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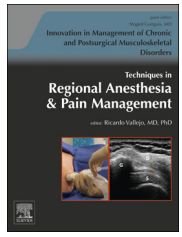

High-frequency peripheral electric nerve block to treat postamputation pain

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ABSTRACT

Postamputation residual limb pain is often a disabling chronic pain condition. Oftentimes, patients are left with a chronic stump pain that is refractory to current pain management modalities, such as medications, peripheral nerve blocks or denervation techniques, nerve or spinal cord stimulation, or surgical revision. Using high-frequency alternating current via a peripheral nerve cuff electrode creates a complete depolarizing nerve block, which blocks painful or unwanted nerve transmission of pain signals; the cuff is placed proximal to the neuroma at the end of the severed nerve. This article demonstrates the technique of placing a peripheral nerve cuff surgically around the peripheral nerves of patients who suffer from debilitating stump pain with lower extremity amputations. In total, 10 patients were implanted with the nerve cuff with 9 patients receiving in-clinic testing and 7 patients progressing onto long-term home-use. The average numerical rating scale pain scale for tested patients decreased from 5.7-1.4 (out of 10) after high-frequency alternating current electrical nerve block therapy with 85% of all testing sessions yielding a >50% pain reduction. Additionally, patients noted improved ability to maintain activity of daily living, as well as noted improvement of quality of life scores, and a reduction in overall pain medication use. Although the study's initial endpoint was 90 days, we have continued to follow our implanted patients who have now reached 36 months.

Introduction

Recently, various types of high-frequency (5000 Hz and above) neuromodulation techniques have been described to treat various types of pain syndromes. The goal of this article is to describe a specific high-frequency neuromodulation technique involving a peripheral nerve cuff applied directly to a nerve to achieve a nerve block in patients who suffer from postamputation pain.

It is been estimated that postamputation residual limb pain is experienced by up to 76% of major limb amputees.[1]

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Currently, there are approximately 2,000,000 patients in the United States, who have major limb amputations with approximately 185,000 new amputations performed annually.[2]

Other approved modalities to treat residual limb pain include opioid analgesics, nonsteroidal anti-inflammatories, physical therapy, spinal cord stimulation, or intrathecal pump. Patients may also undergo amputation revision surgeries or a neurectomy to remove painful neuromas.

Pathophysiology

Postamputation pain usually manifests as 2 different types of painful presentations: phantom limb pain and residual limb (stump) pain. Residual limb pain presents at the end of the stump and may be exacerbated with palpation or pressure placed directly on a neuroma, such as when patients use their prosthetic devices. This, in turn, can limit the patient's ability to perform their activities of daily living.

After an amputation, a neuroma may form at the distal end of the severed nerve. This neuroma is a collection of nerve fibers that can fire aberrant action potentials that may result in unpleasant sensations such as phantom or residual limb pain.[3]

Spinal or central nervous system mechanisms may also influence residual limb or phantom pain. Neuromas, or damaged peripheral (A) fibers, which may subsequently branch into the same lamina. The A fiber inputs may then be reported as noxious stimuli which may then lead to hyperexcitability of the spinal cord, thus producing chronic pain.[4]

Additionally, peripheral mechanisms may influence postamputation pain. At the end of a severed peripheral nerve, a neuroma may form. Within the neuroma, there is often a proliferation of sodium channels that may generate significant aberrant and unwanted action potentials, which can be perceived as painful sensations. If these action potentials could somehow be blocked, then the painful condition could be eliminated. This is the proposed mechanism in which high-frequency electric nerve block is believed to achieve pain reduction.

Types of peripheral neurostimulation modalities

Different neuromodulation methods of peripheral nerve stimulation have been used to treat postamputation pain. These modalities vary from percutaneously placing a linear neuroelectrode lead near the offending peripheral nerve to surgical dissection and placement of paddle leads around or near the target peripheral nerves.

A recent case study demonstrated that percutaneous and remote placement of the lead even as far as 1 cm from the femoral nerve achieved 60% reduction in residual limb pain during a 2-week home stimulation trial.[5] Although this is initially very promising especially considering the fact that the lead was not directly in contact with the peripheral nerve in question, larger sample sizes are needed to determine efficacy. However, it does show the potential promise of percutaneous lead placement near a peripheral nerve in patients with residual limb pain.

These techniques are considered more traditional peripheral neuromodulation options, which is a result of direct stimulation of the target nerve, are felt by the patient as a tingling sensation or paresthesia. Among the recent advances in peripheral nerve stimulation is high-frequency conduction block that is believed to block action potentials from being generated by the painful neuroma. Unlike traditional stimulation, this is believed to prevent the tingling or paresthesia felt by the patient.

High-frequency electric conduction block

High-frequency (10 kHz) electrical nerve block (high-frequency alternating current [HFAC] block) using a surgically implanted peripheral nerve cuff electrode is one of the more recent and promising modalities to treat residual limb and peripherally generated phantom limb pain. In this technique, the electrode is attached to a targeted nerve proximal to a neuroma located near the site of amputation. The cuff electrode is powered by an implantable pulse generator that generates a high-frequency current used to block the pain signals originating in the residual limb as a result of the neuroma.

By placing a cuff electrode around a severed peripheral nerve proximal to a neuroma and administering a high-frequency alternating current, it is possible to block unwanted painful action potentials and prevent neurotransmission of the unpleasant stimuli.[6-12]

Drs Kevin Kilgore and Niloy Bhadra[13] from Case Western Reserve University showed that a high-frequency alternating current using sinusoidal waveforms can be used to block peripheral motor activity in an in-vivo mammalian model. The block threshold amplitudes showed a linear relationship with the frequency, the lowest threshold being at 5 kHz. They showed that in fact HFAC block has three phases; first an onset phase, followed by a period of asynchronous firing, and ending with a period of steady-state complete nerve block. The onset response and the asynchronous firing can be minimized by using an optimal frequency-amplitude combination, thus increasing the duration of total neuro-blockade.[14]

HFAC block creates a complete depolarizing nerve block of the targeted peripheral nerve and its mechanism of action is very similar to that of the amide local anesthetics in that both will block action potential conduction. Therefore, the mechanism of action of HFAC electrical nerve block is different than that of spinal cord or traditional peripheral nerve stimulation modalities. In addition, unlike spinal cord stimulation and traditional peripheral nerve stimulation techniques, no paresthesia is felt by the patient as a result of the neuromoulation therapy. The sensation felt by the patient after HFAC block is similar to that felt after a peripheral nerve block with local anesthetic. This is the proposed mechanism of action that HFAC block has been applied for use in humans with amputation stump pain to achieve a complete nerve block and prevent neurotransmission of pain signals.

Patient selection

The eligibility criteria for peripheral high-frequency neuromodulation includes patients with amputations of the lower