Article type : Case Report

Title: A novel minimally invasive wireless technology for neuromodulation via percutaneous intercostal nerve stimulation (PNS) for post-herpetic neuralgia: A case report with short-term follow-up

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Keywords: Herpes Zoster, Post-herpetic neuralgia, neuropathy, wireless, neuromodulation, minimally invasive, peripheral nerve stimulation

Running Title: Wireless PNS for post-herpetic neuralgia

Abstract

Background

Peripheral nerve stimulation (PNS) of primary afferent neurons provides control of localized chronic pain. This technique applies permanent electrical stimulation at the target area via a minimally invasive, subcutaneous placement of an electrode.

Objective:

To assess analgesic effects of a minimally invasive wireless neuromodulation in the treatment of chronic intractable pain secondary to post-herpetic neuralgia.

Case Summary:

A 78-year-old man presented with severe intractable post herpetic neuralgic pain. He was a known case of non-Hodgkin's lymphoma under remission following treatment with chemotherapy and stem cell transplantation, twice. He also developed steroid induced diabetes mellitus during this treatment. In view of his compromised immune status, he was deemed a suitable candidate for our minimally

invasive neuromodulation technology. Two subcutaneous electrodes were placed right sided, 10cm medial and parallel to spinous process at the level of T7-T8 under fluoroscopic guidance along the T7 intercostal nerve. The external transmitter was worn with a belt over a single layer of clothing and is used to transmit power to the stimulator. The entire procedure required only a small incision for the introduction of the electrode placement.

Results:

After an uneventful procedure, pain score reduced from 8 to 3 with a reduction in pain medication. EQ5D before trial was 0.102; at 1 month: 0.630; at 3 months 0.576.

Conclusions:

Subcutaneous placement of electrodes with our minimally invasive technique and wireless neuromodulation technology was safe and effective. Significant improvements in pain relief ensued and at the end of 3 month- follow up without any adverse events.

Keywords:

Herpes Zoster, Post-herpetic neuralgia, neuropathy, wireless, neuromodulation, minimally invasive

Introduction

One of the most common complaints that take the general population for a medical visit is chronic pain, which is a very prevalent public concern (1,2). A refractory pain is a challenge to both the patient as well as the medical practitioner that would eventually demand an invasive treatment in the form of nerve blocks and epidural injections. The next step in the paradigm is spinal cord stimulation (SCS) that may or may not be able to cover the entire area of pain distribution (3). In some instances, SCS may not work at all. At this juncture, PNS becomes a valuable addition or alternative to the neuromodulation protocol.

PNS is an open option in cases not suitable for SCS. It has been reported to produce sustained paresthesia in difficult to treat regions of the body. This treatment includes placement of electrodes underneath the skin to deliver electric energy to the target nerves or nerve endings in the area of interest. PNS is a relatively new strategy of neuromodulation supported by literature regarding its analgesic effect (4-9).

SCS electrodes placed in spinal epidural space stimulate the large myelinated fibers of the dorsal column, while PNS positioned in the area of pain target the cutaneous afferents leading to the spinal cord (10). The stimulators activate the large afferents and modulate the A-delta and C-fibers possibly producing an anti-inflammatory and membrane depolarizing effect on the dermatomal nerve fibers (11).

The efficacy of this modality was reported in the Austrian retrospective study from 111 Austrian patients. (6).

PNS is commonly used with off label use of SCS device components which lead to technical short comings. Reasons for failed SCS and PNS include device alignment, stimulation parameters and most importantly implant related complications like lead migration, fracture and malpositioning (12,13,14).

We report a novel minimally invasive wireless device, specifically designed to mitigate the complications of conventional devices with PNS, which employ similar instruments but too long and heavy causing possible positional deformations of the electrodes.

Case Report

This 78 year old man was diagnosed in April 1998 to have a high grade Non-Hodgkin's Lymphoma (NHL) and received complete chemotherapy and stem cell transplantation. He had a relapse of NHL in 2008 and in 2010 necessitating repeated chemotherapy and stem cell transplantation. This time he had graft versus host disease complications that were managed successfully. In 2008 he received Valaciclovir treatment for herpes zoster infection which recurred over dorsal part of right shoulder later. This infection resulted in refractory neuropathic pain over his shoulder. He also developed adult onset Diabetes mellitus due to continuous corticosteroid treatment.

Pain management for post-herpetic neuralgia included Amitryptiline, Gabapentine, pregabalin, oxycodone. Additional treatment included the following:

- Thoracic epidural with steroids repeated three times;
- Capsaïcine administration (Qutenza) at pain clinic;
- Botox subcutaneous local injections;
- Tanscutaneous electrical therapy (local) TENS.

However, pain remained refractory to all these treatment modalities and patient was referred for further management. At the time of implant subject presented with allodynia as diagnosed by sensory exam (brush, monofilament, pinprick)

Methodology

After informed consent, patient was taken up for placement of subcutaneous electrodes for neuromodulation.

Device description

Subject was implanted with two Freedom ® stimulator systems (Stimwave Technologies, Pompano Beach, FL, USA) each containing four contacts (3 mm in diameter with 4 mm spacing). The stimulator system utilizes an implantable electrode contact array, microprocessor receiver and antenna embedded within the electrode wire that couples to an external transmitting antenna and pulse generator (figures 1 and 2) The implanted stimulator is 100% passive (i.e., no power source). The external transmitter (figure 3) is worn over a single layer of clothing and is used

to transmit power to the stimulator. The antenna and transmitter are placed in a belt and positioned over the location of the receiver. The external pulse generator is programmed by the clinician to send desired stimulation parameters through a direct electric coupling RF transmitting antenna to the electrode receiver, thereby wirelessly transferring stimulation commands and power to the implanted stimulator. The system uses radiofrequency energy at 915 MHz to transfer power and selected parameters to the implanted stimulator. The implanted stimulator and power source are coupled at such a short distance that the energy emitted from the antenna is relatively low. Wavelengths and product specifications have been designed to decrease risk related to the wireless transmission of energy (REF) and reliably transfer the clinician's desired stimulation parameters. The stimulation parameter spectrum available for clinical use and evaluation include:

- Amplitude: 1 – 24 mA ;
- Pulse Width: 1 – 1000 microSec;
- Frequency: 1 – 20,000 Hz;

Surgical procedure

Under strict aseptic precautions, the skin and subcutaneous tissues were infiltrated with local 1% lidocaine®. A 4 cm wide and 1 cm deep skin incision was made for needle insertion, which was shaped by hand to match the contour to achieve appropriate electrode placement. Insertion of the lead was performed through 16G Tuohy needle; coming from caudal end, right-sided, 10 cm lateral to spinous process

at the level of T7-T8, and along the T7 intercostal nerve. Second identical quad electrode 5 cm was placed lateral to first lead. Subcutaneous placement of the lead was confirmed throughout the procedure by peroperative stimulation to avoid positioning in the muscular plane (intramuscular placement lead to painful stimulations). Both the electrodes could be seen perpendicular to the T7 intercostal nerve (figure 4).

Biplanar fluoroscopic images were used to monitor electrode positioning (figure 5). The stimulator system was subsequently activated wirelessly to confirm electrode positioning with the patient feedback about comfortable paresthesia along the distribution of the targeted field, after retraction of the needle tip exposing electrode contacts. The device was secured in subcutis, 1 cm deep, by a non-absorbable monofilament suture at the skin entry point to prevent distortion, bending or painful motorstimulation as opposed to securing to fascia. No anchor, neither passive nor active, was used to fixate the device. Distal tubing cut at the insertion point, was buried subcutaneously and skin incision was closed.

Stimulation protocol

Stimulation parameters were set at pulse widths of 100-200 microseconds and frequency of 60 Hz. (This is not to be confused with the device communication frequency between the external generator and electrode microprocessor of 915

MHz). A therapeutic stimulation regimen was applied for up to 30 days followed by removal of the trial leads utilizing fluoroscopy and a small incision at the electrode insertion site.

Cyclic stimulation 1/2 , 60Hz, 300μs. He had three programs to adjust intensity.

Post operative Evaluations:

EQ5D before trial: 0.102; at 1 month: 0.630; at present (3 months) 0.576.

Post procedure overall pain scores (VAS) decreased from 8 to 3.

Oxycodone was reduced to 2*10mg instant oxycodone. Patient did not require other medications like Gabapentin, Amitriptyline and Pregabalin.

This patient remained more than 50% better and has a health score of 60% out of 100% (before stimulation 30% (100% being in perfect health, EQ5D).

Decision to put wireless leads was based on:

- Decreased immunity because of chemotherapy and continuous cortisone therapy;
- Secondary diabetes due to steroids;
- Thin skin because of long steroid use;

A wireless system causes less manipulation and requires only one procedure as opposed to conventional systems. It was important for this patient to decrease the risk of infection (no external trial extensions and no battery implant). The subject's ultimate goal was to stop oxycodone therapy (to avoid obstipation problems and cognitive impairment).

Discussion

SCS may not provide the desired results in patients with refractory pain originating from truck, paravertebral and presacaral regions. Similarly, dorsal nerve root stimulation may trigger unpleasant tetanic contractions in the area of stimulation. PNS, however can yield effective pain control, in a limited target area (9,15).

This success could be attributed to the activation of intradermal receptors and neuronal contacts along physiological anterograde conduction. This does not recruit motor fibers and thus no tetanic spasms of the muscles (9).

The efficacy of this modality was reported in the Austrian retrospective study from a large group of 111 patients. There was a significant reduction in the mean pain intensity and reduction in pain medication. However, lead dislocation occurred in 13%, lead fractures in 5%. Infection was reported in 6% cases (6)

PNS is also useful as an add on therapy with SCS for patients with persistent back pain and failed back surgery syndrome (FBSS) providing good pain relief (7-9)

Hamm-Faber et al reported implanted pulse generator (IPG) problems in 27% (3/11) cases and repositioning of the IPG due to pain caused by tilting of the battery in 27% (3/11). They also had connector problem between lead and the extension cable in 1 patient (9%) (16). IPG related complications were also reported in 3/7 cases (42.8%) in a series reported by Buiten et al where a conventional PNS implant system was utilized for control of refractory angina (17). We can conclude complications such as

pain related to the bulk and shape of IPG's are common and significant. In the recently completed 2 year study, HF 10 SCS therapy had incidence of implant site pain (12.9%) and lead migration requiring surgical revision (3%) similar to the traditional SCS (13.4% and 5.2% respectively (18). High-energy consumption was also reported to be an important concern in these patients, with the conventional devices used for PNS (16).

PNS for post herpetic neuralgia (PHN) has been seldom reported. PHN itself is a difficult condition to control and only limited experience is available in literature to draw any conclusions regarding efficacy. SCS is of limited use because of the location of the pain in the chest and abdominal wall as well as midline. Thus, PNS may be considered as an indication even prior to SCS. Yakovlev and Peterson and Tamimi et al reported excellent efficacy with subcutaneous electrodes for chronic neuropathic pain involving intercostals nerve and moderate efficacy for PHN (4,19).

Our case illustrates the analgesic effect of the wireless neuromodulation, emphasizing that this modality is completely devoid of IPG related complications. It is worthwhile to notice that the conventional implant systems have serious limitations due to the lead related as well battery related adverse events. Our technique requires only a small incision (for introduction of a 14-16 G Tuohy needle) to place the electrode. No further incisions or implants are needed during the entire treatment procedure.

Due to the lack of an IPG as an additional anchor point, it is possible, with this technology to observe serious lead dislocation, however the occurrence rate is considered to be very low. Recently, tines have been added to the leads to reduce the risk of migratory leads.

The minimally invasive nature of this technology is offering incomparable benefits to patients with:

- Compromised immunity;
- Retro viral infections;
- Co-morbid conditions like Diabetes mellitus;
- Limited life expectancy in painful conditions associated with malignancy.

The primary limitation of wireless peripheral nerve field stimulation is the lack of larger patient population and randomized–control groups to establish its efficacy and also the potential advantage it has over the available neuromodulation technology.

Nevertheless, the above reported minimally invasive wireless technology offers an attractive treatment option due to its simplicity, low adverse events and cosmetic acceptability compared to the present day systems, yet with comparable pain relief (20).

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Figure 1: Neuro-stimulator electrode, MRI compatible, for both 1.5 and 3 Tesla

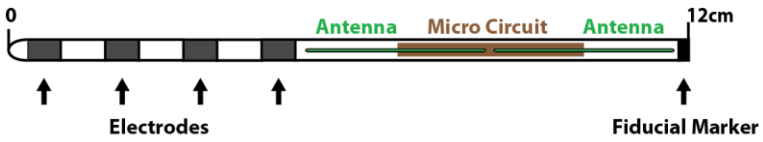

Figure 2: Neurostimulator receiver

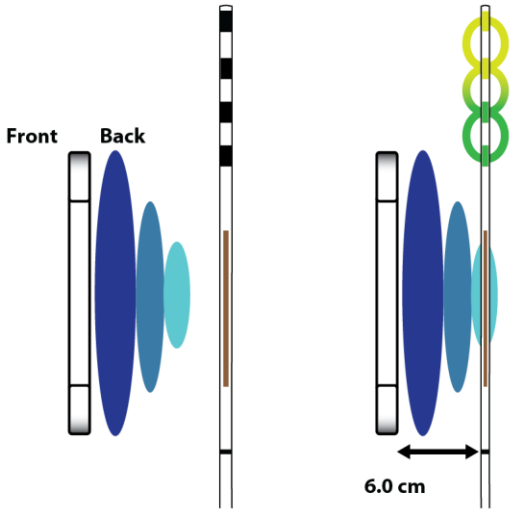

Figure 3: Freedom SCS external device

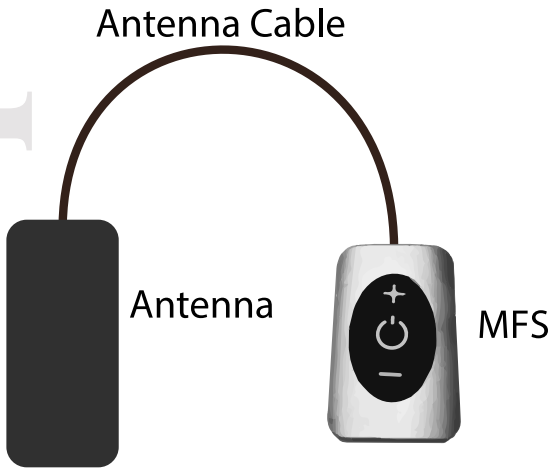

Figure 4: Thoracic, right sided over dermatomes T7 and T8. Leads are placed perpendicular over these two zones. Not longitudinal because of the shoulder-blade. We came from below to put the leads because of the length of the leads, it's also easier for the patient to put the antenna, as you can see (under his clothes).

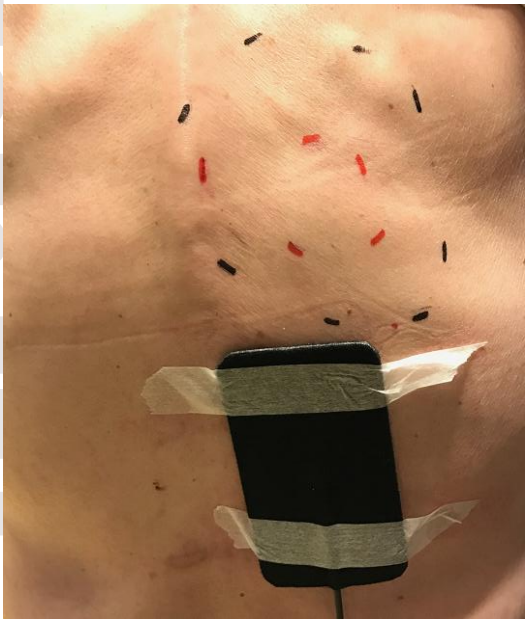

Figure 5: Two leads seen in plain X ray thoracic spine. Both the electrodes seen perpendicular to the intercostal nerve.