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Clinical study

Peripheral nerve stimulation for the treatment of chronic pain

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Abstract

The aim of this retrospective study is to evaluate the role of the implanted peripheral nerve stimulator in patients with pain in a peripheral nerve distribution. The current study is the largest in the literature that examines the role of the implantable peripheral nerve stimulator in the chronic pain patient. Our patient sample included 38 patients (with 41 nerve stimulators), consisting of 19 males and 19 females with a mean age of 44 years (SD = 11 years). Four groups of etiologic factors were identified; blunt or sharp nerve trauma (14/38), iatrogenic injuries from surgery (9/38), inadvertent injection of a nerve (9/38) and post surgery for entrapment or tumour (8/38). Stimulation was attempted in 45 patients, but an initial trial failed in 4. Mean follow-up time from implantation of the stimulator was 31 months (SD = 19 months). Compensation benefit was an issue in 29 cases (76%). Outcome following implantation was assessed based on pain criteria, narcotic usage and return to normal function/ work. Relief from preoperative pain was judged as good (>50% relief) by 23/38 patients (61%). A total of 15 patients reported fair or poor results (39%). Six patients required removal of their stimulators (15%) due to infection or reduction of pain control after an initial good result. A statistically significant decrease in reported pain level was found postoperatively ($p < 0.05$). Workers' compensation patients have equivalent outcomes to non-compensable patients ($p > 0.05$). Eighteen of 38 (47%) patients reported a significant improvement in their activity levels following stimulator implant. In conclusion, over 60% of patients had a significant improvement in their pain and lifestyle following implantation of peripheral nerve stimulators. We therefore conclude that peripheral nerve stimulation can be useful in decreasing pain in well selected patients with severe pain in the distribution of a peripheral nerve.

Keywords: Peripheral Nerve; Pain; Stimulator

1. Introduction

The role of electrical impulses for the treatment of pain has a long history. As early as 400 BC, the *torpedo fish* was used to treat pain with the electric fish placed directly on a painful area of the body. Stimulation-produced analgesia has been used by the Chinese for many centuries, including the use of an electric current applied to acupuncture needles.[1] Electrical stimulation of peripheral nerves using implanted electrodes for treatment of intractable pain has been used over the past 30 years.[2] Difficulties encountered have included defining the appropriate indications, utilizing approved device technology, and standardizing surgical techniques. Circumferential electrodes treating mononeuropathies have given way to paddle-type electrodes, such as the Resume electrode (Medtronic Inc., Minneapolis, MN, USA).

Chronic pain from trauma to a peripheral nerve can be a challenge for both the pain service and surgeon. Type of surgery depends on the type of insult to the peripheral nerve and may include neurolysis, transposition, nerve grafting, division of the painful nerve proximal to the pain source and resection of the nerve.[3,4] Implantation of a nerve stimulator is an option for the patient who continues to have pain despite exhausting surgical and medical options. The aim of this study is to review the results of peripheral nerve stimulation at our institution in an attempt to identify the

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patient population that will most benefit from the procedure and to evaluate the overall value of the procedure in light of the relatively high expense of the implanted electrode and generator complex. In addition, we review the results of other large series and compare them to the study presented.

2. Material and methods

2.1. Patient selection and questionnaire

A retrospective review of patient charts and a telephone questionnaire was conducted. The charts of 42 patients were reviewed to confirm the nerve stimulated and the results of the trial stimulation. Only those patients who had permanent implantation of a stimulator were contacted ($n = 38$). All patients contacted agreed to participate in the phone survey. A questionnaire was devised following consultation with a statistician and the pain management service. The 20-item questionnaire included: assessment of pain preoperatively and postoperatively, using the visual analogue pain scale (VAS);[5] return to work; improvement in activities of daily living; and use of analgesics.

2.2. Technique

The technique for implantation is performed in two stages. The first procedure involves exposure of the affected nerve proximal to the pathology. The use of a nerve stimulator to confirm the nerve has not been necessary in our experience as the operative exposure usually involves a virgin nerve dissection proximal to the level of the pathologic insult to the nerve. We attempt to leave a layer of mesoneurium over the nerve and to dissect just enough nerve to apply the stimulator device. Two Australian surgeons designed a modified Resume electrode (Medtronic) especially for this indication.[6] When the electrode is in place, the mesh is loosely wrapped around the nerve and interrupted 4/0 nylon suture is used to attach the electrode to the nerve. A trial lead exits the skin via a stab incision. A representative from Medtronic visits the patient on day 1 to attach a trial generator. The patient is instructed in the use of the generator and can alter voltage and stimulation settings themselves to find the best combination for their pain. Although some authors have an initial trial period of 24–48 hours, we consider this time course too short as the patient is still recovering from a general anaesthetic and may have long-acting local anesthesia wound infiltration with agents such as Marcaine. Our trial period lasts 3–7 days. If the results of early stimulation are not conclusive, we lengthen the trial for up to 7 days.

If the initial trial is successful, the second procedure involves implantation of the battery/generator unit. Tunneling equipment is included in the package from Medtronic and the electrode and battery are connected. Battery placement is discussed with patients preoperatively and is either pectoral, anterior thigh or abdominal wall above the belt line. Discharge is usually day 2 following the second stage procedure and the patient is sent home on prophylactic antibiotics. All authors were involved in the surgical insertion of the stimulators; however the senior author (PB) was the supervisor for all cases.

2.3. Follow-up

All patients were followed up by the senior author (PB) and by the referring pain clinic. The initial visit was 4–6 weeks following surgery and then as necessary. The patient would contact the Medtronic representative for ongoing advice for generator settings. However, follow-up results for this study were reviewed by an independent non-interested assessor. Over an 8-year period, 41 peripheral nerve stimulators were inserted into 38 patients.

2.4. Statistical analysis

Data collected was analysed in Microsoft Excel (Microsoft Inc., Redmond, WA, USA) format for mean and standard deviation. The *t*-test was used for pre- and postoperative analysis.

3. Results

3.1. Demographics

The total number of stimulators followed was 45. A total of four stimulators (8.9%), in four patients failed the initial trial stimulation period and thus were not included in the final analysis. The location of the failed stimulators included: one brachial plexus; one median; one radial; and one common peroneal nerve. There were a total of 41 peripheral nerve stimulators permanently implanted into 38 patients. The mean age of the patients was 44 years (SD = 11) with a range of 25–68 years. There were 19 men and 19 women. The mean duration of symptoms was 58 months (SD = 36) with a range of 6–144 months. The mean follow-up was 31 months (SD = 19) with a range of 9–89 months. Workers compensation and/or litigation was involved for 29 patients (76%).

The peripheral nerve stimulator was placed in the upper extremity in 34 patients and in the lower extremity in seven. Upper extremity stimulators were placed in the following locations: 11 median; 10 ulnar; nine brachial plexus; three radial; and one suprascapular nerve. Lower extremity stimulators were placed in the following locations: two common peroneal; two sural; two posterior tibial; and one sciatic nerve. The minimal number of lower limb stimulators inserted was a reflection on the poor results that our group encountered early on in the series and thus inserting these devices in the lower extremity was discontinued in favor of spinal cord stimulation.

Of the 38 patients who had permanent implantation, four groups of etiologic factors were identified. The most

Table 1
Indications and outcome for each group of patients

INDICATION	Number (n)	Percentage of patients	Good outcome (>50% relief)
Civilian nerve trauma	14	36%	50%
Iatrogenic: surgery.	9	24%	66%
Iatrogenic: injection/cannulation	9	24%	77%
Nerve entrapment/Tumour	6	16%	50%

common group was blunt or sharp nerve trauma from assault or in the workplace (14/38). Iatrogenic injuries were most likely following surgery for open reduction and internal fixation of fractures (9/38). The third group were also iatrogenic injuries from inadvertent injection of a nerve or attempted cannulation of a vein that damaged a peripheral nerve (9/38). The fourth group consisted of post-surgery patients who initially were treated for nerve entrapment or tumour (6/38) and who remained in pain with no resolution of symptoms following an initial procedure (Table 1).

3.2. Pain and lifestyle outcomes

We defined a good result as a 50% or better improvement in verbal pain scores (VPS) at time of follow-up as compared with preoperative scores. An overall good result was seen in 23 of 38 patients (61%). The mean VPS preoperatively was 9 (SD = 0.96, range 6–10). The documented VPS at the 1-month postoperative visit was 5.1 (SD = 2.73, range 0–10). At the time of independent assessment, the VPS was 5.2 (SD = 2.29, range 2–10). This would indicate that if the patient experiences a good result soon after insertion of the peripheral nerve stimulator, they would continue to benefit from a satisfactory result.

Patients were asked to grade their postoperative activity levels into three broad categories: improved, the same or worse. Activity levels were improved in 47% of patients (18/38), unchanged in 37% (14/38) and worse in 16% (6/38). The issue of analgesic use revealed that 24/38 patients (63%) had reduced or eliminated analgesic use. Using the 2-sample *t*-test the difference between reported levels of postoperative and preoperative pain was statistically significant ($p = 0.034$).

3.3. Factors associated with success and failure

An attempt to determine the overall factors that are associated with success and failure was made. The success with upper extremity stimulation was significant as compared with the lower extremity. The success of the lower extremity (1/7 patients) was 14% as compared with the upper at 65% (22/34 patients). This is a statistically significant result ($p = 0.024$). The average age for successful patients was 41 years, and 48 years for the unsuccessful patients. The duration of symptoms between the two groups was 60 and 62 months respectively. The poor outcome patients had slightly longer average follow-up at 34 months compared with 29 months for the successful patients.

There was no statistically significant difference in postoperative pain levels between men and women ($p > 0.05$), or between cases involving workers compensation or not ($p > 0.05$). Of the seven lower limb stimulators inserted, only one was a success. There is a significant relationship between lower limb stimulation and poor outcome ($p < 0.05$). As a result, no stimulators were inserted at this location after the halfway point of the study period.

3.4. Complications

A total of six stimulators were removed after implantation (15%) (Table 2). Two were removed due to infection, a 5% infection rate. One of these patients had hemophilia and despite factor VIII cover, had an episode of bleeding that was further complicated by infection necessitating removal. Both of these patients were in the first half of the study. Despite a good result during the screening period, one stimulator was removed after a month because of minimal effect post-implantation. This patient subsequently improved again after his workers compensation issues were resolved. One was removed at 4 years post-implantation at the patient's wish as according to her it was no longer needed. Two stimulators in one patient had an initial good effect, lasting 3 months, then a rapid decline in effect. The patient did not wish to have the stimulator re-trialled or reimplanted.

A single lead had to be replaced as it was fractured following a fall from a tree. The stimulator continued to function following revision of the lead. During the follow-up period, two battery generators were replaced because of battery failure and a further two generator/lead combinations had to be repositioned as they were uncomfortable and restricting arm movement.

One electrode was relocated during the trial period owing to a marked uncomfortable motor effect in an adjacent muscle. A further eight electrodes were resutured during

Table 2
Complications necessitating removal of device

Complication	Number (n)
Infection	2
Early failure (<6 months)	3
Late failure (>6 months)	1

the second operation due to position change of the electrode during the trial period. This prompted the senior author (PB) to design the mesh-type electrode to aid in anchoring the electrode.

4. Discussion

The options for electrical nerve stimulation are via the transcutaneous or directly implantable routes. The use of these devices is based on the gate control theory that stimulation of large diameter afferent fibers can "gate" the transmission of noiceptive activity.[7] However, the results of transcutaneous electrical nerve stimulation are inconclusive following a review of 107 published articles.[8] The conclusion by Cochrane investigators is that trials do not provide information on stimulation parameters or answer questions about long-term effectiveness. The current study is the largest in the literature that examines the role of the implantable peripheral nerve stimulator in the chronic pain patient. Stimulation parameters are not discussed, as these are individual and variable for each patient; however, we do hope to answer the question of long-term effectiveness.

The major technique change that we adopt as compared with other authors is the length of the trial period. Although some authors have a relatively short trial period, we believe that a longer trial is beneficial so that no operative factors come into play with the results of trial stimulation. Also, the addition of the mesh electrode aided implantation and reduced the number of times that repositioning was undertaken.

The overall results at a mean follow-up of 35 months is encouraging with 61% of patients experiencing greater than 50% relief from their chronic pain. There have been only seven studies with greater than 20 patients, with our study comparing favourably with the other large studies in the literature. Campbell et al.[1] reviewed 33 patients and had a 45% good–excellent pain reduction result. Picaza et al.[9] reviewed 23 patients with an 87% success rate. Hassenbuschp[10] reviewed 32 patients at 63% favourable outcome. Racz[11] reviewed 23 patients with a 61% favourable outcome. Strege[12] had 24 patients with a 75% good–excellent result with narcotic use eliminated in the same number of patients (Table 3).

Patients suitable for neuromodulation include: peripheral mononeuropathy (traumatic, idiopathic and iatrogenic); plexopathy; and complex regional pain syndromes (CRPS type 1 and 2).[13] Previous authors have stated that response to trial stimulation is the best indicator of long-term prognosis. In our hands, success during the trial period does not always correlate with long-term success as three implanted stimulators have had early failures and have been removed within a 3-month period. The three stimulators were in two patients who both had a long trial period (7 days) and excellent reduction in pain scores during that period.

Peripheral nerve stimulation has undergone a continuous development since the first implanted electrodes on the median and ulnar nerve in 1967 by Wall and Sweet.[14] The original Resume (Medtronic) electrode that has been used by many authors has been adapted to include a mesh-like cuff to aid implantation and help secure the electrode (Fig. 1). This design change was initiated as several early failures were due to electrode migration with inadequate anchoring with the original Resume type electrode.

Early investigators reported the high failure rates associated with peripheral nerve stimulation of the lower limb. Theories include that the posterior tibial nerve is sensitive to stresses and traction with weightbearing and that the sciatic nerve does not provide constant stimulation as sensory fibers are deeper within the nerve.[13] Our experience would seem to reflect these earlier observations and now our practice is to perform spinal cord (dorsal column) stimulation for lower limb pain syndromes, as this procedure achieves higher success rates in our hands, and in the hands of other authors.[15]

Table 3
Peripheral nerve stimulation series

Author/date	Number of patients	Summary of results	Recommendation
Novak CB, Mackinnon SE/2000[2]	17	65% excellent or good outcome	"Peripheral nerve stimulators can be useful in decreasing pain in carefully selected patients with severe neurogenic pain"
Miles J, Lipton S/1978[17]	12 – All phantom limb pain	58% excellent outcome, 25% fair	
Campbell JN, Long DM/1976[1]	33 patients	45% favorable results (24% excellent, 21% good)	"The most dramatic successes occurred in patients with peripheral nerve trauma"
Picaza JA et al./1975[9]	23 patients	87% favorable results	
Hassenbusch et al./1996[10]	32 patients	Long term relief in 63% of patients	"PNS can provide good relief for RSD that is limited to the distribution of one major nerve"
Racz et al./1988[11]	34 patients	61% improvement on preimplant pain	"Implantation for treatment of causalgia caused by electrical burns"
Strege/1994[12]	24 patients	75% good-excellent.	

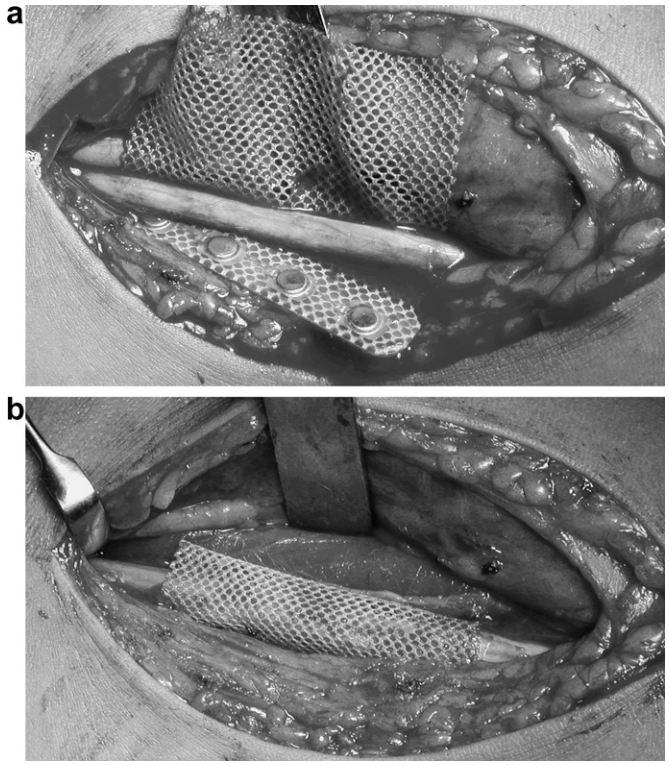

Fig. 1. The mesh Resume electrode (Medtronic Inc., Minneapolis, MN, USA) for peripheral nerve stimulation.

Improvement by the placebo affect has been discussed by previous authors. This is a valid criticism of this retrospective-type analysis; however, most of our patient population had multiple previous procedures and a protracted prior course, including pain clinics, alternative therapies, multiple medications, and therefore a placebo affect should have worked with previous therapeatic attempts.

The authors are unsure as to why one patient lost their chronic pain at a significant time following surgery (4 years after implantation). The device was removed at the patient's request and she did not have ongoing pain for the rest of the study period. We have been unable to find other reports in the literature of this ''pain reprogramming'', but it may be due to reorganization of noiceptive fiber input at the level of the substantia nigra.

The authors accept that the results are retrospective and not based on a randomized control trial (RCT). Although an RCT of peripheral nerve stimulation would be optimal to evaluate its effectiveness as compared with best medical therapy, this would be impracticable. A study that included randomizing patients to a ''best medical therapy'' versus a peripheral nerve stimulator would be ideal, although not feasible as these patients are refereed because they have failed the ''best medical therapy'' option. Second, a study that included a ''sham'' operation as a control group would be unethical.[16] In fact, any trial that attempted to ''blind'' the patient and/or the surgeon would not be possible as after trial implantation, stimulation without the sensation of parasthesia would alert both patient and operator of the assigned study group – thus rendering this option unworkable. Although a Cochrane Review article concluded that a large multi-centre randomised controlled trial of TENS in chronic pain was needed, we do not believe in the feasibility of a similar study for the evaluation of implantable stimulators.

The advantages of peripheral nerve stimulation include: it is a simple surgical procedure; it is non-destructive; and that peripheral nerve stimulation is reversible when the patient turns the stimulator off. Patients can also be trialed, prior to implantation of the complete system, thus reducing cost of permanent implantation if unsuccessful. Disadvantages include the risk of infection, which in our hands was 5% (both patients were early in the series), the risk that the stimulator looses effectiveness in some patients soon after implantation and the cost of implantation which is additional after some time due to battery failure. In addition, there is also the complication of entrapment by the nerve stimulator, necessitating removal of the device (Prof. David Kline, personal communication).

In conclusion we agree with previous reports that peripheral nerve stimulation has a role in the treatment of patients with chronic pain from a peripheral nerve source. Although careful selection is important for success, there is some unpredictability with the long-term outcome of the device.

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