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Review

Different Modalities of Prevention and Treatment in Herpes Zoster

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Abstract

Herpes zoster (HZ) or varicella-zoster virus (VZV) infection is an immersing medical commodity that involves many medical metiers including immunology, dermatology, ophthalmology, and neurology. It can affect patients of any age group ranging from childhood to adulthood and even old age group. Herpes zoster is a transitory disease caused by the recrudescence of latent varicella zoster virus in spinal or cranial sensory ganglia. Herpes zoster is an excruciating vesicular rash in the pretentious dermatome. Varicella is instigated by acute viremia, when the viral infection remains dormant, herpes zoster gets generated, which involves cranial nerve or sensory root ganglia, and it further gets re-activated and spreads from ganglion, through the sensory nerve root, to the main tissue like skin, cornea and auditory canal. Commonly, a solitary dermatome is included albeit two to three neighbouring dermatomes could be included. The lesion rarely crosses the midline. Herpes zoster can likewise give extraordinary or atypical clinical signs, for example, glioma, zoster sine herpete and reciprocal herpes zoster, that is a difficult diagnosis not withstanding for experienced doctors.

Keywords: Herpes Zoster, Post Herpetic Neuralgia, Zoster Sine Herpete, Antiviral Agents, Herpes Zoster Vaccination.

Introduction

Varicella- zoster virus (VZV) infection is an immersing medical commodity that involves many medical metiers including immunology, dermatology (secondary bacterial infection), ophthalmological (keratitis, iridocyclitiss, secondary glaucoma), visceral (pneumonia, hepatitis) and neurological (long term pain, segmental paresis, stroke). It can influence patients from early youth to maturity. Its treatment needs skill in agony the executives and mental help. Reactivation of latent varicella zoster virus is the main cause for Herpes zoster (HZ) in craniospinal sensory neurons and considered as excruciating erythematous rash in its pretentious dermatome. In a lifetime, around 20%-30% of population will be having HZ. Due to ageing and immunosuppressive

disorders or and therapy, incidence of HZ increases when cell-mediated immunity (CMI) against VZV decreases. Varicella-zoster virus is α-herpesvirus. Genotyping has shown that there are five major clades, clade 1 (A), clade 2 (C), clade 3 (D), clade 4 (B) and clade 5 (M1), which have geographical variation (1). The virus gets spread through droplet infection from the nasopharynx. A brief first viraemic stage, when the virus can disseminate to other organs, is followed by a second viraemia coinciding with the onset of the rash.

Patients are infectious to others from about two days before to five days after the onset of the rash and 60–100% of non-immune individuals will contract the infection if exposed to someone in the transmittable period of chickenpox or zoster. Vesicle fluid in either disease contains a large amount of virus or may be a route of droplet infection. Dry scabs are completely un-infectious.

The first is the primary disease characterized by a diffuse, contagious exanthematous vesicular rash known as varicella (chickenpox) and the second is a reactivation disease measured by an aching vesicular dermatome eruption known as herpes zoster (HZ) or shingles. Varicella is instigated by acute viremia, when the viral infection remains dormant, herpes zoster gets generated which involves cranial nerve or sensory root ganglia,and it further gets re-activated and spreads from ganglion, through the sensory nerve root to the main tissuelike **skin**, **cornea** and **auditory canali**. Extension centripetally though the spinal cord and leptomeninges.

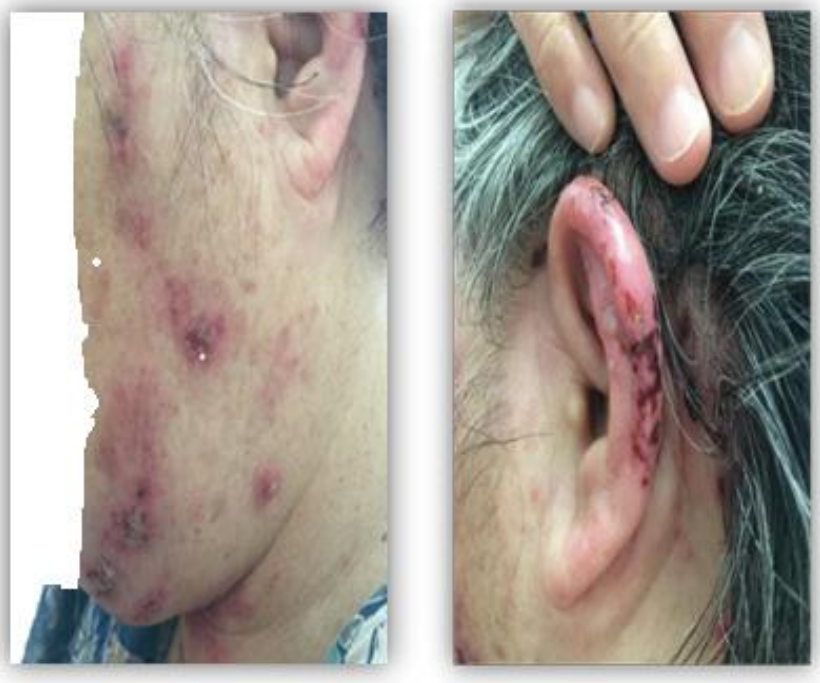

Figure 1. This picture shows the lesions of herpes zoster involving the face and ear following the dermatomes.

Epidemiology

Over 95% of immune compromised individuals aged at least 50years are seropositive for VZV and are therefore **risk of developing Herpes Zoster**. VZV specific cell mediated immunity declines with age concomitantly with the rise in the incidence of HERPES ZOSTER and its complications occurs at about 50years of age. The lifetime risk in incidence of growing Herpes Zoster is between 25% to 30%,

which rise to 50% in aged around at least 80 years. The appraised usual overall incidence of HERPES ZOSTER is about 3.4- 4.82per 1000person years which increments up to more then11 per 1000 person years as compared to those aged up to 80years.

Pathogenesis

Throughout the progression of varicella, Varicella Zoster Virus crosses starting lesions in the skin and a mucosal surface hooked on the transmittable finales of sensory nerves then is elated centripetally up to the sensory fibres to the sensory ganglia. Virus is carried hematogenously to the sensory ganglia across the infected T-cells.

Virus begins a dormant infection which sits for lifetime in the ganglia.The main mechanism behind Herpes Zoster (HZ) is concerned with the dermatomes where the rash associated with varicella attains the maximum density which gets innervated by the first (Opthalmic) division of the Trigeminal nerve and the spinal sensory ganglia starting T1 to L2.

States **like immunosuppression**, emotional stress, irradiation of the spinal column and many other immune compromised states causes the reactivation of VZV.Decline in the VZV-specific immunity which occurs with the increasing age is main responsive factor. Once VZV-specific cellular immunity lowers below some critical level, the virus grows and spread inside the ganglion, resulting neuronal necrosis and intense inflammation,as it is the process which is often go along with severe neuralgia.Varicella- zoster virus **(VZV)**, which are infected spreads consistently towards the sensory nerve, leading to excruciating neuritis, and then it gets released from the sensory nerve endings into the skin, where it produces the characteristic cluster of zoster vesicles. Leptomeninges, cerebral fluid pleocytosis and segmental myelitis is caused mainly due to the transmission through ganglionic infection along the posterior nerve root to meninges and spinal cord (2).

Cerebral or local palsies that convoy the cutaneous eruptions leading to extension within central nervous system is caused by infected motor neurons in the anterior horn and inflammation of anterior nerve root that can result in rare complications of HZ like meningo-encephalitis and transverse myelitis. Herpes also causes viremia.

Clinical Manifestations

1. Prodrome Of Herpes Zoster--

Dermatome involving pain and paraesthesia usually lead to the eruption by several days and differ from shallow itching, tingling, or burning to severe, deep, boring, pain. In the involved dermatome pain could be constant as well as intermittent and is usually carried with tenderness and numbness of the skin. Herpes zoster pain usually coincides with the pain of pleurisy, myocardial infarction, duodenal ulcer, cholecystitis, biliary or renal colic, appendicitis, prolapsed intervertebral disk, and early glaucoma, which may lead to troublesome misdiagnosis and misallocated interventions. Majority of cases with herpes zoster above the age of 60years have prodromal pain but this pain is less common in immune comprised persons below the age of 30. Acute segmental neuralgia without ever developing a cutaneous eruption is experienced by some patients —a condition known as zoster sine herpete.

2. Rash of Herpes Zoster.

Herpes zoster has a common feature which is the location, arrangement, and distribution of the rash, it is always unilateral strictly limitedto areas of skin innervated by a single sensory ganglion. Area which is generally supplied by the 5th cranial nerve,mainly the ophthalmic division, and also trunk following T3 to L2 are most commonly affected; the chest region the sole interpretations for commonly half of generally reported cases, the rash rarely occur distal to the elbows or the knees.

Lesions of herpes zoster usually begins as erythematous macules and papules which usually primarily appear at the main or superficial branches of the exaggerated sensory nerve are weared up, for instance, the posterior primary division alongwith lateral and anterior branches of the anterior primary division of spinal nerves. Generally, within 12-24 hrs, Vesicles are formed which later grow into pustules by 72 hours. Within 7-10 days, these lesions with pustules get dried and crusted. Rash last for longer duration and is most severe in older people whereas in children rash are for shorter duration and less severe (3, 4).

3. Pain of Herpes Zoster.

Commonly, many patients involvedermatomal pains in the acute phase (the 1st 30 days subsequently rash onset) which accounts from mild to severe. The pain is burning type, deep aching, tingling, itching or stabbing type as experienced by patients. Decreased Corporeal functioning, emotive distress, and decreased social functioning is usually associated with acute herpes zoster pain (5, 6).

4. Post Herpetic Neuralgia

It is very common and dreadful clinical consequences of herpes zoster. PHN is a pain syndrome continuously constrained towards originally pretentious dermatome which last for months to year's later persistence of the cutaneous lesions. It is the characteristic neuropathic pain which is extremely severe and debilitating that has a negative effect on the patients physical and mental quality of life (7).

Post herpetic neuralgias are (a) intractable pain, or numerous exanthematous lesions related to the underlying shingles and (b) advanced age are the most important risk factors for future (8). The rule of thumb is that the severity of zoster is directly related to the likelihood of developing PHN. However, accurately predicting which patient will in fact develop this complication is still a clinical challenge.

5. Zoster Sine Herpete

A dermatomal neuropathic pain with puritis with no classical cutaneous manifestations of herpes zoster is known as Zoster sine herpete (9). The diagnosis can be very difficult and depends on positive serology (elevated titres of VZV –specific IgG antibody in serum and CSF) and/ or positive PCR assays (presence of VZV DNA in CSF or in mononuclear cells in peripheral blood) due to the reason there is no rash (9, 10). Only few reports of zoster sine herpeteis registered till now. Many cases remain undiagnosed since many patients suffer from thoracic and abdominal neuropathic pain of unknown origin. To have accurate diagnosis requires a high level of suspicion particularly in patients who complain of persistent, isolated radicular pain. Since Acyclovir treatment has the potential to alleviate pain and improve quality of life so it is very important to diagnose the case (11).

6. Differential Diagnosis

VARICELLA	HERPES ZOSTER
Most Likely	Most Likely
Vesicular exanthems of coxsackieviruses and echoviruses	Zosteriform herpes simplex
Impetigo	Contact dermatitis
Insect bites	Insect bites
Contact dermatitis	Burns
Rickettsialpox	

Consider	**Consider**
Papularurticaria Erythema multiforme Drug eruptions Disseminated herpes simplex Scabies	Papularurticaria Erythema multiforme Drug eruptions Scabies
Rule out	**Rule out**
Secondary syphilis Disseminated herpes zoster Dermatitis herpetiformis Smallpox and other poxviruses	Bullous pemphigoid Pemphigus vulgaris Dermatitis herpetiformis Epidermolysisbullosaherpetiformis

7. Complications

Cutaneous	**Visceral**	**Neurologic**
Bacterial superinfection Scarring Zoster gangrenosum Cutaneous dissemination	Pneumonitis Esophagitis Gastritis Cystitis Hepatitis Arthritis Pericarditis	Post herpetic neuralgia Meningoencepahalitis Transverse myelitis Motor Autonomic Peripheral nerve palsies Cranial nerve palsies Sensory loss Deafness Ocular complications Granulomatous angiitis (causing contralateral hemiparesis)

Diagnosis

Polymerase chain reaction (PCR) assay, skin biopsy, immunofluorescence assay, and viral isolation are the main diagnostic laboratory tests for herpes zoster. Patients having atypical lesions like herpes simplex, as well as contact dermatitis and rash are the main candidates for the diagnosis. But the results of these tests differ in terms of sensitivity, specificity, and time to obtain sample. Therefore, these tests have limitations for application in the clinical management of HZ (12).

Treatment

1. Topical therapy

During the acute phase of herpes zoster, the application of cool compresses, calamine lotion, corn-starch, or baking soda may help to alleviate local symptoms and speed the dehydrating of vesicular lesion.

Occlusive ointments should be avoided, and creams or lotions containing glucocorticoids should not be use. Topical treatment with antiviral agents is not effective.

2. Antiviral drugs

The first line of treatment for three groups of herpes zoster patients are Famciclovir, Valacyclovir and Acyclovir.

The three groups of patients are:

1) Cell-mediated immune-compromised patients.
2) Immuno-competent patients with patients with severe clinical course, i.e. moderate to severe pain, moderate to severe rash, non-truncal involvement and/or manifestations of herpes zoster complications.
3) Patients 50 years old or above (13).

These Guanosine-analogue antiviral drugs are very safe. Goals of therapy are to shorten the duration of the disease, remove the severity of acute pain, and limit viral shedding and the formation of new vesicles (14).

Standard antiviral dosage regimens for non-compromised patient as follows.

a) Normal patients

Age <50 years

Symptomatic treatment alone, or

Famciclovir 500 mg PO every 8 h for 7 days or

Valacyclovir 1 g PO every 8 h for 7 days or

Acyclovir 800 mg PO 5 times a day for 7 days.

Age ≥50 years, and patients of any age with cranial nerve involvement (e.g., ophthalmic zoster)

Famciclovir 500 mg PO every 8 h for 7 days or

Valacyclovir 1 g PO every 8 h for 7 days or

Acyclovir 800 –mg PO 5 times a day for 7 days

b) Immunocompromised patients

Mild compromise, including HIV-1 infection

Famciclovir 500 mg PO every 8 h for 7–10 days or

Valacyclovir 1 g PO every 8 h for 7–10 days or

Acyclovir 800 mg PO 5 times a day for 7–10 days

c) Severe compromise patients

Acyclovir 10 mg/kg IV every 8 h for 7–10 days

Acyclovir resistant (e.g., advanced AIDS) Foscarnet 40 mg/kg IV every 8 h until healed

Usually, patient passivity with valacyclovir and famciclovir is suggestively improved as compared with acyclovir, as valacyclovir and famciclovir are more bio- available than acyclovir. Acyclovir requires dose monitoring (15). Non dependent on viral phosphorylation, which noncompetitively block viral DNA polymerase are Foscarnet, vidabarine and cidofovir. Foscarnet is effective to treat viral infection in patients who have resistance to acyclovir (16).

3. Corticosteroids

Corticosteroids do not play important role in treatment of Postherpetic neuralgia but has significant effect on Herpes Zoster. Pain generating from Herpes Zoster usually gets relieved when combined with antiviral therapy, oral or intravenous administration of corticosteroids, compared with treatment with antiviral therapy alone, but is not effective for the prevention of PHN(17). Corticosteroids brings itself many side effects therefore physicians consider combination of corticosteroids with antiviral treatment for herpes

Zoster patients who have severe symptoms without any contraindications to therapy (16) (17).

4. Analgesics

Though antiviral treatment can reduce the acute pain from HZ, still most patients will require analgesics. PHN progression will be drastically reduced due to administration of analgesics. Non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen usually prescribed, but there is no evidence which proves the analgesic effects of NSAIDs in relieving pain from HZ. In relieving HZ pain, opioids play a great role (18). Adjuvant analgesics such as antidepressants and anticonvulsants are effective to lower down acute pain caused by HZ in addition (16).

5. Post-exposure prophylaxis and infection control

VZV may be transmitted to susceptible individuals where patients who are affected with varicella and herpes zoster. High-titer immunoglobulin (VariZIG) vaccination is used for preventive measures with post-exposure chemoprophylaxis with acyclovir. If in condition within 3 days of exposure, active immunization with the live attenuated varicella vaccine is effective in averting illness or amending varicella severity in children. Protection given by zoster immune globulin is transient, varicella vaccine induces long-lasting (active) immunity to VZV and protection against subsequent exposures. That's the reason when the ACIP recommends varicella vaccine for postexposure prophylaxis in unvaccinated persons without evidence of immunity (19) .

6. Interventional treatments

Sympathetic blockade and neuraxial blockade has been used for the treatment of pain caused by HZ along with the prevention of the development of PHN. A single epidural injection of 80mg methyl prednisolone acetate plus bupicaine drastically reduces pain, but not effective for prevention of PHN, compared to with oral antiviral and analgesic comparison (20). According to the demanding and strong evidence from a recent systemic review on the effect of intervention on HZ altogether, epidural administration of local anesthetics and steroids for the treatment of acute pain from HZ and the prevention of PHN plays the important role. The incidence of PHN can be prevented within 2 months of development of HZ by administration of epidural administration of local anesthetics and steroids (21). Unilateral segmental block that includes the spinal nerve dorsal ramus, communicants, and the sympathetic chain is produces by PVB (para-vertebral block). In comparison to epidural block, PVB is easier with less side effects with similar analgesic efficacy. The clinical trials states that the PVB with local anesthetics and steroids plays effective role in relief of acute pain due to herpes zoster and prevents the rate of occurrence of PHN.

7. Treatment of Post herpetic neuralgia (PHN)

1) Pharmacological treatment

Antidepressants

Antidepressants like Tricyclic antidepressants (TCAs) such as tertiary amines (amitriptyline) and the secondary amines (nortriptyline and desipramine) shows grate effectiveness in lowering down the chronic pain of PHN. Consequently, if conventional analgesic treatment is not effective, TCA are used for controlling pain in Herpes Zoster. The mechanism of action of TCA is to utilize analgesic effects by prohibiting the reuptake of serotonin and norepinephrine at presynaptic nerve terminals and blocking sodium channels. Number needed for the treatment of PHN was2.1 to 2.6 as in clinical trials and meta-analysis of TCAs (22). Side effects are greatly seen using TCAs it prompts several anticholinergic side effects including dry mouth, gastrointestinal discomfort, constipation, urinary retention, nausea, vomiting, blurred vision, orthostatic hypotension, and confusion. Some

life-threatening condition like fatal cardiac dysrhythmias such as QT prolongation, torsades de pointes, and sudden cardiac arrest in patients with conduction abnormalities can also occur (23). Thereby, in order to prevent such conditions clinicians should review a baseline electrocardiogram before initiating treatment with TCAs in elderly patients and patients with a history of cardiovascular disease or hypokalemia. Low dose does not bring adverse effects, side effects are less pronounced. A low dose of TCA of10 mg at bedtime should be started and titrated gradually every week to a target dose of 50-100 mg/day. In elderly patients, nortriptyline and desipramine appear to be better tolerated in comparison with imitriptyline.

SNRIs (serotonin and nor epinephrine reuptake inhibitors) like Duloxetine and venlafaxine are also used for the treatment of acute pain from HZ and PHN. Patients with painful neuropathic disorders have proven to have analgesic effect with these drugs. Pharmacologically and clinically SNRIs may be better tolerated than TCAs due to their favourable side effect (24).

Anticonvulsants

A neuropathic pain disorder which includes trigeminal neuralgia and PHN are significantly reduced using numerous anticonvulsants. The first and second generation's anticonvulsants are used for the treatment of PHN, among which second generation anticonvulsants like pregabalin and gabapentin are safe and well tolerated in comparison with first generation anticonvulsants including valproic acid and carbamazepine. The mechanism of action is unknown. Pregabalin and gabapentin are synergistically agonist drugs.

They act at the a28 subunits of voltage-gated calcium channels, with a consequent reduction in the release of excitatory neurotransmitters including glutamate. Anticonvulsants are not metabolized in liver and remain unchanged in urine. So, dosage should be adjusted according to the reports of the renal function. Gabapentin efficacy was demonstrated with an NNT of 2.8 for moderate improvement in PHN in clinical trials [25]. Dose adjustment is required after the prescription of gabapentin which ranges as 3 to 4 doses per day to minimize the side effects. Gabapentin administration reported somnolence, dizziness, peripheral edema, and ataxia in some patients (25). Predictable and linear pharmacokinetic profile is seen using Pregabalin as compared with gabapentin due to its predictable and linear pharmacokinetic profile. Pregabalin in comparison with gabapentin, which has same analgesic levels but less side effects. So, titration of pregabalin to the therapeutic dose range is more rapid [26]. Pregabalin can be given in two divided doses per day, offering greater convenience than gabapentin (26) (27).

Opioids

Accordingly, the role of opioids in the management of neuropathic pain is Somewhat reduced by administration of opoids recently, however, many clinical studies have demonstrated that the use of opioids is effective to ameliorate neuropathic pain including

PHN (22, 28). Opioid treatment brings many adverse effects which include nausea, pruritus, dizziness, sedation, and constipation. These side effects do not last for long time except the constipation. Consequently, when prescribing opioids, constipation prophylaxis should be kept in mind.

Tramadol

Tramadol, a synthetic 4-phenyl-piperidine analogue of codeine, acts as a ^-opioid receptor agonist and a serotonin and nor-epinephrine reuptake inhibitor. Tramadol has the similarities with an opioid and a TCA. Nausea, dizziness, constipation, somnolence, and headache are the common side effects. Concomitant use with selective serotonin reuptake inhibitors or selective monoamine oxidase inhibitor TCAs can lead to serotonin syndrome or seizures (29).

Topical lidocaine

The local analgesia to affected area is caused using 5% lidocaine patch, without causing local anesthesia. The skin which is affected by the mechanical irritation is treated by lidocaine patch.

2) Interventional treatments

Nerve block

Epidural block, intrathecal injection, and sympathetic nerve block which are the interventional treatments are of very less important for the treatment of PHN (30). Patients with PHN have not got relieved by the use of epidural block with local anesthetics and steroids. Intrathecal administration of steroids has some effects in patients with PHN (31). Risk of developing of adhesive arachnoiditis is high. Sympathetic nerve block brings some impact in patients with acute HZ but has no long term pain relief PHN patients.

Spinal cord stimulation (SCS)

For the management of chronic neuropathic pain disorders SCS has been used (32). SCS provided significant long n clinical trials, the lidocaine patch for PHN term pain relief in 82% of PHN patients. In addition, in 2.5 month period of SCS treatment, the pain was resolves with HZ. Therefore, SCS can act as treatment option for the management of intractable pain from PHN and re-duce the incidence of PHN.

Prevention

Vaccination with live attenuated VZV significantly reduced the incidence of HZ by 51.3% in a large multicenter RCT trial among 38000 population (2,19). Multiplication of latent VZV in the spinal or cranial sensory ganglia mainly occurs as gradual decrease of VZV-specific CMI below the critical threshold. Vaccines bring minor side effects like erythema, pain, and itching sensation at the injection site, along with rise in temperature. Accordingly, we can conclude that vaccination against VZV could be the 1st line for the prevention of HZ and PHN. This live attenuated vaccine is contraindicated in pregnant women and immune compromised individuals.

Conclusion

As the age increases the incidence of HZ also increases. In the future, the general population growth ages, the number of patients with HZ and PHN may increase accordingly. The most common complication of HZ is PHN which is very complicated to treat. Early diagnosis of HZ and prompt treatment with antiviral agents along with the use of interventional treatments gradually and mostly shorten the duration and severity of pain from HZ and prevent the occurrence of PHN. Addition we also conclude that prophylactic vaccination against HZV can be the best opinion to prevent or reduce the incidence of HZ and PHN.

HZ with atypical presentation sometimes brings challenging steps for most clinicians the severity should be judged accordingly and proper management with drugs and therapies should be used. The most important aspect of HZ is pain reduction.

Declaration

1) ***Consent to publication***
   We declare that all authors agreed to publish the manuscript at this journal based on the signed Copyright Transfer Agreement and followed publication ethics.
2) ***Ethical approval and consent to participants***
   We declare that our research protocol involving humans or animals were approved by the Institutional Ethics Committee and they obtained Informed Consent from Participants enrolled in our study.
3) ***Disclosure of conflict of interests***
   We declare that no conflict of interest exists.
4) ***Funding***

None

5) ***Availability of data and material***

We declare that the data supporting the results reported in the article are available in the published article.

6) ***Authors' Contributions***

Authors contributed to this paper with the design (SK), literature search (SK), drafting (SK), revision (SK), editing (SK and MS)and final approval (SK).

7) ***Acknowledgement***

None

8) ***Authors' biography***

None

References

1. Weinberg, J.M., Herpes zoster: epidemiology, natural history, and common complications. J Am Acad Dermatol, 2007. 57(6 Suppl): p. S130-5.

2. Levin, M.J., et al., Decline in varicella-zoster virus (VZV)-specific cell-mediated immunity with increasing age and boosting with a high-dose VZV vaccine. J Infect Dis, 2003. 188(9): p. 1336-44.

3. Arvin, A.M., Humoral and cellular immunity to varicella-zoster virus: an overview. J Infect Dis, 2008. 197 Suppl 2: p. S58-60.

4. Hope-Simpson, R.E., THE NATURE OF HERPES ZOSTER: A LONG-TERM STUDY AND A NEW HYPOTHESIS. Proc R Soc Med, 1965. 58: p. 9-20.

5. Katz, J., et al., Acute pain in herpes zoster and its impact on health-related quality of life. Clin Infect Dis, 2004. 39(3): p. 342-8.

6. Schmader, K.E., et al., The impact of acute herpes zoster pain and discomfort on functional status and quality of life in older adults. Clin J Pain, 2007. 23(6): p. 490-6.

7. Lukas, K., A. Edte, and I. Bertrand, The impact of herpes zoster and post-herpetic neuralgia on quality of life: patient-reported outcomes in six European countries. Z Gesundh Wiss, 2012. 20(4): p. 441-451.

8. Drolet, M., et al., Predictors of postherpetic neuralgia among patients with herpes zoster: a prospective study. J Pain, 2010. 11(11): p. 1211-21.

9. Kennedy, P.G., Zoster sine herpete: it would be rash to ignore it. Neurology, 2011. 76(5): p. 416-7.

10. Blumenthal, D.T., et al., Zoster sine herpete: virologic verification by detection of anti-VZV IgG antibody in CSF. Neurology, 2011. 76(5): p. 484-5.

11. Gilden, D.H., et al., Zoster sine herpete, a clinical variant. Ann Neurol, 1994. 35(5): p. 530-3.

12. Espy, M.J., et al., Diagnosis of varicella-zoster virus infections in the clinical laboratory by LightCycler PCR. J Clin Microbiol, 2000. 38(9): p. 3187-9.

13. Dworkin, R.H., et al., Recommendations for the management of herpes zoster. Clin Infect Dis, 2007. 44 Suppl 1: p. S1-26.

14. Wood, M.J., et al., Oral acyclovir therapy accelerates pain resolution in patients with herpes zoster: a meta-analysis of placebo-controlled trials. Clin Infect Dis, 1996. 22(2): p. 341-7.

15. Shen, M.C., et al., Double-blind, randomized, acyclovir-controlled, parallel-group trial comparing the safety and efficacy of famciclovir and acyclovir in patients with uncomplicated herpes zoster. J Microbiol Immunol Infect, 2004. 37(2): p. 75-81.

16. De Clercq, E., Selective anti-herpesvirus agents. Antivir Chem Chemother, 2013. 23(3): p. 93-101.

17. Whitley, R.J., et al., Acyclovir with and without prednisone for the treatment of herpes zoster. A randomized, placebo-controlled trial. The National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Ann Intern Med, 1996. 125(5): p. 376-83.

18. Dworkin, R.H., et al., A randomized, placebo-controlled trial of oxycodone and of gabapentin for acute pain in herpes zoster. Pain, 2009. 142(3): p. 209-17.

19. Leung, J., et al., Varicella Vaccination Among US Adolescents: Coverage and Missed Opportunities, 2007-2014. J Public Health Manag Pract, 2019. 25(3): p. E19-e26.

20. van Wijck, A.J., et al., The PINE study of epidural steroids and local anaesthetics to prevent postherpetic neuralgia: a randomised controlled trial. Lancet, 2006. 367(9506): p. 219-24.

21. Kumar, V., K. Krone, and A. Mathieu, Neuraxial and sympathetic blocks in herpes zoster and postherpetic neuralgia: an appraisal evidence of current. Reg Anesth Pain Med, 2004. 29(5): p. 454-61.

22. Hempenstall, K., et al., Analgesic therapy in postherpetic neuralgia: a quantitative systematic review. PLoS Med, 2005. 2(7): p. e164.

23. Vieweg, W.V. and M.A. Wood, Tricyclic antidepressants, QT interval prolongation, and torsade de pointes. Psychosomatics, 2004. 45(5): p. 371-7

24. Zin, C.S., et al., An update on the pharmacological management of post-herpetic neuralgia and painful diabetic neuropathy. CNS Drugs, 2008. 22(5): p. 417-42.

25. Rowbotham, M., et al., Gabapentin for the treatment of postherpetic neuralgia: a randomized controlled trial. Jama, 1998. 280(21): p. 1837-42.

26. Sabatowski, R., et al., Pregabalin reduces pain and improves sleep and mood disturbances in patients with post-herpetic neuralgia: results of a randomised, placebo-controlled clinical trial. Pain, 2004. 109(1-2): p. 26-35.

27. Christo, P.J., G. Hobelmann, and D.N. Maine, Post-herpetic neuralgia in older adults: evidence-based approaches to clinical management. Drugs Aging, 2007. 24(1): p. 1-19.

28. Watson, C.P., et al., Controlled-release oxycodone relieves neuropathic pain: a randomized controlled trial in painful diabetic neuropathy. Pain, 2003. 105(1-2): p. 71-8.

29. Boureau, F., P. Legallicier, and M. Kabir-Ahmadi, Tramadol in post-herpetic neuralgia: a randomized, double-blind, placebo-controlled trial. Pain, 2003. 104(1-2): p. 323-31.

[30] Doi, K., et al., Intercostal nerve block with 5% tetracaine for chronic pain syndromes. J Clin Anesth, 2002. 14(1): p. 39-41.

[31] Kotani, N., et al., Intrathecal methylprednisolone for intractable postherpetic neuralgia. N Engl J Med, 2000. 343(21): p. 1514-9.

[32] Jeon, Y.H., Spinal cord stimulation in pain management: a review. Korean J Pain, 2012. 25(3): p. 143-50.

30. Doi, K., et al., Intercostal nerve block with 5% tetracaine for chronic pain syndromes. J Clin Anesth, 2002. 14(1): p. 39-41.

31. Kotani, N., et al., Intrathecal methylprednisolone for intractable postherpetic neuralgia. N Engl J Med, 2000. 343(21): p. 1514-9.

32. Jeon, Y.H., Spinal cord stimulation in pain management: a review. Korean J Pain, 2012. 25(3): p. 143-50.