In this 26th issue of *Challenges in Neuropathic Pain*, we present a review of the management of chronic low back pain, focusing on back pain with a neuropathic component. The fourth in a series on interventional therapies for neuropathic pain provides a summary of recently published recommendations from the International Association for the Study of Pain Neuropathic Pain Special Interest Group, and the case presentation is on neuropathic cancer pain. Visit [www.neuropainhk.org](http://www.neuropainhk.org) for more resources from the MPNP on neuropathic pain.

Review of the management of chronic low back pain

Low back pain (LBP) is a widely prevalent and debilitating condition with high recurrence rates that can lead to substantial healthcare expenses and health resource utilization. With an estimated lifetime prevalence of 84% and a point prevalence of 12%–33%, LBP is perceived as a disability by up to 12% of the population.¹,² This review discusses the general concepts of chronic LBP, with a focus on the diagnosis and management of chronic LBP with a neuropathic component.

**Epidemiology and pathophysiology**

Chronic LBP is defined as pain on most days in a 3-month period, in the back area from below the costal margin to the gluteal fold. The prevalence of chronic LBP is approximately 23%,³ and it is considered the predominant cause of musculoskeletal pain and disability due to LBP.³

The pathophysiology of LBP is complex, with both nociceptive and neuropathic mechanisms implicated.³ Studies show that 20%–35% of patients with back pain suffer from a neuropathic component.³ The processes causing neuropathic pain in chronic LBP include mechanical nerve root compression from a herniated intervertebral disc, damage to local nerve fibres within a degenerated disc, and the effects on nerve fibres of inflammatory mediators arising from a degenerated disc.⁴

**Comorbidity burden**

Chronic LBP is frequently associated with comorbidities, including depression, panic and anxiety disorders, sleep disturbances, and loss of confidence and self-esteem.³ A recent study found a high prevalence of anxiety (55%) and depression (49%) in a cohort of chronic LBP patients, with the levels being significantly higher in females than males (p<0.01 for both comparisons).³

The presence of a neuropathic component in chronic LBP is associated with greater pain intensity, greater number and severity of comorbidities, decreased quality of life, and higher healthcare costs than with nociceptive pain.³ One study found that the cost of treating neuropathic LBP was 67% higher than that of treating nociceptive LBP. In addition, 16% of the total treatment costs...
were attributable to treatment of neuropathic pain.6

Diagnosis

The diagnosis of a neuropathic component of LBP is challenging due to the absence of a gold standard. A systematic approach to evaluation is recommended which includes physical examination, clinical and sensory bedside examination, quantitative sensory testing, radiological examination, neurophysiological testing and use of neuropathic screening tools.4

Patients with neuropathic LBP typically present with specific symptoms expressed with a certain intensity rather than easily recognizable neurological lesions. Sound clinical judgment and history taking are considered the most important skills for diagnosing a neuropathic component in chronic LBP. Currently, several screening tools are available to identify potential patients with neuropathic LBP; these tools are premised on verbal pain description with or without limited bedside testing. These include the LANSS (Leeds Assessment of Neuropathic Symptoms and Signs), the DN4 (Douleur Neuropathique en 4 questions), ID-Pain, and painDETECT.4 The Chinese version of the ID-Pain questionnaire has been validated in Hong Kong Chinese patients and can be useful in the primary care setting as an initial diagnostic tool for neuropathic pain.7 The painDETECT questionnaire is also a reliable, easy-to-use screening tool with high sensitivity (85%) and specificity (80%) that was specifically developed to identify a neuropathic pain component in adults with LBP.8

Management

The goal of treating chronic LBP is to reduce dysfunction and improve quality of life by reducing pain while minimizing the risks and adverse effects of treatments.3 As radiculopathy-induced neuropathic pain often responds poorly to simple analgesics and neuropathic pain medications, a unique care pathway is recommended whereby the condition is diagnosed with early investigations, and appropriate treatment instituted in accordance with symptom severity, and known risks and benefits.9 The British Pain Society has proposed an algorithm which emphasizes a multidisciplinary approach for managing low back and radicular pain.9 The algorithm for radicular pain is shown in Figure 1.9

Non-pharmacological management

Physical, psychological and rehabilitation treatments play an important role in the management of chronic LBP, and are usually offered as part of multimodal and interdisciplinary rehabilitation programmes. Data show that exercise therapy is as effective as...
conventional physiotherapy and may help to increase return of patients to daily activities and work. Psychological interventions including psycho-education, fear-avoidance training, relaxation and mindfulness, aim to help patients better cope and self-manage their disability despite ongoing pain. These show modest benefits in terms of pain reduction and improvement in physical and emotional functioning. Interdisciplinary rehabilitation programmes comprise psychoeducation, cognitive restructuring, acceptance and commitment therapy, physical and vocational rehabilitation, and drug self-management. These interventions significantly reduce pain and the use of prescription drugs and healthcare resources, as well as increase rates of returning to work. 

Pharmacological management
In patients with chronic LBP, pharmacotherapy aims to reduce pain and associated complaints to enable other non-pharmacological approaches. Indications for initiating and continuing medications should be examined and evaluated at regular intervals. Acetaminophen (paracetamol) and non-steroidal anti-inflammatory drugs (NSAIDs) target the nociceptive component and, thus, are not effective for the neuropathic component of chronic LBP. Thus, patients often require combination therapy for managing the nociceptive and neuropathic components of pain.

Opioids
Opioids target both nociceptive and neuropathic components of chronic LBP, and are safe and effective for managing the condition. A meta-analysis of 15 trials found that patients with chronic LBP who received opioids had more pain relief and less difficulty performing their daily activities in the short-term versus placebo. Long-term prescription of opioids should be carefully considered in the context of their adverse effects such as sleep disturbance, nausea, constipation, and risk of misuse and abuse leading to addiction, overdose and death.

Antidepressants
Antidepressants are recommended as first-line drugs for neuropathic pain and are believed to target the neuropathic component of chronic LBP.

Anticonvulsants
Gabapentin and pregabalin are anticonvulsant agents that exert an anti-hyperalgesic effect by binding to the α 2δ subunit of N-type voltage-gated calcium channels. These agents have proven efficacy in treating diabetic peripheral neuropathic pain and postherpetic neuralgia. Pregabalin is effective in chronic LBP when combined with celecoxib or opioids.

Interventional management
Interventional techniques can provide symptomatic relief and facilitate rehabilitation in patients with chronic LBP. The most commonly used interventions include epidural steroid injections and facet joint interventions. Although interventional techniques offer a better balance of benefits and risks than spine surgery, these are often omitted from clinical practice guidelines on chronic LBP due to paucity of high-quality clinical trial data.

Spine surgery
Spine surgery is only recommended in patients with refractory chronic LBP with a pathology who fail to respond to prolonged, appropriate conservative therapies. Currently, no conclusive evidence can be derived from the existing data on the effects of spine surgery on the outcomes of chronic LBP. The three main surgical options offered for chronic LBP include spinal decompression surgery, spinal fusion surgery, and disc arthroplasty. Urgent spinal surgery may be indicated in patients with severe or progressive motor weakness, or signs and symptoms of cauda equina syndrome.

LITERATURE REVIEW

Effects of pregabalin on sleep disturbance in different clinical conditions
Pregabalin is an α,δ ligand approved for the treatment of a variety of clinical conditions and its analgesic, anxiolytic and anticonvulsant properties are well documented. However, its effects on sleep are less known.

This review aimed to summarize all the published data on the effects of pregabalin on sleep in different clinical conditions associated with sleep disturbance. PubMed and Pfizer databases were searched for published papers on the effects of pregabalin treatment on any outcome measure (primary or secondary) related to the assessment of sleep in healthy volunteers, or in patients with clinical conditions such as neuropathic pain, fibromyalgia, partial onset seizures or generalized anxiety disorder.

The data reviewed found that patients reported improved sleep quality in response to pregabalin across several different clinical conditions. Polysomnography revealed fewer awakenings, more time spent in slow-wave sleep and less time spent in stage 1 sleep, suggesting that pregabalin consolidates fragmented sleep and increases depth of sleep. The evidence suggested a beneficial effect of pregabalin on sleep, which may be attributed to its ability to modulate the α,δ subunit of neuronal voltage-gated calcium channels.

According to the authors, polysomnographic studies are warranted to confirm the precise sleep benefits provided by α,δ ligands. Furthermore, additional preclinical/clinical research will serve to elucidate the mechanisms underlying the benefits of pregabalin on sleep.

CASE PRESENTATION

Neuropathic cancer pain

Presentation
A 60-year-old lady with known breast cancer and with lung, liver and left femoral metastases, presented to the clinic with pain in her left thigh. The patient described the pain, which was frequently severe, as tenderness over the thigh, with constant background pain and instances of spontaneous or movement-related exacerbation. An X-ray of the left thigh showed a lytic lesion in the left femoral shaft (Figure 2), which was consistent with a bone metastasis from the breast cancer.

Management strategy
The patient received radiotherapy followed by surgical pinning of the femur. Furthermore, the patient received intravenous bisphosphonate and was given regular opioids and gabapentin. Pain was relieved most of the time, although there was still incidental breakthrough pain on weight-bearing and walking. A physiotherapy programme was then initiated, with transcutaneous electrical nerve stimulation (TENS) for 30 minutes before transferring or mobilizing the patient out of bed. She was also taught a simple diaphragmatic breathing exercise, a relaxation technique that can be used before walking. Timed therapy with fentanyl lozenges and the use of the Zimmer frame also helped. With the different drugs and techniques used over the course of management, the patient was able to get out of bed independently and walk short distances freely.

INTERVENTIONAL THERAPIES FOR NEUROPATHIC PAIN

Part 4: Summary of the International Association for the Study of Pain Neuropathic Pain Special Interest Group recommendations

Patients with neuropathic pain who do not respond adequately to pharmacological treatments used alone or in combination with non-pharmacological treatments are often considered for interventional treatments. These are defined as invasive procedures involving delivery of drugs into targeted areas, or ablation/modulation of targeted nerves for the treatment of pain.1

The International Association for the Study of Pain (IASP) Neuropathic Pain Special Interest Group (NeuPSIG) recently evaluated systematic reviews, clinical trials, and existing guidelines for the interventional management of neuropathic pain to develop evidence-based recommendations. The various interventions for which evidence was summarized included neural blockade, spinal cord stimulation, intrathecal medication, and neurosurgical interventions. The indications for interventional management included herpes zoster and postherpetic neuralgia; painful diabetic and other peripheral neuropathies; neuropathic pain due to spinal cord injury; central post-stroke pain; radiculopathy and failed back surgery syndrome; complex regional pain syndrome; and trigeminal neuralgia and neuropathy.2

Overall, the authors noted a marked paucity of high-quality clinical trials and, therefore, were unable to make any strong or conclusive recommendations for interventional management of neuropathic pain. Four weak recommendations were made, based on the amount and consistency of evidence, including degree of efficacy and safety2:

1. Epidural or paravertebral nerve blocks for herpes zoster
2. Epidural steroid injections for radiculopathy
3. Spinal cord stimulation for failed back surgery syndrome with radiculopathy
4. Spinal cord stimulation for complex regional pain syndrome type 1

It was emphasized that interventional management of patients with chronic neuropathic pain should be considered an integral component of a comprehensive approach that includes pharmacological and non-pharmacological, non-interventional treatments. Interventional treatments for neuropathic pain should ideally be offered in clinical and research settings whereby there is systematic collection and reporting of patient outcome data. More randomized controlled trials, long-term studies, and head-to-head comparisons among different interventional and non-interventional treatments are warranted to improve the quality of evidence in this field.2

References