



Challenges in

Neuropathic Pain

Welcome to the 18th issue of *Challenges in Neuropathic Pain*, a newsletter from the Multidisciplinary Panel on Neuropathic Pain (MPNP). In this issue, the feature article provides a review on the management of fibromyalgia. The series on drugs for neuropathic pain is continued, covering the evidence for cannabinoids, while the Q&A considers the role of radiofrequency procedures for neuropathic pain. The case study discusses how to recognize drug addiction when treating painful conditions.

Visit www.neuropainhk.org for more resources from the MPNP on neuropathic pain.

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Forward any comments
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Review of Fibromyalgia

Introduction

Fibromyalgia is characterized by widespread chronic musculoskeletal pain.^{1,2} Most patients experience fatigue, sleep disturbance and cognitive impairment,² and may also suffer from a range of other symptoms (Table 1).^{1,3} Fibromyalgia is believed to affect 2-4% of the population, with the condition being about seven times more prevalent in women than men.^{3,4} Patients are usually aged 30 to 55 years at symptom onset.² The causes of fibromyalgia are unknown; however, research suggests that a disorder in central pain processing may play a role in its pathogenesis.^{1,2}

Diagnosis

In diagnosing fibromyalgia, physicians must take a thorough history and perform a physical examination. The American College of Rheumatology has developed criteria for the diagnosis of fibromyalgia (Table 2; Figure 1).⁵ However, there are currently no objective laboratory tests or imaging studies that can produce positive results for fibromyalgia.²

Management of fibromyalgia

A multidisciplinary approach is required to manage this potentially disabling condition. Patients with fibromyalgia experience pain, which can include allodynia, hyperalgesia and paraesthesia, in multiple sites.² Therefore, drugs used for neuropathic pain syndromes are of benefit in fibromyalgia²; combination therapy may be required.³ In addition, non-pharmacological strategies should be implemented, such as lifestyle changes, exercise and cognitive behavioural therapy (CBT).³

Table 1. Common symptoms of fibromyalgia: Concomitant with widespread chronic pain³

- | | |
|----------------------------|---------------------------------|
| • Arthralgia | • Myalgia |
| • Paraesthesia | • Headache |
| • Morning stiffness | • Restless legs syndrome |
| • Poor sleep | • Cramps |
| • Fatigue | • Concentration/memory deficits |
| • Irritable bowel symptoms | • Depression |

Table 2. The American College of Rheumatology 1990 criteria for fibromyalgia

1. History of widespread pain

Pain must be present on the left and right sides of the body, and above and below the waist. In addition, axial skeletal pain must be present.

Widespread pain must have been present for at least 3 months.

AND

2. Pain in 11 of 18 tender point sites on digital palpation (See Figure 1)

The sites are (bilaterally): occiput, low-cervical, trapezius, supraspinatus, second rib, lateral epicondyle, gluteal, greater trochanter, knee.

For a tender point to be considered "positive", the subject must state that the palpation was painful.

Adapted from reference 5

Figure 1. Tender point sites for diagnosis of fibromyalgia

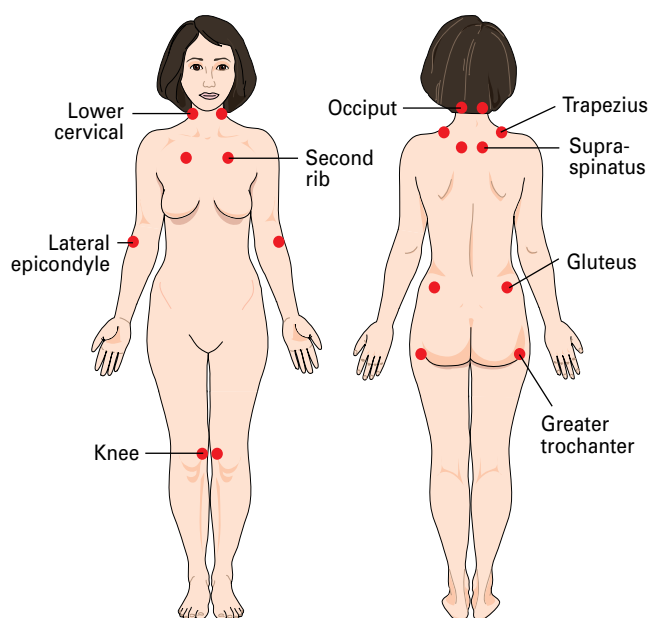
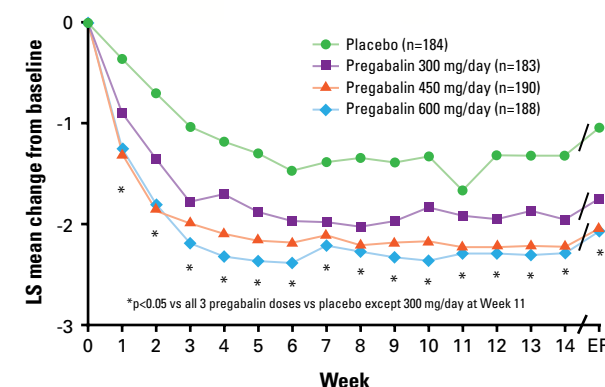


Figure 2. Change in pain score from baseline in patients treated with pregabalin or placebo⁷



EP, endpoint; LS, least squares

for pregabalin-treated patients than those on placebo ($p < 0.0001$), demonstrating durability of benefit in longer-term treatment.

Tricyclic antidepressants

Tricyclic antidepressants (TCAs) provide some benefit to patients with fibromyalgia and are recommended treatment options.¹⁰ Others consider that for first-line treatment of fibromyalgia, the efficacy of TCAs is limited by poor tolerability.⁴

Serotonin-norepinephrine reuptake inhibitors

The serotonin-norepinephrine reuptake inhibitors duloxetine and milnacipran are newer options for fibromyalgia treatment. The efficacy and safety of duloxetine has been studied in four randomized placebo-controlled trials of 3 or 6 months' duration, and two 6-month extension trials.⁴ These studies demonstrated that duloxetine 60 or 120 mg/d significantly improved pain severity and Patient Global Impression of Improvement scores, as well as other clinical outcomes.⁴ Common side effects include insomnia and dry mouth.⁴

Milnacipran, at a dose of 100-200 mg/d, has also been investigated in four randomized placebo-controlled trials, and shown to improve pain scores and the proportion of responders compared with placebo.⁴ Side effects tend to be similar to those reported with duloxetine.¹

Other agents

Recommendations from the European League Against Rheumatism (EULAR) suggest that simple analgesics, such as paracetamol, and weak opioids can be considered in the treatment of fibromyalgia.¹⁰ In addition, tramadol is recommended for the management of pain in fibromyalgia.¹⁰

Pharmacotherapy

α_2 - δ Ligands

Pregabalin* can be considered as a first-line treatment option in patients with fibromyalgia.⁶ Pregabalin has been studied in randomized, double-blind, placebo-controlled trials as monotherapy for fibromyalgia.^{7,8} In these two trials, patients received placebo or pregabalin (300, 450 or 600 mg/d) for 13-14 weeks. In all pregabalin groups, there was a significant improvement in endpoint mean pain score (Figure 2), Patient Global Impression of Change (PGIC) and assessment of sleep. The benefit of pregabalin was evident after only 1 week's treatment (Figure 2). Pregabalin was well tolerated, with the most frequently reported adverse events being dizziness and somnolence.

A 6-month, randomized, double-blind, placebo-controlled, discontinuation trial was designed to evaluate the efficacy of pregabalin monotherapy for durability of effect on fibromyalgia pain.⁹ Patients who responded to initial open-label treatment with pregabalin ($\geq 50\%$ decrease in pain visual analogue scale and at least 'much improved' on PGIC) were eligible to enter the double-blind phase. Time to loss of therapeutic response ($< 30\%$ reduction in pain from open-label baseline or worsening of fibromyalgia symptoms) was significantly longer

Non-pharmacological treatment options

Non-pharmacological treatments should complement drug therapy in the management of fibromyalgia.^{2,3} While the evidence for these options is not as well documented, physical therapy, such as a tailored exercise programme that includes aerobic exercise and strength training, is recommended.^{1,10} Physiotherapy, aquatherapy and CBT can provide benefit to some patients.^{2,10} Furthermore, lifestyle changes such as improving sleep hygiene, eating a healthy diet and practicing meditation or relaxation techniques can be beneficial.² Results from studies on acupuncture are conflicting.¹

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Summary

Fibromyalgia is a chronic disabling condition requiring a multidisciplinary approach to treatment. Treatment should be tailored individually, including pharmacotherapy and non-pharmacological treatments, with an aim to decrease pain, improve sleep and establish a regular exercise programme.

* Pregabalin is currently the only drug in Hong Kong with a licensed indication for fibromyalgia monotherapy

DRUGS FOR THE TREATMENT OF NEUROPATHIC PAIN

In this issue, Part 9 of our series on drugs for the treatment of neuropathic pain discusses the current position of cannabinoids.

Part 9 – Cannabinoids

Pain models in animals, including models of neuropathic pain, have shown that cannabinoids display antinociceptive activity, which is mediated at the peripheral, spinal and supraspinal levels.¹ Such research has generated interest in the potential role of cannabinoids in the treatment of neuropathic pain, particularly when traditional neuropathic pain therapies prove inadequate.

Fontelles and Garcia recently published a review of controlled clinical trials investigating cannabis or cannabinoids (eg, dronabinol, nabilone) for the relief of neuropathic pain.¹ Overall, individual studies showed mild but statistically significant improvements in pain symptoms unresponsive to standard treatments. Around half the studies were in patients with multiple sclerosis-related neuropathic pain, although trials in HIV-associated peripheral neuropathy and chronic neuropathic pain patients also gave positive findings.¹ The effect on

pain perception was generally weak and its clinical relevance remains to be established. Another review concluded that cannabinoids were generally well tolerated in the treatment of pain, with acceptable adverse event profiles.² However, most published clinical trials have been small and short, and there are few data from comparative trials of cannabinoids and approved neuropathic pain therapies.¹

Although cannabinoids show promise for intractable neuropathic pain, more data are needed to better assess their benefit-to-risk profile. In addition, widespread acceptance as therapeutic agents is unlikely until the issue of psychotropic adverse effects has been addressed.^{1,2}

References

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Q & A

Forward any questions on neuropathic pain to the MPNP at mpnp@asia.cmpmedica.com.

What is the role of radiofrequency procedures in treating neuropathic pain?

Radiofrequency is classified as a percutaneous, minimally invasive, neurolytic procedure for patients with pain that does not respond to appropriate medical and physical therapy.¹ Two types are available – conventional radiofrequency and the newer technique of pulsed radiofrequency. In clinical practice both have successfully reduced intractable pain in several chronic neuropathic pain conditions,^{1,2} including trigeminal neuralgia, postherpetic neuralgia and complex regional pain syndrome. The pain relief obtained may last for several months, after which the procedure needs to be repeated.¹

Conventional radiofrequency has a relatively low incidence of side effects and complications, but it occasionally leads to worsening, and even new onset, of neuropathic pain.¹ A review of pulsed radiofrequency studies found few reports of noticeable side effects or complications directly attributable to the procedures, although the authors acknowledged the potential for complications including bleeding, infection, nerve damage from needle placement and post-procedure neuritis.²

Conventional and pulsed radiofrequency have been used clinically for more than 25 years¹ and 10 years,² respectively, and many uncontrolled and observational studies documenting positive outcomes have been published. However, the benefits have not been corroborated in well-designed, randomized, controlled trials. As a result of this lack of high-quality published evidence proving its efficacy, the role of radiofrequency interventions for the treatment of intractable neuropathic pain remains under some debate.¹ Nevertheless, clinical experience justifies its use by skilled physicians in certain situations. The use of radiofrequency can be considered an option for refractory trigeminal neuralgia; in other neuropathic pain conditions, radiofrequency should be used with caution and only by an experienced physician.

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CASE STUDY

In this issue, a case of psychological analgesic drug addiction and pain management in a patient with cancer is discussed.

Recognizing drug addiction when managing painful conditions

History

A 35-year-old man with lymphoma had undergone treatment with combination chemotherapy. Soon after commencing chemotherapy, he developed severe pain on swallowing; upper gastrointestinal (GI) endoscopy revealed herpes simplex oesophagitis. He is unable to swallow solid foods because of the pain and he can only tolerate some liquids.

Management

The patient is given paracetamol with codeine elixir 4 hourly, but this does not relieve the pain. The medication is subsequently changed to morphine sulphate elixir 15 mg 4 hourly. It provides transient relief, but the patient requests higher doses at more frequent intervals. The nursing staff consider the patient's demands unreasonable, and suspect that he may be an addict. On careful history taking, the patient revealed a history of poly-drug abuse about 2 years ago, but denied taking any recreational drugs in the past 2 years.

Questions

1. What are the pros and cons of further increasing the dose of morphine sulphate?
2. How can you differentiate a genuine need for greater pain relief from drug addiction?

Discussion

1. Increasing the opioid dosage may provide better pain relief but there are certain inherent risks, including the patient becoming an addict and the possibility of respiratory depression and cardiovascular and GI complications.
2. Behaviour that might suggest the patient is in fact an addict or prone to attention-seeking include excessive body language, facial grimacing, repeated clock watching, demanding behaviour, finding used syringes or needles in the bedside locker, being overly sedated after "friends" visit, or requesting or demanding specific drugs.

Source: MPNP members

NEWS

Conjoint HKPS and MPNP Scientific Meeting cum HKPS ASM 2009

Pain Management in Daily Practice



The Multidisciplinary Panel on Neuropathic Pain (MPNP) was pleased to partner with the Hong Kong Pain Society (HKPS) to co-organize the "Conjoint HKPS and MPNP Scientific Meeting cum HKPS ASM 2009 on Pain Management in Daily Practice". Held on Saturday, 12 September 2009 at the Langham Place Hotel, the meeting attracted more than 150 delegates. Sessions covered a number of painful conditions commonly encountered in daily practice: neuropathic pain; generalized musculoskeletal pain; and facial pain and headache.

LITERATURE REVIEW

Pérez C, Navarro A, Saldaña MT, Martínez S, Rejas J. Patient-reported outcomes in subjects with painful trigeminal neuralgia receiving pregabalin: evidence from medical practice in primary care settings. Cephalalgia 2009;29:781-790.

This article provides results of a secondary analysis from a larger prospective study that aimed to assess the cost of treatment in patients with refractory neuropathic pain treated in the primary-care setting. In this analysis, 65 patients with trigeminal neuralgia refractory to previous analgesia were treated with pregabalin, either as monotherapy (n=36) or add-on therapy (n=29), for 12 weeks. The mean age of patients was approximately 56 years, 60% were female, and the mean time since diagnosis was 2.4 years. At the baseline visit, the mean number of concomitant analgesics was 2.1, most commonly non-steroidal anti-inflammatory drugs (NSAIDs; 52%), paracetamol (29%), antiepileptic drugs (34%), opiates (19%) and tricyclic drugs (17%). In the add-on group, other medications patients received during the study period included NSAIDs (34%), paracetamol (20%) and opiates (11%).

After 12 weeks' treatment with pregabalin, patients experienced significant reduction in intensity of pain (-40.0 ± 22.1 mm, $p < 0.0001$) and 59.4% achieved pain reduction of $\geq 50\%$. Pregabalin therapy also improved anxiety and depression symptoms, sleep and patient functioning. The authors conclude that pregabalin, as monotherapy and combination therapy, is effective for short-term treatment of trigeminal neuralgia, and suggest that additional randomized controlled trials be undertaken to confirm efficacy, dosage and benefits in longer-term maintenance therapy.



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