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Phantom Limb Pain

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Introduction

Phantom limb pain (PLP) is clinically defined as the perception of pain or discomfort in a limb that no longer exists. Although PLP most commonly presents as a pathological sequelae in amputee patients, the underlying pathophysiology remains poorly understood. PLP can present along a wide clinical spectrum and varying severity of symptoms. The condition should be differentiated from other related but separate clinical conditions, including residual limb pain (RLP). RLP (formerly known as "stump pain") is pain that originates from the actual site of the amputated limb. It is most common in the early post-amputation period and tends to resolve with wound healing. Unlike PLP, RLP is often a manifestation of an underlying source, such as nerve entrapment, neuroma formation, surgical trauma, ischemia, skin breakdown, or infection.

In the United States, 30,000 to 40,000 amputations are performed each year. Amputations can occur for many reasons including severe trauma, tumors, vascular disease, and infection. Pain after amputation of a limb is a common symptom and is separated into two types of pain: residual limb pain (RLP) and phantom limb pain (PLP). Ninety-five percent of patients report experiencing some amputation-related pain, with 79.9% reporting phantom pain and 67.7% reporting residual limb pain. It is important to know the difference between the two because the causes and treatment for each differ, but also be aware that both of these elements can coexist at the same time.

Etiology

The exact etiology of phantom limb pain is unclear. Multiple theories have been debated, and the only agreement is that multiple mechanisms are likely responsible. The predominant theory for years involved the irritation of the severed nerve endings causing phantom pain. This was enforced by evidence that almost all amputation patients will develop neuromas in the residual limb. Over the last few decades, advances in imaging and laboratory techniques have shown evidence of central nervous system involvement. Imaging studies such as MRI and PET scans show activity in the areas of the brain associated with the amputated limb when the patient feels phantom pain. The pain is now thought to involve many peripheral and central nervous system factors.

Epidemiology

In 2005, there were 1.6 million people (1 in 190) living with limb loss in the United States. This same study projected a striking increase to 3.6 million cases by 2050. The literature reports PLP affecting 60% to 85% of amputee patients. The following underlying causes are given clinical consideration:

- Vascular etiologies (most common)
- Trauma
- Cancer/Malignancy
- Congenital conditions

Pathophysiology

Peripheral Nerve Changes

During the amputation, there is a significant amount of trauma that occurs in the nerves and surrounding tissues. This damage disrupts the normal afferent and efferent signals involved with the missing limb. The proximal portions of the severed nerves start to sprout neuromas, and the nerves become hyper-excitabile due to an increase in sodium-channels and resulting spontaneous discharges.

Spinal Cord Changes

In the spinal cord, a process called central sensitization occurs. Central sensitization is a process where neural activity increases, the neuronal receptive field expands, and the nerves become hypersensitive. This is due to an increase in the N-methyl-D-aspartate, or NMDA, activity in the dorsal horn of the spinal cord making them more susceptible to activation by substance P, tachykinins, and neurokinins followed by an upregulation of the receptors in that area. This restructuring of the neural components of the spinal cord can cause the descending inhibitory fibers to lose their target sites. The combination of increased activity to nociceptive signals as well as a decrease in the inhibitory activity from the supraspinal centers is thought to be one of the major contributors to phantom limb pain.

Brain Changes

Over the past few years, there has been significant research into cortical reorganization and is a commonly cited factor in phantom limb pain. During this process, the areas of the cortex that represent the amputated area are taken over by the neighboring regions in both the primary somatosensory and the motor cortex. Cortical reorganization partially explains why nociceptive stimulation of the nerves in the residual limb and surrounding area can cause pain and sensation in the missing limb. There is also a correlation between the extent of cortical reorganization and the amount of pain that the patient feels.

Psychogenic Factors

Chronic pain has been shown to be multi-factorial with a strong psychological component. Phantom limb pain can often develop into chronic pain syndrome and for treatment to have a higher chance of success the patient's pain behaviors and pain processing should be addressed. Depression, anxiety, and increased stress are all triggers for phantom limb pain.

History and Physical

Phantom limb pain is often described as tingling, throbbing, sharp, pins/needles in the limb that is no longer there. It occurs more commonly in upper extremity amputations than lower extremity and tends to be intermittent in frequency. Pain severity varies, and onset can be immediate or years afterward. It is important to try and distinguish phantom limb pain from residual limb pain.

The goal of the physical exam is to rule out causes of residual limb pain. First, the skin should be carefully inspected for evidence of wounds or infection. Sensation needs to be tested, along with looking for allodynia and hyperalgesia. The joint above the amputated limb should be examined for any signs of dysfunction.

Evaluation

The diagnosis of phantom limb pain is primarily a diagnosis of exclusion and heavily dependent on the patient's history. Because of this lab tests are often not needed. A complete blood count (CBC) can help rule out infection. An ultrasound can be ordered to look for neuromas as a possible pain generator. A psychology evaluation may be indicated if the patient is having a significant amount of extrinsic triggers that may be contributing to his or her pain.

Treatment / Management

Treatment, unfortunately, for phantom limb pain has not proven to be very effective. While treatment for residual limb pain tends to focus on an organic cause for the pain, phantom limb pain focuses on symptomatic control.

Pharmacotherapy

NSAIDs/Tylenol are the most commonly used treatment for phantom limb pain. The mechanism of action is unknown.

Opioids: Randomized controlled trials have demonstrated the effectiveness of opioids for neuropathic pain and phantom limb pain. Should be used in conjunction with antidepressants or neural modulating agents (i.e., gabapentin, pregabalin).

Antidepressants are commonly used for phantom limb pain. Amitriptyline, in particular, is the TCA of choice as it has shown good results, but other studies looking at Nortriptyline and desipramine have shown them to be equally effective. Duloxetine is another medication that has been showing some positive results.

Anticonvulsants (Gabapentin, Pregabalin) have shown mixed results.

Calcitonin has no clear evidence.

NMDA Receptor antagonist mechanism is not clear. Memantine has had mixed results.

Beta-blockers (propranolol) and calcium channel blocker (nifedipine) show unclear data.

A sympathetic block may also help.

Non-pharmacological Treatments

TENS shows moderate evidence supporting its use. Low-frequency and high-intensity are thought to be the most effective for phantom limb pain.

Hyperhidrosis (excessive sweating) can not only hinder the use of a prosthetic but can adversely affect the course of phantom limb and residual limb pain. Treatment of the hyperhidrosis with botulinum toxin type B injections has shown in several small studies to reduce residual limb pain, phantom limb pain, and sweating.

Mirror therapy: A randomized trial of mirror therapy in patients with lower leg amputation showed a significant benefit of phantom limb pain. Another study was minimally helpful

Biofeedback shows limited evidence.

Acupuncture research is still ongoing.

Dorsal Column Stimulator(DCS) (an implantable device which stimulates transdural the dorsal columns of the spinal cord) is often an effective therapy for phantom limb pain. The exact mechanism of pain relief from DCS is unknown.

Questions

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