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POSTHERPETIC NEURALGIA

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ABSTRACT: Post Herpetic Neuralgia, generally referred to as PHN, a commonplace complication in herpes zoster, occurs with intolerable, unrelenting pain which remains a formidable challenge throughout treatment. Although several ways of managing PHN have been propounded, none could evince a definite gratifying effect. This article intends to succinctly delve into the etiopathogenesis, clinical features and management of PHN.

KEYWORDS: Postherpetic, Neuralgia, Oro facial pain.

INTRODUCTION: Neuralgia, as from the Greek origin, (neuro= nerve; algos = pain) denotes that the pain occurs along the distribution of a nerve. Neuralgias are most common in the maxillofacial region and are the most difficult to treat, where in the patient's psychological trauma has to be considered apart from just symptomatic management. Any agony in the oro-facial region warrants the attention of a dexterous maxillofacial specialist who is endowed with a set of specific skill and knowledge to handle such situations and provide relief to the patient. Of all the neuralgias in the maxillofacial region, Post Herpetic Neuralgia is infrequent but is demanding in the process of cure and invites debate. This paper works on the current concepts in the development and management of PHN.

DEFINITION: Post herpetic neuralgia has been variedly defined by authors of distinct knowledge and opinion:

- Postherpetic neuralgia is defined as pain that persists or relapses within 30–120 days at the site of acute herpes zoster after rash healing.¹
- Chen N et al gave the distinction between acute herpetic neuralgia (within 30 days of rash onset), subacute herpetic neuralgia (30 to 120 days after rash onset), and PHN (defined as pain lasting at least 120 days from rash onset).²
- Post herpetic neuralgia can also be defined as pain along the course of a nerve following the characteristic acute segmental rash of herpes zoster.³

ETIOPATHOGENESIS: PHN is the most frequent complication of herpes zoster, which is the most common neurological illness.⁴ Herpes zoster usually affects the dermatomes from T3 to L3. If the ophthalmic branch of trigeminal nerve is involved, zoster ophthalmicus results. (Fig. 1)

PHN is thought to be due to the destruction of the larger myelinated nerve fibers which are responsible for carrying inhibitory impulses, leaving out the smaller myelinated and unmyelinated fibers which are responsible for carrying nociceptive stimuli through the dorsal horn of spinal cord and hence pain is perceived. The characterization of afferent nerve fiber function using quantitative sensory testing and histamine-induced flare analysis showed that PHN is associated with damage of afferent fibers. Central sensitization (i.e. allodynia) also might contribute to PHN pain. A striking association between anxiety, depression and age, and the magnitude of PHN pain was established.⁵

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Fields and Botham clearly emphasized that both peripheral and central pathophysiological mechanisms contribute to PHN pain.

Some PHN patients have irritable nociceptors, which characteristically have minimal sensory loss. Other patients have pain associated with small fiber deafferentation in whom pain and temperature sensation are profoundly impaired but light moving mechanical stimuli can often produce severe pain (allodynia). In these patients, allodynia may be due to the formation of new connections between non-nociceptive large diameter primary afferents and central pain transmission neurons. Other deafferentation patients have severe spontaneous pain without hyperalgesia or allodynia and presumably have lost both large and small diameter fibers. In this group the pain is likely due to increased spontaneous activity in deafferented central neurons and/or reorganization of central connections.⁶

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Clinical Features: Once the acute rash of HZ heals, the affected skin exhibits reddish, purple or brownish hue which subsides leaving a pale scar. This scar may be characterized by allodynia/ hyperaesthesia/ hyperalgesia. The pain may be continuous or paroxysmal and both are usually aggravated by any contact with involved skin such as friction even from the lightest clothing.³

Unrelenting pain, sleep disturbance, anorexia, lassitude, constipation and decreased libido are the other complaints⁷. Pain often leads to depression, fatigue, insomnia, altered activities of daily living and decreased socialization and decreased ability to concentrate.⁸ PHN makes undertaking basic tasks (for example, bathing, dressing, eating) and complex activities (for example, travelling, performing household chores, shopping) difficult.⁹ Institutionalization and a loss of autonomy can occur in elderly patients with PHN.¹⁰

TREATMENT: The management of PHN can be broadly classified into;

- I. Conservative management.
- II. Surgical management.

CONSERVATIVE MANAGEMENT:

1. **Tricyclic Antidepressant Drugs (TCA):** TCA are important components of therapy for postherpetic neuralgia as they block the reuptake of norepinephrine and serotonin, and may relieve pain by increasing the inhibition of spinal neurons involved in pain perception.¹¹ Amitriptyline was suggested as useful in treating postherpetic neuralgia and may not act as an antidepressant.¹² A therapeutic approach for post herpetic neuralgia in which pharmacological therapy began with TCA, usually Amitriptyline was proposed.⁷

Adverse reactions to tricyclic antidepressant drugs, including confusion, urinary retention, postural hypotension, and arrhythmias, limit their usefulness in older patients, and plasma concentrations should be monitored to ensure compliance and help determine the optimal dose.¹¹

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2. **Anti Convulsants:** Carbamazepine (Tegretol) and gabapentin (Neurontin) are often used to control neuropathic pain. The use of Carbamazepine should be supervised, especially in the elderly as they can cause severe cutaneous reactions.¹³ Gabapentin appears to be effective and well tolerated for the short-term treatment of PHN.¹⁴ The efficacy of gabapentin in the treatment of PHN was evaluated by Ahmed Beydoun who confirmed that the lack of drug to drug interactions and excellent safety profile of the drug along with its efficacy in reducing PHN pain apart from having beneficial effects on sleep, overall mood, quality of life, makes it a drug of choice in the treatment of PHN.¹⁵
3. **Opioids:** Opioids have been effectively used to treat PHN without impairing cognition.¹⁶ Watson et al in their study of 208 cases with PHN noted that opioids were useful in achieving pain relief in patients with intractable pain.³ The effectiveness of epidural morphine in the control of pain in PHN was evaluated and found that, it more likely produced side effects than pain relief.¹⁷ Opioids like oxycodone and hydrocodone when used as the predominant therapies in patients being treated with gabapentin, it was observed that if patients reached efficacious dosages of gabapentin, opioid use in PHN might be reduced.¹⁸
4. **Topical agents:** Local anesthetics, capsaicin preparations, NSAID preparations are the three forms of topical agents used in management of PHN:
 - **Anesthetic Patch:** The effectiveness of topical local anesthetics in the relief of PHN has been evaluated and it has been observed that, they are a definitive treatment option for the relief of pain in PHN. Topical 5% lidocaine (lignocaine) medicated plaster is a treatment option for pain of PHN.¹⁹ Some authors suggest the use of the 5% lidocaine medicated plaster as one of the first-line therapies in patients with PHN.²⁰ Comparative efficacy of 5% lidocaine medicated plaster versus pregabalin showed that anesthetic patch has better efficacy than pregabalin in patients with PHN.²¹
 - **Capsaicin:** The mechanism of action of topical capsaicin has been ascribed to depletion of substance P. 0.075% Capsaicin cream is considered safe and effective treatment option for the pain in postherpetic neuralgia patients.²² Topical capsaicin provides improvement in pain relief in patients with PHN.²³ Capsaicin, may be used either as repeated application of a low dose (0.075%) cream, or as a single application of a high dose (8%) patch, which may provide a degree of pain relief to some patients with painful neuropathic conditions.²⁴
 - **NSAIDs Preparations:** De Benedittis G suggested that the aspirin/diethyl ether mixture provided pain relief in patients with PHN better than indomethacin and diclofenac drug/ether mixtures.²⁵ It is also suggested that Topical aspirin dissolved in chloroform is an effective means of reducing pain due to PHN.²⁶
5. **NMDA Antagonist (N -Methyl D- Aspartate):** Memantine, an NMDA receptor antagonist is ineffective in reducing spontaneous and evoked pain in patients with PHN.²⁷ Efficacy of Dextromethorphan was evaluated and it was found that it is ineffective in relieving pain of PHN.²⁸ Ketamine was observed to reduce pain of PHN significantly as compared to morphine and even reduced allodynia and wind-up like pain of PHN in a double blind study conducted by Eide PK.²⁹
6. **Intrathecal Steroids:** Studies have shown that corticosteroids inhibit the activity of IL-8 and decrease IL-8 concentration, and this decrease correlated with the degree of pain relief. Corticosteroids work by stabilizing neural cell membranes and suppress ectopic discharge

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from C-fibers. Allodynia, which is due in part to increased excitation of injured C-fibers, was eliminated because corticosteroids attenuate peripheral C-fiber activity, thereby suppressing hyperexcitability of the CNS. Intractable PHN was successfully treated with three consecutive weekly intrathecal administration of preservative-free dexamethasone and hyperbaric bupivacaine at the level of pathology.³⁰ Kotani N Kushikata T achieved pain relief in patients with intractable PHN by intrathecal administration of methylprednisolone and lidocaine proving it to be an effective treatment option³¹ while Rijsdijk M, van Wijck AJ did not observe any beneficial effects of intrathecal administration of methylpredisone with lignocaine in patients with PHN.³²

7. **Modified Jaipur Block:** Neerja puri proposed a modified jaipur block for treatment of PHN, which consisted of local subcutaneous infiltration of 2% Xylocaine, 0.5% bupivacaine and methylprednisolone and stated that it is very effective in resistant cases of pain, especially those persons who do not respond to topical and other oral medications.³³

SURGICAL MANAGEMENT:

1. **Peripheral Nerve Stimulation:** Peripheral Nerve Stimulation for Intractable Postherpetic Neuralgia was performed by Alexander E. Yakovlev et al and they achieved excellent pain relief in a patient refractory to all other treatment modalities.³⁴ Johnson et al stated that Peripheral nerve stimulation of the supraorbital or infraorbital branches of the trigeminal nerve is an effective method for relief of neuropathic pain in post herpetic infection.³⁵
2. **Spinal Cord Stimulation:** The effects of spinal cord stimulation in relieving pain of PHN was evaluated and an improvement in 82% of patients with PHN who were not relieved of pain by pharmacological therapy was observed.³⁶ Meglio M et al observed spinal cord stimulation to give satisfactory pain relief in patients with PHN and recommend a percutaneous test trial of SCS in every case of postherpetic neuralgia resistant to medical treatment.³⁷
3. **Deep Brain Stimulation:** Studies have shown that, patients with neuropathic pain of peripheral origin responded well to DBS while those with central pain syndrome did not give satisfying results.³⁸ Deep brain stimulation for intractable pain was studied by kumar k et al who suggested that it did not provide long term effective pain control in patients with PHN.³⁹
4. **Dorsal Root Entry Zone (DREZ) Coagulation:** Friedman et al in the treatment of 12 patients with PHN used DREZ Lesions and found it to be a satisfactory treatment option in patients refractory to conservative therapy⁴⁰ while Rath SA, Braun V did not support the DREZ coagulation for management of PHN as they observed minimal relief of pain post operatively.⁴¹

PREVENTION: As quoted aptly by Benjamin Franklin, "An ounce of prevention is worth a pound of cure", Prevention of development of PHN should be one of the tenets in the management of Herpes Zoster.

Several studies done with the premise that, management of acute phase of herpes zoster might prevent the chronic pain state have shown differing results. A review on the use of antiviral drugs in preventing PHN was done by Chen N, Li Q, Yang J et al, in which acyclovir and famciclovir were evaluated for the efficacy in preventing development of PHN in patients with shingles and found that both these drugs were no better than placebo in preventing PHN.⁴² Ying Han et al interventionally reviewed the efficacy of corticosteroids in preventing PHN and observed that they are not effective in preventing postherpetic neuralgia.⁴³ The Relationship between time of treatment

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of acute herpes zoster with sympathetic blockade and prevention of post-herpetic neuralgia was evaluated and emphasis that sympathetic blockade if applied within 2 months of the onset of herpes zoster prevented damage to the large nerve fibers, thus avoiding the development of PHN was given. Also, sympathetic blockade after two months of acute onset of PHN does not prevent development of PHN as the large fibers are damaged irreversibly.⁴⁴ A novel approach for preventing PHN wherein vaccination for herpes zoster was proposed. A definite reduction of herpes zoster was observed but no direct evidence could be drawn about the effectiveness in preventing PHN beyond its effect in reducing herpes zoster.⁴⁵

CONCLUSION: Post Herpetic Neuralgia presents with pain of such severe intensity that it affects the social life of the patient, thus making the treatment essential. This neuralgia tends to regress with time or may even continue for several years. Several treatment options have been proposed in the literature, each of which has merits and demerits. A planned approach to relieve the patient symptomatically and to improve the quality of life is the base for management of such patients.

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