporary electrodes removed.

Statistical Analysis

In this pilot study, all patients served as their own control. The paired samples *t*-test was used to compare the means of the total symptom and the quality of life scores and furthermore to compare the means of the different symptom and quality of life domains. $P<0.05$ was considered statistically significant.

RESULTS

Temporary stimulation was successful for 21 days in all patients. The mean total GSRS-IBS score was reduced from 48.9 before sacral nerve stimulation to 28.3 during stimulation ($P=0.004$). Symptom clusters depicting pain, bloating, and diarrhea were reduced significantly from 7.9, 13.5, and 17.3 to 4.4, 7.2, and 10.6, respectively ($P=0.02$, $P=0.01$ and $P=0.03$; Fig. 1). There was no significant difference in symptom score in the constipation and satiety domains before and during stimulation of the sacral nerves. Table 1 shows the GSRS-IBS data in details for all six patients.

The impact of irritable bowel syndrome on patients' quality of life measured by the mean total IBS-IS score was significantly reduced from 99.3 to 59.6 ($P=0.009$). The dimensions—daily activities, emotional distress, eating habits, and fatigue—were all significantly reduced during stimulation (Fig. 2). There was a tendency to a reduction in sleep disturbances ($P=0.06$). Table 2 shows the details of the IBS-IS data for all six patients before and during sacral nerve stimulation.

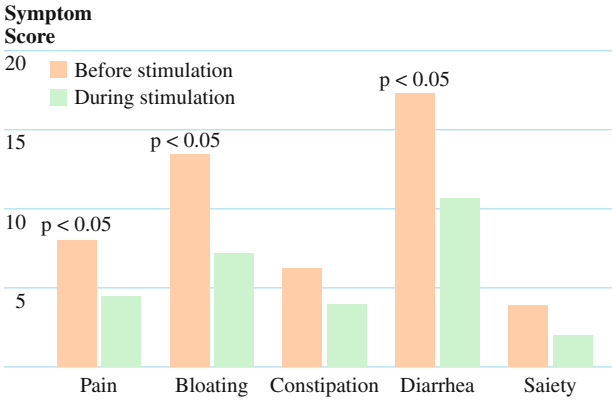

FIGURE 1. Mean symptom score for the five symptom clusters before and during stimulation. *$P<0.05$.

Rectal volume tolerability was evaluated at baseline and after three weeks of sacral nerve stimulation just before the temporary electrodes were removed. Median "first sensation," "desire to defecate," and "maximal tolerable volume" did not change significantly during stimulation.

There was a nonsignificant reduction in the number of bowel movements per day from 3.5 to 2.1 ($P=0.07$). The inability to defer defecation, classified as episodes with urgency per day, decreased from 1.9 to 0.5 ($P=0.08$) during the test period.

Two patients, Patient 1 and Patient 5, also suffered from fecal incontinence. For both, there was a reduction in incontinence episodes per week from 3.3 and 1.3 to 0.3 and 1, respectively. There was no operative morbidity in any of the six patients after placement of the temporary stimulation system.

Two weeks after the temporary electrodes were removed, patients were interviewed by telephone. IBS symptoms were specified to be as before stimulation. Five patients wanted implantation with a permanent neurostimulator, and one patient wanted to consider the possibility of implantation.

DISCUSSION

This pilot study is the first to demonstrate a beneficial effect of temporary sacral nerve stimulation in patients suffering from severe irritable bowel syndrome. IBS is a functional disorder with a significant impact on daily function and quality of life of the patients, on the health care system, and the society as a whole.[2,3] Symptoms result from what appears to be a disturbance in the interaction between the gut or intestines, the brain, and the autonomic nervous system that alters regulation of bowel motility or

Table 1. Mean symptom score three weeks before stimulation and during three weeks of stimulation

	Pt 1		*Pt 2*		*Pt 3*		*Pt 4*		*Pt 5*		*Pt 6*		*Total*		
Patients	*Before*	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*	***P***
Total symptom score	**50**	**32**	**52.8**	**17.7**	**42**	**23.2**	**52.7**	**47.3**	**45.6**	**30.3**	**49.7**	**19.8**	**48.9**	**28.3**	0.0047
Pain	**6.6**	**5.7**	**8.6**	**2.7**	**5**	**4**	**9.7**	**8.7**	**8**	**3.3**	**9.3**	**2.3**	**7.9**	**4.4**	0.02
Abdominal pain	4.3	4	4.3	1.7	4	3	5	4	3,7	1.3	5.3	1	4.4	2.5	
Defecation pain	2.3	1.7	4.3	1	1	1	4.7	4.7	4.3	2	4	1.3	3.4	2	
Bloating	**14**	**10.3**	**12**	**3.3**	**16.3**	**5.3**	**10.6**	**11**	**13**	**5**	**15.3**	**8.3**	**13.5**	**7.2**	0.01
Feeling of bloating	4.7	3.3	3.7	1	5.7	2.3	3.3	3	4	1	5.3	3	4.5	2.3	
Passing gas	5.3	3.3	5	1.3	4.6	1	4	5	7	3	5	3	5.2	2.8	
Visible abdominal swelling	4	3.7	3.3	1	6	2	3.3	3	2	1	5	2.3	3.9	2.1	
Constipation	**2.3**	**2.3**	**3.6**	**3**	**4.7**	**5.3**	**9.7**	**9.3**	**8.3**	**2**	**8.7**	**2.6**	**6.2**	**4**	0.16
Constipation	1.3	1	1.3	1	2	2.3	5.7	5.3	4.3	1	3.7	1.3	3.1	1.9	
Hard stools	1	1.3	2.3	2	2.7	3	4	4	4	1	5	1.3	3.2	2.1	
Diarrhea	**22.7**	**11.4**	**19.6**	**6.7**	**14**	**6.6**	**20.7**	**16.3**	**14.3**	**18**	**12.7**	**4.6**	**17.3**	**10.6**	0.035
Diarrhea	5	2.7	5.7	1.7	5	1.3	3.7	3	1.3	5	2	1	3.8	2.5	
Loose bowel movements	7	4.7	5	2.7	4	2.3	5.7	4	2	5	3.7	1.3	4.6	3.3	
Urgency	6.7	2.7	2.7	1	3	1	6	4	7	7	3.7	1	4.9	2.9	
Incomplete emptying	4	1.3	5.7	1.3	2	2	5.3	5.3	4	1	3.3	1.3	4.1	2	
Satiety	**4.4**	**2.3**	**9**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**3.7**	**2**	**3.9**	**2**	0.153
Full shortly after meal	2.7	1	5	1	1	1	1	1	1	1	1.7	1	2.1	1	
Full long after eating	1.7	1.3	4	1	1	1	1	1	1	1	2	1	1.8	1.1	

A total of 13 items that combine into 5 domains.

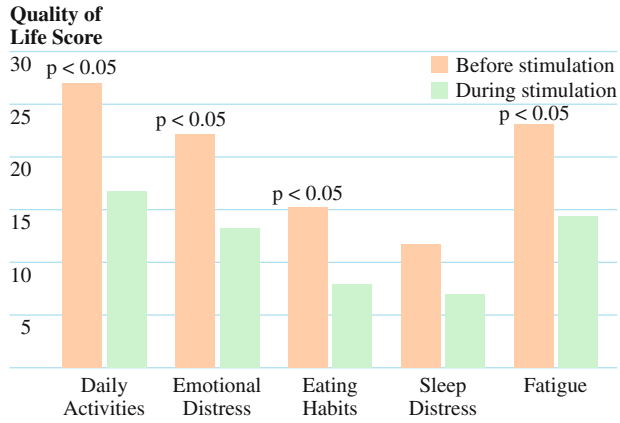

FIGURE 2. Mean IBS-specific Quality of Life score for the five domains before and during stimulation. *$P<0.05$.

sensory function. Traditional treatment of IBS has been bulking agents, antidiarrheal medications, antispasmodics, tricyclic antidepressants, and agents that affect serotonergic pathways, but the clinical efficacy of these treatments has not yet been confirmed.[1]

In this study we used questionnaires as a tool to evaluate the efficacy of treatment before and during sacral nerve stimulation. The GSRS-IBS and IBS-IS questionnaires are disease-specific score systems to assess the patient's own perception of symptoms over time and to demonstrate the impact of irritable bowel syndrome on quality of life. The questionnaires are short, simple to complete—focusing on the most pronounced impact of IBS—and easy to score using a mean item score. Therefore, these questionnaires are useful to measure changes in symptoms and quality of life in response to a new treatment as SNS.[15,16]

Patients with mild or moderate IBS are usually treated by the general practitioner. The patients included in this study were classified as severe IBS by the gastroenterologist, they have undergone thorough examinations, and several different treatment options have been tried without effect.

This study suggests that the application of temporary sacral nerve stimulation to patients with diarrhea-predominant irritable bowel syndrome leads to a substantial reduction both in symptoms and improvement in quality of life. The total symptom score was reduced by more than 40 percent with a significant relief of the symptom clusters pain, bloating, and diarrhea. Symptoms of constipation and satiety were of no significance in these patients. Several studies have shown that the quality of life of IBS patients often is more severely impaired than of patients with other chronic diseases.[3] The total score of the irritable bowel syndrome impact scale was distinctly reduced during sacral nerve stimulation from 99.3 to 59.6 and the reduction was significant for all domains except for sleep disturbances. The reduction in IBS symptoms and the improvement in quality of life had disappeared two weeks after cessation of the stimulation.

The exact mechanism of action of SNS still remains unclear. Stimulation of the sacral nerves results in a "neuromodulatory" effect where the sensory afferent, efferent, and autonomic nerve pathways are altered. The advantageous effect of SNS on fecal incontinence in patients with partial spinal cord injury[7] and in patients with scleroderma[8] supports this theory. It seems that an underlying autonomic disturbance may be corrected or overridden by the stimulation.

The number of patients in this study is small, and it is well known that a placebo effect must be considered when treating IBS patients. The patients underwent temporary stimulation and the long-term benefit of stimulation is still unknown. However, the effect of temporary SNS on symptoms and the impact on quality of life is encouraging. Further studies are necessary with permanent implantation of neurostimulator and double-blind crossover ON-and-OFF-stimulation to evaluate the effect of SNS on symptoms and quality of life on a long-term basis and to determine the impact of placebo.

Table 2. Mean IBS-specific Quality of Life score three weeks before stimulation and during three weeks of stimulation

	Pt 1		*Pt 2*		*Pt 3*		*Pt 4*		*Pt 5*		*Pt 6*		*Total*		
Patients	*Before*	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*	***P***
Total QOL score	**131.3**	**57.3**	**63.3**	**28.7**	**88**	**60**	**125.6**	**108.3**	**77.9**	**60.7**	**108.9**	**42.6**	**99.3**	**59.6**	**0.0099**
Daily activities	40.7	16.3	18	7	16	16	37.3	29	21.3	20	28.3	13.3	26.9	16.9	**0.021**
Emotional distress	29.3	13	6	5	27	13	27	25.3	22.3	15.7	21.3	8	22.2	13.3	**0.026**
Eating habits	18.7	7	11.3	4	13	11.7	16.3	13	10.3	6.3	21.3	6	15.2	8	**0.025**
Sleep disturbances	11.3	6	13	4	7	6	15.3	14.7	7.3	6.7	16.7	4.3	11.8	7	**0.062**
Fatigue	31.3	15	15	8.7	25	13.3	29.7	26.3	16.7	12	21.3	11	23.2	14.4	**0.007**

A total of 26 items that combine into 5 domains.

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