Review Article

Peripheral Nerve Stimulation and Percutaneous Electrical Nerve Stimulation in Pain Management: A Review and Update on Current Status -

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INTRODUCTION

Chronic pain is a common symptom necessitating hospital visits. Several medical, non-invasive, minimally invasive and invasive treatments are available implicating the complex nature of pain as an intractable problem. Electrical stimulation of the nervous system, both peripheral and central, has been an accepted therapeutic method with or without breaching the integument. Accordingly transcutaneous and percutaneous stimulation techniques have emerged with remarkable advancements in the technology. Peripheral Nerve Stimulation (PNS) is a reasonably less invasive treatment option compared to stimulation of the central nervous system. Percutaneous Electrical Nerve Stimulation (PENS), by definition implies the route of administration, distinguishing itself from the Transcutaneous Electrical Nerve Stimulation (TENS), and engages the non-neural elements more than the nerve itself. PNS targets a nerve trunk supplying the painful body parts to provide relief.

Nomenclature Of Peripheral Nerve Stimulation

The remarkable work of Ronald Melzak and Patrick Wall in 1965, introduced the theory of pain [1], while William Sweet along with Wall provided the proof of concept of PNS in 1967, when they stimulated their own infraorbital nerve by a needle electrode thereby experiencing the effects of electrical stimulation first hand [2].

Following this, PNS was enthusiastically employed for chronic pain relief but had mixed results mostly due to lack of selection criteria, technical difficulties and failure of systematic application [3]. This explains the distinctly sparse literature on PNS in spite of the awe-inspiring beginning [4].

However, PNS is capable of catering to multiple somatic as well as visceral conditions apart from pain, such as diaphragm palsy, intractable epilepsy, autonomic as well as somatic nerve stimulation for urinary bladder [5,6]. It is important to define PNS, thus, to understand its efficacy.

Peripheral Nerve Stimulation: PNS is electrical stimulation of a specific nerve with a specific name that supplies a very distinct area of body. There is a territory of that nerve and stimulation results in changes in the function of the particular nerve. PNS provides unidirectional paresthesia along that selected peripheral nerve with a better stimulation quality [7]. Accordingly, indication for PNS therapy is neuropathic pain along the nerve distribution so the stimulation is effective along the affected nerve [8]. This can be achieved by open method, wherein the nerve is exposed surgically and the electrodes are placed overlaying it or by minimally invasive percutaneous technique.

In case a specific nerve is not stimulated, the procedure is called Peripheral Subcutaneous Field Stimulation (PSFS).

Percutaneous Nerve Stimulation (PENS): A combination of TENS, a surface stimulation method and acupuncture, intradermal needle insertion according to Chinese land marks on the body, is PENS. Acupuncture acts by mechanical stimulation but Electroacupuncture (EA) employs electrical stimulation (2-100 Hz) for analgesic effects mediated through opioid receptors [9,10].

TENS also can be applied with either low (2Hz) or high (50-100 Hz) frequency stimulation on the skin; but not at the same time. At high as well low frequencies TENS produces analgesia by activating smaller motor afferents while high frequency is more selective in stimulating larger diameter a beta afferents to cut down the nociceptor cell activity [11]. PENS delivered via percutaneous insertion of needles in the vicinity of peripheral nerves, however, utilizes both high and low frequencies in a rapidly alternating rhythm to achieve similar effects of stimulation as above [12]. This is particularly useful in patients intolerant to TENS (due to skin irritation or allodynia) and as such avoiding skin resistance, delivers the stimulation to its full potential [13].

Advancements with PNS

The initial pioneering work of Wall, Sweet and Sheldon continued for 20 years with limited expertise and technology [2,14,15]. Difficulties were encountered due to ineffective on and off stimulation method and surgical trauma to the nerves followed by scar tissue formation [8,16,17].

A percutaneous electrical nerve stimulator was developed by Long in 1973, much similar to the indigenous method of Wall and Sweet, using cordotomy electrodes within 18 G needles, initially for PNS screening but later became more of a prototype for PENS [18]. Percutaneous epidural insertion of cylindrical electrode for epidural and PNS had set in the initiative for minimally invasive procedures by Urban and Nashold in 1982 [19]. A simple and less invasive technique introduced by Weiner and Reid for occipital neuralgia [20] improved the confidence in PNS of occipital and trigeminal nerves [21-23] expanding the gamut of indications, implantation methods and type of electrodes. Further safety and simplification of
the technique ensued with ultrasound guidance to place electrodes for stimulation of any named peripheral nerve throughout the body [24,25]. Trigeminal and occipital nerves remained to be major nerves to receive PNS for a variety of indications like postherpetic neuralgia, trigeminal neuropathy/neuralgia, migraines and cluster headaches [21,26-32].

The minimally invasive nature of PNS increased the indications to relieve postsurgical pain, low back pain, scapular pain, coccydynia and chronic regional pain syndrome- type 2 by placing the stimulator in close proximity to the peripheral nerve [32-37].

As the popularization of PNS continued, evaluation of outcomes and adverse events started to get attention not only to audit the procedure but to refine the technology also [38,39]. Electrode migrations, fractures, disconnections, erosion of leads and failure of stimulation prompted several modifications [40,41].

**Wireless, minimally invasive nano-technology in PNS:**
Most of the device related complications in PNS arise from its off label application of a conventional Spinal Cord Stimulation (SCS) equipment [42]. The long and bulky SCS device components may not be suitable for the peripheral nerve space and the related complications could be avoided with proper device components.

A miniature Nano electrode system operated by wireless technology is one such advancement in the field of PNS.

The conventional SCS system is bulky with electrodes enclosed in a catheter, attached to long connectors leading to an Implantable Pulse Generator (IPG). All components are placed inside the patient’s body and the system can fail due to malfunction of any of these. Research is ongoing to reduce the bulk of the equipment without compromising the efficiency and IPG life.

Stimwave device has a novel external Wireless Power Generator (WPG) that uses a dipole antenna for electric field coupling accomplished with very short length pulsed electromagnetic wave at Giga Hertz Frequencies (GHz), ‘microwaves’. This enables miniature implants to be embedded deeper inside the body and also affords minimal loss of power due to the higher frequency at play [43]. The small implants can be successfully placed by percutaneous minimally invasive approaches.

**Device description**

The stimrelieve® stimulator system (StimRelieve LLC, Fort Lauderdale, FL, USA) implants contain four or eight contacts (3 mm in diameter with 4 mm spacing) and accessed by an implantable electrode contact array, a microprocessor receiver and an antenna embedded within the electrode wire that couples to an external WPG (figures 1 and 2). The implant is passive and maneuvered by the WPG according to the patient-physician protocol (figure 3) required for therapeutic effects.

The spectrum of parameters available for stimulation include amplitude of 1-24 ma, pulse width of 1-1000 msec, and frequency of 1-20,000 hz.

**Percutaneous Nerve Stimulation (PENS)**

When Wall and Sweet applied temporary electrical stimulation to the infraorbital nerves, they put forth the prototype of PENS [2] similar to the implanted electrodes of Sheldon et al that became models for PNS [14,15]. Placement of electrodes either on the skin or in subcutaneous tissues with TENS, PENS or PNS leads to alterations in blood flow, concentrations of local neurotransmitters and endorphins along with cell membrane polarization thereby inhibiting the nociceptive transmission [44].

For PENS, bipolar needle electrodes are inserted into tissues for pain relief and removed after the therapy, in conditions like back pain, sciatica, diabetic neuropathy, herpetic neuralgia and headache [45-49]. It combines the simplicity and mechanisms of TENS and EA to stimulate the dermatomal sensory nerve endings to produce analgesia better than TENS and Sham controlled therapy. PENS was shown to reduce consumption of opioids in a systematic randomized study [12,45,49].

**DISCUSSION**

Chronic pain is a common complaint that takes the general population for a medical visit and is a very prevalent public concern [50,51].

Short term benefits with repetitive administration would be provided by local therapies and topical agents including injectable forms only leading to subsequent failures along with continued suffering. Electrical stimulation of nerves provided better relief with long lasting results but with complex apparatus and power supply as well as variable energy requirements.
PENS, however does not require the complex surgical implantation since the bipolar needle electrode required to stimulate the nerve endings is removed after the therapy and does not demand great technical skills. Selection of the area of stimulation is also not particularly difficult since there is an area of sensory derangement marked out clearly by the patient.

Ghoneame et al did a randomized crossover study on PENS to show that the results are superior to TENS in patients with low back pain [45]. Consistently encouraging results with PENS have been published [48,49] for a variety of painful conditions.

However, the sham treatment reported was an issue in its accuracy and as Cummings comments probably reflect the concerns. In his review, Cummings stated that “PENS is neither different in principle nor in practice from EA, and whilst the term accurately reflects the nature of the treatment, there is no substantial justification for referring to PENS as a ‘novel analgesic therapy’ while the term is acceptable for reporting purposes [52].

This might explain why PENS did not become a popular, sustainable neuromodulation approach even though it is less invasive and temporary.

PNS, as a complementary treatment to SCS in nonresponsive cases of neuropathic pain, though was promising in its days of inception, could not meet with the safety requirements, predominantly due to the off-label use of the bulky SCS equipment. PENS (and TENS also) was helpful as a trial stimulation for PNS, along with electrophysiological studies and nerve blocks to make better selection of indications [44,53]. Limited success could only be achieved with the extremity pain, especially in the lower extremities until the morphological configuration of the electrodes was altered to a cylindrical percutaneous type, thus reducing the interface with epineurium and minimizing scar tissue formation [22,54,55]. The modified configuration has improved the access to the sensory afferents in head and face regions as well as extremity peripheral nerves.

Currently available neurostimulator systems, however, have not been designed for use in the peripheral nerve space, and are thus associated with complications and side effects [56,57,58]. Further refinements to the bulky apparatus deemed necessary to make the PNS more acceptable for its efficacies and applications.

The wireless technology, as described above, due to its inherent design mitigates the negative issues related to these “implantable-only” components of the SCS assembly. Wireless neuromodulation shows promise and paves pathway to expanding number of indications and indications for the relief of chronic pain conditions. A significant reduction in hardware components associated with complications would follow due to the minimally invasive nature of both the technique as well as the technology. A simple lead placement without the need to tunnel and attach an implanted pulse generator can be advantageous to the patient, the surgeon and the health care system in reducing costs, procedure time, postoperative pain, and adverse events while achieving the desired pain control [59]. Stimwave wireless technology has been reported to be safe and effective, as PNS modality in cases of craniofacial pain, occipital neuralgia and postherpetic neuralgia [60-61].

Additionally, the minimally invasive nature of this technology may be offering incomparable benefits to patients with:

1. Compromised immunity as in cases of herpetic neuralgia, retro viral infections, chronic debilitating diseases and malignancy.
2. Comorbid conditions like Diabetes mellitus, chronic renal failure, and anemia.
3. Fragile skin conditions secondary to neuropathy, psoriasis, chronic limb ischemia.
4. Limited life expectancy in painful conditions and those associated with malignancy.

**SUMMARY AND PERSPECTIVE**

From surface electrical stimulation with TENS to implantation of electrodes and power generators, pain management has progressed to a minimally invasive therapy with significant improvement in disability. PENS and AE in spite of their ease of application have not been popular in neuromodulation most likely due to the lack of evidence based literature. PNS on the other hand found increasing acceptance as a preferred method to control intractable pain following the percutaneous technique. However, the technology, being an off-label use of SCS, required finesse and further advancements in terms of its energy delivery as well reduced bulk of implanted material. Wireless neuromodulation with nanomaterials provide the required technological substrate missing in application so far. Initial experience in cases with refractory occipital neuralgia, craniofacial pain and intercostal neuralgia due to herpes zoster have been encouraging. Further experience in larger groups of patients would be expected to make this wireless stimulation technology to replace the bulky, cumbersome implantation devices in the limited peripheral nerve space.

**REFERENCES**


