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POSTHERPETIC NEURALGIA - a patient's guide

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What is postherpetic neuralgia?

Although herpes zoster (HZ) is not a fatal disease, the legacy of postherpetic neuralgia (PHN) often causes prolonged and significant misery and distress. There are now several therapeutic options, but management of PHN can be challenging.

Postherpetic neuralgia is defined by the International Association for the Study of Pain as chronic pain with skin changes in a dermatomal distribution following HZ infection.

There are over 100 known forms of the Herpes virus, but only seven can infect humans. It was only in the 1950s that the varicella zoster virus (VZV) was shown to be the initial culprit in causing chicken pox. Following this illness, the VZV persists in a dormant state and many years later the virus reactivates causing the shingles rash.

It remains a mystery as to what triggers this event. However, there is an increased incidence of shingles with aging. There is some evidence that shows a slight decrease in the incidence of shingles after widespread chicken pox epidemics, suggesting that immunity is boosted by further contact with VZV.

Epidemiology

The incidence of HZ (shingles) infection rises dramatically with increasing age. It occurs at the rate of about one case per 1000 population, with a peak in the over-60 age group of about one in 100.

There is a higher incidence in females, probably reflecting a larger number of women in older age groups.

The most common sites for the shingles rash is the trunk (thoracic dermatomes) and face (ophthalmic division of the trigeminal nerve). Repeat attacks are uncommon (1 to 5%), and are usually associated with weak immunity or cancer.

Zoster-associated pain

This term is now applied to the spectrum of pain symptoms associated with HZ, which begins with the virus prodrome (the time when there is pain prior to the development of the classical rash) and progressing through to both the acute and chronic states.

It is of interest to note that in a recent study, doctors considered rash to be the main diagnostic indicator of HZ, whereas patients considered pain to be the primary feature.

The pain of acute HZ is due to inflammation and damage in the local tissues. It is characterised as a sharp stabbing pain.

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The mechanism of the persisting pain of postherpetic neuralgia (PHN) is most likely due to the type of nerve cells involved (more unmyelinated) and the way in which the nerve signals are modified on their way to the brain. The illness is characterised by a more burning type of pain.

Age has a significant effect on zoster-associated pain. One study showed that 50 percent of patients older than 70 years have pain at six months. For those between 50 and 70 years, however, it was down to 9 percent and only about 1 percent for those younger than 50 years.

The pain duration also appear to be equated to the severity of the initial infection and the presence of prodromal pain before the rash appears.

The important point, fortunately, is that there is a decline in the incidence of PHN with time, even if there is no treatment in the acute phase (the onset of the rash). In that time however, the pain can be intolerable. Not only because of the severe pain, but also the additional profound disturbances in physical, psychological and social function.

Early treatment of Herpes Zoster

Does early treatment of HZ alter the incidence of postherpetic neuralgia? This question continues to polarise doctors. Studies seeking to show long-term benefit from the treatment of acute HZ must have age-matched, and time-from-onset-matched patient groups, in order to validate benefits. Unfortunately, few studies meet these criteria.

It is recommended that antiviral therapy should be considered early in the illness, preferably at the time of the herpes zoster (shingles) infection.

TREATMENT OF ACUTE HERPETIC PAIN (SHINGLES PAIN):

Antiviral therapy

Acyclovir

In 1981, acyclovir was introduced as the first nontoxic potent inhibitor of the herpes viruses. Acyclovir has been particularly successful in preventing recurrences of genital herpes.

One study of acyclovir (800 mg five times daily for seven days) has shown that the duration of zoster-associated pain was shortened by more than 55 percent and PHN by 67 percent.

Acyclovir is currently accepted as the drug of choice for antiviral therapy of herpes zoster, although valaciclovir (Valtrex) and famciclovir (Famvir) appear to have similar effectiveness. Acyclovir has an excellent safety profile.

Valaciclovir

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Valaciclovir is well absorbed orally after which it is hydrolysed to acyclovir. It is taken three times a day. It provides significantly better acyclovir exposure, and presumably, patient compliance.

Famciclovir

Famciclovir is a derivative of penciclovir. Its mode of action is different to acyclovir and its long-term toxicology has not been determined.

Corticosteroids

There have been several uncontrolled studies claiming a reduction in PHN in a small number of patients having shingles, treated with prednisone 40 to 60 mg daily for 2 to 4 weeks. The most valid studies do report significantly fewer patients with pain lasting more than 8 weeks in the treated groups, but with no difference at 1 year of follow-up.

A recent study in which prednisolone was added to the acyclovir course showed no alteration in rash healing, but some improvement in the acute zoster-associated pain. There was no difference in the incidence of PHN. This must be weighed against the potential risks of high-dose corticosteroids in the elderly. Corticosteroids have also been injected at the rash sites, and while reduction in acute pain and the incidence of PHN have been claimed, again there have been no controlled trials of this method.

Neural blockade

Local anaesthetic nerve blocks can be very effective for pain relief in the acute phase of the illness.

Analgesics

The use of regular analgesic pain relief at full dose is appropriate and desirable in the early stages of the disease. If the pain is of significant intensity, strong opioids should be used. Side effects, however, will often limit the dose in the elderly.

Debate continues as to the merits of tricyclic antidepressants for any residual pain at this stage. There is a consensus advocating their early introduction, but this recommendation is intuitive rather than having any scientific foundation.

It now seems that the successful treatment of PHN may be correlated with the interval between the onset of shingles and the initiation of antiviral treatment. Also, early complete and sustained relief of pain in the first few weeks is probably crucial to the prevention of a chronic pain syndrome.

TREATMENT OF POSTHERPETIC NEURALGIA

Apart from those treatments which are aimed at preventing the onset of PHN, most approaches are directed to the care of the patient when the chronic pain syndrome has developed two months or more after the infection.

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Topical therapies

Capsaicin

Capsaicin is the major ingredient of hot peppers. Capsaicin cream has been marketed for topical use, with the recommendation that it be applied five times daily for three weeks. Studies have shown it to provide improvement in PHN. When applied during the shingles phase, it may also reduce the incidence of PHN. However, it does cause burning and stinging at the affected site.

Aspirin in chloroform

Aspirin in chloroform has been reported to produce significant pain relief in both herpes zoster and PHN. The preparation is made by crushing two soluble aspirin tablets in chloroform 15 ml. This is applied to the skin with cotton wool. Care must be taken to prevent burning. This application can be repeated up to four times daily. No controlled studies of this treatment have been published.

Topical local anaesthetics

Local anaesthetics have been administered by a wide variety of routes to relieve the pain of herpes zoster and PHN. Unfortunately, although some patients will experience sustained pain relief that lasts long enough, most patients will have such brief pain relief that repetitive use of local anaesthetics is not justified.

Systemic therapies

Opioid analgesics

Morphine and its derivatives can continue to have an analgesic benefit in the chronic state, but like other neuropathic conditions, that effect is variable. A significant improvement in activity and pain must be demonstrated to continue their use in the long term.

Psychoactive drugs

Tricyclic antidepressants (TCAs) are frequently used in the management of neuropathic pain. This is due to their effect as a potential analgesic agent. Relief of pain does not depend upon the presence of psychological depression.

The careful use of a TCA should be considered as a first-line step in the management of PHN. The choice of TCA does not appear to be crucial. Patient preference is based on the relative incidence of side effects. The newer antidepressants, selective serotonin reuptake inhibitors, appear to be disappointing in treating this condition.

Antiepileptic agents

The use of anticonvulsants such as carbamazepine, sodium valproate and clonazepam may also have a place in the management of PHN. The rationale for their use is that in some

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cases the pain syndrome presents with episodes of apparent spontaneous burst activity akin to sensory neuronal discharge. All too often however, patients are plagued by their side effects, because these agents may need to be taken at full dose.

Physical treatments

A part of the genesis of the PHN syndrome appears to be the loss of normal sensory activity. Reinstitution of sensory stimulation, such as the use of 'transcutaneous electrical neural stimulation' (TENS) therapy, or gentle acupuncture, can help bring about effective pain control.

Surgery

A newer brain surgery option, dorsal root entry zone lesions and spinal cord stimulation, showed initial promise, but has also proved disappointing in the longer term.

Conclusion

Treatment for PHN should start early, preferably at the time of shingles infection, and should involve antiviral agents as well as oral analgesics and possibly neural blockade and steroids. Close daily symptom monitoring is required to manage this phase adequately.

In the chronic, postherpetic neuralgia stage, treatment with topical creams, tricyclic antidepressants, active sensory and motor stimulation, or occasionally antiepileptic agents, may provide benefit when pain has been sustained over a longer time.

In all instances such patients need to be monitored closely by their family doctor to ensure medication is being taken as required and to assess any untoward side effects. Social support and psychological interventions should also be considered. Although the measures described above will benefit many patients, the management of PHN remains, in some cases, an intractable problem.