Pain Medicine

Pain Medicine 2011; 12: 1515–1522
Wiley Periodicals, Inc.

NEUROPATHIC PAIN SECTION

Original Research Articles

Randomized Double-Blind Sham-Controlled Crossover Study of Short-Term Effect of Percutaneous Electrical Nerve Stimulation in Neuropathic Pain

Jon H. Raphael, MD,* Tarek A. Raheem, MB BCh,* Jane L. Southall, RN,† Alan Bennett, FRCA,‡ Robert L. Ashford, PhD,* and Sharon Williams, RN‡

*Faculty of Health, Birmingham City University, Birmingham;

†Pain Management, Russells Hall Hospital, Dudley;

‡Anaesthetics, Kidderminster Treatment Centre, Kidderminster, UK

Reprint requests to: Jon H. Raphael, MD, Graduate School, Ravensbury House, Faculty of Health, Birmingham City University, Westbourne Campus, Westbourne Road, Birmingham B15 3TN, UK. Tel: +44 (0)1384 244809; Fax: +44 (0)1384 244025; E-mail: jon.raphael@bcu.ac.uk.

Disclosure: Algotec Ltd. has previously provided unrestricted funding support for research but was not involved in the design, undertaking, analysis, and writing of this study. This research activity was supported by the Higher Education Funding Council for England.

Abstract

Background. Percutaneous electrical nerve stimulation (PENS) is an electrical neuromodulation technique that has shown its therapeutic potential in various chronic pain conditions over the past few years, but well-blinded controlled studies are lacking.

Patients and Methods. A randomized double-blind sham-controlled crossover trial on 31 patients with chronic pain with surface hyperalgesia to investigate the efficacy of PENS.

Results. For the active PENS therapies, the median numerical rating scale (NRS) for pain changed from 7.5 (standard deviation [SD] ± 1) (range 6–10) before therapy to 0.5 (range 0–8.5) after therapy ($Z = -4.206$, $P < 0.0005$ [two-tailed]). The mean pain pressure threshold (PPT) measured with the von Frey aesthesiometer changed from 202 gm (SD ± 137 gm) (range 55–800 gm) before therapy to 626 gm (SD ± 228 gm) (range 45–800 gm) after therapy ($Z = -4.373$, $P < 0.0005$ [two-tailed]). There was a statistically significant difference between the changes in NRS for the active (3.9 [±3.2] [0–8]) compared with the sham (0.1 [±0.4] [0–1.5]) therapies, $U = 40$, $Z = -3.484$, $P < 0.0001$ (two-tailed). There was a statistically significant difference between the changes in PPT for the active (310 gm [±267 gm] [0–670 gm]) compared with the sham (8 gm [±4 gm] [0–15 gm]) therapies, $U = 48.5$, $Z = -2.699$, $P = 0.007$ (two-tailed).

Conclusion. PENS therapy appears to be effective in providing short-term pain relief in chronic pain conditions. Studies, involving larger sample sizes and longer follow-up are recommended.

Key Words. Chronic Pain; CRPS; Percutaneous Electrical Nerve Stimulation (PENS); Neuromodulation; Neuropathic Pain

Introduction

Percutaneous electrical nerve stimulation (PENS), also known as percutaneous neuromodulation therapy [1], is a technique of electrical neuromodulation for pain relief that has become more popular in recent years with availability of the technologies. It provides for high and low-frequency electrical stimulation for a period of several minutes via probes inserted through the skin of the perceived painful area [2–6].

There have been an increasing number of open cohort studies [7,8] and several randomized controlled trials [2,3,5,9–13]. These have reported benefit in a range of chronic pain conditions such as low back pain [2,3,5,12,13], headache [10], diabetic neuropathic pain [4], post-herpetic neuralgia [9], sciatica [11], and chronic cervical pain [6]. It has, however, been difficult to evaluate

the efficacy of this treatment because of the challenges of blinding patients to an active treatment that is associated with a paresthetic sensation.

In this study, we have investigated the efficacy of PENS in chronic pain conditions with surface hyperalgesia in a design with a sham device to which patient and observer were blinded and have used the objective technique of pressure algometry.

Methods

We conducted a multicenter, double-blinded, crossover, placebo-controlled, randomized clinical trial of active PENS therapy compared with sham treatment. The study protocol was approved by the R&D department at Russells Hall Hospital, Dudley, UK and the R&D department at Worcestershire Acute Hospitals NHS trust, UK. Ethical approval was granted by the Black Country Research Ethics Committee, Redditch, UK.

The inclusion criteria were adult patients with hyperalgesia from various chronic pain conditions who were scheduled for PENS therapy at the two centers (Russells Hall Hospital, Dudley, West Midlands and Kidderminster Treatment Center, West Midlands, UK). Scheduling was based upon the clinicians deciding to offer this treatment for chronic pain conditions with surface hyperalgesia for which more conservative measures such as medications and transcutaneous electrical nerve stimulation (TENS) had failed. For inclusion to the study, patients were required to have pain of more than 6 months duration, with a localized area of hyperalgesia on the body surface, and to not have obtained pain relief with previous medical treatments.

A sample size of 30 patients was computed on the advice of a statistician (PN) based on power analysis judged by taking account of projections from previous studies of the degree of change with treatment, the predicted placebo effect, and the clinically meaningful difference in the levels of pain.

Their pain diagnoses were surgical scar pain N = 7, occipital neuralgia N = 4, posttraumatic neuropathic pain N = 3, stump pain N = 2, inflammatory neuropathic pain N = 3, chronic low back pain N = 5, complex regional pain syndrome N = 1, pain following total knee replacement surgery N = 3, chronic cervical pain N = 1, and post-herpetic neuralgia N = 2.

The outcome measure variables were perceived pain intensity level, measured by the numerical rating scale (NRS) and the pressure pain threshold (PPT), measured by pressure algometry with the Electronic von Frey Aesthesiometer™ (IITC Life Science, CA, USA). The left end of the NRS had the words “No Pain,” and the right end had the words “Worst Possible Pain.” The scale was numbered from zero to 10 at regular intervals. The patient was asked to mark the point along the line that corresponds to their current pain intensity.

The aesthesiometer was calibrated before each clinic using standard acrylic weights and also recalibrated before each patient. These measurements were taken by the same clinician and the patient was present in the examination room for 10–15 minutes prior to the actual examination. Depending on the locality of pain, the examination was performed with the patient either sitting or lying down. The point of maximum tenderness was located through manual palpation and marked using a skin marker. The round tip of the probe was applied in a perpendicular manner to the marked spot, and the clinician began to increase the pressure very gradually. The patient was asked to shut his or her eyes, and verbally indicate immediately when the sensation of pressure turned into a sensation of pain, at which point compression was stopped and the pressure reading was made. A total of three readings were taken from the same point, with 30-second intervals in between, and the mean was used as the final reading for analysis.

Data were collected from the patients prior to the therapy and 1 week after the therapy.

Participants were assigned randomly to either group A (active treatment first) or group B (control treatment first). At the next treatment, patients were crossed over to the opposite treatment. The randomization was achieved by means of numbered sealed envelopes containing computer generated random assignments provided by a statistician at the University of Birmingham (PN). The envelopes were held by an administrator uninvolved in the study (JE) and located in a separate building. A copy of the randomization sequence was kept in a locked cabinet away from the study personnel. The administrator was contacted by telephone to obtain the randomization envelope and the information was passed to the treating physician who was not involved in recruitment or outcome assessment of the patients.

Due to the potential carryover effect from crossover design, a washout period of 4 weeks was provided between treatments.

To establish double-blinding in this trial, the PENS device was operated from outside of the patients’ screens by a nurse independent of the study (GB) and the treating physician worked from behind an opaque curtain. The physician, patient, and research team were not aware whether the device was electrically powered or not.

For the sham therapies, the wires connected to the probes inserted through the patients’ skin were not connected to the PENS device but taped to the working surface. The wires connected to the PENS device were connected to a resistance box to simulate the electrical resistance of human tissue and thus creating a closed electrical circuit so that with the device switched on it simulated normal functioning and provided the set algorithm of alternating frequency stimulation for the set time of 25 minutes (Figure 1).

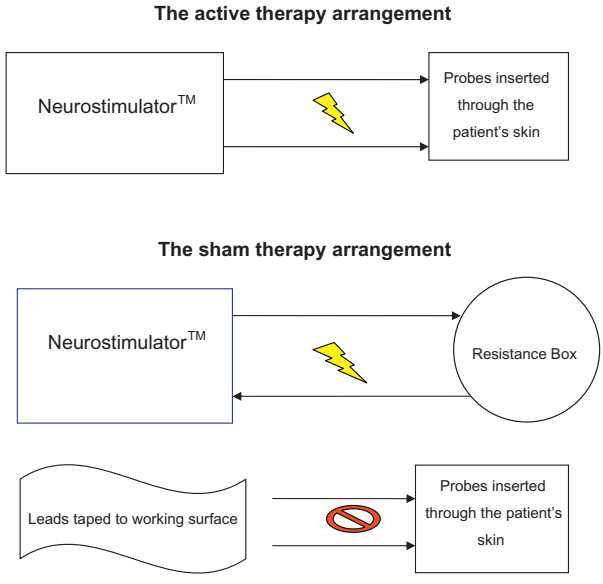

Figure 1 Active and sham experimental arrangements.

The patient's area of primary pain was identified and mapped prior to the treatment. A percutaneous probe was passed into the area and electrical neurostimulation therapy provided via conduction cables to the probe and to an earth plate on another non-painful skin site (Neuro-Stimulator™, Algotec Ltd., Haywards Heath, UK). Electric currents with frequencies automatically alternating between 2 and 100 Hz, at a rate of every 3 seconds, were provided for a total duration of 25 minutes.

All data analyses and graphs were produced using the SPSS 16.0 statistics software package (SPSS Inc., Chicago, IL, USA). Data were analyzed by the Wilcoxon matched pairs signed rank sum test and the Mann–Whitney test.

Results

Patients meeting the inclusion criteria of listing for PENS therapy and a localized area of hyperalgesia were sequentially approached. Four (two male, two female, mean age 56.3 years) declined to enter the study. Their diagnoses were back pain (N = 2), post-herpetic neuralgia (N = 1), and osteoarthritis of knee (N = 1); their pretreatment NRS were 6, 7, 8, and unrecorded.

The ages of the patients entering the study ranged from 23–84 years, with a mean age of 55.8 years (standard deviation [SD] ± 15.5 years). The sex distribution was female N = 18, male N = 13. Their pain diagnoses were surgical scar pain N = 7, occipital neuralgia N = 4, post-traumatic neuropathic pain N = 3, stump pain N = 2, inflammatory neuropathic pain N = 3, chronic low back pain N = 5, complex regional pain syndrome N = 1, pain following total knee replacement surgery N = 3, chronic cervical pain N = 1, and post-herpetic neuralgia N = 2.

The duration of time they had suffered from pain before having PENS therapy ranged from 1 to 35 years, with a mean of 8.1 years (SD ± 8.3 years). During this period, they had received a number of other therapies and medication that were either ineffective or of limited efficacy. These therapies included co-codamol (N = 9), guanethedine (N = 1), paracetamol (N = 9), gabapentin (N = 4), pregabalin (N = 3), carbamazepine (N = 1), amitriptyline (N = 3), tramadol (N = 7), morphine (N = 1), fluoxetine (N = 2), escitalopram (N = 2), steroid/nerve block injections (N = 9), lidocaine patches (N = 1), TENS therapy (N = 3), acupuncture (N = 7), physiotherapy (N = 7), hypnotherapy (N = 2), chiropractic therapy (N = 2), osteopathic therapy (N = 1), and herbal remedies (N = 1) (see Appendix 1 for further details).

One patient left the study after the first (active treatment) arm, his diagnosis was post-herpetic neuralgia and his NRS changed from 8 to 6.

For the active PENS therapies, the median NRS score for pain (Figure 2A) changed from 7.5 (SD ± 1) (range 6–10) before therapy to 0.5 (range 0–8.5) after therapy ($Z = -4.206$, $P < 0.0005$ [two-tailed], Wilcoxon matched pairs signed rank sum test). The mean PPT (Figure 3A) changed from 202 gm (SD ± 137 gm) (range 55–800 gm) before therapy to 626 gm (SD ± 228 gm) (range 45–800 gm) after therapy ($Z = -4.373$, $P < 0.0005$ [two-tailed], Wilcoxon matched pairs signed rank sum test). No adverse events were reported.

For the sham PENS therapies, the median NRS score (Figure 2B) for pain was 7.5 (SD ± 1) (range 6–10) before and after therapy ($Z = -1$, $P = 0.317$ [two-tailed], Wilcoxon matched pairs signed rank sum test).

The mean PPT (Figure 3B) changed from 202 gm (SD ± 134 gm) (range 65–800 gm) before therapy to 206 gm (SD ± 133 gm) (range 60–800 gm) after therapy ($Z = -1.915$, $P = 0.055$ [two-tailed], Wilcoxon matched pairs signed rank sum test).

There were responders in all diagnostic groups; the numbers in each group are too small for comparative analysis.

The blinding procedure in this study was evaluated by asking patients which therapy (i.e., active or sham) they thought they had after each arm of the study. After the first therapy, none of the patients could tell whether they had the active or the sham. However, after the second therapy, all the patients knew due to the characteristic tingling vibratory effect of the electrical stimulation, which is only present in the active therapies. We therefore analyzed the first treatment arm. There was a statistically significant difference between the changes in NRS for the active (3.9 [±3.2] [0–8]) compared with the sham (0.1 [±0.4] [0–1.5]) therapies (Figure 4A), $U = 40$, $Z = -3.484$, $P < 0.0001$

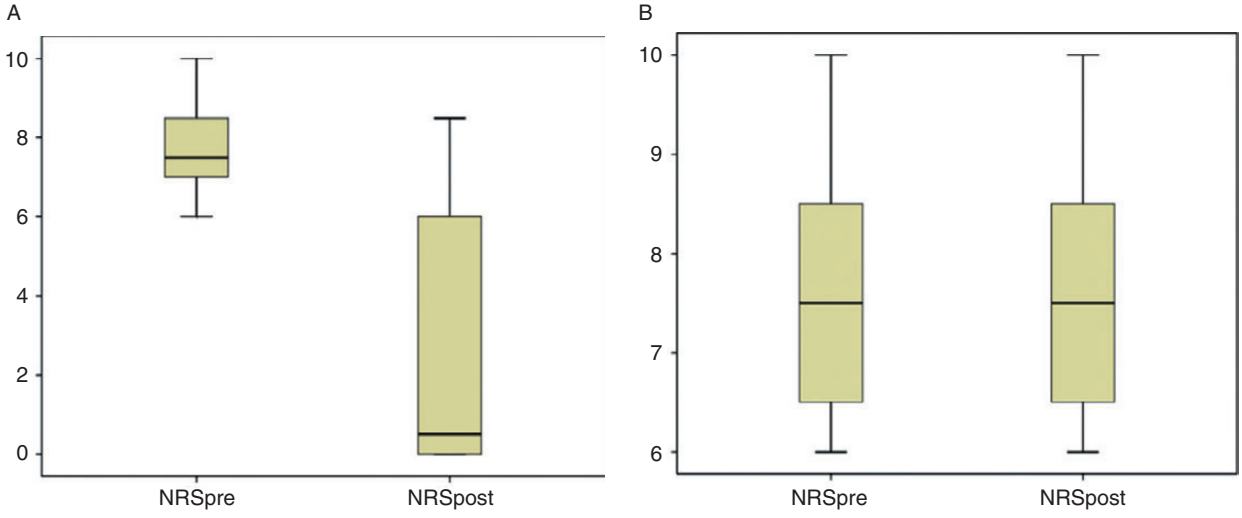

Figure 2 The *y*-axis represents the numerical rating scale (NRS) score for pain out of 10: (A) NRS scores before and after active therapy: (B) NRS scores before and after sham therapy.

(two-tailed) (Mann–Whitney test). There was a statistically significant difference between the changes in PPT for the active (310 gm [±267 gm] [0–670 gm]) compared with the sham (8 gm [±4 gm] [0–15 gm]) therapies (Figure 4B), $U = 48.5$, $Z = -2.699$, $P = 0.007$ (two-tailed) (Mann–Whitney test).

Discussion

In this randomized, sham-controlled crossover study, we have found evidence for short-term effectiveness of PENS compared with placebo. There were both clinically and statistically significant improvements in the NRS for pain and PPT after active therapy compared with sham. For the active treatments, 23 out of the 30 patients responded to therapy. The majority of patients treated with sham showed no improvement. One patient reported improvement following the sham therapy; however, this was not accompanied by a parallel change in the PPT.

Our results are comparable with those obtained from other sham-controlled crossover studies. In an active comparator study, Ghoname et al. found that PENS was more effective than TENS in providing short-term pain relief in patients with chronic low back pain [2] and in patients with sciatica [11]. Furthermore, in a third study,

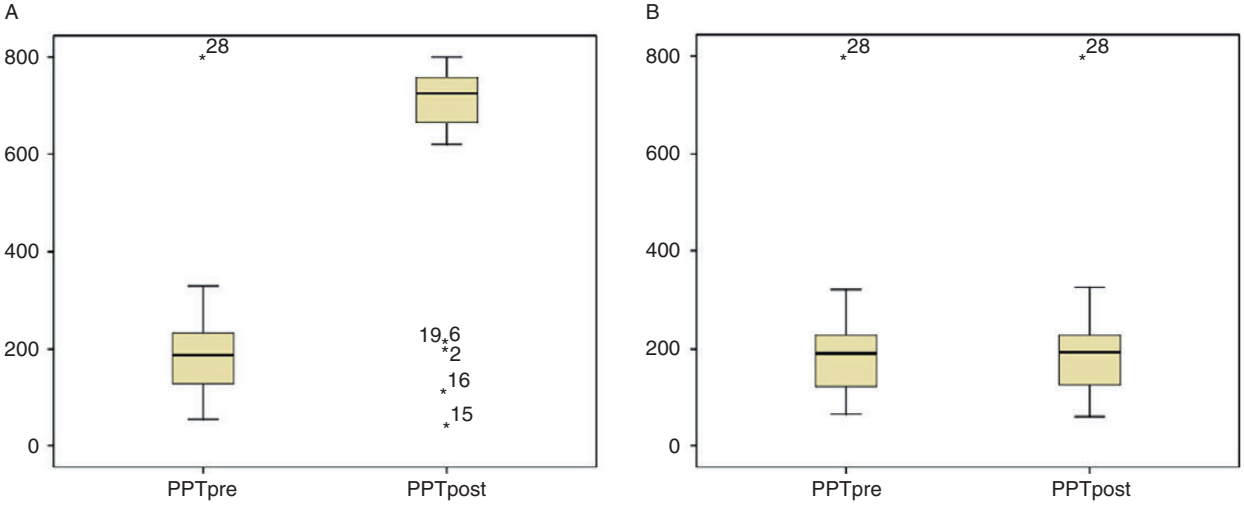

Figure 3 The *y*-axis represents the PPT in grams: (A) PPT before and after active therapy; (B) PPT before and after sham therapy.

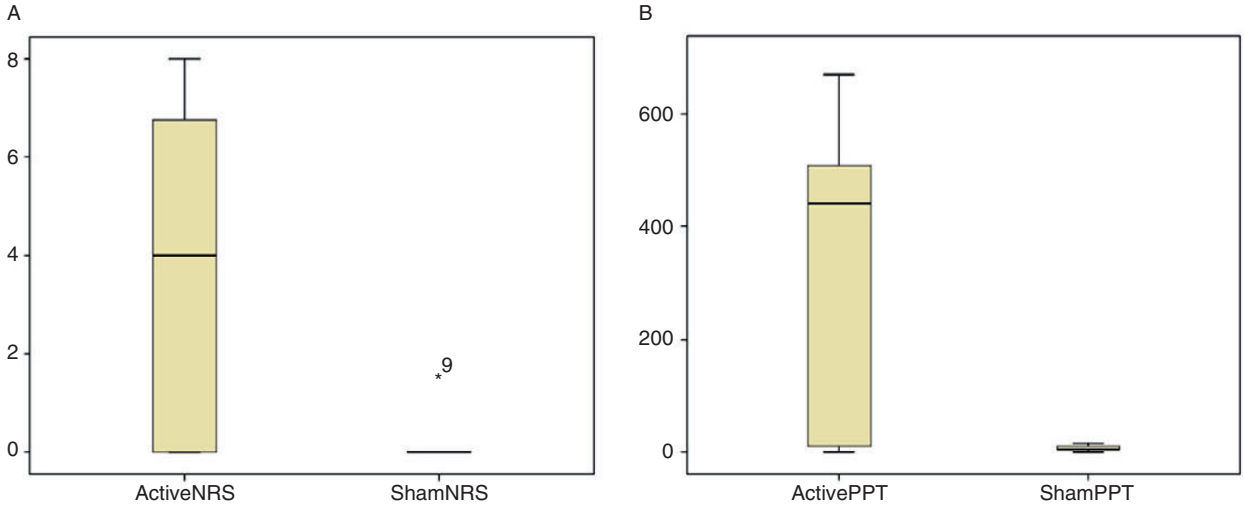

Figure 4 (A) Magnitude of change in NRS for the active and sham therapies of first arm (the *y*-axis represents the NRS score for pain out of 10). (B) Magnitude of change in PPT for the active and sham therapies of first arm (the *y*-axis represents the PPT in grams).

the same authors found that a mixed (both low and high) frequency electrical stimulation was more effective than either low or high frequencies alone in the treatment of patients with chronic low back pain [3]. Ahmed et al. have found benefit of PENS for the management of chronic headache [10], and Hamza et al. have found PENS to be a useful therapy for treating diabetic neuropathic pain [4].

These sham-controlled crossover studies used subjective pain ratings. In our study, we have additionally used pressure algometry to provide a measure of pain evoked with pressure in addition to global pain as reported by the NRS.

Blinding for interventional treatments can be challenging. For a treatment where the active treatment produces a sensation of paresthesia, this is even more so. We undertook a blinded crossover study with sham treatment. The treating physician and study investigator were blinded to the treatment arm. The patients were only blinded to their first treatment since they could determine the type of their second treatment by comparing it with the first. As such, this study was double-blinded for first treatment but not for the crossover. We therefore analyzed the first treatment and found that only for the active therapies was there a significant reduction in NRS pain scores accompanied by a significant elevation of the PPT after therapy.

PENS is a form of subcutaneous stimulation, which in practical concept, is related to acupuncture and TENS. In acupuncture, needles are inserted intradermally or into the muscle in accordance with the traditional Chinese points and meridians but at times, following a dermatomal distribution. The needles themselves act as a mechanical stimulation agent, but at times, low-frequency electrical stimulus is applied. At low-frequency (2 Hz), analgesic effects are induced through μ and δ opioid receptors and at a high-frequency stimulus (100 Hz), through activating the κ opioid receptors [14,15]. In the case of PENS, however, the needle-like probes are inserted percutaneously below the skin surface and based upon anatomical and physiological considerations. The probes act as mere vehicles to deliver the electrical stimulus through the skin, bringing it into closer proximity to the peripheral nerves. The physical insertion of the probes themselves had no pain-relieving effect in our study.

TENS is applied electrical stimulation to the skin surface. Both high (50–100 Hz) and low (2 Hz) frequencies can be applied and are thought to work by different mechanisms. High-frequency TENS is thought to selectively activate large diameter non-noxious A beta afferents to reduce nociceptor cell activity and sensitization at a segmental level in the central nervous system [16]. High-intensity and low-frequency TENS can be applied and activates small diameter motor afferents to elicit extra-segmental analgesia [9,16]. However, it is not possible to use both frequencies within a short time frame. With PENS applied by the Neurostimulator™, the algorithm provides for a rapidly alternating frequency, of 2 and 100 Hz, at 3-second intervals. The mechanism of action is presumed to involve a combination of the aforementioned low and high frequency effects [3].

With PENS, the probes can be introduced through skin from outside of the area of skin hyperalgesia, thus aiding compliance in patients intolerant of TENS due to allodynia. A further advantage of percutaneous probe insertion is that it bypasses the resistance of the skin, thus delivering the full magnitude of the electrical stimulus and in closer proximity to the stimulated peripheral nerve.

Although we have found statistical significance, the numbers in this study are small and a larger cohort is advisable. The patients had tried a variety of treatments prior to PENS but many had not tried alternatives such as TENS and gabapentinoids. While this study lends support to the efficacy of PENS by providing a proof of concept, its utility in clinical practice requires comparison against the alternatives. Data on longer term efficacy of this treatment are also needed to determine its value in the clinical context.

Acknowledgments

The authors wish to thank Dr. Peter Nightingale for calculating the sample size and providing the randomization sequence and Mrs. Julie Emms for ensuring the safe keeping of the randomization envelopes.

References

1 White PF, Li S, Chiu JW. Electroanalgesia: Its role in acute and chronic pain management. Anesth Analg 2001;92:505–13.

2 Ghoname E-SA, Craig WF, White PF, et al. Percutaneous electrical nerve stimulation for low back pain: A randomized crossover study. JAMA 1999;281(9):818–23.

3 Ghoname E-SA, Craig WF, White PF, et al. The effect of stimulus frequency on the analgesic response to percutaneous electrical nerve stimulation in patients with chronic low back pain. Anesth Analg 1999;88:841–6.

4 Hamza MA, White PF, Craig WF, et al. Percutaneous electrical nerve stimulation: A novel analgesic therapy for diabetic neuropathic pain. Diabetes Care 2000;23:365–70.

5 Weiner DK, Perera S, Rudy TE, et al. Efficacy of percutaneous electrical nerve stimulation and therapeutic exercise for older adults with chronic low back pain: A randomized controlled trial. Pain 2008;140:344–57.

6 White PF, Craig WF, Vakharia AS, et al. Percutaneous neuromodulation therapy: Does the location of electrical stimulation effect the acute analgesic response? Anesth Analg 2000;91:949–54.

7 Borg-Stein J, Seroussi RE, Gomba L, et al. Safety and efficacy of percutaneous neuromodulation therapy in the management of subacute radiating low back pain. Pain Pract 2003;3(2):125–34.

8 Seroussi RE, Gliner BE, Steinitz E, et al. Effectiveness of percutaneous neuromodulation therapy for patients with chronic and severe low back pain. Pain Pract 2003;3(1):22–30.

9 Ahmed HE, Craig WF, White PF, et al. Percutaneous electrical nerve stimulation: An alternative to antiviral drugs for acute herpes zoster. Anesth Analg 1998;87:911–4.

10 Ahmed HE, White PF, Craig WF, et al. Use of percutaneous electrical nerve stimulation (PENS) in the short—Term management of headache. Headache 2000;40:311–5.

11 Ghoname E-SA, White PF, Ahmed HE, et al. Percutaneous electrical nerve stimulation: An alternative to TENS in the management of sciatica. Pain 1999;83:193–9.

12 Weiner DK, Rudy TE, Glick RM, et al. Efficacy of percutaneous electrical nerve stimulation for the treatment of chronic low back pain in older adults. J Am Geriatr Soc 2003;51:599–608.

13 White PF, Ghoname E-SA, Ahmed HE, et al. The effect of montage on the analgesic response to percutaneous neuromodulation therapy. Anesth Analg 2001;92:483–7.

14 Goldstein A, Naidu A. Multiple opioid receptors: Ligand selectivity profiles and binding site signature. Mol Pharmacol 1989;36:265–72.

15 Sun SL, Han J. High and low frequency electroacupuncture analgesia are mediated by different types of opioid receptors at spinal level: A cross tolerance study. Acta Physiol Sin 1989;41:416–20.

16 Johnson MI. Transcutaneous electrical nerve stimulation. In: Kitchen S, ed. Electrotherapy: Evidence Based Practice. Edinburgh: Churchill Livingstone; 2002:259–86.

Appendix 1: Sample of Patients

Surgical Scar Pain

For the 7 patients included in this diagnostic group, their ages ranged from 23–64 years, with a mean age of 43.9 years (SD ± 14.6 years).

The sex distribution was female n = 3, male n = 4.

The duration of time that they had suffered from pain before having PENS therapy ranged from 3–27 years, with a mean of 9 years (SD ± 8.5 years). During this period, they had received a number of other therapies and medication that proved to be either completely ineffective, or had very limited efficacy in terms of both magnitude and duration. These therapies included: tramadol, paracetamol, escitalopram, co-codamol, local steroid injections, scar revision, silica gel, amitriptyline, pregabalin, lidocaine patches, TENS, as well as various other pain killers.

The duration of time that the maximum level of pain relief lasted ranged from 0–28 days, with a mean duration of 11.4 days (SD ± 11.6 days).

Chronic Low Back Pain

For the 5 patients included in this diagnostic group, their ages ranged from 52–70 years, with a mean age of 61.6 years (SD ± 7.7 years).

All patients were female.

The duration of time that they had suffered from pain before having PENS therapy ranged from 2–26 years, with a mean of 8.2 years (SD ± 10 years). During this period, they had received a number of other therapies and medication that proved to be either completely ineffective, or had very limited efficacy in terms of both magnitude and duration. These therapies included: paracetamol, co-codamol, morphine, ibuleve maximum gel, facet joint injection, epidural, acupuncture, physiotherapy, chiropractic, osteopathic, and spiritualist therapy.

The duration of time which the maximum level of pain relief lasted ranged from 8–35 days, with a mean duration of 18.4 days (SD ± 10.4 days).

Occipital Neuralgia

For the 4 patients included in this diagnostic group, their ages ranged from 34–62 years, with a mean age of 54.8 years (SD ± 13.8 years).

The sex distribution was female n = 2, male n = 2.

The duration of time that they had suffered from pain before having PENS therapy ranged from 8–17 years, with a mean of 12 years (SD ± 3.9 years). During this period, they had received a number of other therapies and medication that proved to be either completely ineffective, or had very limited efficacy in terms of both magnitude and duration. These therapies included: neurofen, ibuprofen, co-codamol, amitriptyline, meloxicam, fluoxetine, pregabalin, tramadol, paracetamol, steroid/nerve block injections, acupuncture, TENS, physiotherapy, chiropractic, hypnotherapy, and herbal remedies.

The duration of time that the maximum level of pain relief lasted ranged from 7–28 days, with a mean duration of 17 days (SD ± 11.6 days).

Pain Following Total Knee Replacement Surgery

For the 3 patients included in this diagnostic group, their ages ranged from 56–73 years, with a mean age of 65 years (SD ± 8.5 years).

All patients were female.

The duration of time that they had suffered from pain before having PENS therapy ranged from 1–3 years, with a mean of 2 years (SD ± 1 year). During this period, they had received a number of other therapies and medication that proved to be either completely ineffective, or had very limited efficacy in terms of both magnitude and duration. These therapies included: paracetamol, co-codamol, tramadol, gabapentin, nerve block injection, and physiotherapy.

Only one patient responded to therapy in this group. The duration of time that the maximum level of pain relief lasted was 6 days.

Post-Traumatic Neuropathic Pain

For the 3 patients included in this diagnostic group, their ages ranged from 55–61 years, with a mean age of 57.3 years (SD ± 3.2 years).

The sex distribution was female n = 1, male n = 2.

The duration of time that they had suffered from pain before having PENS therapy ranged from 2–35 years, with a mean of 13.3 years (SD ± 18.8 years). During this period, they had received a number of other therapies and medication that proved to be either completely ineffective, or had very limited efficacy in terms of both magnitude and duration. These therapies included: amitriptyline, co-codamol, escitalopram, acupuncture, TENS, and physiotherapy.

The duration of time that the maximum level of pain relief lasted ranged from 8–28 days, with a mean duration of 19 days (SD ± 10.1 days).

Post-Inflammatory Neuropathic Pain

For the 3 patients included in this diagnostic group, their ages ranged from 37–71 years, with a mean age of 49 years (SD ± 19.1 years).

The sex distribution was female n = 2, male n = 1.

The duration of time that they had suffered from pain before having PENS therapy ranged from 3–7 years, with a mean of 4.3 years (SD ± 2.3 years). During this period, they had received a number of other therapies and medication which proved to be either completely ineffective, or had very limited efficacy in terms of both magnitude and duration. These therapies included: co-codamol and nerve block injections.

The duration of time that the maximum level of pain relief lasted ranged from 0–14 days, with a mean duration of 5.3 days (SD ± 7.6 days).

Stump Pain

The 2 patients included in this diagnostic group were 37-year-old female and an 84-year-old male.

The duration of time that they had suffered from pain before having PENS therapy was 10 and 9 years, respectively. During this period, only the female patient had received a number of other therapies and medication that proved to be either completely ineffective, or had very limited efficacy in terms of both magnitude and duration. These therapies included: tramadol, gabapentin, pregabalin, fluoxetine, carbamazepine, acupuncture and hypnotherapy.

Only the female patient responded to therapy. The duration of time that the maximum level of pain relief lasted was 21 days.

Complex Regional Pain Syndrome

The 1 patient included in this diagnostic group was a 46-year-old male.

The duration of time that he had suffered from pain before having PENS therapy was 10 years. During this period, he had received a number of other therapies and medication that proved to be either completely ineffective, or had very limited efficacy in terms of both magnitude and duration. These therapies included: guanethidine, gabapentin, sympathetic nerve block, and various other painkillers.

This patient did not respond to therapy.

Chronic Cervical Pain

The 1 patient included in this diagnostic group was an 81-year-old female.

The duration of time that she had suffered from pain before having PENS therapy was 1.5 years. During this period, she had only received paracetamol, which had very limited efficacy in terms of both magnitude and duration.

The duration of time that the maximum level of pain relief lasted was 7 days.

Post-Herpetic Neuralgia

The 1 patient included in this diagnostic group was a 79-year-old male.

The duration of time that he had suffered from pain before having PENS therapy was 1 year. During this period, he had received the following medication that proved to have very limited efficacy in terms of both magnitude and duration; gabapentin, tramadol, and capsaicin cream.

The duration of time that the maximum level of pain relief lasted was 28 days.