Interventions in Neuropathic Pain: Options for Management of the Hidden Hurt

Neuropathic pain can be complex, as the nerve fibres themselves are damaged, dysfunctional or injured. As a result, they transmit incorrect signals, at times with minimal provocation or, in fact, without stimulus. Treatment of neuropathic pain can be difficult, because developing a care plan first relies on understanding the individual aetiologies of the condition, in order to delineate and address the underlying mechanisms and different symptoms that arise. Perhaps because of these complicating factors, only a minority of people with neuropathic pain experience a clinically relevant benefit from any one intervention. A multidisciplinary approach that combines pharmacological, physical and cognitive interventions, as appropriate, is now advocated.

Pain has been defined by the International Association for the Study of Pain as “an unpleasant sensory and emotional experience that is associated with actual or potential tissue damage … pain is always subjective”. This definition is most suitable for chronic pain that involves some type of tissue damage (Gerhart, 2000).

However, neuropathic pain is a specialised type of pain that can be much more complex than this definition. The nerve fibres themselves are damaged, dysfunctional or injured. As a result, they transmit incorrect signals, at times with minimal provocation or, in fact, without stimulus (Boots WebMD, 2016). Treatment of neuropathic pain can be difficult, because developing a care plan first relies on understanding the individual aetiologies of the condition, in order to delineate and address the underlying mechanisms and different symptoms that arise (Beniczky et al, 2005).

Underlying conditions that can result in neuropathic pain include:

- Diabetic neuropathy
- Post-herpetic neuralgia
- Trigeminal neuralgia
- Radicular pain
- Post-surgical chronic pain
- Neuropathic cancer pain after chemotherapy
- Neuropathic pain after direct invasion of neural structures.

Neuropathic pain can also arise due to stroke, spinal cord injury and multiple sclerosis (Multiple Sclerosis Trust, 2016).

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**Presentation of pain**
Neuropathic pain can be intermittent or constant. Patients describe shooting, stabbing pains — such as an electric shock — burning, tingling, tightness, numbness, a pricking or itching and, often, a pins-and-needles sensation. Alldynia (pain from gentle stimulus) and hyperalgesia (an over-exaggerated response to minimal stimulus) can also cause problems (International Association for the Study of Pain, 2007; NICE, 2013).

The extent of incidence of neuropathic pain in the population is unknown. An epidemiological review of chronic pain was unable to provide an accurate estimate of prevalence (Smith et al, 2012).

We do know, however, that an individual’s beliefs and perception of their pain and its causes will affect their coping strategies (Tasso and Behar-horenstein, 2004). Probable mood changes, disturbed sleep and anxiety all need to be addressed. As all pain is subjective, treatment plans are must be individually tailored to acknowledge the inherent differences in the experience of pain.

**Goals of treatment in neuropathic pain**
The clinician must acknowledge that pain-free status is not always achievable. In many clinical trials involving pharmacological and physical therapies, a reduction in pain of 50% is commonly considered an adequate and successful endpoint (Hanna et al, 2006). Healthcare professionals have a duty of candour with patients to manage their expectations of their treatment goals (Greater Manchester Medicines Management Group, 2014).

A thorough, holistic assessment of the condition, the presentation of the pain, and the underlying disease is needed to determine the strategies for management of neuropathic pain. Treatment is likely to require more than one type of intervention. Certain underlying causes may make management of neuropathic pain more straightforward. In diabetic neuropathy, for example, ensuring diabetes is well-controlled may help improve the resultant painful neuropathy or prevent it from worsening (NHS Choices, 2016).

**Multidisciplinary approach**
Neuropathic pain is difficult to treat effectively, with only a minority of people experiencing a clinically relevant benefit from any one intervention. Once treatment of underlying causes has been optimised, treatment of symptoms can be more effective. A multidisciplinary approach that combines pharmacological, physical and cognitive interventions, as appropriate, is now advocated (Ju et al, 2006).

**Oral medications**
Use of nonsteroidal anti-inflammatory drugs (NSAIDs; e.g. ibuprofen, aspirin) can relieve mild pain. For more severe pain, a prescription-only NSAID, such as diclofenac, may be considered. Opioids, such as tramadol and oxycodone, should be approached with caution due to potential issues with dependency and addiction, and should be considered only when other methods had failed.

Tricyclic antidepressants such as amitriptyline, doxepin and nortriptyline are considered by many as first-line treatment, although neuropathic pain is an unlicensed indication for use. Anticonvulsants initially developed as treatment for epilepsy (e.g. gabapentin, pregabalin) are recognised as effective against nerve pain.

Duloxetine, a heterocyclic antidepressant in the serotonin-norepinephrine reuptake-inhibitors class, and venlafaxine, an extended-release antidepressant, also have a place in neuropathic pain relief. Broadly, these drugs work by reducing the nerve cell’s ability to reabsorb neural transmitters, such as serotonin and noradrenaline. If these transmitters fail to be absorbed, pain messages are suppressed (Pain Concern, 2013). Side effects of these medications include: dizziness, nausea, dry mouth, drowsiness, blurred vision and loss of appetite. As a result, these these drugs are often titrated to build effectiveness, while minimising side effects.

**Topical preparations**
Capsaicin cream, a prescription-only medicine, licensed for use under specialist supervision, can be used. The preparation is made from hot peppers to capture substance P, which blocks mild pain distal to the area of application. However, the cream can result in skin irritation and burning at the site of application. Lidocaine patches can be deployed, but are rarely used outside of specialist centres; their use can result in drowsiness and dizziness.

A transparent, quick-drying spray film dressing (e.g. Opsite® Spray, Smith & Nephew) can be applied to the skin to form a direct-contact, and constant, low-level touch stimulation of sensory nerves. This may be effective for neuropathic pain in accordance with the gate control theory. The idea is this: only a limited number of pain signals can be carried along the nerves. When the ‘nerve gates’ are open, pain messages ‘get through’ more easily, and the pain experienced can be intense. But if the nerve gates are ‘overwhelmed’ by a primary signal, other pain messages may be prevented from reaching the brain and may not even be experienced. According to this model, the stimulus of the light film on the skin may provide the priority message...
that blocks many of the other pain signals, reducing discomfort without the aforementioned side effects (Foster et al, 1994).

**Physical therapies**
Use of transcutaneous electrical nerve stimulation (TENS) may be used for effective relief of neuropathic pain. Strategically positioned pads deliver a current at varying frequencies, affecting the central and peripheral nervous systems. Areas in the brain stem and spinal cord that use opioid and serotonin neurotransmitters are stimulated by TENS activity. In the peripheral system, at the actual site of TENS application, opioid and α-2 noradrenergic receptors produce the pain-relieving effect (Sluka, 2008).

There have been a number of literary reviews collating TENS studies. Many have found statistically significant improvements in pain compared to placebos, but there are differences in length of individual session times and whether treatment can be prolonged. The majority of the evidence recommends the use of TENS therapy for the management of painful diabetic peripheral neuropathy. However, evidence is often limited by the short duration of trial period in the research and a lack of standardisation of TENS therapy for the condition (Merghani, 2015).

Other physical therapies may aim to improve muscle strength. Effective use of hand or foot braces, walking aids and physiotherapy to improve movement and balance (depending on the underlying cause of the pain) can be very beneficial (Sein, 2017).

**Surgical intervention**
The need for surgery arises when the neuropathy is caused by pressure from tumours or inflammation, and the pressure must be relieved to resolve the pain. Examples include carpal tunnel surgery and excision of a cancerous mass.

**Alternative therapies**
Acupuncture — the practice of inserting sharp, thin needles into the skin along ‘meridians’ of the body — has been a central tenet of Chinese medicine for millennia. It is used in the West mainly as a means of pain relief. Acupuncture appears to affect the peripheral and central nervous systems in subtly different ways. In the periphery, polymodal-type receptors in deep tissue are activated when the needles are inserted at points that trigger specific afferent nerve fibres (Dhond et al, 2008; Kim et al, 2008; Zhang et al, 2005). In the central nervous system, it is thought to be the deactivation of several limbic areas that produce descending inhibitory variations to help control pain (Takeshige et al, 1992; Paola and Arnold, 2003; Hui et al, 2010).

In a meta-analysis of randomised, controlled trials on the effects of alpha-lipoic acid (ALA) for symptomatic peripheral neuropathy in patients with diabetes mellitus, results favoured the effectiveness of ALA administration (Ziegler et al, 2004). When given intravenously at a dosage of 600 mg/day over a period of 3 weeks, ALA leads to a significant and clinically relevant reduction in neuropathic pain (grade of recommendation A), the authors concluded. However, it was unclear if longer-term improvements were clinically relevant. In addition, ALA administration can increase sensitivity to insulin and result in hypoglycaemia in people with diabetes (Ziegler et al, 2004).

Evening primrose oil has also been trialled in tackling neuropathy. A review of three randomised controlled trials identified symptom relief with doses of 360–480mg; no effect on blood-glucose levels was seen (Ford, 2001; Halat and Dennehy, 2003).

**Ongoing assessment**
The importance of individual assessment, incorporation of patient-specific considerations, and need to manage patient expectations cannot be underestimated. The degree of neuropathic pain and its influence on daily-to-day life and sleep patterns must be deliberated. The clinician must understand the aetiology of the pain and whether its intensity has recently changed. Other important aspects of assessment include physical or psychological issues, and the potential for drug interactions with existing medication. Patients should understand any medication regimen, and be educated about how to incrementally build up dosage, if appropriate.

Reassessment should include a review of all interventions that have been/are being used to determine:
- The level of pain control achieved
- Impact on lifestyle
- Sleep disturbance
- The patient’s physical and psychological wellbeing
- Any side effects they may be experiencing.

Reassessment should also consider whether treatment(s) need to continue. If treatment is to cease, then careful tapering of pharmacological interventions should be undertaken (Mayo Clinic, 2016).

**The NICE guidelines**
Current NICE guidelines regarding the pharmacological treatment of neuropathic pain can be found in clinical guideline 173. They differentiate between trigeminal neuralgia, which requires specialist intervention and the use of carbamazepine and/or surgery; and all other neuropathic pain (NICE, 2013).

NICE-recommended first-line treatment is the use of amitriptyline,
Neuropathic pain can be a real burden for our patients. It is also a condition that requires careful diagnosis, understanding and specific treatment. Ongoing review of effectiveness and titration of medication is essential, as is holistic management of the physical and psychological neuropathic pain can produce.

Taking a holistic approach
The NICE guidelines are designed to assess the pharmacological management of painful neuropathy, but there are many other methods available. Anecdotally, patients have reported the effective use of bed cages in an effort to avoid the weight of even a thin sheet, to achieve a decent night’s sleep. Conversely, other patients wear socks in bed to have something in contact with their feet to ‘calm’ their nerves. Others insist that silk sheets are the only possible option to tackle their sleepless nights.

The discomfort that can be generated by endless sleep deprivation and ongoing pain should never be underestimated. Many patients with neuropathic pain will have complex medical conditions, with multiple demands on their already-stretched capabilities. And yet, many report that their burning feet or hands are the things that worry them most.

Neuropathic pain can be a real burden for our patients. It is also a condition that requires careful diagnosis, understanding and specific treatment. Ongoing review of effectiveness and titration of medication is essential, as is holistic management of the physical and psychological neuropathic pain that can produce.

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