Original article

Sacral neuromodulation in the treatment of fecal incontinence. The GINS experience.

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SACRAL NEUROMODULATION IS AN OPTION IN THE TREATMENT OF FECAL INCONTINENCE.

Summary: Eighty-eight patients treated and enrolled in the registry of the Italian Sacral Neuromodulation Group (Gruppo Italiano di Neuromodulazione Sacrale - GINS) were evaluated after permanent implantation of a sacral neuromodulation device, with a median follow-up of 12 months. A statistically significant average improvement was observed in Quality of Life (QoL) and General Health Status, according to the Cleveland Clinic Fecal Incontinence Scoring System. Similar results were also observed in the three sub-groups of patients with: idiopathic neuropathy, iatrogenic sphincter dysfunction, and post-rectal resection. Manometric measurements at follow-up were compared with baseline measurements, and did not show a significant difference in total or in the different patient sub-groups. In conclusion, sacral neuromodulation can be regarded as an effective treatment for fecal incontinence in a selected group of patients. Further studies are required to better define the indications for this treatment.

Key words: Sacral neuromodulation; Fecal incontinence; Idiopathic neuropathy; Sphincter lesion; Rectal resection.

INTRODUCTION

Fecal Incontinence (FI) is the inability to control leakage of feces (liquid, solid, flatus) from the anus. The estimated mean prevalence of this condition in the general population is as high as 3.5% in females, and 2.3% in males[1], with a tendency to increase with age. Due to patient embarrassment and reluctance to report FI, these figures probably underestimate its true prevalence[2]. FI is thought to cause significant social consequences for affected people, and to generate high direct and indirect costs, for the individual patient and the total community.

Traumatic anal sphincter lesions, idiopathic sphincter degeneration, spinal cord injuries, and other neurogenic lesions account for the majority of cases of FI in adults. In females, childbirth trauma plays a pivotal role: it is reported that FI can occur in 4-6% of women after a vaginal delivery[3]. A number of patients develop FI from a condition of idiopathic pelvic neuropathy, or from pelvic nerves injury, either of iatrogenic origin, or subsequent to other pelvic dysfunctions. It is believed that all these different clinical conditions might affect the integrity of the anorectal nerve supply, and in particular the sacral nerves which include somatic and autonomic (orthosympathetic and parasympathetic) fibers[4].

Initial treatment of FI is generally conservative, consisting of dietary modification, anti-diarrhoeal drugs, pelvic floor training and biofeedback[5-7]. A number of patients rely only on the use of pads or anal plugs. Different injectable biomaterials have been experimented with in the past, and others are currently under clinical trials, in patients presenting with passive FI, secondary to internal sphincter dysfunction[8, 9]. An overlapping sphincter plasty can be electively performed in cases of external sphincter injury. Although short term results of these procedures show an improvement of FI in 70-80% of operated patients[10, 11], the long term efficacy of this surgical procedure decreases with time[12]. Dynamic gracilo-plasty, or implantation of an artificial anal sphincter may be indicated in cases with wide or multiple sphincteric lesions[13, 14]. The first option offers a significantly higher cure rate, with a lower complication rate. A permanent bowel diversion represents the last option in treatment. It is to be reserved for severe and otherwise intractable cases, or for patients deemed unsuitable for the above-mentioned procedures.

More recently, electrical stimulation of sacral nerves has been used to treat FI, mainly of neurogenic origin, in order to obtain a "modulation" effect on their specific activities, by supplying additional electrical stimulation to both pelvic floor muscles[15], and sensitive neurological pathways[16]. This therapeutic approach is referred to as Sacral Neuromodulation (SNM).

Indications for SNM are still to be clearly defined. Currently an accepted indication is severe FI, with at least one episode per week of leakage of solid or liquid stool after failure of conservative treatment. The largest group of patients in the initial trials demonstrated pelvic floor muscle dysfunction without any evidence of sphincter injury[17]. Recently, other more specific indications for the use of SNM have been identified: FI from idiopathic sphincter degeneration[7, 18], iatrogenic injuries to the internal sphincter[19], incomplete spinal cord lesions[7, 20, 21], scleroderma[22], limited injuries to internal and/or external sphincter[17, 23-25], rectal prolapse[19, 26], and anterior lower rectal resection[27-31]. Patient selection should take into consideration the results of previous conservative treatment, and be based upon the evidence of pre-operative clinical assessment: ano-rectal manometry, endo-anal ultrasound scan, and electrophysiologic studies. Selected patients should undergo a Percutaneous Nerve Evaluation test (PNE Test), in order to assess their response to the SNM. The patient response to a PNE Test is the most significant factor in predicting the therapeutic outcome of a permanent SNM implant.

MATERIALS AND METHODS

SNM Implantation Technique

SNM differs from other surgical options in that the first step, the PNE Test, is a diagnostic tool that also predicts the efficacy of treatment. Permanent implantation of the SNM system should only be performed when there is a significant improvement of FI after a PNE Test.

PNE Test

The PNE Test evaluates the clinical effects of sacral nerve stimulation on anorectal dysfunction at the time of lead implantation. A positive response to the PNE Test shows a positive predictive value for a good long-term re-

sponse to the permanent SNM implant as high as 100%[7, 22, 25, 32, 33].

The temporary lead traditionally used in a PNE Test is monopolar. Developments in implantation techniques allow the PNE Test to be undertaken with the same quadripolar lead that will be left in at the time of permanent implantation. Since sacral nerve stimulation causes contraction of the striated pelvic muscle, and possible changes in pelvic sensation, the PNE Test is best performed under local anaesthesia. After positioning the patient prone on the table, the cutaneous landmarks corresponding to anatomical features of the bony pelvis are identified. The needle-guide is directed to the sacral foramina S2, S3, or S4. The S3 foramen is preferably used, since sacral nerves pass much closer to its ventral aspect. To confirm the correct position of the needle-guide in S3, an electrical stimulation is given and the typical "bellows-like" response should be observed: contraction/relaxation of the external anal sphincter, and of the levator ani complex, plantar bending of the big toe and/or of other toes of the foot ipsilateral to the side of stimulation. A sensitive response is also produced, at the level of the vagina/scrotum, perineum, and perianal area. Confirmation of the correct positioning of the needle-guide is then obtained using fluoroscopy. When a clear and correct response to electrical stimulation is observed, the lead is implanted through the needle-guide, and its position is checked again with both electrical stimulation and fluoroscopy. The implant is then covered with an appropriate dressing, and the lead connected to an external stimulator device, properly set (pulse duration 210 μs, frequency 25 Hz, amplitude: from 1 to 10 V). The minimal duration of the PNE test is 14 days. During the test, the patient is asked to complete a diary where normal episodes of micturition and defecation are reported, as well as any episodes of urinary and/or fecal incontinence. At the end of the PNE test, a QoL questionnaire is administered, and anorectal manometry performed. If a temporary lead was used then it should be removed at the end of the PNE test. Should the patient experience a reduction of at least 50% of fecal incontinence episodes, and a significant improvement in QoL, a definitive SNM device can be implanted. There are cases in which, a double lead implantation can be considered to achieve bilateral sacral nerve stimulation[7, 27, 34].

Permanent Implantation

The Permanent Implantation technique has changed over time. It was initially performed under general anaesthesia, without using muscle relaxants, so the response of the striated muscles to the electrical stimulation could be observed. The needle-guide was inserted in the same foramen previously used for the PNE test. A 10-12 cm long median skin incision was performed in the presacral region and a wide dissection performed to directly expose the sacral foramen. The lead was fixed directly to the sacral periosteum. Further modifications have greatly simplified the lead implantation technique, firstly by reducing the size of the skin incision over the sacral foramen[35] and secondly by developing a percutaneous insertion procedure[36, 37]. Both these steps can be performed under local anaesthesia, simplifying the procedure, and allowing the patient's cooperation in identifying the correct responses to the electrical stimulation. A subcutaneous tunnel is created to seat the lead, and to reach a pouch, which is generally located in the gluteal region, and where the stimulating device is implanted.

The permanent stimulator device is then set to the same stimulation parameters that were identified at the time of the PNE test. These parameters can be subsequently changed, guided by the clinical response, using a remote control.

RESULTS

The Italian Sacral Neuromodulation Group (Gruppo Italiano di Neuromodulazione Scrale – GINS) was constituted in 1996, and now includes 20 Centres in Italy. All data is recorded in a central registry. Prior to December 2005, eighty-eight patients had been treated with a Permanent implant for FI, and registered: 15 males (17%), 73 females (83%); median age 55 ± 12 years, range: 23-81 years of age. The median follow-up after the Permanent implant was 12 months (range: 7-84 months). Five patients (5.7%) required explantation. Indications for SNM were defined in a protocol, which was agreed by all participating Centres. All selected patients were suffering from severe FI (according to the number of weekly episodes of FI, and the Cleveland Clinic Scoring System[38]), and had failed to respond to previous conservative treatments. A thorough clinical assessment was performed, including: anorectal manometry, anorectal electrophysiologic studies, endoanal ultrasound scan, defecatory/urinary diary, Rockwood QoL questionnaire[39], and a health status questionnaire SF-36[40]. Of the 83 patients suitable for a final evaluation, with a still functioning implant, 49 had been implanted for neuropathy (of idiopathic origin in 40, iatrogenic in 9), 19 for a sphincteric dysfunction (iatrogenic in 17, congenital anomalies in 2), 11 patients for FI secondary to rectal resection, 2 for FI secondary to rectal prolapse. In 2 patients the aetiology of the FI remained unknown. The complete set of data, from enrolment in the registry, to the last follow-up was not available for all patients. FI score data were complete in 66 patients, anorectal manometry data was complete in 32 patients, QoL questionnaires were completed by 34 patients, and the SF-36 was completed by 33 patients.

In all the treated patients, SNM caused a significant reduction in the Cleveland Clinic Score, from a median basal score of 15.2, to 6.9 ($p<0.0001$). A similarly significant reduction was observed in those subgroups of patients that were identified according to the aetiology of FI, and where patient numbers were high enough to make a statistical analysis possible. In 33 patients with idiopathic neuropathy, the Cleveland Clinic Score went from basal values of 15.5, to 8.1 at follow-up ($p<0.0001$), in 13 patients with iatrogenic sphincter damage, the Cleveland Clinic Score went from basal values of 19.4, to 5.2 at follow-up ($p<0.0001$), in 8 patients with FI after rectal resection, the Cleveland Clinic Score went from basal values of 16.1, to 5.5 at follow-up ($p<0.0001$).

As far as QoL is concerned, in all the 34 patients assessed with the Rockwood questionnaire, a significant improvement of physical, psychological, and social performance was observed (Table 1). A similar significant improvement was observed in 17 assessable patients with idiopathic neuropathy, as well as in 6 assessable patients with FI after rectal resection. In 8 assessable patients with iatrogenic sphincter damage, the improvement was only statistically significant in the physical and psychological domains (Table 1).

In table 1 are also reported the results of health status evaluation using SF-36. In all the 33 assessable patients, all the explored domains showed a statistically significant improvement, except for physical pain. In the 16 assessable patients with idiopathic neuropathy, significant improvements were evident for physical, mental, social, and general health status domains. In the 8 assessable patients with FI due to iatrogenic damage, a significant improvement was observed in emotional status, whilst less evident improvements were seen in the other domains. The SF-36 evaluation in the 6 assessable patients with FI after rectal resec-

TABLE 1. – *Results of QoL evaluation (Rockwood's questionnaire) and of health status (SF-36), basal and in the follow up (median: 12 months; range: 7-84 months) after Permanent implantation of SNM for FI.*

		Total Cases		*Idiopathic Neuropathy*		*Jatrogenic Sphincter Damage*		*Rectal Resection*	
		basal	FU	basal	FU	basal	FU	basal	FU
	Physical Dominion	2.1a	2.9 a	2.2 b	2.8 b	2.2 d	3.1 d	1.7 f	2.8 f
	Psychological Dominion	1.5 a	2.7 a	1.5 b	2.6 b	1.5 e	2.9 e	1.1 g	2.8 g
	Social Dominion	2.2 a	2.9 a	2.2 c	2.7 c	2.2	3.0	2.1 g	3.0 g
	Physical Function	57.0 h	68.7 h	51.2	62.5	68.8	75.8	56.3 c	78.3 c
	Physical Role	28.9 h	56.7 h	19.6 c	48.2 c	53.1	59.4	5.0 l	85.0 l
	Physical Pain	57.5	65.0	56.7	64.8	52.4	64.6	62.2	77.3
	Health General Status	37.9 i	48.4 i	30.1 c	46.3 c	54.0	53.1	24.5	50.2
	Vitality	41.7 c	53.9 c	35.7	48.3	54.3	62.4	35.0 g	56.7 g
	Social Function	45.1 h	61.7 h	4.0 h	64.1 h	56.3	62.5	33.3 g	62.5 g
	Emotional Role	29.0 b	58.1 b	26.2	38.1	37.5 c	70.8 c	11.1 m	88.9 m
	Mental Health	45.4 e	61.8 e	40.5 g	62.1 g	55.4	58.0	34.0 n	66.7 n

a p<0.0001; b p<0.002; c p<0.02; d p=0.004; e p=0.006; f p=0.009; g p<0.03; h p=0.008; i p<0.04; l p=0.001; m p=0.005; n p<0.06.

tion, showed significant improvements in vitality, physical, social and emotional functions. The anorectal manometry did not show, in all the 32 assessable patients, statistically significant differences between the median basal values and values measured at follow-up. More specifically, the basal tone changed from 60.5 to 71.9 mmHg, the contraction tone from 84.5 to 99.3 mmHg, the threshold sensitivity from 54.3 to 46.5 ml, and the urgency sensitivity from 119.9 to 97.9 ml. In patients with idiopathic neuropathy, the average values have been: basal tone from 61.8 to 69.8 mmHg, contraction tone from 82.7 to 99.7 mmHg, threshold sensitivity from 51.5 to 40.4 ml, urgency sensitivity from 129.7 to 95.6 ml (p=0.022). In patients with iatrogenic sphincteric damage, the manometric recorded values have been: basal tone from 44.0 to 59.0 mmHg, contraction tone from 71.6 to 124.4 mmHg, threshold sensitivity from 63.8 to 65.2 ml, urgency sensitivity from 123.6 to 113.0 ml. In patients with FI after rectal resection, the manometric recorded values have been: basal tone from 77.4 to 82.3 mmHg, contraction tone from 98.0 to 86.8 mmHg, threshold sensitivity from 46.0 to 51.0 ml, urgency sensitivity from 85.0 to 95.0 ml.

DISCUSSION

A decade since it was first introduced, SNM is now a recognised therapeutic option in the management of FI. Despite the good, and sometimes excellent, documented results of this procedure, the mechanisms of action remain poorly understood. In order to define the correct indications for SNM, a systematic analysis of data collected from a population of implanted patients, although heterogeneous, can be helpful. The GINS registry has made this type of evaluation possible. Results of SNM treatment have been changing over time, due to modifications in the implantation technique, and to changes in patient selection criteria. Enrolment in the Registry shows all the limitations that are due to the collection of data from several different Centres, with its resultant variability, although the treatment evaluation tools applied in each individual Centre have all been very similar. Unfortunately, both basal and follow-up data were not available for all the enrolled patients. On the other hand, a major advantage of this kind of evaluation is the opportunity to analyse data from a large series of patients, and to obtain more specific data from subgroups of patients with an adequate sample size.

All the patients treated with SNM reported a significant improvement of their FI, with a reduction in both the daily and weekly frequency of FI episodes. Improvement in FI brought to these patients a positive impact both on QoL and on general health status. More specifically, a significant improvement was observed in all the domains examined in the Rockwood questionnaire (physical, psychological, and social), and in almost all of the domains in the SF-36 questionnaire (physical function and role, physical pain, general health status, vitality, social function, emotional role, mental health). The data from the GINS group are similar to data reported from other Authors of multicentric trials[7, 19, 24, 25, 29, 32, 41-47]. In a recent review, Jarrett[48] reports rates of 41-75% of complete continence to both solid and liquid stools, and reduction greater than 50% in major incontinence episode in 75-100% of patients treated with SNM. A European multicentric trial reported a complete control of FI in 37% of 34 patients treated, with the ability to postpone defecation and with complete evacuation[44]. In our series of 16 patients, SNM restored a full rectal discriminative capacity, and, in the majority of them, the sensation of complete evacuation[49].

Clinical results appear homogeneous, unlike the data from instrumental diagnostic exams, especially manometric data, which is not comparable, and is sometimes contradictory. This is partly due to different examination techniques, but is mainly related to the different aetiology of FI in different groups of patients. These figures are evident also in the GINS experience. Treatment with SNM did not lead to significant changes from the baseline, with regard to anal tone (both resting tone, and contraction tone), and with regard to rectal sensitivity (threshold and urgency). Differences in anal pressures seldom were statistically significant, whereas in other series, variations in rectal sensitivity before and after SNM showed a greater variability. This variability can be explained considering the wide range of differences that may exist in each individual patient (e.g. hyper/normal/hypotonic anal canal, or rectal hyper/normal/hyposensitivity), and that make explain the different manometric findings, although the vast majority of patients share a good clinical response to SNM. If, on one hand, it can be said that these considerations do not help in understanding the SNM's true mechanisms of action, and on the other hand they support the hypothesis that SNM provides a "modulatory effect" on the electrical stimuli directed to the sacral nerves, and from here both to pelvic target organs, and to upper CNS areas. On the base of this hypothetical mechanism of action, it may be possible to treat a number of multifactorial neuromuscular dysfunctions, even though they may be very different from one another.

Nevertheless, in order to better define the indications for SNM, it is mandatory to investigate the effects of this treatment on both specific and homogeneous groups of patients. On the base of data analysis of the GINS Registry, three large enough subgroups of treated patients can be identified, so as to obtain a specific profile of treatment outcome in each group. FI of idiopathic neurogenic origin proved to be the most responsive to SNM. In this study the efficacy of SNM in this sub-group of patients has been confirmed: a significant reduction of the average number of episodes of FI, and of the FI evaluation score, a significant improvement of QoL and of general health status over several domains. There is also a significant reduction in the rectal sensation of urgency in these patients.

The outcomes of patients treated with SNM for FI secondary to iatrogenic sphincter damage, including lesions deriving from vaginal childbirth and from anorectal surgical procedures were very interesting. This sub-group included both patients that have had a previous unsuccessful external sphincter overlapping sphincter-plasty, and patients with an external sphincter lesion, possibly associated also with an internal sphincter lesion, for who SNM was the primary treatment. The effectiveness of SNM in these patients was made evident by the significant reduction in the Cleveland Clinic score, and by the improvement in QoL and health status indices. Also in this group, the manometric findings failed to show statistically significant differences, although the anal contraction tone was increased. Values of rectal sensitivity after SNM appear to be similar to the baseline values. Baseline values are assumed to be normal, since they should not be altered in the sphincter lesion, and this seems to suggest that SNM is acting only on the altered mechanisms, which are responsible for the FI, and not exerting any "modulatory" effect on normally functioning mechanisms.

A new interesting frontier for SNM is in treatment of patients suffering from FI after rectal resection, often performed for rectal cancer. Ultra-low rectal resection with adjuvant radiotherapy and chemo-radiotherapy is becoming more and more frequent in the treatment of these patients. Risk factors for FI include complete ablation or volume reduction of the rectal pouch, possible damage to the internal sphincter due to the use of a mechanical stapler and damage to pelvic nerves, and to sensitive peripheral anorectal structures from radiotherapy. Further damage can occur during surgery: trauma to sympathetic nerve fibers in the para-aortic/caval, superior hypogastric plexus, or hypogastric nerves, to parasympathetic nerves (S2, S3, S4), and to mixed sympathetic/parasympathetic nerves in the inferior hypogastric plexus, and in terminal fibres to the pelvic organs. Treatment with SNM in these patients produced a significant reduction of FI score, and an improvement of both QoL and in the majority of SF-36 domaines, whereas the significance of the manometric data remains uncertain. In these patients SNM is an interesting treatment option.

In conclusion, SNM is an effective treatment option for patients suffering from FI, particularly if of idiopathic neurogenic origin, but also if secondary to other causes. The good results obtained in patients with FI after rectal resection and neoadjuvant radiochemotherapy, and those observed in patients with a continuous internal sphincter lesion, appear to be of particular interest. In all these conditions, SNM had a positive impact on QoL and health general status, while the manometric data is unclear. A better understanding of the intimate mechanisms of action of SNM, thus allowing a better patients selection, can derive from this and from other similar studies.

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