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How do we manage Post Herpetic Neuralgia (PHN) ?

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ABSTRACT

Postherpetic neuralgia is a neuropathic pain syndrome characterized by pain that persists for months to years after resolution of the herpes zoster. Postherpetic neuralgia appears as a result from peripheral and central neurons damage that may by product of inflammatory response accompanying varicella zoster virus reactivation. Management of postherpetic neuralgia consists of the prevention through vaccination and/or antiviral treatment, and pain treatment using specific medications. Recommendation of treatment for postherpetic neuralgia uses tricyclic antidepressants, anticonvulsants, opioids, and topical agents. These medications should be selected based on individual patient characteristics. Many of these medications require dosing adjustment in older patients an in those with reduced creatinine clearance. Health-care professionals play a key role in pain management through early assessment, recommending evidence-based treatment, monitoring and evaluation of the treatments.

KEYWORDS : postherpetic neuralgia, management, prevention

1. Introduction

Postherpetic neuralgia (PHN) is a neuropathic pain syndrome characterized by pain that persists for months to years after resolution of the herpes zoster[1]. Herpes zoster, also known as shingles, presents as a painful vesicular rash and is caused by reactivation of the varicella-zoster virus within the dorsal root or cranial nerve ganglia, leading to pain in the affected dermatome. Postherpetic neuralgia occurs in approximately 30 percent of patients older than 80 years and in approximately 20 percent of patients 60 – 65 years; it is rare in patients younger than 50 years. Pain may be divided into three different stages: acute, subacute and chronic. The acute stage is defined as pain starting within 30 days after the appearance of skin rashes. The subacute stage is characterized by pain persisting beyond the acute stage, but resolved before PHN diagnosis. The third stage is PHN itself, with pain persisting for 120 days or more after the exanthema[1,2].

The risk factors of postherpetic neuralgia are older age, moderate to severe rash, moderate to severe acute pain during the acute phase, history of prodromal pain and ophthalmic involvement. Postherpetic neuralgia may persist from 30 days to more than six months after the lesions have healed, and most cases resolve spontaneously[2,3].

Pain is the most uncomfortable symptom for patients. Pain persistence significantly impairs quality of life and increases health care costs. Currently, recommendation of treatment for postherpetic neuralgia is available. Several approaches use anticonvulsants, opioids, tricyclic antidepressants and topical agents to control pain[2,3].

This study aimed to overview the management of postherpetic neuralgia based on clinical history of post herpetic neuralgia and focusing on pain control.

2. Reviews

2.1. Post herpetic Neuralgia Definition

Postherpetic Neuralgia is characterized by chronic neuropathic pain that persist at least one month in the pathway of the affected nerve, starting between one and six months after herpes zoster rash healing and may last for years[2,3]. The incidence of PHN varies from 10% to 20% in immunocompetent adults. There is no predominance with regard to gender. Age is a major PHN predictor because prevalence significantly increases with age. Postherpetic neuralgia occurs in approximately 30 percent of patients older than 80 years and in approximately 20 percent of patients 60 – 65 years; it is rare in patients younger than 50 years.

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2.2. Clinical manifestation and diagnosis

Postherpetic pain may take several forms of pain and sensory symptoms. The type of pain is chronic, characterized by burning or pricking and may be associated to allodynia (nonpainful stimulus perceived as painful), hyperpathia (slightly painful stimulus perceived as very painful), and dysesthesia (abnormal sensation with no stimuli)[3,4].

The anatomic distribution of postherpetic neuralgia follows the pattern of dermatomes involved with HZ. The dermatomes from T3 to L3 more commonly involved[3,4]. Diagnosis of postherpetic neuralgia is clinical, with differential diagnosis depend on pain characteristics and location of the affected nerve[3,4].

The risk factors of postherpetic neuralgia are older age, moderate to severe rash, moderate to severe acute pain during the acute phase, history of prodromal pain and ophthalmic involvement. The impact to patient quality of life is considerable because it affects sleep and the ability to work and perform daily activities[3,4,5].

2.3. Management of postherpetic neuralgia

Theoretical models suggest that reducing pain during the acute phase of herpes zoster may stop the initiation of the mechanisms that cause chronic pain, thus reducing the risk of posthepetic neuralgia[5,6,7]. If postherpetic neuralgia develops, treatment should be with the drugs to control and relieve pain that focuses on preventing a chronic pain syndrome. The first line drugs are anticonvulsants and tricyclic antidepressants. Second line drug include opioids. The other options include topical agents[5,6,7,8].

Tricyclic antidepressants

These drugs are used for postherpetic neuralgia as single therapy[1,6,9]. The mechanism of action is blockade of serotonin and norepinephrine reuptake and also the inhibition of voltage-dependent sodium channels. The most common drug is amitriptyline, and the other drugs such as nortriptyline, imipramine and desipramine. In older patients, these drugs should be started at lower doses given at bedtime, and the patient should be monitored for adverse effects, including interactions with other medications.

Anticonvulsants

Anticonvulsants drugs have been used for different conditions inducing neuropathic pain[1,6,9]. Studies involving anticonvulsants showed that gabapentin and pregabalin reduce pain from postherpetic neuralgia by approximately 50%. Gabapentin and pregabalin are drugs analog to gamma aminobutyric acid (GABA), that acts on the α-2-δ sub-unit of voltage-dependent calcium channels, decreasing calcium flow and inhibiting excitatory neurotransmitters release on primary afferents of spinal cord dorsal horn, similarly to pregabalin. It is possible that gabapentin has effect on N-methyl-D-as- partate type receptors (NMDA), decreasing glutamate levels to better control allodynia. Daily gabapentin dose may vary from 1800-2400 mg. Recommended dose for pregabalin is 300 – 600 mg/day.

Opioids

Opioids have analgesic effects and are helpful for postherpetic neuralgia, especially if pain is moderate to severe[6,9]. Opioids should be carefully adjusted in all patients for clinical

response, such as dose titration to minimize side effects, drug tolerance and abuse. A common recommendation is to use codeine (30-60 mg) every 6 hours, when needed. Studies have shown that patients taking oxycodone, morphine, or methadone have better pain relief than those taking placebo. A Cochrane review found that tramadol to be effective for neuropathic pain including postherpetic neuralgia. Tramadol analgesic action occurs in μ-agonist opioid recep-tors and in norepinephrine and serotonin reuptake inhibi-tion, promoting pain relief and improved QL. In cases of difficult pain management, a combination of tramadol and amitryptiline has been used[6,9].

Topical agents

The FDA has approved two topical medications for treatment of postherpetic neuralgia, such as capsaicin and lidocaine[6,9]. Capsaicin is a pepper-derived alkaloid Capsicum frutescens that stimulates a peripheral discharge od sunstance P, leading to its storage depletion. The unavailability of substances P on primary afferent fibers (C fibers) inhibits the generation of the painful phenomenon. Topical lidocaine acts by blocking sodium channels and decreasing abnormal ectopic discharges. It is uses as 5% lidocaine skin patches or as a cream, such as the Eutectic Mixture of Local Anesthetics (EMLA) containing 2.5% prilocaine and 2.5% lidocaine. Topical lidocaine is effective and safe, with low incidence of systemic adverse reactions and few side effects; in general, patients have mild local reactions. The topical 5% lidoacine should be applied in the painful skin area for a maximum period of 12 hours per day. It may be used in association with anticonvulsants, opioids and tricyclic antidepresants[6,9].

3. Prevention

The number of herpes zoster and postherpetic neuralgia patients may increase in the future because of ageing general population. A prophylactic vaccine able to improve specific immunity of T cells against varicella zoster virus is a promising clinical approach to limit herpes zoster and postherpetic neuralgia. The Centers for Disease Control and Prevention recommends one dose of the herpes zoster vaccine for persons 60 years and older in USA or for persons 50 years and older in Europe. This vaccine is being contraindicated for immunocompromised patients, children and pregnant women[9].

Prevention of the occurrence of postherpetic neuralgia is important issue to be considered when a patient has already contracted herpes zoster. The management for this condition should include antiviral drug therapy in the early phase of herpes zoster, proper topical therapy for skin lesions, aggressive treatment of neuralgia and education for daily life such as the importance of rest, recreation and nutrition[9].

4. Conclusion

Early herpes zoster diagnosis and treatment are important in the attempt to optimize pain management in the acute stage and to prevent the occurrence of postherpetic neuralgia. Management of postherpetic neuralgia has several therapeutic options. The available drugs tact to control and relieve pain that focuses on preventing a chronic pain syndrome. However, further researches are needed to better evaluate drug combination and develop new therapies to manage postherpetic neuralgia. A prophylactic vaccine against varicella zoster virus is a promising approach to decrease the incidence of herpes zoster and post herpetic neuralgia.

References

1. Fashner J, Bell AL. Herpes zoster and postherpetic neuralgia: prevention and management. Am Fam Physician [Internet]. 2011Jun;83(12):1432–1437. Available from https://www.ncbi.nlm.nih.gov/pubmed/21671543
2. Gharibo C, Kim C. Neuropathic pain of postherpetic neuralgia. Pain Med News. 2011;9:84–92.
3. Mallick-Searle T, Snodgrass B, Brant JM. Postherpetic neuralgia: epidemiology, pathophysiology, and pain management pharmacology. Journal of Multidisciplinary Healthcare [Internet]. 2016 [cited 2018 May 2]:9:447-454. Available from https://www.ncbi.nlm.nih.gov/pubmed/27703368 DOI 10.2147/JMDH.S106340
4. Nagasako EM, Johnson RW, Griffin DR,

Dworkin RH. Rash severity in herpes zoster: correlates and relationship to postherpetic neuralgia. J Am Acad Dermatol [Internet]. 2002 Jun;46(6):834–839. Available from https://www.ncbi.nlm.nih.gov/pubmed/12063479 DOI: 10.1067/mjd.2002.120924

5. Forbes HJ, Thomas SL, Smeeth L, Clayton T, Farmer R, Bhaskaran K, Langan SM. A systematic review and meta-analysis of risk factors for postherpetic neuralgia. Pain. 2016;157(1):30–54. Available from https://www.ncbi.nlm.nih.gov/pubmed/26218719 DOI: 10.1097/j.pain.0000000000000307
6. Portella AVT, de Souza LCDB, Gomes JMA. Herpes-zoster and post-herpetic neuralgia. Rev Dor. Sao Paulo [Internet]. 2013 jul-set;14(3):210-215. Available from http://www.scielo.br/pdf/rdor/v14n3/en_12.pdf
7. Argoff CE. Review of current guidelines on the care of postherpetic neuralgia. Postgrad Med [Internet]. 2011;123(5):134–142. Available from https://www.tandfonline.com/doi/pdf/10.3810/pgm.2011.09.2469?needAccess=true DOI 10.3810/pgm.2011.09.2469
8. Dworkin RH, O'Connor AB, Backonja M, et al. Pharmacologic management of neuropathic pain: evidence-based recommendations. Pain [Internet]. 2007;132(3):237–251. Available from https://www.ncbi.nlm.nih.gov/pubmed/17920770 DOI 10.1016/j.pain.2007.08.033
9. Ozawa A, Treatment of postherpetic neuralgia. JMAJ [Internet]. 2004;47(1):529 – 536. Available from http://www.med.or.jp/english/pdf/2004_11/529_536.pdf