Parameters of successful sacral root neuromodulation of the pelvic floor: a retrospective study

A. Bin Mahfooz, MD, N. Elmayergi, MD, M. Abdelhady, MD, Y. Wang, MD, M. Hassouna, MD

Division of Urology, Toronto Western Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada

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Introduction/objective: *Neuromodulation of the pelvic floor (InterStim®) is a relatively new technique in the field of urology. We present our observations for effective neuromodulation on our patient population.*

Materials and methods: *In a retrospective case review study, we studied the charts of 67 patients, who underwent InterStim® operations between the years 1993 to 2002. All 67 patients had a good response to InterStim®. Patients with inefficient or inconclusive responses were not included in the study. All the relevant patient data was recorded from their charts. For each patient, the following was recorded; the amplitude in volts, the pulse width (in microseconds) and rate, the mode (cycling versus continuous), the electrodes and their position, the load impedance, and the change in amplitude over time.*

Results: *Amplitude over time showed an initial plateau, followed by a small increase that gets larger.*

Conclusions: *Long-term management of InterStim® recipients requires increasing amplitude following the implantation of the IntreStim® to maintain the same satisfactory levels of urinary control.*

Key Words: neuromodulation, sacral nerve stimulation, voiding dysfunction, prothesis

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Address correspondence to Magdy M. Hassouna, MD, Division of Urology, Toronto Western Hospital, 399 Bathurst Street, MP 8-306, Toronto, Ontario M5T 2S8 Canada

Introduction

Galvani and Volta made the connection between electricity and muscular contraction in the 18th century. This facilitated study of the functional anatomy of individual muscles and of neuromuscular contraction.[1] Animal studies were conducted in the 1960's, and in 1963 Caldwell described his clinical experience with

the first implantable pelvic floor stimulator.[2] In the early 1970's Nashold et al were the first to achieve micturition via spinal cord stimulation.[3] Since the late 1980's and early 1990's sacral neuromodulation has evolved as an established treatment modality for patients with chronic voiding dysfunction.

Sacral neuromodulation has been shown to be effective in treating patients refractory to traditional therapies for urge incontinence and urgency/frequency,[4-6] idiopathic "non obstructive" chronic urinary retention,[7,8] pelvic pain[5,9,10] and interstitial cystitis.[11]

The US FDA has approved sacral root neuromodulation for patients with chronic voiding dysfunctions in the form of urinary urge incontinence, urgency frequency syndrome, or voiding (difficulty either with incomplete voiding, incomplete retention, or complete retention with inability to initiate normal micturation).[12]

Our experience with the InterStim® (electrical stimulation) is discussed below.

Patients and methods

In this study, a retrospective chart review was preformed on all patients who successfully underwent IntreStim® operations from 1993 to 2002 at the Toronto Western Hospital.

During this time period, 197 patients with voiding dysfunction (including urge incontinence, urgency/frequency, and chronic urinary retention) not responding to conventional therapy were seen in the clinic and underwent peripheral nerve evaluation (PNE) as a screening test. Of these, 67 (34.01%) were successful and henceforth implanted with a neurostimulator on the third or fourth sacral nerve root. Fifty-eight were female and 9 male, with ages ranging from 29 to 75 years old (average = 48.29). Patients were followed up after implantation for periods ranging from 3 months to 7 years.

The implantable device used in 63 patients was the ITREL III. Four patients were implanted with the ITREL II. ITRELL III is the more recent model and allows for more versatility and patient control than previous models.

Screening test and procedure

All patients underwent PNE as a screening test. The steps of this test have been previously described.[13,14] Patients were asked to complete a baseline-voiding diary before and during PNE, conducted for 3-7 days. The baseline-voiding diary is a standardized form of questions covering aspects of voiding function. The questions include frequency/voiding per day, voiding volume, number of pads used (in incontinent patients), degree of urgency, and the post void residual volume (through self catheterization) in retention patients.

A 50% improvement in baseline voiding symptoms during test stimulation is considered as the cutoff value for the patient to qualify for surgical implantation of neuroprothesis as previously described.[13,14] The stimulation parameters for the PNE were not recorded.

All patients included in this study had achieved and maintained successful outcomes in one or more voiding parameters in the voiding diary.

Implantation of the InterStim® device was done under general anesthesia and involved the placement of a permanent electrode into the S3 foramen on one side through a small (5 cm - 7 cm) vertical incision over the sacrum. The electrode lead was tunneled under the skin and connected to the stimulating device implanted in the upper buttock through a second horizontal incision. The detailed description of the surgical technique has been described in a previous publication.[14]

Follow up evaluations after implantation were done for each patient during visits at 1, 3, 6, 9, and 12 months after implantation, and every 6 months thereafter. In each visit the patient is requested to fill a voiding diary to document the efficacy of the therapy and side effects. The stimulation parameters were collected through an InterStim® programmer (7432 Neurological Programmer Medtronic).

In the current work, we assessed the parameters of stimulation used by the patients during the period of follow-up. The stimulation parameters were recorded during each visit and kept in the patient's chart.

The data collected and presented in this study are the following: the amplitude required to achieve sensation in volts, the pulse width (in microseconds), the rate (pulse per second), the mode of the implant (continuous versus cycling), the on and off time of stimulation (in seconds), and the site of the active electrodes used. The load impedance was recorded in the active electrode. Finally, the change in amplitude required to achieve proper bladder control over time was recorded.

All this data was then tabulated and presented, with the averages calculated for the different variables over time.

Results

Amplitude

Amplitude (v) average: 1.462
Amplitude (v) upper limit average: 5.007

Amplitude (v) lower limit average: 0.3
The amplitude of stimulation in 67 patients ranged between 0.2 – 6.8 volts. The average was 1.462.

Pulse width (ms)
Pulse width (ms) average: 204.090 μsec.
The pulse width ranged between 120 – 270 microseconds. The majority of patients (58) had a 210 m second pulse width. This is based on patient comfort level.

Rate (pulse/s)
Rate (pulse/s) average: 9.018
The Pulse Rate ranged from 2 – 20 pulse/s. The majority of patients (49) had a pulse rate of 10 pulse/s. This is also based on patient tolerance and comfort level.

Mode (cycling versus continuous)
Sixty-one patients had cycling mode (91%), while only six patients (9%) were in continuous mode. Cyclic mode has the benefit of maintaining the patients sense of awareness of the pelvic floor. Sixty-one patients had cycling mode of stimulation for 10 seconds On and 5 seconds Off. The stimulation cycle starts at 2 seconds ramping.

On time (s)
On time (s) average: 12.243.

Off time (s):
Off time (s) average: 4.765

Electrode assignment
All patients except one had the stimulator in monopolar fashion, with the case of IPG being positive. The active electrodes were arranged mainly between the distal 2. See Figure 1.

Electrode laterality and position
The majority of electrodes were placed in the third right sacral foramina (33) and the third left sacral foramina (23). One patient had stimulation in both foramina, and three patients underwent the new tined lead sacral stimulation.

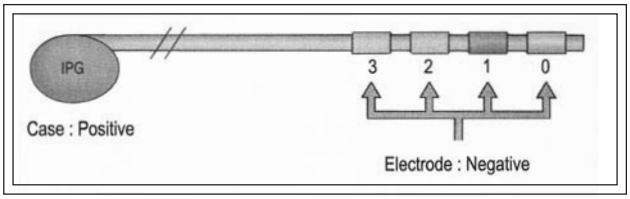

Figure 1. IPG electrode assignments

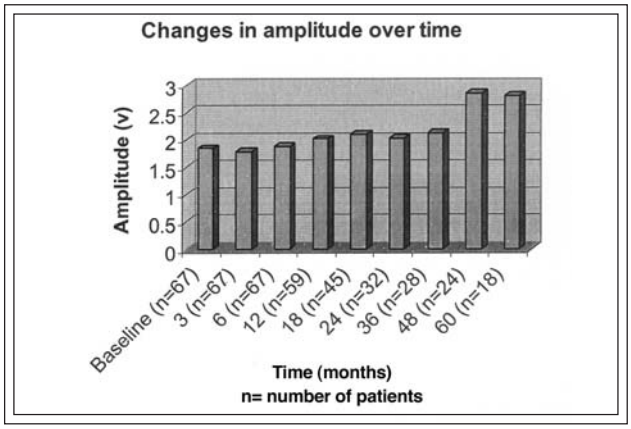

Figure 2. Changes in amplitude over time

Load impedance:
The load impedance was found to range from 578 – 1537 Ohms (W). None of the patients had an impedance of more than 2000 W

Change in amplitude over time
The patients were able to increase the amplitude to ensure proper perception of stimulation in perineal area. There was a gradual increase in amplitude starting from 6 months until 36 months, with this increase getting significantly larger after that. See Figure 2.

Discussion

It is difficult to compare our study with others since there have been no previous studies conducted for this purpose (i.e. long term observations for patients undergoing successful IntreStim® procedures). This procedure is becoming common, and is conducted in several centers throughout North America.

However, from the chart review several key points have been made clear.

The starting amplitude recorded for the 67 patients varies. This starting amplitude is based on the patient's level of comfort and sensation. The amplitude is increased in 0.1 volt implements until it reaches a comfortable and tolerant level based on the patients' verbal feedback. The average starting amplitude was 1.462 volts.

Cyclic mode was found to be effective in maintaining the degree of sense of awareness of the pelvic floor. The on and off time averaged at 12.2 and 4.7 seconds respectively.

The far majority of patients had the return (positive) electrodes attached to the case of the IPG. Most of the negative electrodes were attached either

TABLE 1. **The mean, standard deviation, and ranges of the Amplitudes of the SNS at the different time intervals in which they were seen at the clinic (i.e. at implantation, then at 1, 3, 6, 9, and 12 months after implantation, then every 6 months after that till 60 months)**

		Statistics at each time period				
Variable	**Label**	**N**	**Mean**	**Standard deviation**	**Minimum**	**Maximum**
a0	baseline	67	1.8395522	1.3037689	0.2	6.8
a1	1 mo	67	1.7619403	1.2958000	0.1	6.8
a3	3 mo	67	1.7768657	1.0997358	0.1	5.7
a6	6 mo	67	1.8716418	1.2105040	0.1	5.7
a9	9 mo	66	1.9196970	1.1768236	0.1	5.7
a12	12 mo	59	2.0135593	1.2060491	0.1	5.7
a18	18 mo	45	2.0900000	1.3124232	0.3	7.9
a24	24 mo	32	2.0234375	0.9809462	0.7	4.15
a30	30 mo	32	2.2000000	1.2072362	0.7	5.2
a36	36 mo	28	2.1089286	1.3253269	0.7	6.8
a42	42 mo	26	2.5076923	1.5901379	0.8	7.7
a48	48 mo	24	2.8500000	1.7018532	0.8	7.7
a54	54 mo	19	2.9157895	1.7170754	1.0	7.5
a60	60 mo	18	2.8111111	1.7667314	1.0	7.5

to electrode 0 or 1. The presence for multiple electrodes enabled the surgeon to choose among the electrodes that gave the least resistance. Should displacement of electrodes occur in the postoperative period, re-assignment of the electrode is possible without the need of surgical revision. Almost all patients had their implants in the third Sacral Foramina, either left or right. Only one patient needed implants in both the foramina, with three patients undergoing the new tined lead implant procedure. Contrary to bipolar, the unipolar stimulation is found to be more effective at lower amplitudes.

The impedance load (in Ohm) is a function of electrical conductivity between the active electrodes and the tissue surrounding the nerve root. The impedance recorded was noted to be < 2000 Ohms. The increase in the impedance was found to increase with the increase in the amplitude.

Finally, the initial amplitude was compared with the amplitude at different intervals, starting from 1, 3, 6, 9, and 12 months, then every 6 months thereafter. It appears that there is an initial plateau, followed by a small increase that gets larger later. See Table 1. This table gives the means, standard deviations, and ranges for baseline through 60 months. Table 2 provides means, standard deviations, and p-values of the increases from baseline to 60 months. It is noticed that there is a slight decrease through 3 months, followed by a very small increase through 12 months and somewhat larger increases after that. Beginning at 42 months, the increases are statistically significant.

In order to use the most important intervals and the larger sample sizes at those intervals, tables 3 and 4 use only the 32 patients with data at baseline, 6, 12, and 24 months. Table 3 shows the means, standard deviations, and p-values of the increases from baseline. None of the three intervals was statistically higher than baseline. A repeated measures analysis of variance (ANOVA) of the relationship between amplitude and time for these four intervals was performed. The p-value was 0.30, indicating no statistical differences across time for these patients. Table 4 shows the mean amplitudes for these 32 patients at the four intervals, where again you can see a small increase through 24 months.

This increase in amplitude over time is due to local tissue reaction around the active electrode.[15] The role of current density as an independent parameter in the induction of neurolgic damage has not been investigated thoroughly. Charge density and the current density are manipulated independently according to the duration of the stimulus pulse or, more generally, the shape and duration of each phase of the stimulus waveform. The pulse duration does not appear to strongly influence the threshold of the neural damage in the feline cerebral cortex, for pulse durations in the range of 100-250 microseconds.[15] There has been no clinical evidence of neuronal

TABLE 2. **The mean, standard deviation, and p-values of the increases in baseline to 60 months of the Amplitudes of the SNS at the different time intervals in which they were seen at the clinic (i.e. at implantation, then at 1, 3, 6, 9, and 12 months after implantation, then every 6 months after that till 60 months)**

Statistics for the increases at each time period						
Variable	**Label**	**N**	**N missing**	**Mean**	**Standard deviation**	**Minimum**
a1	Base to 1 mo	67	0	-0.0776119	0.8348146	0.4494
a3	Base to 3 mo	67	0	-0.0626866	0.9851682	0.6042
a6	Base to 6 mo	67	0	0.0320896	1.1200210	0.8153
a9	Base to 9 mo	66	1	0.0568182	1.1466971	0.6886
a12	Base to 12 mo	59	8	0.0906780	1.2675484	0.5848
a18	Base to 18 mo	45	22	0.3888889	1.3984524	0.0688
a24	Base to 24 mo	32	35	0.3046875	1.1457748	0.1426
a30	Base to 30 mo	32	35	0.4812500	1.3853933	0.0584
a36	Base to 36 mo	28	39	0.5285714	1.4556676	0.0653
a42	Base to 42 mo	26	41	0.8634615	1.7612244	0.0193
a48	Base to 48 mo	24	43	1.2333333	1.8675528	0.0037
a54	Base to 54 mo	19	48	1.1105263	2.0029547	0.0265
a60	Base to 60 mo	18	49	0.9500000	1.8995355	0.0488

TABLE 3. **The means, standard deviations, and p-values of the increases of Amplitude from baseline at key intervals, which are the most important intervals and the larger sample sizes at those intervals, using only the 32 patients with data at baseline, 6, 12, and 24 months.**

Statistics at key intervals through 24 months					
Variable	**Label**	**N**	**Mean**	**Standard deviation**	**P- value**
a6	Base to 6 months	32	0.1875000	0.7056226	0.1429
a12	Base to 12 months	32	0.2156250	0.8824853	0.1768
a24	Base to 24 months	32	0.3046875	1.1457748	0.1426

TABLE 4. **The mean amplitude, standard deviations, and p-values of the increases from baseline at key intervals, which are the most important intervals and the larger sample sizes at those intervals, using only the 32 patients with data at baseline, 6, 12, and 24 months**

Mean amplitude at key intervals through 24 months						
Variable	**Label**	**N**	**Mean**	**Standard deviation**	**Minimum**	**Maximum**
a0	Baseline	32	1.718750	0.9820773	0.3	4.15
a6	Base to 6 months	32	1.906250	0.9516327	0.6	4.5
a12	Base to 12 months	32	1.9343750	0.8887684	0.6	3.8
a24	Base to 24 months	32	2.0234375	0.9809462	0.7	4.15

damage in our study population.

The mechanism of electrode-induced neural damage is not fully understood. It is suggested that the electrode configuration itself (incorrect fit to the nerve), surgical trauma, and pressure caused by post surgical oedema are physical causes for nerve damage. With continued excitation of the nervous tissue, there is an increase in the release of potassium electrolyte into the extracellular compartment, with simultaneous uptake of sodium by the neurons. Over time this causes a "cytotoxic" edema, and an increase in electrical stimulation is required to produce the same results. Excessive scar formation (which can bind the nerve to surrounding tissue) and tension on the electrode cables are also all potential contributors to neural damage. The charge density provided by the present stimulator parameters was found to be in the safe zone.[15]

The configuration of electrode lead (model 3080 Medtronic Inc) does not allow any local pressure on the nerve roots. The electrodes are located in proximity of the nerve root with minimal direct contact within the sacral foramina, causing minimal scarring of the nerve roots. The long-term effects show no evidence of neuronal damage.

Our main goal of this study is to present this data to serve as guidelines for future surgeons interested in performing this procedure. We feel many more successful patient examples need to be collected, and it would be interesting to see what other centers' standards of parameters are in comparison to ours.

In conclusion, InterStim® is a therapy that has demonstrated impressive results in treating voiding dysfunctions. The parameters for this technique have not been established, as comfort level differs from one patient to another. However, we present our observations as guidelines, and believe it would decrease trial and error attempts. More importantly, it is an indication of what to expect in the long-term management of these patients. □

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