

Diagnosis and management of postherpetic neuralgia

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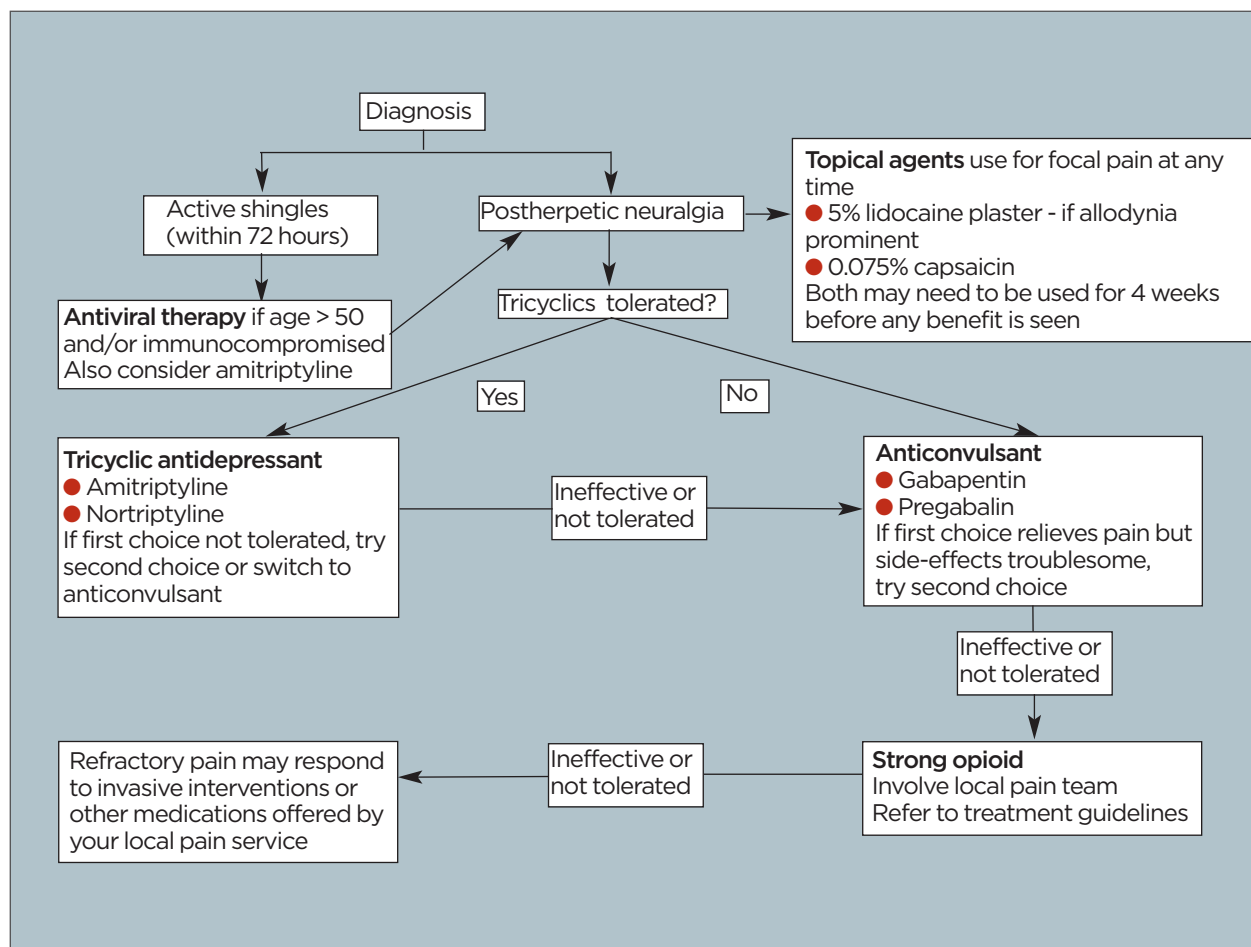


FIGURE 1
Treatment algorithm
for postherpetic
neuralgia

How do patients present?



FOLLOWING AN INITIAL CHICKENPOX INFECTION WITH VARICELLA-ZOSTER IN CHILDHOOD OR EARLY

adulthood, the virus remains dormant in the nerve cell bodies of the asymptomatic host.¹ Less commonly it becomes latent in the satellite cells of the dorsal root, cranial nerves or autonomic ganglia.²

Reactivation of the latent herpes zoster virus occurs in 50% of those who reach the age of 85. The reduction in cell-mediated immunity that accompanies ageing is thought to be accountable for this viral recrudescence which, in

What are the treatment approaches?

turn, leads to an acute, often painful rash commonly referred to as shingles or acute herpetic neuralgia.¹

Pain usually subsides within three to five weeks, but a significant number of patients develop persistent pain classified as sub-acute herpetic neuralgia, 30-120 days following rash onset, and postherpetic neuralgia (PHN), 120 days following rash onset.^{3,4}

Risk factors for PHN include:

- Increasing age. Age confers considerable risk with 40% of patients over 50 and 75% of those over 75 going on to develop PHN following resolution of the rash⁵⁻⁷

Which patients should be referred?

- A prodrome of pain before rash onset
- The degree of spread of the rash, particularly if it extends beyond a single dermatome
- Severity of pain during the acute attack⁵

The exact pathogenesis of why some individuals go on to develop PHN is yet to be fully established. Examination of pathological specimens from the ganglia of those with persistent pain has demonstrated a diffuse infiltration of chronic inflammatory cells.^{8,9} The discovery of varicella-zoster proteins incorporated»

within mononuclear cells of the peripheral blood of patients with PHN further supports the theory that a chronic low-grade ganglionitis is responsible.^{10, 11}

'75% of those over 75 go on to develop postherpetic neuralgia following resolution of the rash'

PRESENTATION

Following a history of acute herpes zoster infection with a resultant rash, patients may present with pain within the timescales defined above.

Pain in PHN can be either constant or paroxysmal and is commonly described as burning, stabbing or itching in character and located in the same dermatomal distribution as the shingles rash.

Precipitation of the pain by a non-painful stimulus such as touch or pressure (e.g. from clothing) is referred to as allodynia, which can accompany hyperalgesia (intense exaggerated pain from a painful stimulus). These are frequently distressing features of PHN, which can lead to sleep disturbance, anorexia, reduced socialisation and reactive depression.¹²

PREVENTION

A detailed approach to the management of acute herpetic neuralgia is beyond the scope of this article. However, the way that acute herpetic neuralgia is managed does have implications for the subsequent development of PHN. The antiviral agents aciclovir, valaciclovir and famciclovir are known to reduce the pain of acute shingles and hasten the resolution of the skin lesions.¹³⁻¹⁵ Despite this, antiviral treatment is probably underprescribed with some studies reporting treatment rates in the community setting of approximately 40%.¹⁶

In addition to treating the acute presentation, earlier evidence in the literature tended to support the use of antiviral agents for reduction of both the incidence and severity of PHN.¹⁷

Treatment has been shown to be effective as prophylaxis, particularly when started within 72 hours of the rash,¹⁸ but also when initiated beyond three days if the rash is continuing to spread.¹⁹ Despite these findings, a Cochrane review published online in 2014, has questioned the level of evidence to support the use of antivirals as prophylaxis for PHN.²⁰

It neither affirms nor refutes their routine use but rather suggests that further trials focusing on outcomes such as pain severity and quality of life are required before such recommendations can be made.

Perhaps because of their proven efficacy in treating acute herpetic neuralgia and low incidence of adverse events, NICE guidelines published in May 2013 (later than any of the trials included in the Cochrane review) advocate the use of antivirals for all patients over 50 in the acute phase of herpes zoster reactivation.²¹

A typical prescription would be valaciclovir 1,000 mg tid for seven days, which has a simpler dosage regimen than the alternative aciclovir 800 mg five times daily.

'Pain can be either constant or paroxysmal and is commonly described as burning, stabbing or itching'

The prescription of corticosteroids during the acute stage can cause a significant reduction in symptoms.²²⁻²⁴ Interestingly, this effect is only seen when they are prescribed alongside an antiviral agent. As a result, NICE recommends their use be reserved for those with severe pain and in whom the side effects of systemic corticosteroids would not adversely impact on any comorbidity such as diabetes mellitus.²¹

A suggested regimen is prednisolone 40 mg daily for seven days, then tapering the dose down by 5-10 mg every three days over a total treatment period of 21 days.

Unfortunately, despite their anti-inflammatory effect, they have no impact, when administered alone, on the subsequent development of PHN

when given for acute varicella-zoster infection.²²⁻²⁴

MANAGEMENT

Initial assessment of the patient presenting with PHN allows the opportunity to explain the diagnosis and set realistic expectations in terms of symptom duration and the likely success of the different treatments.

'Pain is located in the same dermatomal distribution as the shingles rash'

The approach to managing the patient's symptoms requires treatment to be tailored to individual factors such as stage of illness (acute herpetic neuralgia or PHN), pain severity and the limitations of specific treatments when considered alongside patient factors such as age and any significant comorbidities.

An algorithm to simplify the approach to management has been previously described by one of the authors,²⁵ see figure 1, p21.

Simple analgesia

Paracetamol should be tried initially for mild to moderate pain, either alone or in combination with codeine. Two different guidelines recommend this initial approach,^{26,27} although NICE Clinical Knowledge Summaries could find no evidence to support this.

Patients taking codeine should be reviewed regularly and the duration of treatment kept to a minimum, in accordance with expert opinion.²⁸

There is no evidence to support the use of NSAIDs in the context of PHN. Simple analgesia such as co-codamol may provide some benefit but the likelihood in clinical practice is that the patient will require treatment with an anticonvulsant or tricyclic antidepressant (TCA).

Tricyclic antidepressants

Amitriptyline and nortriptyline are known to be effective in the context of PHN.²⁹ A randomised controlled trial found that amitriptyline 25 mg per night for 90 days, starting within two days of the onset of the rash, can reduce the incidence of postherpetic neuralgia from 35% to 16%; number needed to treat = 6.³⁰

key points

SELECTED BY

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Risk factors for postherpetic neuralgia (PHN) include:

increasing age; a prodrome of pain before rash onset; the degree of spread of the rash, particularly if it extends beyond a single dermatome; and severity of pain during the acute attack. Forty per cent of patients over 50 and 75% of those over 75 develop PHN following resolution of the rash. The exact pathogenesis of why some individuals go on to develop PHN is yet to be fully established but some evidence supports the theory that a chronic low-grade ganglionitis is responsible.

Patients develop persistent pain classified as PHN

120 days following rash onset. It can be either constant or paroxysmal and is commonly described as burning, stabbing or itching in character and located in the same dermatomal distribution as the shingles rash. Pain can lead to sleep disturbance, anorexia, reduced socialisation and reactive depression.

Antiviral agents are known to reduce the pain of acute

shingles and hasten the resolution of the skin lesions. NICE guidelines advocate the use of antivirals for all patients over 50 in the acute phase of herpes zoster reactivation. Corticosteroids prescribed during the acute stage can cause a significant reduction in symptoms but only when prescribed alongside an antiviral agent.

Paracetamol should be tried initially for mild to moderate

pain, either alone or in combination with codeine but there is no evidence to support the use of NSAIDs. Tricyclic antidepressants are the most likely to confer benefit in neuropathic pain, in frail elderly patients nortriptyline appears to be tolerated best.

Both gabapentin and pregabalin can reduce pain and

improve sleep patterns in patients with PHN. Strong opioids provide similar pain relief to tricyclic antidepressants but their use is complicated by a greater incidence of side effects including neuropsychiatric and gastrointestinal disturbance. There is evidence to suggest an additive or even synergistic effect when combined with gabapentin for neuropathic pain.

Capsaicin 0.075% can be applied four times per day once

the skin lesions have healed. The uncomfortable burning sensation tends to settle with ongoing use, but can be ameliorated by mixing the capsaicin with GTN paste or EMLA cream. Lidocaine 5% plasters are particularly useful where allodynia is a prominent feature, or in patients in whom other treatments are not tolerated. Patients with severe pain or those whose condition is affecting their daily activities and function should be referred to a specialist in pain management.

Compared with other antidepressants, TCAs are the most likely to confer benefit in neuropathic pain.³¹ Their use has to be carefully considered against the side effects which include urinary retention, dry mouth, ataxia and constipation. More serious adverse effects include hypotension and cardiac dysrhythmias. These can be particularly problematic in frail elderly patients, in whom nortriptyline appears to be better tolerated. Furthermore, by up-titrating the dose gradually these effects can be minimised.

'Allodynia and hyperalgesia are frequently distressing features of postherpetic neuralgia...

A reasonable approach in patients over 50 is to start with nortriptyline 10 mg nocte. This can be titrated upwards in increments of 10 mg every 3-7 days to a maximum dose of 100 mg. It is worthwhile explaining to patients that the maximal effect typically takes at least three weeks and that the analgesic effects of these medications are separate from their historical use as antidepressants. If this fails to control symptoms, or is not tolerated because of side effects, then treatment with an anticonvulsant is indicated.

Anticonvulsant therapy

Both gabapentin and pregabalin can reduce pain and improve sleep patterns in patients with PHN.^{32,33} A small randomised controlled trial showed pregabalin to be superior to amitriptyline when used for PHN.³⁴ A single bedtime dose of 100 mg gabapentin for frail elderly patients can be up-titrated to a maximum of 1,200 mg tid. Pregabalin 75 mg 12 hourly up to a maximum of 300 mg bd can be tried if sedation or ataxia limits gabapentin use. Abrupt withdrawal should be avoided.

Opioids

In isolation, strong opioids provide similar pain relief to TCAs but their use is complicated by a greater

incidence of side effects including neuropsychiatric and gastrointestinal disturbance.³⁵ There is evidence to suggest an additive or even synergistic effect when combined with gabapentin for neuropathic pain.^{36,37} Their use is complicated by addiction and drug diversion, therefore it is vital to monitor patients' usage frequently and have defined treatment goals. The British Pain Society provides guidance for the use of strong opioids in non-cancer pain.³⁸

Tramadol has the additional benefit of modulating descending inhibitory pain pathways by its inhibitory effect on serotonin and noradrenaline reuptake. It may provide some benefit but there is as yet insufficient evidence for its use in PHN.³⁹

Topical therapy

Capsaicin 0.075% can be applied four times per day once the skin lesions have healed. Acutely it produces a burning sensation which overwhelms peripheral sensory nerves by calcium influx. A delayed benefit is seen after four weeks, when it is thought to reduce pain transmission by depletion of neurotransmitters and blockade of neurogenic inflammation.⁴⁰

The uncomfortable burning sensation tends to settle with ongoing use, but can be ameliorated by mixing the capsaicin with GTN paste or EMLA cream.⁴¹

...which can lead to sleep disturbance, anorexia, reduced socialisation and reactive depression'

Lidocaine 5% plasters are approved by the MHRA as third-line therapy for PHN, applied over the area of pain for 12 hours followed by 12 hours off. This is particularly useful where allodynia is a prominent feature, or in patients in whom other treatments are not tolerated – adverse events occur in 6% of patients compared with 42% with pregabalin when used for PHN.⁴² In the authors' experience, using the »

SYMPOSIUM CARE OF THE ELDERLY

POSTHERPETIC NEURALGIA

plaster continuously for 36 of the initial 48 hours can reduce the pain from repeated application and removal.

REFERRAL

Postherpetic neuralgia remains a common and difficult condition to manage in the elderly population. Patients with severe pain or those in whom the condition is affecting their daily activities and function should be referred to a specialist in pain management.²¹

This can facilitate a multidisciplinary approach to the assessment and management of the pain and provide additional treatments such as opioids, cannabinoids, ketamine, perineural local anaesthetic injections, physiotherapy, TENS and psychological coping strategies.

NEW DEVELOPMENTS

In future, management may focus on increasing attempts to prevent the development of PHN. In 2013 the Scottish Government introduced a vaccination programme for those over 70, with the NHS in England and Wales following suit.⁴³

In addition, there is increasing research interest in the role of biomarkers to identify which patients are at greatest risk of developing this debilitating condition.

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Useful information

The British Pain Society
www.britishpainsociety.org

Pain Concern
www.painconcern.org.uk

Shingles Support Society
www.shinglesupport.org

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