

CZERWIK, Julia, CIESZKOWSKA, Joanna, DMOCHOWSKA, Joanna, CZUBALA, Marta and WRÓBLEWSKI, Wiktor. How should we treat postherpetic neuralgia? *Quality in Sport*. 2024;17:53070. eISSN 2450-3118. <https://dx.doi.org/10.12775/QS.2024.17.53070>  
<https://apcz.umk.pl/QS/article/view/53070>

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.

Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).

Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.

Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

© The Authors 2024;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland

Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 04.07.2024. Revised: 15.07.2024. Accepted: 17.07.2024. Published: 23.07.2024.

## How should we treat postherpetic neuralgia?

Julia Czerwik (1), Joanna Cieszkowska (2), Joanna Dmochowska (3), Marta Czubala (4),  
Wiktor Wróblewski (5)

<sup>1</sup> julia.czerwik26@gmail.com, Medical University of Lublin

<sup>2</sup> joasia.cieszkowska.99@gmail.com, Medical University of Lublin

<sup>3</sup> joannadmochowska.um@gmail.com, Medical University of Lublin

<sup>4</sup> marta.czubala99@gmail.com, Medical University of Lublin

<sup>5</sup> wiktowroblewski10@gmail.com, Military Clinical Hospital in Lublin

## Abstract

Postherpetic neuralgia (PHN) is the most common long-term complication of varicella-zoster virus (VZV) reactivation. It is characterized primarily by persistent pain more than 90 days after the illness at the site where the rash was. This pain is sharp, burning, stabbing in nature. Postherpetic neuralgia can lead to a reduced quality of life and negatively affect sleep and daily

functioning. The first line of treatment is currently conservative methods, which include anticonvulsants, antidepressants, topical lidocaine, as well as opioids and topical capsaicin. If these measures are ineffective, individually tailored interventional methods may be necessary. Among these, botulinum toxin A injection is the most common. Other methods focus on neuromodulation (which is the alteration of nerve activity through targeted delivery of a stimulus) or blocking individual elements of the nervous system.

**Key words:** Anticonvulsants, Antidepressants, Botulinum toxin, Capsaicin; Lidocaine, Nerve block, Opioids, Postherpetic neuralgia, Quality of life, Spinal cord stimulation, Transcutaneous Electrical Nerve Stimulation

## **Introduction**

Herpes zoster is an infectious disease caused by the varicella zoster virus (VZV, now referred to as Human Herpesvirus-3 - HHV-3). The same virus when first infected causes chickenpox, after which it travels to the spinal ganglia, cranial nerve ganglia and posterior horns of the spinal cord, where it can be reactivated as herpes zoster even after many years of latency. The main symptom of herpes zoster is the presence of unilateral, painful blisters located within a single dermatome, an area of skin innervated by a single spinal root. The heraldic symptoms of the disease include continuous or intermittent pain in the same area of a burning, stabbing, throbbing nature. There may also be a headache, fever, malaise, a feeling of fatigue. The heraldic symptoms usually appear 3-4 days before the skin lesions. Herpes zoster is treated with antiviral drugs (acyclovir, valacyclovir, famcyclovir), which reduce the severity and duration of herpes zoster. (1)

The most common complication of herpes zoster is postherpetic neuralgia. The occurrence of neuralgia is associated with nerve damage and its irritation in a specific part of the body. It manifests as unilateral chronic pain in the dermatomes previously occupied by the rash, which lasts for at least 90 days after herpes zoster. The nature of the pain is burning, stabbing, piercing with exacerbations caused by cold and stress, often disturbing sleep. In addition, patients may develop allodynia (pain caused by a non-nociceptive stimulus), hyperalgesia (pain hypersensitivity) and hypoesthesia (weakened sensation of touch and temperature). Postherpetic neuralgia negatively affects quality of life, mental well-being and mental health functioning. Risk factors for this complication include older age, female gender, significant pain intensity at the time of the rash, location within the trigeminal branch, diabetes mellitus, cancer and other immune-compromising diseases. The prevalence of neuralgia in people who

have survived herpes zoster is estimated at about 20%. Antiviral treatment of herpes zoster has not been proven to prevent the occurrence of postherpetic neuralgia. The main goal of treating postherpetic neuralgia is effective pain control. Conservative treatment is used first: topical (lidocaine and capsaicin) and systemic (gabapentin, pregabalin, antidepressants, opioids). However, drugs alone are not always effective, especially in patients with long-term neuralgia. In addition, pharmacotherapy in some patients is associated with side effects such as nausea, dizziness and drug dependence, so sometimes interventional methods are necessary. These include subcutaneous botulinum toxin A injection, steroid injections, Transcutaneous Electrical Nerve Stimulation (TENS), spinal cord stimulation, pulsed radiofrequency, peripheral nerve stimulation, stellate ganglion block and dorsal root ganglion destruction. (2, 3, 4)

### **Conservative methods**

First-line drugs for the treatment of postherpetic neuralgia include gabapentin, pregabalin, tricyclic antidepressants and lidocaine 5% patches, while second-line drugs include capsaicin and opioids. Therapy should begin with lidocaine patches, then expand therapy with other drug groups as needed. (5,6)

#### **1. Topical lidocaine**

Lidocaine is an amide derivative with local anesthetic effects. In the treatment of postherpetic neuralgia, patches containing 5% lidocaine are mainly used. It stabilizes cell membranes by inhibiting the rapid flow of sodium ions and preventing the cell from depolarizing under the influence of an incoming stimulus. Pathological voltage-dependent sodium channels accumulate in the damaged nerve and cause ectopic excitations. Lidocaine, by binding to the channels, prevents the formation of these extra excitations, but does not block afferent conduction, so it does not cause numbness. There is also a second mechanism of action of lidocaine, which is to inhibit the release of pain mediators by keratinocytes. These cells make up 95% of epidermal cells, are involved in signal transduction, and their activation can lead to stimulation of nociceptive sensory endings. Lidocaine also has a cooling effect on the affected area, and the patch itself provides mechanical protection. Lidocaine in the patch is minimally absorbed into the vessels, so it does not disturb the circulatory system or the functioning of the liver and kidneys. Also beneficial in long-term therapy is the way the patch is applied - it is stuck once a day for 12 hours, up to 4 patches at a time. Side effects include mainly local skin irritation. Lidocaine patch products also have the disadvantage of a relatively high price, which prevents some patients from using them. Superficially applied lidocaine is the drug of first

choice, both alone and in combination with other first-line drugs (gabapentin or antidepressants). The value of the NNT factor (number needed to treat), which determines the number of patients in whom the drug must be administered in order to achieve a positive effect of therapy in 1 of them to achieve a positive treatment effect, for lidocaine in the treatment of postherpetic neuralgia is 2. (7-11)

## **2. Topical capsaicin**

Capsaicin is an alkaloid found in hot chili peppers of the genus *Capsicum* and is also a highly selective agonist of TRPV1 channels located in nerve fibers in the skin. Its mechanism of action involves activation of TRPV1 nociceptors, followed by an influx of  $K^+$  and  $Ca^{2+}$  ions into the cell and the release of vasoactive neuropeptides, primarily substance P, resulting in skin irritation and erythema. A late consequence of surface application of capsaicin is the abolition of nociceptor sensitivity to stimuli, referred to as “anesthesia.” This effect is reversible and passes after a few weeks. According to several studies, capsaicin in low concentrations (0.025% or 0.075%) provided only partial relief, and had to be repeatedly reapplied. Therefore, currently the most favorable form of application is patches with 8% capsaicin - each is  $14 \times 20$  cm ( $280 \text{ cm}^2$ ) and contains 179 mg of capsaicin. The patch is applied to the painful area for 60 minutes at a time. Pain relief can last about 12 weeks, and in case of recurrence the therapy can be repeated after 90 days. Patches can only be applied to intact skin, up to 4 at a time. The most common side effects include burning at the application site, pain, erythema and pruritus, so it is recommended to use an anesthetic before applying the capsaicin patch. Despite this most patients require analgesics to alleviate the pain associated with the immediate effects of the patch. The patch is not recommended for use in patients under the age of 18. (12, 13,14)

## **3. Gabapentin and pregabalin**

Gabapentin and pregabalin (its derivative) are new-generation antiepileptic drugs that can be used to treat neuropathic pain. They are analogs of the neurotransmitter, gamma-aminobutyric acid (GABA), but without affecting GABA receptors. Their mechanism involves binding to proteins within the alpha-2-delta subunit of voltage-gated calcium channels. The analgesic effect of gabapentin is achieved by increasing the action of the GABA-dependent inhibitory pathway, antagonistic activity against the NMDA (N-methyl-D-aspartic) receptor and inhibition of conduction from peripheral nerves. Both drugs are not metabolized in the liver and rarely interact with other drugs. The use of gabapentin starts at a dose of 100 mg per day. In contrast, the target dose extends from 600 to 3600 mg per day. An effective therapeutic dose is

achieved within 30 days. The NNT value for gabapentin is 3.2. The bioavailability of gabapentin depends on the dose administered and decreases as the dose increases. In the case of pregabalin, this effect does not occur, it is absorbed in a linear relationship, so the maximum dose for it is 6 times lower than for gabapentin. The preparation is used at a dose of 150-600 mg/d. in 2-3 divided doses. Adverse effects of both drugs include dizziness, imbalance, excessive drowsiness, and peripheral edema. Gabapentin can also cause ataxia, gait disturbances and diarrhea. Pregabalin and gabapentin are oral first-line drugs for the treatment of postherpetic neuralgia. Of the two drugs, pregabalin has been shown to have a better analgesic effect and improved sleep quality in patients. (15, 16)

#### **4. Antidepressants**

Many antidepressants are used in low doses to treat postherpetic neuralgia, producing an analgesic effect without an antidepressant component. Mainly used are substances from the group of tricyclic antidepressants (TCAs), especially amitriptyline. The analgesic effect with the use of these drugs is achieved by blocking the transport of the neurotransmitters noradrenaline and serotonin from the synaptic space back into the neuron, that is, inhibiting the reuptake of these substances, as well as blocking sodium channels and alpha-adrenergic receptors. For amitriptyline, the initial dose is 10 to 25 mg orally at bedtime, then increase by 10 to 25 mg per week to target of 75 to 150 mg per day. A meta-analysis of four randomized controlled trial comparing amitriptyline, nortriptyline, and desipramine with placebo estimated an NNT (Number Needed to Treat) of 3 to achieve meaningful pain relief. Tricyclic antidepressants, however, cause a large number of side effects, which include dry mouth, constipation, urinary disturbances cardiac arrhythmias and double vision. There are also cognitive impairment, excessive sedation, orthostatic hypotonia and decreased libido. Caution should be taken with the use of TAC in patients with prostatic hypertrophy, glaucoma, serious cardiovascular disease, and o patients who are at risk of suicide. SSNRIs for the treatment of postherpetic neuralgia - duloxetine and venlafaxine - are also shown to be effective in controlled trials. Duloxetine is used at a dose of 60-120 mg/d, and venlafaxine at 75-150 mg/d. (3, 17)

#### **5. Opioids**

Opioids are a group of analgesics on the second and third steps of the analgesic ladder. They are not routinely used in the treatment of postherpetic neuralgia due to the risk of addiction and overdose. They are chosen as the second (tramadol) or even third line of treatment (other opioids). Opioids act directly on three types of opioid receptors:  $\mu$  (MOR),  $\delta$  (DOR) and  $\kappa$

(KOR). Opioid receptors are located in structures of the central and peripheral nervous systems. They belong to the family of G protein-coupled receptors. Following the action of opioids, the release of pronociceptive neurotransmitters is halted and the conduction of impulses in nerve fibers is slowed or inhibited. The most commonly observed side effects include nausea, pruritus, central nervous system disorders (confusion, hallucinations) and opioid-induced bowel dysfunction (OIBD) - primarily constipation, to the most dangerous - respiratory center depression.

Tramadol, which is a weak opioid that acts on the  $\mu$ -receptor, has been used in the treatment of postherpetic neuralgia. Its maximum dose is 400 mg per day, or 300 mg per day in patients over 75. Use should start at 50 mg per day and increase by 50-100 mg to a tolerable dose. Tramadol is less effective in reducing neuropathic pain than other opioids, but is safer to use. (18)

### **Interventional Treatments**

Patients who experience persistent pain despite conservative treatment or develop intolerable adverse effects to medications may benefit greatly from interventional therapies. Interventional methods are not routinely used by some specialists due to lack of awareness of their benefits and because of absence of training. It is important to carefully select a specific method from a wide range of options, with an individualized approach for each patient. (19, 20)

#### **1. Botulinum Toxin A Injection**

Botulinum toxin type A (BTX-A) is an exotoxin produced by *Clostridium botulinum* bacilli. It is composed of 2 chains - a light chain (50 kD) and a heavy chain (100 kD) connected by a disulfide bridge. Botulinum toxin type A is a potent biological poison. It is used in aesthetic medicine to treat dystonia, spasticity, contractures, as well as chronic pain of various origins, including postherpetic neuralgia. The exact analgesic mechanism of botulinum toxin is not known, but it inhibits the release of pain mediators (substance P, glutamate, and calcitonin gene related protein - CGRP) from nerve endings and dorsal root ganglia. For the treatment of postherpetic neuralgia pain, botulinum toxin at a dose of 100-200 IU is injected subcutaneously within 1-2 cm of the site of pain. The same benefits were observed in two randomized, double-blind, placebo-controlled trials, which evaluated the effectiveness of subcutaneous botulinum toxin A injection for postherpetic neuralgia. Patients showed reduced pain intensity as measured by VAS, increased sleep duration and reduced opioid use. Botulinum toxin A has a NNT of 1.2 for a 50% reduction in the VAS score. (21-24)

## **2. Steroid Injection**

Steroids have found use in the treatment of postherpetic neuralgia by several means. The first is local triamcinolone injection. Triamcinolone is a synthetic, fluorinated glucocorticosteroid with stronger anti-inflammatory, anti-edema, anti-itch, anti-pruritic and anti-allergic effects than prednisolone. It inhibits capillary permeability, thereby reducing edema. The underlying cause of postherpetic neuralgia is neuronal damage and inflammation with edema caused by reactivation of the VZV virus. The therapeutic profile of corticosteroids may allow pain relief in postherpetic neuralgia by quieting this inflammatory process. A study was conducted in which patients received three injections of triamcinolone plus lidocaine in the painful lesion with two-week intervals. 100% of them reported a reduction in pain. The NNT was determined to be 2.1. However, due to the specific site of the study, which was a military hospital, further trials should be conducted on a more diverse population. A second option is to administer steroids intrathecally. Patients with postherpetic neuralgia have been shown to have subacute or chronic inflammation around the spinal cord. In addition, they have been found to have increased levels of interleukin-8 in the cerebrospinal fluid. To counteract these changes, methylprednisolone with local anesthetics or midazolam is administered intrathecally. That method cannot be used for PHN involving the trigeminal nerve. (25, 26)

There is also the possibility of injection in paravertebral area, which is called paravertebral block. It is more beneficial for patients in whom pain is unilateral and involves a limited number of spinal segments. (27)

## **3. Transcutaneous Electrical Nerve Stimulation**

Transcutaneous Electrical Nerve Stimulation (TENS) is a non-invasive, non-pharmacological method used to treat many painful conditions. Nerve stimulation is achieved by applying surface electrodes to the site of the ailment. The mechanism of pain relief is believed to be due to central and peripheral mechanisms. TENS activates the release of endogenous opioids, modifies electrical transmission and dilates blood vessels, reducing neuropathic pain. We distinguish between: traditional high-frequency TENS, low-frequency TENS, burst TENS and modulated TENS. TENS can be used alone or in combination with a drug to reduce the dose. To test the efficacy of this method in the treatment of postherpetic neuralgia, a study was conducted in which TENS was combined with oral cobalamin, and another in which TENS was used with cobalamin and lidocaine. In both studies, TENS was used for 30 minutes a day over a period of 4 to 8 weeks. The studies showed significant improvements in average worst pain

intensity, average continuous pain intensity, reduced allodynia and paresthesia, and increased quality of life for patients. The NNT for the first combination was 3.3, and the NNT for the second was 4.3. Another study combined the use of pregabalin with TENS, using this treatment for 4 weeks. The group treated with pregabalin 300 (P300)+TENS had a reduction of pain of 30% and the group treated with pregabalin 600 (P600)+TENS had a reduction of pain of 40%. Moreover, the comparison between group P600+TENS versus group P600+TENS placebo has shown a statistically significant reduction of VAS. Furthermore, transcutaneous electrical nerve stimulation has also been used in patients with acute-stage herpes zoster in prevention of postherpetic neuralgia. (28-32)

#### **4. Peripheral Nerve Stimulation**

Underlying the pain of postherpetic neuralgia are central mechanisms involving neuronal necrosis and the inflammatory process. However, the pathophysiology of this neuralgia also has a peripheral basis. According to the pain gate theory, neuralgia neuralgia may be a type of deafferentation pain. Therefore, methods that affect the peripheral nerve can be used. Peripheral nerve stimulation, frequently referred to as PNS, is a commonly used approach to treat chronic pain. It involves surgery that places a small electrical device next to one of the peripheral nerves. (nerves that are located beyond the brain or spinal cord). The electrode delivers rapid electrical pulses that are felt like mild tingles (so-called paresthesias). During the testing period (trial), the electrode is connected to an external device, and if the trial is successful, a small generator gets implanted into the patient's body. The stimulation settings include pulse widths of 150-450  $\mu$ s, frequencies of 50-60 pulses per second, and amplitudes of off to 5 V (or 3 mA). PNS can be used in continuous or intermittent mode. Reported adverse events are: skin irritation, painful or uncomfortable stimulation and other medical events such as swelling or pain at the lead exit site comprising the rest. A randomized clinical trial has not been conducted to date, but in the case studies described, patients undergoing PNS have reported pain relief, minimization or cessation of medication, and improved sleep. PNS is used in patients with refractory postherpetic neuralgia, especially with neuralgia originating from cranial nerves, which precludes the use of spinal cord stimulation. (33, 34, 35)

#### **5. Spinal cord stimulator**

A spinal cord stimulator is an implanted device that sends low levels of electricity directly into the spinal cord to relieve pain. The mechanism of action of the spinal cord stimulator remains incompletely explained. Currently, its action is based on the "Gate control theory" given by



Wall and Melzack. Stimulation of large-diameter A- $\alpha$  and A- $\beta$  neurons inhibits the transmission of the pain signal carried by C fibers. In this way, the spinal cord stimulator would have an effect on pain modulation. In addition, it affects  $\gamma$ -aminobutyric acid and adenosine levels, reducing neuropathic pain. Spinal cord stimulators consist of thin wires (electrodes) and a small, pacemaker-like battery (generator). The electrodes are placed between the spinal cord and vertebrae (epidural space), and the generator is placed under the skin, usually near the buttocks or abdomen. Permanent placement of the device is always carried out after a successful temporary trial. This method of pain treatment was first used in 1967. In addition to postherpetic neuralgia, the spinal cord stimulator is used in pain associated with Lyme disease, root pain, cancer pain, Raynaud's disease, cluster headaches and ischemia-related pain. Studies suggest that patients with pain and allodynia due to central sensitization and those with preserved neuronal and dorsal column function would respond well to spinal cord stimulation. In contrast, patients with marked sensory loss and those experiencing continuous pain without allodynia would not benefit from spinal cord stimulation, as the predominant mechanism may be deafferentation and degeneration of the dorsal column. (36, 37, 38)

## **6. Pulsed radiofrequency stimulation**

Pulsed radiofrequency stimulation (PRF) is increasingly being applied to ease several types of pain including neuralgia, joint pain, and muscle pain. This technique works by delivering an electric field and heat bursts to targeted nerves or tissues via a catheter needle tip without damaging these structures. The underlying mechanism is attributed to the effects of a rapidly changing electrical field on neuronal membranes, which results in electrolyte conduction and subsequent depolarization. This procedure was first performed in 2008. In four randomized clinical trials on the effects of PRF on postherpetic neuralgia, patients showed improvement in their condition (reduced pain, improved emotional state and daily functioning) 2-3 days after the procedure, which persisted for up to 2-3 months. No serious side effects were observed, only local symptoms and transient bradycardia occurred. (39, 40)

## **7. Stellate Ganglion Block (SGB)**

Sympathetic nervous system has its role in pathophysiology of chronic pain. There is abnormal activation of adrenergic receptors in primary afferent neurons and direct interaction between primary afferent and efferent sympathetic nerves due to collateral sprouting after a nerve injury or tissue trauma. A stellate ganglion block is an injection of local anesthetic to block the sympathetic nerves located on either side of the larynx in the neck. The anesthetic is injected at

the C6 or C7 vertebral level, historically with the Chassignac's tubercle, the cricoid cartilage, and the carotid artery serving as the anatomic landmarks to the procedure, nowadays it is ultrasound-guided. A study conducted on 252 patients showed that ultrasound-guided ropivacaine SGB is more effective than lidocaine in treating upper limb PHN. Other studies have confirmed that early SGB can not only effectively relieve herpes acute pain but also reduce the incidence of PHN. However, due to the short maintenance time after a single SGB treatment, multiple injections are generally required for maintenance treatment, which increases the risk of injection complications. Repeated treatments can lead to distress, poor compliance, increased financial burden, and poor quality of life. (41, 42)

### **8. Dorsal Root Ganglion Destruction**

Patients with severe postherpetic neuralgia experience loss of axons, cells and myelin, and consequently, pain sensation due to ectopic discharge in nociceptors. When the above methods are ineffective, dorsal root ganglion destruction can be considered. This is performed with adriamycin, also known as doxorubicin, which is a topoisomerase II inhibitor associated with cytotoxic effects such as apoptosis, autophagy and necrosis. Adriamycin can be absorbed by peripherals of nervous fibers and retrogradely transport along axoplasm to corresponding distributed neurons resulting in neuronal degeneration and necrosis, which is named as fatal and retrograde axoplasm transport and suicidal transport effect. Thus, Adriamycin affects cell growth in the body and destruction of the dorsal root ganglion with it contributes to pain relief by disrupting the associated signaling pathway. It should be remembered, however, that this is an off-label effect, as adriamycin has not been registered for this purpose. Patients treated with adriamycin and dexamethasone reported improved VAS scores 1 week after treatment, and the effect lasted up to 6 months. In contrast, another study showed that dorsal root ganglion destruction by adriamycin was significantly more efficacious than dexamethasone in reducing pain of PHN, without any serious side-effect. Patients could accept the second or third operation when the pain returned or they still feel pain after the first operation. (43)

### **Summary**

Postherpetic neuralgia is a complicated and burdensome neuropathic pain, which influences the individual's daily function and quality of life. Successful management of PHN can be complicated and challenging, especially with the fact that there is no definitive treatment algorithm specifically for patients with PHN. Effective therapy often requires multiple drugs. The most common combination is anticonvulsants, antidepressants and topical lidocaine.

However, the use of these agents can be ineffective and cause bothersome side effects. This is when interventional strategies should be used. The choice of intervention will depend on the region involved, cost, invasiveness and patient opinion.

### **Authors contributions**

Julia Czerwik: Conceptualization, Writing - rough preparation, Methodology, Investigation, Project administration

Joanna Cieszkowska: Formal Analysis, Visualisation

Joanna Dmochowska: Software, Resources

Marta Czubala: Writing – review and editing

Wiktor Wróblewski: Supervision, Data curation

*All authors have read and agreed with the published version of the manuscript.*

### **Funding Statement**

The study did not receive special funding.

### **Institutional Review Board Statement**

Not applicable.

### **Informed Consent Statement**

Not applicable.

### **Data Availability Statement**

The data presented in this study is available upon request from the corresponding author.

### **Acknowledgments**

Not applicable.

### **Conflict of Interest Statement**

All authors declare that they have no conflicts of interest.

## References

1. Saguil A, Kane S, Mercado M, Lauters R. Herpes Zoster and Postherpetic Neuralgia: Prevention and Management. *Am Fam Physician*. 2017;96(10):656-663.
2. Mielniczek K. Botulinum toxin in the treatment of neuralgia and neuropathic pain. *J Educ Health Sport* [Internet]. 2021 Sep. 19 [cited 2024 Jun. 19];11(9):310-4. <https://doi.org/10.12775/JEHS.2021.11.09.038>
3. Borkowska A, Marosz S, Marosz K, Chilimoniuk Z, Sobstyl A, Dudziński D, Chałupnik A, Krupska K, Piecewicz-Szczęśna H. Raising awareness about the importance of chickenpox vaccination in children. *J Educ Health Sport* [Internet]. 2023 Sep. 19 [cited 2024 Jun. 20];19(1):119-28 <https://doi.org/10.12775/JEHS.2023.19.01.012>
4. Johnson RW, Rice AS. Clinical practice. Postherpetic neuralgia. *N Engl J Med*. 2014;371(16):1526-1533. doi:10.1056/NEJMcp1403062
5. Massengill JS, Kittredge JL. Practical considerations in the pharmacological treatment of postherpetic neuralgia for the primary care provider. *J Pain Res*. 2014;7:125-132. Published 2014 Mar 10. <https://doi.org/10.2147/JPR.S57242>
6. Iłżecka J. Hydrotherapy in nervous system diseases. *Pedag Psychol Sport* [Internet]. 2019 Jan. 9 [cited 2024 Jun. 20];5(1):55-60. <https://doi.org/10.12775/PPS.2015.05.01.005>
7. Budzeń K, Wesołowski P, Bąk S, Stachura T, Żelazny P. Lidocaine, old drug - new possibilities. Treatment of postoperative pain and reduction of postoperative complications with intravenous administration. *J Educ Health Sport* [Internet]. 2022 Sep. 14 [cited 2024 Jun. 20];12(9):763-72. <https://doi.org/10.12775/JEHS.2022.12.09.090>
8. Fornasari D, Magni A, Pais P, Palao T, Polati E, Sansone P. Changing the paradigm in postherpetic neuralgia treatment: lidocaine 700 mg medicated plaster. *Eur Rev Med Pharmacol Sci*. 2022;26(10):3664-3676. [https://doi.org/10.26355/eurrev\\_202205\\_28862](https://doi.org/10.26355/eurrev_202205_28862)
9. Baron R, Mayoral V, Leijon G, Binder A, Steigerwald I, Serpell M. Efficacy and safety of 5% lidocaine (lignocaine) medicated plaster in comparison with pregabalin in patients with postherpetic neuralgia and diabetic polyneuropathy: interim analysis from an open-label, two-stage adaptive, randomized, controlled trial. *Clin Drug Investig*. 2009;29(4):231-241. <https://doi.org/10.2165/00044011-200929040-00002>
10. Binder A, Bruxelle J, Rogers P, Hans G, Bösl I, Baron R. Topical 5% lidocaine (lignocaine) medicated plaster treatment for post-herpetic neuralgia: results of a double-blind, placebo-controlled, multinational efficacy and safety trial. *Clin Drug Investig*. 2009;29(6):393-408. doi:10.2165/00044011-200929060-00003

11. Hans G, Sabatowski R, Binder A, Boesl I, Rogers P, Baron R. Efficacy and tolerability of a 5% lidocaine medicated plaster for the topical treatment of post-herpetic neuralgia: results of a long-term study. *Curr Med Res Opin.* 2009;25(5):1295-1305. <https://doi.org/10.2165/00044011-200929060-00003>
12. Yong YL, Tan LT, Ming LC, et al. The Effectiveness and Safety of Topical Capsaicin in Postherpetic Neuralgia: A Systematic Review and Meta-analysis. *Front Pharmacol.* 2017;7:538. Published 2017 Jan 10. <https://doi.org/10.3389/fphar.2016.00538>
13. Derry S, Rice AS, Cole P, Tan T, Moore RA. Topical capsaicin (high concentration) for chronic neuropathic pain in adults. *Cochrane Database Syst Rev.* 2017;1(1):CD007393. Published 2017 Jan 13. <https://doi.org/10.1002/14651858.CD007393.pub4>
14. Irving GA, Backonja MM, Dunteman E, et al. A multicenter, randomized, double-blind, controlled study of NGX-4010, a high-concentration capsaicin patch, for the treatment of postherpetic neuralgia. *Pain Med.* 2011;12(1):99-109. <https://doi.org/10.1111/j.1526-4637.2010.01004.x>
15. Saldaña MT, Pérez C, Navarro A, Masramón X, Rejas J. Pain alleviation and patient-reported health outcomes following switching to pregabalin in individuals with gabapentin-refractory neuropathic pain in routine medical practice. *Clin Drug Investig.* 2012;32(6):401-412. <https://doi.org/10.2165/11599400-000000000-00000>
16. Piotrowska K, Pabianek Łukasz. Physical activity – classification, characteristics and health benefits. *Qual Sport [Internet].* 2019 Aug. 24 [cited 2024 Jun. 20];5(2):7-14. <https://doi.org/10.12775/QS.2019.007>
17. Hempenstall K, Nurmikko TJ, Johnson RW, A'Hern RP, Rice AS. Analgesic therapy in postherpetic neuralgia: a quantitative systematic review. *PLoS Med.* 2005;2(7):e164. <https://doi.org/10.1371/journal.pmed.0020164>
18. Duehmke RM, Derry S, Wiffen PJ, Bell RF, Aldington D, Moore RA. Tramadol for neuropathic pain in adults. *Cochrane Database Syst Rev.* 2017;6(6):CD003726. Published 2017 Jun 15. <https://doi.org/10.1002/14651858.CD003726.pub4>
19. Lin CS, Lin YC, Lao HC, Chen CC. Interventional Treatments for Postherpetic Neuralgia: A Systematic Review. *Pain Physician.* 2019;22(3):209-228.
20. Aggarwal A, Suresh V, Gupta B, Sonthalia S. Post-herpetic Neuralgia: A Systematic Review of Current Interventional Pain Management Strategies. *J Cutan Aesthet Surg.* 2020;13(4):265-274. [https://doi.org/10.4103/JCAS.JCAS\\_45\\_20](https://doi.org/10.4103/JCAS.JCAS_45_20)

21. Xiao L, Mackey S, Hui H, Xong D, Zhang Q, Zhang D. Subcutaneous injection of botulinum toxin a is beneficial in postherpetic neuralgia. *Pain Med.* 2010;11(12):1827-1833. doi:10.1111/j.1526-4637.2010.01003.x
22. Apalla Z, Sotiriou E, Lallas A, Lazaridou E, Ioannides D. Botulinum toxin A in postherpetic neuralgia: a parallel, randomized, double-blind, single-dose, placebo-controlled trial. *Clin J Pain.* 2013;29(10):857-864. <https://doi.org/10.1097/AJP.0b013e31827a72d2>
23. Park J, Park HJ. Botulinum Toxin for the Treatment of Neuropathic Pain. *Toxins (Basel).* 2017;9(9):260. Published 2017 Aug 24. <https://doi.org/10.3390/toxins9090260>
24. Peng F, Xia TB. Effects of Intradermal Botulinum Toxin Injections on Herpes Zoster Related Neuralgia. *Infect Drug Resist.* 2023;16:2159-2165. Published 2023 Apr 12. <https://doi.org/10.2147/IDR.S401972>
25. Cui Y, Zhou X, Li Q, et al. Efficacy of different acupuncture therapies on postherpetic neuralgia: A Bayesian network meta-analysis. *Front Neurosci.* 2023;16:1056102. Published 2023 Jan 10. <https://doi.org/10.3389/fnins.2022.1056102>
26. Watson CPN, Deck JH, Morshead C, Van der Kooy D, Evans RJ. Post-herpetic neuralgia: further post-mortem studies of cases with and without pain. *Pain.* 1991;44(2):105-117. [https://doi.org/10.1016/0304-3959\(91\)90124-G](https://doi.org/10.1016/0304-3959(91)90124-G)
27. Rijdsdijk M, Svensson CI, van Wijck AJ, Kalkman CJ, Yaksh TL. Analgesic properties of intrathecal glucocorticoids in three well established preclinical pain models. *Scand J Pain.* 2016;10:90-102. <https://doi.org/10.1016/j.sjpain.2015.10.006>
28. Ing MR, Hellreich PD, Johnson DW, Chen JJ. Transcutaneous electrical nerve stimulation for chronic post-herpetic neuralgia [published correction appears in *Int J Dermatol.* 2018 Mar;57(3):371]. *Int J Dermatol.* 2015;54(4):476-480. <https://doi.org/10.1111/ijd.12385>
29. Bates JA, Nathan PW. Transcutaneous electrical nerve stimulation for chronic pain. *Anaesthesia.* 1980;35(8):817-822. <https://doi.org/10.1111/j.1365-2044.1980.tb03926.x>
30. Barbarisi M, Pace MC, Passavanti MB, et al. Pregabalin and transcutaneous electrical nerve stimulation for postherpetic neuralgia treatment. *Clin J Pain.* 2010;26(7):567-572. <https://doi.org/10.1097/AJP.0b013e3181dda1ac>
31. Eid MM, Hamed NS, Abdelbasset WK, Elkholi SM, Eladl HM, Bahey El-Deen HA. A comparative study between transcutaneous electrical nerve stimulation and pulsed electromagnetic field therapy in the management of post-herpetic neuralgia of the sciatic nerve. *Medicine (Baltimore).* 2022;101(44):e31433. <https://doi.org/10.1097/MD.00000000000031433>

32. Xu G, Xú G, Feng Y, Tang WZ, Lv ZW. Transcutaneous electrical nerve stimulation in combination with cobalamin injection for postherpetic neuralgia: a single-center randomized controlled trial. *Am J Phys Med Rehabil.* 2014;93(4):287-298. <https://doi.org/10.1097/PHM.0000000000000002>
33. Kalava A, Mihaylov SV, Austin HK, Acharya S. Peripheral Nerve Stimulation for a Refractory Case of Postherpetic Neuralgia in the Upper Limb: A Case Report. *Cureus.* 2024;16(2):e55168. Published 2024 Feb 28. <https://doi.org/10.7759/cureus.55168>
34. Zhao L, Song T. Case Report: Short-Term Spinal Cord Stimulation and Peripheral Nerve Stimulation for the Treatment of Trigeminal Postherpetic Neuralgia in Elderly Patients. *Front Neurol.* 2021;12:713366. Published 2021 Aug 3. <https://doi.org/10.3389/fneur.2021.713366>
35. Niv D, Maltsman-Tseikhin A. Postherpetic neuralgia: the never-ending challenge. *Pain Pract.* 2005;5(4):327-340. <https://doi.org/10.1111/j.1533-2500.2005.00035.x>
36. Dones I, Levi V. Spinal Cord Stimulation for Neuropathic Pain: Current Trends and Future Applications. *Brain Sci.* 2018;8(8):138. Published 2018 Jul 24. <https://doi.org/10.3390/brainsci8080138>
37. Huang M, Chen Q, Wu S, et al. Treatment Efficacy and Technical Advantages of Temporary Spinal Nerve Root Stimulation Compared to Traditional Spinal Cord Stimulation for Postherpetic Neuralgia. *Pain Physician.* 2022;25(6):E863-E873.
38. Isagulyan E, Tkachenko V, Semenov D, et al. The Effectiveness of Various Types of Electrical Stimulation of the Spinal Cord for Chronic Pain in Patients with Postherpetic Neuralgia: A Literature Review. *Pain Res Manag.* 2023;2023:6015680. Published 2023 Mar 24. <https://doi.org/10.1155/2023/6015680>
39. Saxena AK, Lakshman K, Sharma T, Gupta N, Banerjee BD, Singal A. Modulation of serum BDNF levels in postherpetic neuralgia following pulsed radiofrequency of intercostal nerve and pregabalin. *Pain Manag.* 2016;6(3):217-227. <https://doi.org/10.2217/pmt.16.3>
40. Chang MC. Efficacy of Pulsed Radiofrequency Stimulation in Patients with Peripheral Neuropathic Pain: A Narrative Review. *Pain Physician.* 2018;21(3):E225-E234.
41. Fan Z, Zheng X, Li D, Chen H, Li L. Comparison of lidocaine and ropivacaine stellate ganglion blockade in treating upper limb postherpetic neuralgia. *Medicine (Baltimore).* 2022;101(23):e29394. Published 2022 Jun 10. <https://doi.org/10.1097/MD.00000000000029394>
42. Luo Q, Wen S, Tan X, Yi X, Cao S. Stellate ganglion intervention for chronic pain: A review. *Ibrain.* 2022;8(2):210-218. Published 2022 May 28. <https://doi.org/10.1002/ibra.12047>

43. Chun-Jing H, Yi-Ran L, Hao-Xiong N. Effects of dorsal root ganglion destruction by adriamycin in patients with postherpetic neuralgia. *Acta Cir Bras.* 2012;27(6):404-409. <https://doi.org/10.1590/s0102-86502012000600008>