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Treatment of post-herpetic neuralgia in the elderly

Notes for doctors by Dr David Bowsher, MA, MD, PhD, FRCPed, FRCPath, *co-founder of the Pain Relief Foundation and consultant neurologist at the Pain Research Institute, Rice Lane, Liverpool L9 1AE*

1. Postherpetic neuralgia (PHN) is defined as pain persisting or recurring at the site of shingles three or more months after the appearance of the acute rash. It occurs in about 50% of the over 65s who get shingles, rising to 75% at age 80. Based on the 1992 census population figures, it can be calculated that 200,000 people in the UK will be suffering from PHN at any one time [1, 2]. It can be one of the most intense, and if untreated, persistent, pains known - and may render the patient's final years an unendurable misery. PHN is perhaps best regarded as a condition *caused* by having had shingles rather than as a continuation of shingles.

2. Treatment of acute shingles with antivirals within 72 hours of rash appearance has some preventive effect on the subsequent development of PHN. It does certainly:
   a) relieve the pain of acute zoster,
   b) to a large extent prevent subsequent scarring (25% of cases occur on the face),
   c) in those PHN patients who respond to tricyclic antidepressants, treatment with antivirals reduces the time to pain relief by half [3]. There is suggestive evidence that patients treated with antivirals may actually show a reduction in the proportion still in pain after 6 months.

   It appears that treatment of acute shingles with gabapentin has some effect in preventing the later development of PHN.

3. Conventional analgesics, however powerful, are of little help.[4,5] Tablets containing dextropropoxyphene seem best at "taking the edge off the pain". A recent trial found that controlled-release morphine 91 mg or methadone 15mg "effectively relieved pain" and did not cause fuzziness, unlike the tricyclic antidepressants. Methadone is metabolised differently from other opioids. Recently Tramadol has been found to be an effective analgesic for PHN.

4. **Gabapentin** and **pregabalin** have received licenses for use in PHN. They have been shown to be effective therapies for this condition.[6] *(Other anticonvulsants are of unproven value: there is little, if any, indication for their use*). Gabapentin should be given three times daily in doses rising over a few weeks to an average of 400 mg three times a day. In most patients, gabapentin is remarkably free of side-effects, so large doses can often be tolerated (even up to 3,600 mg/day) though a daily total of between 900mg and 1,800mg is usually adequate. Pregabalin treatment can be started at a dose of 150 mg per day (divided in two or three doses). Based on individual patient response and tolerability, this may be increased to 300 mg per day after an interval of 3 to 7 days, and if needed, to a maximum dose of 600 mg per day after an additional 7 day interval.

Patients who report unpleasant side effects on higher doses should be pegged at a dose they can tolerate. The dosage should tailed off gradually in the same stages by which it was increased.

A recent trial has found that gabapentin and morphine [or oxycodone hydrochloride [7,8]] combined achieved better analgesia at lower doses of each drug than either single agent, with constipation, sedation and dry mouth as possible adverse side effects [9].

5. Before the advent of gabapentin and pregabalin, the best treatment was with tricyclics such as amitriptyline [3] or nortriptyline, 25 mg/day rising by weekly increments of 25 mg/day; or in the elderly 10 mg/day, rising by weekly increments of 10 mg/day. It is these particular drugs and not *"tricyclics"* in general; in fact, they work in proportion to their adrenergic activity as opposed to their serotonergic activity [10, 11], upon which latter their antidepressant action depends. If patients can't tolerate amitriptyline, try nortriptyline (a metabolite of amitriptyline) in the same dose. More recently, duloxetine has been found to be effective, with fewer side effect.[12]

   WARN PATIENTS NOT TO EXPECT PAIN RELIEF UNTIL TISSUE LEVELS ARE ESTABLISHED i.e. 2 or 3 weeks. It is also necessary to explain that although invented as antidepressants, these drugs have a separate and independent action on "nerve pain" and they are not being fobbed off as having "imaginary pain".

   The cheapest way to overcome *dry mouth* the most common cause of non-compliance, is to prescribe *artificial saliva spray* (BNF); chewing gum will also do the trick, for those prepared to use it.

   Tricyclic antidepressant drugs should be continued at full dose for 3 months after the pain has disappeared, then tailed off gradually. The patient should be warned to re-start (or increase the dose) *immediately* if the pain recurs.

   What it all depends on, is how soon appropriate treatment is started. PHN so treated within three months of acute shingles shows >90% recovery. If treatment does not start until after a year, only about 30% get relief [13]. All acute shingles patients over 60 years of age should be given low-dose antidepressants (e.g. 10 or 25 mg nocte) immediately on diagnosis and told to return to the surgery after 6 weeks to be asked by the practice nurse *"Do you still have pain where you had the shingles?"* If the answer is "yes", increase the tricyclic antidepressant by weekly increments to 50 or 75 mg at bedtime.

   A number of centres are currently co-prescribing tricyclics and gabapentin.

6. Versatis is medicated plaster containing lidocaine (formerly called lignocaine) that is placed directly on the site of pain, providing rapid, cooling relief from nerve pain associated with PHN. Each plaster contains 700 mg (5% w/w) lidocaine in an aqueous adhesive base and offers fast and continuous pain relief from 30 minutes after application.[8, 14] The soft felt-like backing helps prevent allodynia. It is worn for 12 hours in every 24 hours. It is particularly suitable for some patients: experiencing confusion, are polymedicated, or for whom first line treatments are contraindicated.

7. Allodynia (pain elicited by normally non-painful stimulus, such as touch) is the bugbear of PHN. A few patients get help from a layer of plastic over the area, preventing contact

(rubbing) by clothes; we use *'Opsite'* spray (use several layers; buy from chemist) as *'clingfilm'* is usually too thin (but try it first). Depending on the location of the pain, some patients benefit from a pad firmly bandaged in place, as they find pressure does not cause allodynia. Cotton underclothes seem to be less allodynogenic than other materials.

8. If there's no improvement in 8-12 weeks, the patient should be referred to a pain clinic without stopping the antidepressant.

9. These simple measures would reduce referrals to pain clinics for PHN by 80 or 90% and save an unquantifiable amount of human misery and suffering.

SUPPLEMENTARY TREATMENTS (concomitantly with antidepressants)

a) Capsaicin cream ('Axsain') has been introduced for the treatment of PHN; it stimulates and then inactivates C nociceptors. Stimulation of C nociceptors is exceedingly unpleasant, so lidocaine 5% ointment or 'Emla' cream should be applied half an hour before the capsaicin cream 4 times daily for the first two weeks[15]. Relief is said to take up to 6 or 8 weeks. But N.B. while shingles is a disease of the peripheral nervous system, the pathophysiology of PHN is central [16]; perhaps capsaicin works so slowly (when it does) because the effect is due to transsynaptic (within the cord) action rather than inactivation of primary peripheral C afferents, which are already knocked out by the disease anyway. Contrary to the situation in tissue-damage *(nociceptive)* pain, C fibres are NOT responsible for the pain experienced in PHN and other neurogenic pains. This has important pharmacological/ therapeutic implications!

b) Alternatively, a 4% dispersible aspirin in chloroform (weight to volume) may help, provided it doesn't irritate the skin too much or get into open sores or the eyes. [17]

c) T(E)NS (transcutaneous electric nerve stimulation) can be very helpful; it may be necessary to apply it in the contralateral (mirror-image) dermatome for the first 10 minutes because of allodynia. NB: Acupuncture depends mainly on enkephalinergic mechanisms, which neurogenic pain emphatically doesn't, and is therefore very rarely of benefit in our experience - but others have reported good results.

d) Positive relaxation techniques can also be very useful, as they reinforce the autonomic-dependent diminution of pain at rest or in sleep; they should be prescribed in all long term cases for use at least twice and preferably three times a day. Audiotapes are available for this purpose. (W.L.A.P. PO Box 1, Wirral, L47 7DD Tel: 0151 632 0662)

e) One-off sympathetic ganglion blockade has never, in our experience, given any lasting relief in PHN (as opposed to acute shingles); others have however claimed that repeated blocks at 48 or even 24 hour intervals may achieve something.

David Bowsher, 2008

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