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Postherpetic Neuralgia Management

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Abstract

Postherpetic neuralgia (PHN) is a neuropathic pain that occurs in the sensory nervous system after herpes zoster virus outbreak (Zhang, 2018). It is described as persistent burning, sharp pain that can last many months to several years. PHN is caused by deterioration of the spinal nerve sensory system when the herpes zoster virus is reactivated in the dorsal root ganglion (Zhang, 2018). A 70-year-old woman presented to the clinic with a shingles outbreak. She was treated with valacyclovir with instructions to return to the clinic the following week to assess for PHN. Pain management of PHN can be incredibly difficult with several pharmacological intervention options and potential referral to a pain clinic. A literature review was completed to address whether pain management of PHN was better attained to a tolerable level with the use of anticonvulsant medications versus the use of narcotic medications. The literature review was conducted using both Cumulative Index of Nursing and Allied Health Literature (CINAHL) and PubMed databases using key words “post herpetic neuralgia”, “anticonvulsants”, “narcotics”, and “pain management.” The initial review identified 131 articles, limitations of English language, 8-10 years old or less, and peer reviewed articles were used. This reduced articles to 49, upon further review, 10 were identified as pertinent for this review and were the highest levels of evidence based on the Melnyk levels of evidence scale. The results are discussed as learning points at the conclusion of this report. This literature review will better guide providers in the treatment of PHN.

Background

A 70-year-old patient presented to the clinic with a chief complaint of low back pain for the past two days. The pain increased when clothing rubbed against the right side of her back, or when she laid on her right side at night. On examination her skin to her right lower back was noted to be erythematous with a vesicular rash. She was diagnosed with herpes zoster and prescribed valacyclovir. Her history and physical exam are described in detail in the case report, she was instructed to follow up in one week to reassess her symptoms and recovery.

Dunphy et al. (2019) state, "One in three individuals in the United States will develop shingles. An estimated one million cases occur each year" (p. 131). Shingles or herpes zoster is an infection by the varicella-zoster virus that happens along dermatomal pathways causing a vesicular skin rash (Dunphy et al., 2019). PHN is seen most often in people 50 years and older, especially in those in immunocompromised state or on immunosuppressant drugs (Koshy et al., 2018). The varicella-zoster virus becomes latent in sensory ganglia neurons after an initial infection of chickenpox and reactivates later in life (Dunphy et al., 2019).

Postherpetic neuralgia (PHN) is chronic, persistent pain that can occur for more than three months after shingles disease has run its course (Dunphy et al., 2019). It is the most common complication of herpes zoster that can be disabling (Tovalino, 2018). With initiation of antiviral drugs and analgesics within the first three days of herpes zoster outbreak the severity of complications are reduced (Koshy et al., 2018). However, if untreated, PHN occurs in up to one-half of people over age 60 (Dunphy et al., 2019). PHN leads to unbearable pain that can difficult to treat (Tovalino, 2018). Treatment options include narcotics, NSAIDs, anticonvulsants, corticosteroids, tricyclic antidepressants, topical capsaicin, and more invasively a regional block with corticosteroids along with referral to a pain center (Koshy et al., 2018). With so many

treatment options for PHN, a literature review was conducted to answer the question: In patients experiencing postherpetic neuralgia after shingles outbreak does treatment with anticonvulsants or narcotics better manage pain to a tolerable level?

Case Report

HPI

A 70-year-old Caucasian female presents with a chief complaint of back pain for two days. The back pain is located on her lower right back, near her waist. The pain occurred consistently throughout the day, she described it as shooting, sharp pain, especially when her clothing rubbed against it. She had taken Tylenol without relief. She reported ice pack helped temporarily. The pain increased at night when she would lay on her right side. She denied any recent injury or trauma.

Medical History

She has a medical history significant for hypertension, arthritis, and hysterectomy. Her medication list includes daily lisinopril 20 mg tablet for her hypertension. Her rheumatologist also prescribed prednisone as needed for arthritis. She reported taking this about two times per year. She took over the counter acetaminophen as needed for pain. She has no known allergies. The patient also denied any significant family history, specifically denying cancer or early cardiac death.

Social History

She is currently retired from doing secretarial work. She lives with her husband in a single-family home. She denied use of any tobacco products, e-cigarettes, or vaping. She

consumed alcoholic beverages very rarely at social occasions. She also denied any illicit drug use. Her vaccines were up to date except for the Shingrix vaccine.

Review of Systems

She denied any headache, dizziness, chest pain, palpitations, shortness of breath, wheezing, abdominal pain, any loss of bowel or bladder control, diarrhea, constipation, dysuria, urinary urgency, urinary frequency, nausea, or vomiting. Review of symptoms was positive for myalgias to right lower back.

Physical Exam

On presentation her vitals included blood pressure 154/90, pulse 78, temperature 99.1, oxygen saturation 96%. On examination she appears well-groomed and in no acute distress. Her heart sounds are normal, S1, S2, no murmur, click, or gallop. Lung sounds are clear to auscultation, no wheezing or rhonchi noted. When inspecting her right lower back, a vesicular, erythematous rash is noted unilaterally. There are multiple small fluid-filled lesions localized to her right lower back along the lumbar 1-3 dermatome. This area is tender to palpation and light touch. Her range of motion is intact. She has a non-antalgic gait.

Assessment and Plan

This patient's history and physical exam are consistent with herpes zoster, or shingles. Since she presented within the first 72 hours of symptom onset, therefor she was prescribed valacyclovir 1,000 mg by mouth every eight hours for seven days. She was given the first Shingrix vaccine in the clinic prior to leaving and was counseled to return in 2-6 months for her second vaccination. She was advised to wear loose clothing to prevent rubbing of the area. Lotions, such as calamine, may help to soothe the area. She may continue to take NSAIDs for

her acute pain and may attempt utilizing Lidoderm patches to the area. Decreasing scratching and rubbing should improve healing time. As the lesions open and drain, she was educated to avoid contact with pregnant women and practice strict hand hygiene to prevent the spread to her husband. A follow-up appointment was scheduled for the following week to ensure her skin lesions do not become infected and to assess for PHN.

Literature Review

Valacyclovir is the first line recommendation in treatment of herpes zoster that presents within 72 hours of onset to decrease the severity and duration of the eruptive phase and reduce intensity of herpes zoster pain in the acute phase (Gan et al., 2013). Prescribing antiviral drugs on the onset of herpes zoster also decreases the risk of post-herpetic neuralgia, but does not prevent it (Koshy et al., 2018). Pain management becomes more difficult if PHN is present after this initial treatment. Even with treatment, 10% of patients with herpes zoster will develop PHN and will require pain management for several months, and 2% may have pain that persists up to five years (Khadem & Stevens, 2013). To address whether pain management of PHN is better attained to a tolerable level with the use of anticonvulsant medications versus the use of narcotic medications research was done utilizing the University of North Dakota's Harley E. French Library of Health Sciences. Applying evidence-based treatment will allow for better patient outcomes and reduce morbidity.

For this literature review Cumulative Index of Nursing and Allied Health Literature (CINAHL) and PubMed were used. In CINAHL, the following key words were searched "post herpetic neuralgia", "anticonvulsants", "pain management", and "narcotics", the initial search yielded 58 articles. The search was narrowed by specifying articles in the English language, published within the past eight years, and peer reviewed articles as limitations. This reduced the

search to 35 articles. Upon further analysis, five articles were identified as relevant for this review. The same key words were utilized in the Pubmed search. Initially 73 articles were retrieved. The search was narrowed by specifying English language, articles published within the past ten years, and peer reviewed articles. This search yielded 14 articles. Five of the 14 articles were deemed relevant to the topic and sources were chosen that were published within the past eight years. On the Melnyk Level of Evidence scale, all articles chosen were Level 1 to Level 2 ratings, which include systematic reviews, meta-analysis, clinical guidelines, and one or more randomized control trials (Melnyk & Fineout-Overholt, 2015).

Authors agree that PHN management is challenging because of its severity, long duration, and potential for debilitation. The Food and Drug Administration (FDA) approves the use of capsaicin and lidocaine patches, gabapentin, and pregabalin for the treatment of PHN (Khadem & Stevens, 2013). Calcium channel blocking anticonvulsants gabapentin and pregabalin are currently utilized as first line treatment for PHN. Narcotics are typically recommended as second- and third-line treatment of PHN (Thakur & Philip, 2012). When used for PHN narcotics are used off-label of FDA recommendation, as FDA requires demonstration of efficacy in each pain syndrome for label indication (Khadem & Stevens, 2013). In general, the pain management community agrees that drugs effective for management of one type of pain syndrome may be useful in another (Khadem & Stevens, 2013).

The two drug classes are often utilized in combination to reach pain reduction to a tolerable level. In order to prescribe ideal treatment, providers must consider safety, efficacy, and tolerability in relation to patient objectives, preferences, and adherence concerns (Khadem & Stevens, 2013).

Anticonvulsants

Anticonvulsants are also referred to as “anti-seizure” medication. Anticonvulsant medications that were assessed in the review of literature include gabapentin, pregabalin, carbamazepine, and divalproex sodium. These medications possess central analgesic effect and inhibit the ectopic discharge of the peripheral nerves after injury (Zhang et al., 2018). Gabapentin specifically affects gamma aminobutyric acid (GABA), which is an inhibitory neurotransmitter, and its mechanism of action is not well understood (Woo & Robinson, 2016).

Gabapentin was found to be typically well tolerated, lacks medication interactions, and has few significant adverse effects (Miao, 2017). It is not metabolized, it is excreted unchanged in the urine and feces (Woo & Robinson, 2016). So, it is imperative to note that gabapentin is expelled by the kidneys and should be used cautiously in patients with renal insufficiency (Thakur & Philip, 2012). Patient education should be provided to advise patients not to abruptly stop taking this medication, patients should be weaned off to prevent possible seizure activity (Woo & Robinson, 2016).

Throughout the literature review gabapentin was the most prominently mentioned anticonvulsant medication in relation to PHN treatment. It has been shown to significantly reduce pain, improve sleep, and quality of life when taken for PHN pain (Thakur & Philip, 2012). Another systematic review found improvement in short-term pain intensity with the use of gabapentin and a 50% reduction in pain after treatment compared to those taking a placebo (Salah et al., 2016). Gabapentin was found to be dose dependent, with higher doses up to 3600 mg per day results showed larger reduction in pain intensity (Khadem & Stevens, 2013). It is advised to start at a lower dose and increase the dose as the patient responds with improved pain management. For the treatment of PHN, the dose is started at 300 mg per day on day one,

increased to 300 mg twice a day on day two, and on day three the dose is 300 mg three times per day. This dosing can be titrated up to 600 mg three times a day based on pain relief (Woo & Robinson, 2016).

Dosenevic et al. (2017) completed an overview of systematic reviews that notes safety of use of anticonvulsant medications was not mentioned or was reported as inconclusive in most systematic reviews of PHN pain management, two of the 16 reviews reported gabapentin as safe (p. 647). Many studies emphasize that future research should explore the different dosing, durations, and frequencies of gabapentin administration in the treatment of PHN (Zhang et al., 2018). Fan et. al (2014) agree that more trials are needed to look at long term efficacy and tolerance of gabapentin in PHN patients.

Narcotics

If nonopioid medications are ineffective for pain relief, narcotics are considered the next step in treatment of PHN pain (Woo & Robinson, 2016). Opioids control pain via the various opioid receptors located within the central nervous system and the peripheral afferent nerve terminals (Gan et al., 2013). They alter the perception and response to painful stimuli (Woo & Robinson, 2016). Throughout the literature review the primary narcotics studied in the treatment of PHN include oxycodone, morphine, methadone, and tramadol.

These medications are metabolized in the liver and excreted in the urine (Woo & Robinson, 2016). Side effects of narcotic use include constipation, cardiorespiratory depression, sedation, nausea, vomiting, hallucinations, paresthesia, and histamine release (Woo & Robins, 2016; Gan et al., 2013; Khadem & Stevens, 2013). The use of narcotics also poses a risk of physical dependence and development of analgesic tolerance (Gan et al., 2013). There are also

drug interactions when narcotics are taken in combination with alcohol, antihistamines, sedative-hypnotics, barbiturates, and antipsychotics (Woo & Robins, 2016). When compared to the anticonvulsants, narcotics have increased side effects and potential risks.

The use of tramadol, specifically, over a 28-day period was found to provide significant pain improvement in PHN (Saxena et al., 2012). A double-blind crossover trial found oxycodone treatment resulted in superior scores of effectiveness, disability reduction, and patient preference in the treatment of PHN (Thakur & Philip, 2012). Khadem and Stevens (2013) state, "Oxycodone, morphine, methadone, and tramadol, a partial opioid receptor agonist, have all demonstrated to be significantly superior to placebo" (p. 277). This is promising as a treatment option for patients with PHN struggling with pain management, however this systematic review did not specify duration of treatment. The studies reviewed assessed treatment for greater than four weeks but did not include the total length of treatment. A more recent systematic review also found substantial pain relief noted with the use of buprenorphine, morphine, oxycodone, and tramadol compared to placebo in the treatment of PHN for 4-12 weeks (Sommer et al., 2020).

The most recent evidence-based guidelines recommend 90-150 mg morphine equivalent per day (Sommer et al., 2020). Many patients require increased doses of narcotics higher than these recommendations. This increased dosing may be due to tolerance or ineffective pain control with opioids. Referral to a pain specialist for expert management should be considered if stronger opioid medications are needed (Gan et al., 2013). It is recommended that risk factors for prescription opioid abuse be assessed prior to prescribing and at each prescription renewal (Sommer et al., 2020).

In the literature review, many systematic reviews point out that combination therapy of pregabalin and oxycodone showed decrease pain intensity and improved quality of life (Koshy et

al., 2018). Thakur & Philip (2012) emphasize that, “the combination of gabapentin and morphine was superior to either of these medications alone” (p. 12). Overall, even with several therapeutic modalities it is agreed that treatment of PHN remains challenging (Koshy et al., 2018). This literature review has established that combination therapy appears to be a trend to reach optimum pain management.

Learning Points

- PHN is persistent burning, sharp pain that can last many months to several years and is the most common complication of shingles that often leads to difficult pain management.
- Capsaicin and lidocaine patches, gabapentin, and pregabalin are considered first line treatment of PHN, whereas narcotics are typically recommended as second- and third-line treatment of PHN.
- Gabapentin was mentioned most often in relation to PHN treatment and has been shown to significantly reduce pain, improve sleep, and quality of life when taken for PHN pain.
- Multiple studies confirm that combination therapy using anticonvulsants with narcotic medications was shown to be more effective for pain management in PHN patients than either medication used alone.
- In order to prescribe ideal treatment, providers must consider safety, efficacy, and tolerability in relation to patient objectives, preferences, and adherence concerns; with the use of narcotics, abuse and dependence should be assessed at each prescription refill.

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