Introduction to Neuropathic Pain Syndromes

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KEYWORDS

• Pain • Neuropathic • Nociceptive • Chronic • Epidemiology • Treatment outcomes

KEY POINTS

- Chronic pain impairs the quality of life for millions of individuals and therefore presents a serious ongoing challenge to clinicians and researchers.
- Debilitating chronic pain syndromes cost the US economy more than $600 billion per year. This article provides an overview of the epidemiology, clinical presentation, and treatment outcomes for craniofacial, spinal, and peripheral neurologic pain syndromes.
- Although the authors recognize that the diagnosis and treatment of the chronic forms of neuropathic pain syndromes represent a clinical challenge, there is an urgent need for standardized classification systems, improved epidemiologic data, and reliable treatment outcomes data.

Chronic pain impairs the quality of life for millions of people, and therefore presents a serious ongoing challenge to clinicians and researchers.[1] Debilitating chronic pain syndromes cost the US economy more than $600 billion per year.[2] The annual cost of pain treatment is greater than the combined annual costs of heart disease, cancer, and diabetes. A recent epidemiology review reports that prevalence rates of neuropathic pain as a global clinical entity range from 0.9% to 17.9%.[3]

For many years, clinicians have understood that nociceptive pain sensation serves as a crucial, adaptive physiologic response to noxious stimuli through primary nociceptive afferent activation. In contrast, neuropathic pain arises by activity generated within the somatosensory system without adequate stimulation of peripheral afferents.[4] This maladaptive plasticity in the neuropathic pain state is often a consequence of lesions to the peripheral or central nervous system. Alterations such as ectopic generation of action potentials, facilitation and disinhibition of synaptic transmission, loss of synaptic connectivity and formation of new synaptic circuits, and neuroimmune interactions contribute to the multifaceted pathogenesis of complex neuropathic pain syndromes.[5,6]

Historically, neuropathic pain syndromes have been classified based on their cause or on the anatomic distribution of pain. Although this classification has some use for diagnostic purposes, it offers no good framework for the clinical management of pain or for the evaluation of the available therapies.[7] A range of positive and negative neurosensory symptoms usually characterize

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these syndromes.[8] This clinical heterogeneity makes the development of standardized diagnostic and evaluation tools for pain increasingly challenging. Consequently, patients are frequently misclassified and treatment outcomes are not recorded in a reliable and efficient manner.[3,9–11] Modern pain research has explored genetic and molecular modulation of nociceptive systems to develop new analgesic strategies. Such examples of backward translation from the clinic to basic science are starting to become increasingly important. For this approach to be successful, it is of utmost importance to first develop an effective way of assessing treatment outcomes in the clinic. Successful exploration of genetic and molecular tools to better define neuropathic pain syndromes requires the tandem improvement of clinical outcome measurements.[12,13] This article categorizes the existing literature for neuropathic pain, focusing on craniofacial, spinal, and peripheral pain syndromes.

CRANIOFACIAL PAIN SYNDROMES

Epidemiologists estimate that approximately 39 million adult Americans are suffering from chronic craniofacial pain.[14] Despite the high prevalence, in the last few years, the classification of craniofacial pain disorders has been a matter of active debate, and there are no established criteria to evaluate the efficacy or effectiveness of available pharmacologic and nonpharmacologic therapies.[15] This section details recently reported epidemiology and neurosurgical treatment outcomes for craniofacial pain syndromes.

Primary Headaches

Primary headaches, such as tension-type, migraine, and cluster headaches, are prevalent conditions that affect the US population. **Table 1** provides a comprehensive overview of the available neurosurgical interventions for cluster and migraine headaches.

Patients suffering from cluster or migraine headache often do not find pain relief from conventional management. Considerable progress has been made in neurostimulative and neuroablative approaches to treat chronic headache syndromes. However, the effectiveness of each treatment approach varies widely in terms of pain relief. Some of the studies that were reviewed report moderate to significant pain reduction, whereas others report decrease in frequency of pain attacks. The level of evidence for the treatment outcomes ranges from case reports to quasi-randomized studies, thus unmasking a clear need for prospective randomized controlled studies to rigorously evaluate current surgical treatment interventions effective for craniofacial neuropathic pain.

Cranial Neuralgias

Cranial neuralgias comprise various painful paroxysmal disorders of the head. Although trigeminal neuralgia has an incidence that ranges from 3 to 5 new cases for 100,000 persons per year and a prevalence that ranges from 12.6 to 28.9 per 100,000 persons, it is still a rare disease that is easily misdiagnosed among the duplicative and inconsistent nomenclature of craniofacial neuralgias (**Table 2**).[3,16]

Despite the low incidence and prevalence of cranial neuralgias, a wide range of surgical and nonsurgical interventions are available, most of which have good success rates. Classification criteria (eg, International Headache Society, International Classification of Headache Disorders 2nd edition) have long been purely based on the clinical presentation of pain, which can sometimes be subjective. Thus, it makes it easy to misdiagnose or misclassify patients with chronic conditions. To have more reliable outcomes data, one must first have a more effective classification system for these conditions. Classification systems, such as the one proposed by Burchiel in 2003, attempt to reduce misclassification by standardizing the nomenclature.[17] However, this system is based on empirical observations rather than on prospective data.

Other Types of Craniofacial Pain

Other types of craniofacial pain, such as temporomandibular joint (TMJ) disorders, are not uncommon; however, most of the available treatment options do not fall in the scope of the neurosurgery practice. Persistent idiopathic facial pain (PIFP), also known as atypical facial pain, is a rare condition that includes facial pain that does not have the characteristics or distribution of any of the cranial neuralgias. Likewise, anesthesia dolorosa (AD) is a pain syndrome that arises as a complication of the surgical treatments of neuralgias and trauma, among other causes. PIFP and AD are rare chronic pain conditions that are commonly treatment refractory; consequently, there is a limited literature on success rates of the available treatments (**Table 3**).

Neuroablative and neurostimlative approaches used to treat these conditions have had questionable success rates that can be attributed to the rarity of these conditions, as well as the limited body of published literature on successful intervention. The level of evidence that supports the effectiveness of the available treatments for PIFP, AD, and TMJ disorders ranges from case