



Review Article

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Management of Herpes zoster: a review

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Abstract

Streblus asper Lour. (Moraceae) is a small tree found in tropical regions of the world and used for the treatment of fever, diarrhea, dysentery, elephantiasis, filariasis, gingivitis, leprosy, piles, skin diseases, toothache and wounds. Phytochemical investigation of a methanol extract of the roots led to the isolation of two new compounds characterized as lup-20(29)-en-3 β -olyl octadec-9'-enoate (1) and stigmast-5-en-3 β -olyl-26-oic acid-3 β -hexadecanoate (4) together with the four known constituents identified as lupeol linoleate (2), stigmasterol palmitate (3), cerotic acid (5) and octacosanoic acid (6). The structures of all these compounds were elucidated on the basis spectral data analysis and chemical reactions.

Keywords: Herpes zoster, Management of Herpes zoster, Antiviral Agents

Introduction

Herpes zoster (HZ) or "shingles" is one of the most common neurological conditions worldwide. It occurs as a result of a reactivated varicella zoster virus (VZV) infection. Anaesthetists and pain specialists may find themselves consulted to manage the often severe and disabling pain of an acute episode. To prevent progression to post herpetic neuralgia (PHN), a potentially crippling persistent disorder, early intervention is imperative. The purpose of this paper is to review current guidelines for the management of HZ.

Management

The principal goals for the treatment of herpes zoster involve reduction of pain and cessation of viral replication. The treatment protocol includes^[1,2]

1. Patient Education
2. Conventional Medicinal Regimen
 - Antiviral agents
 - Corticosteroids
 - Analgesics and non-steroidal anti-inflammatory drugs (NSAIDS)
 - Tricyclic antidepressants
1. Natural treatment options
 - Dietary/ multiple nutrients
 - Enzyme therapy
 - Botanicals with special efficacy for herpes zoster
2. Others

1. Patient Education

The treatment of herpes zoster should occur in conjunction with appropriate education and support from the health care providers. Careful explanation of the disease regarding the risk of viral transmission to individuals and the proposed treatment plan is essential for adherence to therapy. It is beneficial to patients so as to reassure and educate them regarding the dispel myths or fears about herpes zoster and its implications for their health. Encouragement, reassurance and advice on quality of life are also important and include supporting adequate nutrition and optimal levels of mental, physical, and social activity. Patients should be advised:-

- To keep the rash clean and dry so as to reduce the risk of bacterial super infection.
- To avoid use of topical antibiotics and dressings with adhesive that can cause irritation and delay in rash healing.

2. Conventional Medicinal Regimen

A. Antiviral Agents

Currently treatment of herpes zoster with antiviral medication appears to be the method of choice, particularly when treating elderly and immunocompromised patients. Although multiple clinical investigations have demonstrated efficacy in reducing both duration of the rash and severity of the associated pain^[3], but benefit has only been demonstrated in patients who received treatment within 72 hours after onset of the rash. The three most commonly used antiviral agents used in treatment of herpes zoster are:-

- ❖ Acyclovir (Zovirax)
- ❖ Valacyclovir (Valtrex)
- ❖ Famciclovir (Famvir)

Medication	Dosage	Duration Of Treatment
Acyclovir	800 mg five times daily	7-10 days
Famciclovir	500 mg three times daily	7 days
Valacyclovir	1000 mg three times daily	7 days

These medications are generally well-tolerated with the most common side effects being abdominal pain, nausea, vomiting, dizziness and headache.

Administration of gabapentin (1000 mg thrice daily) in conjunction with these antiviral agents during the acute phase of zoster may offer further protection against post herpetic neuralgia^[4].

B. Corticosteroids

Oral corticosteroids have commonly been used for pain management in herpes zoster although clinical trials have yielded inconsistent results for reducing development of post herpetic neuralgia. One study has also demonstrated a significant reduction in pain associated with herpes zoster by usage of a combination of prednisone and acyclovir^[5,6].

C. Analgesics and NSAIDs

The pain associated with herpes zoster covers a broad spectrum of intensity. Generally individuals with mild-to-moderate pain find sufficient relief via topical or oral analgesics and anti-inflammatory agents. Several studies have observed that topical aspirin preparations can provide effective temporary relief in cases of acute herpetic neuralgia and post herpetic neuralgia^[7]. In one randomized trial comparing the efficacy of a topical aspirin-moisturizer (75 mg aspirin/ml of moisturizer three times daily) to oral aspirin (375-750 mg three times daily) for 21 days, has shown that topical preparation provided quicker and longer pain relief as compared to oral aspirin^[8,9].

D. Tricyclic Antidepressants

Low-dose tricyclic antidepressants (TCAs) have also been used for PHN. Although TCAs lessens the pain by inhibiting the reuptake of serotonin and norepinephrine but they require at least three months for positive effects^[10]. Antidepressants usually prescribed for herpes zoster includes:- Amitriptyline (Elavil), Nortriptyline (Pamelor), Imipramine (Tofranil) and Desipramine (Norpramin)^[11].

• Amitriptyline (Elavil)	10 to 25 mg orally once a day at bedtime; increase dosage by 25 mg every 2 to 4 weeks until response is adequate or to maximum dosage of 150 mg per day.
• Nortriptyline (Pamelor)	10 to 25 mg orally once a day at bedtime; increase dosage by 25 mg every 2 to 4 weeks until response is adequate or to maximum dosage of 125 mg per day.
• Imipramine (Tofranil)	25 mg orally once a day at bedtime; increase dosage by 25 mg every 2 to 4 weeks until response is adequate or to maximum dosage of 150 mg per day.
• Desipramine (Norpramin)	25 mg orally once a day at bedtime; increase dosage by 25 mg every 2 to 4 weeks until response is adequate or to maximum dosage of 150 mg per day.

3. Natural Treatment Options

Acyclovir and other antiviral drugs have provided a major advancement in the treatment of herpes zoster and post herpetic neuralgia. However, area of growing concern is the appearance of acyclovir-resistant Herpes strains among immunosuppressed patients, such as organ transplant recipients and patients with HIV/AIDS^[12]. As with conventional protocols, the objective of natural therapeutics in the prevention and treatment of herpes zoster and post herpetic neuralgia is to facilitate healing of skin lesions, reduce pain and prevent complications. An underlying goal for employing natural therapies is to strengthen cell-mediated immunity thereby allowing the body's natural defence mechanisms to control the virus and prevent recurrence. Henceforth, natural therapies can prevent and treat complications and can minimize the risk of developing viral resistance.

• Dietary/Multiple-Nutrient Effects

Incidence of herpes zoster rises sharply after the age 50 years. One possible explanation is the potential decline in immune competence (immunosuppression). Maintaining adequate nutrition is one contributing factor to ensuring healthy cell-mediated immunity. A study by Thomas *et al.* in 2006 reviewed 243 cases of herpes zoster and concluded that individuals who ate less than one serving of fruit or vegetables weekly had a three-fold greater risk of zoster as compared to those who ate more than three servings daily^[13]. Hence, it is thought that nutrients may act synergistically to maintain healthy immune function and consequently decreases the risk of herpes zoster.

Vitamin A functions both as a fat-soluble vitamin and a hormone, contributing to the visual pigment rhodopsin and controlling gene transcription that allows normal proliferation and differentiation of epithelial cells. It is a key immune modulator, involved in the synthesis of lymphocytes, neutrophils, cytokines and immunoglobulins. Its deficiency has also been associated with increased susceptibility to numerous infectious diseases including herpes zoster^[14].

• Enzyme Therapy

Prior to the introduction of acyclovir, pancreatic enzyme preparations were used effectively in Germany as a treatment for herpes zoster. Such historical application led researchers to conduct a comparison trial^[15].

In a double-blind controlled trial two groups of 96 herpes zoster patients were given either acyclovir (800 mg) or an enzyme preparation (120 mg trypsin, 40 mg chymotrypsin, and 320 mg papain) five times daily for seven days and were followed for 14 days. During the course of the study, the intensity of pain and reddening of skin lesions were measured. No statistically significant difference was seen between the two groups either in pain intensity or reddening of skin lesions during the first seven days. However, on day 14 a significant decrease in skin reddening was noted in the acyclovir group while no other parameters

revealed statistically significant differences. Overall the study concluded that the enzyme preparation was just as effective as acyclovir. The suspected mechanisms of action for the enzyme formula included stimulating breakdown of immune complexes and enhancing cell-mediated immunity^[16].

Botanicals with Specific Efficacy for Herpes Zoster

a. Capsaicin (from *Capsicum frutescens*)

Capsaicin is an alkaloid derived from cayenne pepper (*Capsicum frutescens*). Capsaicin causes an increase in the release of substance P. Eventually the substance P is depleted and further releases from the nerve ending are reduced^[17]. Creams containing capsaicin have reduced post-operative pain associated with mastectomy patients and for amputees suffering from phantom limb. Prolonged use of the cream has also been found to reduce the pain occurring because of shingles (Herpes zoster).

b. Licorice (*Glycyrrhiza glabra*)

Licorice is one of the most widely used herbs in traditional medicine spanning many generations and several continents. It possesses properties of an anti-inflammatory, mucoprotectant and antiviral agents. This suggested that it may have potential value in the treatment of herpes zoster^[18]. One of its constituent named glycyrrhizin can inhibit viral growth and may also inactivate viral particles. It has demonstrated antiviral activity in vitro against various forms of herpes virus including varicella zoster virus^[143].

c. Madonna Lily (*Lilium candidum*)

In northern Italy, traditional folk medicine has identified *Lilium candidum* as an herbal treatment for herpes zoster.¹⁹ Bulbs of cultivated *L. candidum* have yielded successful results when fried in olive oil and applied externally as a poultice on herpes zoster lesions. Healing properties are thought to come from the presence of eight spirostanol saponins and two furostanol saponins identified in the bulb of the plant^[20].

d. Reishi Mushroom (*Ganoderma lucidum*)

A few small studies have documented the effect of *Ganoderma lucidum* alone or in combination with other herbs for the treatment of herpes zoster or post herpetic neuralgia^[21]. One case study on two patients with herpes zoster and two patients with post herpetic neuralgia demonstrated that administration of hot-water-soluble extracts of *Ganoderma lucidum* (36-72 g dry wt/day) had a dramatic effect on decreasing pain. In another small clinical trial, five patients with herpes zoster experienced almost complete pain relief within 10 days of treatment with an oral preparation consisting of *Ganoderma lucidum*, *Wisteria floribunda*, *Trapa natans*, *Miristica agrans*, *Coix lachryma-jobi*, *Elfuinga applanata*, *Panax ginseng* and *Punicagranatum*^[22].

e. Bi Phaya Yaw (*Clinacanthus nutans*)

Clinacanthus nutans a small shrub found in Southeast Asia has long been used in Thailand as a traditional medicine for snake and insect bites and various other skin ailments.²³ Several studies have documented its benefit for herpes zoster. One randomized, placebo controlled trial was performed on 51 herpes zoster patients using a topical preparation of *C. nutans* extract applied five times daily for 7-14 days. This was followed by resolution of the herpetic lesions^[24].

f. Other Botanical Considerations

The following botanicals or plant extracts when used in vitro or vivo have demonstrated efficacy against HSV type 1 and 2. They have also been highlighted to be possibly considered in the management of herpes zoster^[25-30]. These include:-

- Honey/Propolis
- Sangre de Grado (*Croton lechleri*)
- Aloe (Aloe vera)
- St John's wort (*Hypericum perforatum* and spp)

4. Others

• Acupuncture

Acupuncture has long been regarded as an effective therapy for pain management. Several cases have been documented on its use in herpes zoster and post herpetic neuralgia. One study documented a case of a 52-year-old male with post herpetic neuralgia that was successfully treated after four treatments using a combination of acupuncture and moxibustion^[31,32].

• TENS

Use of transcutaneous electrical nerve stimulation (TENS) therapy has been beneficial in the management of post herpetic neuralgia^[33,34].

In one review the use of combination therapy consisting of amitriptyline, topical capsaicin and transcutaneous electrical nerve stimulation was recommended for the treatment of post herpetic neuralgia over antiviral therapy^[35].

Conclusion

Herpes zoster infection is an often painful condition which may progress to persistent pain. It is imperative to manage the symptoms early and aggressively. Evidence based management guidelines are useful for both the primary care physician and the specialist. The management of HZ may affect the patient's outcome including future quality of life. Future studies should address the effect of management on both pain and quality of life.

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