

Challenges in

NEUROPATHIC PAIN

Newsletter

Welcome to the third issue of *Challenges in Neuropathic Pain*, a newsletter brought to you by the members of the Multidisciplinary Panel on Neuropathic Pain. In this issue, the first in a series of treatment recommendations for neuropathic pain is presented. These recommendations aim to provide Hong Kong clinicians with up-to-date information and assist in everyday clinical practice. Trigeminal neuralgia is the topic for the first set of recommendations. We also continue our series of case presentations, looking at diabetic neuropathy. Our regular features, including a literature review, Q&A, useful Web sites and a calendar of upcoming conferences, will keep Hong Kong clinicians informed of the latest news on neuropathic pain.



Multidisciplinary Panel on
Neuropathic Pain

神經痛跨學科研究小組

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RECOMMENDATIONS FOR THE MANAGEMENT OF TRIGEMINAL NEURALGIA



One of the key initiatives of the Multidisciplinary Panel on Neuropathic Pain is the development of recommendations on a number of common neuropathic pain syndromes. This will better assist general practitioners (GPs) to recognize the signs and symptoms of neuropathic pain, to initiate appropriate treatment and provide guidance on when to refer. In this issue, a summary is provided of the recommendations for trigeminal neuralgia management. The project leader for the development of the trigeminal neuralgia recommendations was Dr Joseph Lam.

Background

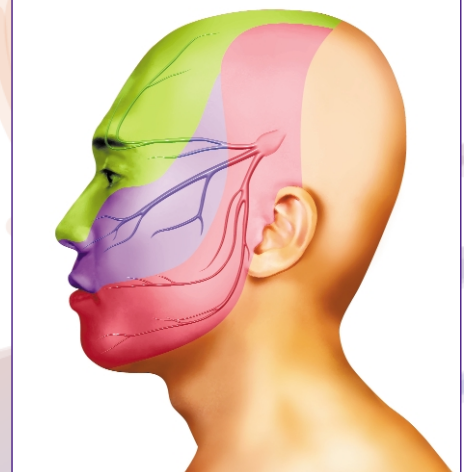
Trigeminal neuralgia (TN) is sometimes described as the most excruciating pain known. In severe cases, patients may experience sleep deprivation, depression or weight loss because of pain when trying to eat. Accurate diagnosis and prompt, appropriate treatment can markedly reduce a patient's suffering.

Diagnosis

The diagnosis of idiopathic TN should be based on the clinical symptomatology and the exclusion of pathological causes.

- Idiopathic TN has 5 major characteristics:
 - A history of shooting, stabbing, jabbing, electric shock-like pain in the distribution of the trigeminal nerve (Figure 1).
 - Unilateral pain attacks that start abruptly and last for several seconds to 2 minutes.
 - Pain triggered by talking, chewing, kissing, drinking, shaving or brushing teeth.
 - A normal neurological examination.
 - Relatively pain-free periods between attacks.
- The main differential diagnoses include: temporal tendonitis; temporomandibular joint disorders; occipital neuralgia; glossopharyngeal neuralgia; postherpetic TN; atypical facial pain and the SUNCT (short-lasting, unilateral, neuralgiform pain with conjunctival injection and tearing) syndrome.
- To exclude pathological causes of TN, such as tumour or multiple sclerosis, a high quality magnetic resonance image of the brain is required.

Figure 1: Distribution of the trigeminal nerve



Treatment

Pharmacotherapy is the mainstay of treatment for TN and may be initiated by GPs. Full product information should be consulted before prescribing pharmacotherapy. If a patient remains refractory to 2 or 3 agents, they should be referred to a multidisciplinary pain management centre. These recommendations also include background information for doctors on approaches that may be undertaken, which encourage more effective communication with patients suffering from ongoing pain about treatment options. The overall approach to the treatment of TN is summarized in Figure 2.

Pharmacotherapy

First-line treatment

Carbamazepine is effective in treating neuropathic pain and tends to be the usual first-line treatment for TN.¹² The maximum dose of carbamazepine in TN is 1,200 mg daily in divided doses. Unfortunately, side effects of carbamazepine, such as dizziness, ataxia, allergic skin reactions, leucopenia and vomiting, are common and limit its use in some patients. Rarely, agranulocytosis, aplastic anaemia or pancytopenia may occur, so it is important to monitor laboratory parameters.

Other pharmacotherapy options

When carbamazepine is contraindicated or is not well tolerated, a number of other agents can be used for second-line treatment. These include other anticonvulsant agents, such as gabapentin, phenytoin, lamotrigine and baclofen. Antidepressants, such as amitriptyline, are also effective in the treatment of neuropathic pain.

Gabapentin is approved for all neuropathic pain syndromes, although its efficacy has been most evident in painful diabetic neuropathy and postherpetic neuralgia.³ Gabapentin may be an effective first-line therapy for some patients. It should be commenced at 300 mg once daily and titrated up to 1,800 mg daily in divided doses.

Peripheral trigeminal nerve block

Peripheral trigeminal nerve block can be used as an adjunct to pharmacotherapy to achieve immediate and intermediate-term pain relief. A number of agents (including alcohol, phenol, glycerol or local anaesthetic agents) can be used. The technique provides immediate pain relief in the majority of cases. However, the effect may only be temporary, with median duration of relief from 2 to 19 months.

Interventions on the trigeminal nerve

In general, interventions and operations on the trigeminal nerve are much more effective, but have higher associated risks, than pharmacotherapy. These procedures should not be performed unless therapy with 2 or 3 medications has been tried for a reasonable period of time (ie, 3 to 6 months).

Microvascular decompression (MVD)

In MVD, the trigeminal root close to the brain stem is identified, the offending compressing blood vessel is isolated and a sponge is placed between the vessel and nerve, relieving the compression and, thus, the pain.⁴ Pain relief is immediate in most cases, and offers long-term relief for 70%-80% of patients, and preservation of trigeminal nerve function in 85% of cases. There is a small risk (<5%) of complications, such as facial numbness, facial weakness, double vision, infection or deficiencies in hearing or balance. The major disadvantage of this procedure is the need for craniotomy, which has associated risks. The risk of mortality or severe morbidity with MVD is around 1%.

Percutaneous procedures

Percutaneous radiofrequency rhizotomy (PRFR), balloon compression rhizotomy (BCR) and percutaneous retro-Gasserian glycerol rhizotomy (PRGR) all involve destruction of part of the trigeminal nerve or ganglion to relieve TN. However, these procedures are less frequently available in Hong Kong. PRFR uses radio waves, BCR requires inflation of a balloon and PRGR involves injection of glycerol into the ganglion. Although initial pain relief may be achieved with these procedures, there tends to be high recurrence rates. Side effects include facial numbness, diminished corneal reflexes, anaesthesia dolorosa and trigeminal nerve dysfunction.

Gamma knife radiosurgery (GKR)

In this newer technique, focal irradiation is applied to the proximal part of the trigeminal nerve near the pons.⁵ The duration between treatment and onset of effect is between 1 day and

8 months. Studies have shown that 2 years after GKR, only 40%-75% of patients were pain free, with or without medications. Major complications include increased sensory loss in the trigeminal nerve distribution (10%-34% of cases) and corneal numbness (up to 8% of patients). The major advantage of GKR is the avoidance of mortality or other serious complications.

Summary

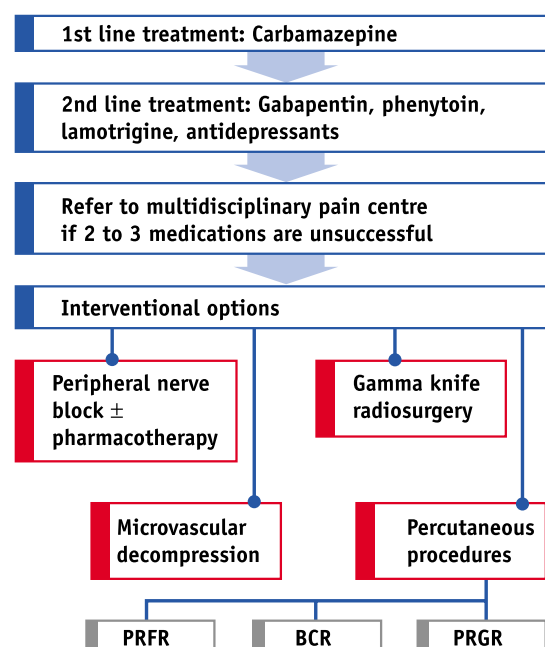
Pharmacotherapy, as outlined in Figure 2, may be initiated by GPs. If the response to a first-line treatment is unsuccessful, one or two second-line agents may be tried. However, if a patient remains refractory to treatment, they should be referred to a multidisciplinary pain centre for further treatment, including surgical intervention on the trigeminal nerve. The most appropriate treatment should then be based on the patient's clinical symptoms and the clinical experience of the pain management team.

Patients should be allowed to consider all available therapeutic options. In general, for patients younger than 70 years, who have a low surgical risk and prefer to preserve trigeminal nerve function, MVD should be recommended. The best non-surgical treatment choice is PRFR. In cases where TN pain involves the ophthalmic division or all 3 divisions, BCR should be considered over PRFR. GKR should be reserved for patients who have failed to respond to both surgical and percutaneous procedures.

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Figure 2: Treatment options for trigeminal neuralgia



PRFR: Percutaneous radiofrequency rhizotomy

BCR: Balloon compression rhizotomy

PRGR: Percutaneous retro-Gasserian rhizotomy

CASE PRESENTATION

In each issue, a case study is presented on a relevant neuropathic pain syndrome. Reviewing case studies will help to improve your diagnostic approach to neuropathic pain and increase your understanding of selecting treatment strategies based on presenting symptoms. In this issue, a case of diabetic neuropathy with paraesthesia is discussed.

Diabetic neuropathy

Presenting symptoms

A male, aged 67 years, with type 2 diabetes was admitted to a local Accident and Emergency (A&E) department with chemical burns to both feet. He had applied an improper dilution of potassium permanganate solution for treating his foot blisters.

Medical history

The patient was diagnosed with diabetes 20 years previously and was prescribed oral hypoglycaemic agents. He suffered an episode of pulmonary tuberculosis in 1995 and was treated for 9 months with drug therapy. He stopped smoking and drinking alcohol as a result of the tuberculosis. In 1995, the patient had poor glycaemic control (HbA_{1c} of 9% and fasting glucose of 10 mmol/L) and a body mass index of 24 kg/m². After consultation with a dietician, a strict diet resulted in lowering his HbA_{1c} to 8%. He continued on oral hypoglycaemic agents: glibenclamide 10 mg bd and metformin 1,000 mg tds.

In 2001, he started to experience excruciating, dull, aching pain and numbness in both feet and lower legs. This pain disturbed him so much that he used ointment on his feet and foot massage instruments daily. However, these only brought short-term relief. The patient purchased a new pair of shoes, hoping to relieve the numbness, but developed blisters on the soles of both feet after wearing the new shoes for just one day. A GP at an outpatient clinic recommended that he use a potassium permanganate bath to treat the blisters. The patient forgot the dilution method advised by the nurse, and added too little water to the potassium permanganate solution. After soaking his feet for 2 minutes, he noticed that they had turned red and he had skin lacerations on all toes. Although he did not experience any pain, his wife convinced him to go to A&E for medical advice.

Clinical examination

The patient was diagnosed with chemical burns to both feet (Figure 3). He also had peripheral neuropathy with loss of sensation in the lower third of both calves, absent tendon reflexes, dilated veins and weak dorsalis pedis pulses, indicating co-existing peripheral vascular disease.

Interpretation

The patient had diabetic neuropathy, autonomic neuropathy and peripheral vascular disease. These conditions commonly co-exist in long-standing, poorly controlled diabetic patients. Insensitivity to painful stimuli, injury and noxious stimuli are often unnoticed, which can result in severe sequelae. Polymicrobial infection is a common

problem in the infected, diabetic foot. The prognosis for patients with diabetic neuropathy is mostly dependent on the adequacy of blood circulation to the feet.

Management

The specific approaches for treating this patient are:

- 1) Prompt commencement of antibiotics if signs of infection are present. A multidisciplinary approach to treatment – involving an orthopaedic surgeon, podiatrist, endocrinologist, diabetic nurse and community nurses – is essential. In this case, epithelization of the skin and improved circulation to the second and third toes became evident after 2 weeks of treatment.
- 2) Education on home monitoring of blood glucose by the diabetic nurse. Improved awareness resulted in better glucose control, with HbA_{1c} of 7% and fasting blood glucose of 6.5 mmol/L. The patient was referred to an ophthalmologist to monitor background retinopathy and other co-existing microvascular complications.
- 3) Treating the symptoms of neuropathic pain presenting with paraesthesia. Amitriptyline was commenced at 25 mg nightly and titrated to 100 mg nightly. As there was no response to treatment after 4 weeks, gabapentin was commenced at a dose of 300 mg bd. Symptoms improved after a further 2 weeks of treatment.
- 4) Advice on foot care and self-examination of his feet on a daily basis.

Figure 3: Appearance of chemical burns to the feet of a patient with diabetic neuropathy



WEB SITES ON NEUROPATHIC PAIN

Various Web sites are devoted to neuropathic pain or pain management. Most of these are not based in the Asia-Pacific region but, nevertheless, provide useful information on pain for clinicians and patients.

The Web site of the National Institute of Neurological Disorders and Stroke (<http://www.ninds.nih.gov>) in the USA provides recent news on all aspects of neuroscience and patient information on a range of neurological disorders, including neuropathic pain syndromes.

The Neuropathy Association (<http://www.neuropathy.org>) is a patient support network in the USA. According to the Web site, it was “established by people with neuropathy, their families and friends, to provide support and education”.

Q&A

Readers are encouraged to send questions to members of the Multidisciplinary Panel on Neuropathic Pain. Please forward your questions concerning any aspect of neuropathic pain and its management to mpnp@medimedia.com.hk or fax to (852) 2559 6910.

Some of my patients have chronic pain. How do I know if it is neuropathic pain?

Patients with chronic pain should be assessed for symptoms consistent with neuropathic pain. This includes tingling, burning, shooting or lancinating pain, sensory impairment, allodynia and hyperalgesia. Neuropathic pain is caused by injury to the peripheral or central nervous system and tends not to respond to simple analgesics, such as non-steroidal anti-inflammatory drugs and paracetamol. Peripheral causes of neuropathic pain include trauma, surgery, diabetes mellitus, infection (eg, shingles), ischaemia and exposure to toxins (eg, drugs or alcohol). Central causes of neuropathic pain include stroke, multiple sclerosis and tumours. Neurological examination may be useful to diagnose some types of neuropathic pain, such as diabetic neuropathy. However, patients with trigeminal neuralgia will have normal outcomes from a neurological examination. When diagnosis is difficult, patients should be referred to a pain management team for assessment and treatment.

LITERATURE REVIEW

Serpell MG, et al. Gabapentin in neuropathic pain syndromes: a randomised, double-blind, placebo-controlled trial. Pain 2002;99:557-566.

This double-blind, randomized, placebo-controlled trial, recently published in *Pain*, evaluated the efficacy and safety of gabapentin in various neuropathic pain syndromes. A symptom-based approach was taken, recruiting neuropathic pain patients with at least two of the following: allodynia, burning pain, shooting pain or hyperalgesia. The most common neuropathic pain syndromes were complex regional pain syndrome (28%), postherpetic neuralgia (14%) and radiculopathy (9%), while 22% of patients suffered from postsurgical pain, such as postlaminectomy, postinguinal hernia repair and postmastectomy pain. Patients were randomized to receive gabapentin (initial dose of 900 mg/day titrated over 3 days, with a maximum dose of 2,400 mg/day in divided doses) or placebo for the 8-week treatment period.

The primary outcome measure of change in average pain score (recorded in a diary) between baseline and the final week was greater in gabapentin-treated patients than in placebo-treated patients, (21% versus 14%; $p=0.048$). Clinician and Patient Global Impression of Change ratings were significantly greater in patients treated with gabapentin; 34% of gabapentin-treated patients compared with 16% of placebo-treated patients considered their pain as very much or much improved ($p=0.03$). Quality of life, as assessed by the Short Form-36 survey, improved more in gabapentin-treated patients, with changes significantly greater than placebo in the domains of bodily pain, social functioning and role emotional. Although there was a trend for relief of symptoms with gabapentin, a significant improvement was seen only in burning pain and hyperalgesia. Gabapentin was well tolerated, with 79% of patients completing the study compared with 73% of control subjects. Mild to moderate dizziness and somnolence were the most common adverse events with gabapentin, and were mostly transient, occurring during the titration phase. The authors concluded that, in patients with various neuropathic pain syndromes, gabapentin reduces pain and improves some quality of life measures.

CONFERENCE CALENDAR

| MEETING | 5th South Asian Confederation of Anaesthesiologists & 1st South Asian Regional Pain Societies Congress | Australian Pain Society 24th ASM & New Zealand Pain Society 29th ASM | 55th Annual Meeting of the American Academy of Neurology |
|-----------------|---|--|--|
| LOCATION | Dhaka, Bangladesh | Christchurch, New Zealand | Honolulu, Hawaii, USA |
| DATE | February 18-20, 2003 | March 9-13, 2003 | March 29-April 5, 2003 |
| CONTACT DETAILS | Dr Lutful Aziz Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka-100 Bangladesh Tel: (+880 2) 861 9115 Fax: (+880 2) 966 9444 E-mail: sacabd@dhaka.net Web site: http://www.sacabd2003.com | Conference Secretariat: DC Conferences Pty Ltd PO Box 571 Crows Nest, NSW 1585 Australia Tel: (+61 2) 9954 4400 Fax: (+61 2) 9954 0666 E-mail: mail@dcconference.com.au Web site: http://www.apsoc.org.au/conference/RegInfo.html | Lori Wiener Tel: (+1 651) 695 2706 E-mail: lwiener@aan.com Web site: http://am.aan.com |

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