Effective pain management of post-herpetic neuralgia

Post-herpetic neuralgia is a neuropathic pain syndrome that is notoriously difficult to manage. It is preceded by an acute attack of herpes zoster (shingles) and usually occurs at the site of shingles skin lesions. While acute herpetic pain occurs before and during the presence of the shingles rash, post-herpetic neuralgia is pain that continues beyond the normal healing time of the rash.

Post-herpetic neuralgia has been variously defined as pain persisting, or recurring, beyond one, three and six months after the onset of the rash. Since many cases resolve spontaneously in the first few months, it seems reasonable to assume a diagnosis of post-herpetic neuralgia if the pain continues beyond three months after the acute rash (Dworkin and Portenoy, 1996).

The reported incidence of post-herpetic neuralgia depends on the definition used. National data suggest that there are 25,000 new cases in the UK each year, and an annual prevalence approaching 50,000 (Bowsher, 1997).

The condition is frequently underdiagnosed (Padfield, 1997), despite being consequent to having had shingles. Management is difficult with traditional analgesics because the shingles virus can cause so much nerve damage in the few days before a patient seeks medical help. Specific analgesic regimens for relieving nerve pain, therefore, are required.

In total, 10-25 per cent of patients who have pain one month post-shingles will have pain one year later (Ragozzino et al, 1982; Fig 1). This is likely to have a devastating impact on their quality of life. Health care practitioners have a duty to help people obtain both a swift diagnosis and offer early, appropriate treatment.

Varicella zoster

Shingles is by far the most common condition that can affect the nervous system. However, it has been less than 50 years since we were able to medically confirm that the varicella zoster virus, which causes shingles, is also responsible for chickenpox. It is only in recent years that we have begun to fully understand the disease profile and its potential long-term complications.

Once the virus has passed through the chickenpox stage, it migrates along the sensory axons towards the dorsal horn (the junction box between all sensory nerves and the spinal cord). When it reaches this area it will live a dormant, parasitic existence. The patient will be unaware it is there, since there will be no pain or symptoms.

If the varicella zoster virus is reactivated it will travel back along the nerve paths, causing nerve damage to the skin, which will erupt into the familiar shingles rash. Reactivation is usually attributed to suppression of the immune system, infection or malignancy.

Acute shingles usually involves a single nerve root on one side of the body. A band or patch of raised dots will appear within a few days in the corresponding dermatome. The most common sites are the torso and face. Chills, fevers, and aches are also common. In some cases, the affected area becomes flushed and hypersensitive to touch before the rash erupts, making diagnosis difficult.

Such early discomfort may be an indication of the level of nerve damage (Nurmikko, 2001). Any patient with a rash around the brow or eye should be referred immediately to an ophthalmologist since herpes zoster infection of the optical nerve can cause blindness or other eye problems, including corneal ulcers. After a few more days, the spots will turn into painful fluid-filled blisters that may multiply over the next week or so. If shingles is treated within the first two to three days of infection, the symptoms usually disappear within five weeks.

Treatment

Treatment of the varicella zoster virus includes administration of antiviral drugs such as aciclovir, farniclovir and valaciclovir. To be effective, the drugs need to be started within 48 to 72 hours of the emergence of the viral vesicles. Treatment taken for a week to 10 days can reduce the period of viral shedding and accelerate the rate of healing; it may also shorten the duration of pain from the acute attack and reduce scarring.

However, treatment with oral antiviral drugs does not appear to prevent the development of post-herpetic neuralgia, although starting them early is thought to reduce the duration of pain (Wood et al, 1996).

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Development of post-herpetic neuralgia

Post-herpetic neuralgia develops when pain from the acute phase is unrelenting, and persists beyond resolution of the rash. Patients characteristically describe their pain as a constant burning, throbbing or aching, with intermittent shooting or stabbing sensations. Itching and numbness in the scars often accompanies the pain. Over 90 per cent of patients experience allodynia, which is pain produced by a non-noxious stimulus, such as the movement of clothes over the skin or a draught on exposed areas (Bowsher, 1997).

Post-herpetic neuralgia pain is probably one of the most severe types of pain. It can be both debilitating and isolating, leading to sleep disturbance, anorexia and loss of libido. People who experience long-term pain are four times more likely to suffer from anxiety and depressive disorders, and twice as likely to suffer moderate to severe work interference than those who do not experience pain (Gureje et al, 1998).

Anyone who has had chickenpox is at risk of developing shingles. The risk is increased in people predisposed to severe infections or nervous-system damage, including older people, recipients of organ transplants, diabetes patients, people with HIV or cancer, and those taking steroids. Future vaccination programmes may play an important part in reducing the incidence of chickenpox generally, or through vaccination of middle-aged people in boosting immunity to varicella zoster virus and its latent phase (Johnson, 1997).

There is currently no way of determining who is at risk of developing post-herpetic neuralgia after shingles, although the incidence dramatically increases with age, particularly for people over 50 years old. In those aged over 60 who have had shingles, the occurrence is estimated at 27-68 per cent (Schmader, 1998). Other risk factors include pain prior to shingles, an extended rash period, a rash on the face or lower back, and being female.

Pain management

Acute herpetic pain and post-herpetic neuralgia can be viewed as separate phases on a pain continuum. Pain intensity fluctuates and patients sometimes have pain-free intervals. Patients must be reassured should they experience post-herpetic neuralgia that treatments and support are available.

The key to effective management is to start it early. Primary care practitioners are often best placed to do this. Effective management regimens are multimodal and involve medication, non-pharmacological therapies and psychosocial support.

In the acute phase, aggressive treatment with a range of analgesics is invariably required (Box 1). Tramadol, a synthetic centrally acting analgesic with both opioid and antineuralgic properties, can be an effective option (Gobel and Stadler, 1997). A short course of opioids, such as morphine or oxycodone, may be necessary to treat severe pain in the early stages of shingles, but their efficacy tends to be limited in post-herpetic neuralgia.

Non-stereoidal anti-inflammatory drugs (taken orally or applied topically) may reduce the sensitisation of nerves from an abnormal inflammatory process involved in mediating post-herpetic neuralgia. Stellate ganglion blocks, usually performed by anaesthetists, can provide short-term relief from acute herpes pain by blocking sympathetic nerves in the affected region (a stellate ganglion is a large irregular ganglion on the lowest part of the cervical sympathetic trunk). In established post-herpetic neuralgia, the aim is to focus on curtailing the neuropathic element of the pain. Neuropathic pain is caused by a misinterpretation of messages in the brain and spinal cord. In effect, the nervous system signals are ‘scrambled’ or ‘amplified’.

Tricyclic antidepressants, which have been used in neuropathic pain conditions for many years, are the most studied class of drugs used for treating post-herpetic neuralgia. They produce analgesia by inhibiting neuronal uptake of catecholamines, such as noradrenaline and serotonin, thus increasing synaptic levels of these neurotransmitters. They are not used to offer pain relief by reducing depression, as their analgesic effect is produced at lower doses and more quickly than their antidepressant effect.

The impact of post-herpetic neuralgia is likely to be lower if tricyclic antidepressants are commenced early in combination with antivirals. Pre-emptive administration of low-dose amitriptyline has been shown to reduce pain prevalence by half (Bowsher, 1997). People who do not respond to one tricyclic antidepressant may benefit from administration of another with similar efficacy, such as nortriptyline.

Patients should be made aware that these drugs are also used for people with depression and that it will take a few weeks of treatment before they will feel the benefits (hence the advantage of starting early). Doses usually start at 10-25mg at night and are increased gradually.

One of the side-effects of such drugs is sedation, but this can be a benefit to patients who have difficulty sleeping because of the chronic pain. Some people experience intolerable dryness, drowsiness or constipation. These drugs are contraindicated for people with cardiac tachyarrhythmias. Older people, who are particularly prone to post-herpetic neuralgia, tend to experience...

**REFERENCES**


the worst side-effects.

The newer anti-epileptic drugs are another important group of drugs for which there is mounting evidence of efficacy in treating post-herpetic neuralgia: for example, gabapentin is licensed for the treatment of neuropathic pain. Its exact mode of action is not yet fully understood, although it appears to target calcium channels.

Its effectiveness in treating post-herpetic neuralgia has been demonstrated in two large controlled studies (Rowbotham et al, 1998; Rice et al, 2001). As well as a reduction in pain, patients reported better sleep, mood and quality of life. Doses are usually commenced at 300mg a day and titrated up to 1800mg–2400mg a day.

In the Rice et al (2001) study, patients treated with gabapentin reported a significant reduction in pain scores after one week. Side-effects tended to be uncommon, transient and mild but included dizziness, lethargy, headache and confusion.

Small studies that compared gabapentin with amitriptyline showed similar efficacy, although some patients may be more tolerant of the former. Its safety profile, suitability for use in older patients and comparative lack of adverse drug interactions make it a useful treatment for post-herpetic neuralgia.

The role of other newer anti-epileptics, such as topiramate and lamotrigine, in post-herpetic neuralgia has yet to be studied, although case reports have indicated that they may be beneficial.

Evidence is emerging to support use of topical lignocaine in post-herpetic neuralgia (Galer et al, 1999). The five per cent lignocaine patch, while not generally available in the UK at present, is attracting increasing interest. Applied to the most painful area, it works on the skin, tissues and peripheral nerves and can be particularly effective at reducing allodynia. Alternatively, lignocaine gel may be applied. The lack of systemic side-effects and absence of drug interactions make topical lignocaine particularly important in treating older people.

Application of a eutectic mixture of local anaesthetics, such as Emla cream, to the affected area appears to be effective in reducing paraesthesiae, although the effect on ongoing pain appears limited. Another topical treatment, capsaicin cream, made from red chilli peppers, has demonstrated efficacy in a minority of cases. It requires application two or three times a day, can be messy and can often cause local irritation. However, there are no systemic side-effects, making it a potentially useful option (Aronoff and Gallagher, 1999).

Non-pharmacological treatments

Non-pharmacological methods of treating post-herpetic neuralgia include protecting the skin from external stimulation by covering the affected area with a clear adhesive dressing. Domestic kitchen film wrap can be used as a simple alternative. There is anecdotal evidence that some patients can derive great benefit from the use of transcutaneous electrical nerve stimulation (TENS). This involves attaching electrodes from a small machine to the painful area, and it is safe and simple to use. It should therefore be given a trial for a week or so, unless it elicits intolerable allodynia (Galer and Argoff, 1999). Acupuncture can also be effective for a minority of patients and represents a safe adjuvant therapy (Wu and Akande, 1999).

Because stress and anxiety exacerbate pain, it makes sense to offer the patient support with relaxation and reassurance as part of the analgesic regimen. In addition, those experiencing excessive disability and distress may benefit from cognitive behavioural therapy.

Conclusion

Post-herpetic neuralgia can be a disabling and life-changing condition. It is imperative that health-care professionals recognise shingles and post-herpetic neuralgia, because early diagnosis and treatment will yield the best results.

It is not possible to predict which patients who have shingles will continue to have pain for weeks, months or even a lifetime, but older people, those with a compromised immune system and those who experience pain before the rash are particularly at risk.

It is important to make a swift diagnosis, to enable affected patient to obtain the appropriate antiviral and analgesic drugs necessary to halt the progression of chronic pain. Successful management of post-herpetic neuralgia requires the use of therapies that specifically relieve nerve pain. Tricyclic antidepressants, gabapentin, topical and non-pharmacological treatments, and psychological