Received: May 11, 2016 Revised: August 10, 2016 Accepted: September 7, 2016

(onlinelibrary.wiley.com) DOI: 10.1111/ner.12536

Trigemino-Cervical Neuropathic Pain Relieved by Serially Repeated Peripheral Nerve Field Stimulation Without Tolerance: Case Report

Brian A. Simpson, MD; Ravindra Nannapaneni, MS

Background: With its relative simplicity and safety, peripheral nerve field stimulation (PNFS; PENS) is contributing to the re-emergence of peripheral nerve stimulation as an effective therapy for neuropathic pain (NPP).

Case Presentation: A 70-year-old woman had developed severe, medically refractory NPP unilaterally in the scalp and face 20 years earlier, following a maxillofacial surgical procedure. PNFS gave substantial relief of the pain and allodynia and was repeated successfully on a further 25 occasions over the subsequent five years. Tolerance did not develop.

Conclusion: Serially repeated PNFS can provide sustained relief of NPP over long periods, without tolerance, where a permanent implant may be inappropriate, unavailable, or declined.

Keywords: Allodynia, neuropathic pain, peripheral nerve field stimulation, tolerance, trigeminopathic pain

Conflict of Interest: The authors reported no conflict of interest.

INTRODUCTION

Although the analgesic effect of direct nerve stimulation was first demonstrated (using the infraorbital branch of the trigeminal nerve) nearly half a century ago (1), technical problems have hindered its clinical application. In recent years, interest has increased through the use of occipital nerve stimulation for occipital neuralgia and headache, particularly migraine (2,3). The relatively simpler approach of stimulating within peripheral nerve fields (PNFS; also referred to as PENS) is now gaining acceptance in treating neuropathic pain (4), whether used alone or in combination with spinal cord stimulation. We present a case which indicates that PNFS with a single electrode may effectively influence more than one nerve field, may generalize from spinal to cranial nerve field, and can be repeated safely on a large number of occasions without loss of efficacy.

Case Report

A 70-year-old woman presented with severe neuropathic pain in the left side of her face and scalp, which had developed soon after she underwent an operation on the ipsilateral temporomandibular joint/mandible 20 years earlier. That operation completely relieved her contralateral pain and jaw clicking. The healthy surgical scar was anterior to, and above, the left pinna. The left-sided pain was in the scalp, extending suboccipitally, and into the forehead and cheek. It was accompanied by allodynia which included the pinna, eyebrow, cheek, upper lip, and side of the nose. The pain was continuous and she rated the intensity as varying 7–10/10. The allodynia made washing and hair care extremely difficult, sometimes unbearable. There was variable reddening and swelling of the painful parts of the face plus dysmorphism when the pain was most intense, in that she felt her eye to be in the region of her cheek. Motor impairment was expressed in impairment of smiling and she was unable to wink on the left. The symptoms were medically refractory but had earlier responded to injections of botulinum toxin to the stellate ganglion. Each of approximately ten injections had given complete or nearly complete relief for six weeks to six months but two subsequent injections were ineffective.

After giving her fully informed written consent on each occasion, the patient underwent 26 sessions of PNFS over five years and two months. Both authors performed the procedure on different occasions, identically and with no difference in outcome. After injecting a 2–3 mm bleb of lidocaine 1% and puncturing the skin with an IV cannula, a 21 gauge 50 mm electrode was inserted upwards subdermally over the left mastoid process to 20–25 mm. The entry point was approximately 5–10 mm below the tip of the mastoid process. The electrode passed along the long axis of the mastoid process and approximately over its midline. Stimulation alternated between 2 and 100 Hz at three-second intervals and was delivered, above sensory threshold, at 1.4–2.4 volts (typically 1.7–2.2 volts) for 25 min (Algostim™; Algotec Research and Development Ltd., Crawley, UK). The stimulation paradigm was based on published evidence for an increased release of encephalin, β-endorphin, and endomorphin with peripheral stimulation at 2 Hz and of dynorphin at 100 Hz, with a combination of the two frequencies accelerating the release of all four (5).

Address correspondence to: Brian A. Simpson, MD, Department of Neurosurgery, University Hospital of Wales, Cardiff, CF14 4XW, UK. Email: briansimpson48@btinternet.com

Department of Neurosurgery, University Hospital of Wales, Cardiff, CF14 4XW, UK

For more information on author guidelines, an explanation of our peer review process, and conflict of interest informed consent policies, please go to http://www.wiley.com/WileyCDA/Section/id-301854.html

Source(s) of financial support: None.

The stimulation was felt throughout the affected area and sometimes also in the lower face. The allodynia diminished radially from the position of the electrode, starting after approximately three minutes. By five minutes, it was absent within a four to five-centimeter radius and was abolished throughout by seven to eight minutes. The presence or absence of allodynia could be supported by touching without warning from behind. The pain relief began at the same time and on some occasions was reported as "100%" by the end of the session, although the usual pattern was for the relief to increase gradually over several days. Motor function returned to normal by the end of the session.

Apart from the fifth treatment, which resulted in complete relief for four weeks, the degree of reported pain relief increased over the first eight sessions (from 60% to 80–100%) and the duration of the relief increased over the first three sessions (from three weeks to a maximum nine weeks). The outcome was then consistently 70–90% pain relief (on some occasions 100%) combined with complete relief of the allodynia and motor impairment for four to seven weeks (nine weeks on one occasion and only ten days on another, the latter coinciding with a family tragedy). The pain and allodynia would recur gradually over approximately two weeks, starting with an increasingly intense formication. No adverse effects occurred. The patient was offered a permanent implant on several occasions but adamantly declined.

DISCUSSION

PNFS is a relatively simple procedure and the present case demonstrates that it is safe and well tolerated in an elderly patient. It was consistently very effective for the severe pain and allodynia and for the motor impairment, for several weeks after each treatment session. The response increased over the first few treatments and no tolerance developed during 26 treatments over five years. The response was relatively short-lived on one occasion and it seems reasonable to attribute this to a simultaneous personal tragedy, reflecting a limbic influence on the pain or on the mechanism of its relief. It may, however, have been coincidental. Scarring was not an issue despite the multiple reinsertions of an electrode; there was no increase in difficulty of inserting the electrode nor of the threshold voltage over time.

Stimulation was in the territory of the great auricular nerve and/or the lesser occipital nerve (both C2,3). The evoked sensation was felt simultaneously in this spinal distribution and throughout the trigeminal distribution. The relief of the allodynia spread seamlessly through the same territories. Although it is possible that the stimulation over the mastoid process also affected the trigeminal nerve directly, it raises the intriguing suggestion that the effects of PNFS may not be restricted to the nerve field occupied by the electrode. In the present case, there appeared to be generalization from spinal to cranial nerve fields. It is anticipated that this would involve the brainstem trigeminocervical complex. The radial (rather than dermatomal) spread of the abolition of the allodynia from the point of stimulation, which occurred over several minutes, also suggests central activity. Even if some trigeminal fibers were stimulated directly, the effect generalized beyond one division of that cranial nerve. Although the stimulation paradigm employed was based on knowledge of the increased release of four intrinsic opioid peptides, there is no evidence that this was relevant to its mechanism of action in the present case.

Although the limitations of an uncontrolled single case report apply, the persistence of the response with a large number of treatments over several years, the objective evidence of abolition of allodynia, the radial spread of the relief and her description of the return of the symptoms, all argue against a placebo mechanism. The effect of subthreshold stimulation might have informed this further but was not tried in this therapeutic situation. Furthermore, evoked paresthesiae appear to be an important predictor of success with PNFS (4).

Our elderly patient was adamant throughout that she found the prospect of an implanted system aversive and unacceptable to her. She was content to travel to the hospital and to endure some discomfort to obtain the prolonged periods of relief. Her case illustrates the feasibility of intermittent treatments, even over several years, if an implant is unacceptable (this may be particularly likely in the elderly), unsuitable or unavailable. It was possible to adjust the timing of treatments to optimize relief at special times such as Christmas, vacations, and a family wedding. Heterogeneous economic status and pressures create wide geographical variations in the availability of implantable neuromodulation devices; the technique described here may provide a substantially cheaper alternative in many cases.

Acknowledgement

The authors wish to acknowledge the technical support provided by Gillian Bassett and Coral Winslow-Llewellyn.

Authorship Statements

Both authors performed the procedure and made and recorded the assessments, on different occasions. Dr. Simpson drafted the manuscript and it was critically reviewed and approved by both authors.

How to Cite this Article:

Simpson B.A., Nannapaneni R. Trigemino-Cervical Neuropathic Pain Relieved by Serially Repeated Peripheral Nerve Field Stimulation Without Tolerance: Case Report.
Neuromodulation 2016; E-pub ahead of print. DOI: 10.1111/ner.12536.

REFERENCES

1. Wall PD, Sweet WH. Temporary abolition of pain in man. *Science* 1967;155:108–109.
2. Weiner RL, Reed KL. Peripheral neurostimulation for control of intractable occipital neuralgia. *Neuromodulation* 1999;2:217–221.
3. Silberstein SD, Dodick DW, Saper J, Huh B, Slavin KV, Sharan A. Safety and efficacy of peripheral nerve stimulation of the occipital nerves for the management of chronic migraine: results from a randomized, multicenter, double-blinded, controlled study. *Cephalalgia* 2012;32:1165–1179.
4. Kloimstein H, Likar R, Kern M, Neuhold J, Cada M, Loinig N. Peripheral nerve field stimulation (PNFS) in chronic low back pain: a prospective multicentre study. *Neuromodulation* 2014;17:180–187.
5. Han JS. Acupuncture and endorphins. *Neurosci Lett* 2004;361:258–261.

