

NICE neuropathic pain guidelines: clarity for initial treatment

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This recently published NICE guideline on *The Pharmacological Management of Neuropathic Pain in Adults in Nonspecialist Settings* (CG173) replaces CG96, which was first issued in March 2010. Both of these guidelines were produced to help clinicians manage neuropathic pain in nonspecialist settings, and start by listing the symptoms and range of conditions that may cause neuropathic pain.

Neuropathic pain

The International Association for the Study of Pain (IASP) has defined neuropathic pain as 'pain caused by lesion or disease of the somatosensory system'. This is a more specific definition and requires the demonstration of abnormalities within the sensory pathways. In the UK, it is estimated that 7 per cent of the population has neuropathic pain. Half of those affected are either unemployed or underemployed.

The direct and indirect healthcare costs and negative impact on quality of life are considerable. The presence of neuropathic pain alone is associated with significant morbidity and mortality. For example, 95 per cent of patients with neuropathic pain report sleep interference and two-thirds have depression, anxiety or both.

In a Taiwanese study of over 300 patients with type 2 diabetes, the hazards ratio of all deaths increased by five-fold in those with diabetic painful neuropathy compared to those without. This increased mortality is independent of other risks, such as hypertension or hyperlipidaemia. There is therefore an imperative to improve the diagnosis and management of neuropathic pain.

Recommendations

This recent guideline recommends that patients with neuropathic pain be offered a choice of amitriptyline (unlicensed indication), duloxetine (Cymbalta), gabapentin or pregabalin (Lyrica) as initial treatment except for those with trigeminal neuralgia. It further recommends that if initial treatment is ineffective or not tolerated, then one of the remaining three drugs should be tried. Tramadol should only be used as an acute rescue medication.

For those with localised peripheral neuropathic pain who wish to avoid or cannot tolerate systemic treatment, topical capsaicin cream should be considered.

The guideline specifically recommends that nonspecialists avoid the use of a number of other medications including cannabis, strong opioids such as morphine and the long-term use of weaker opioids such as tramadol.

Trigeminal neuralgia was considered a separate condition where carbamazepine is suggested as initial treatment. If initial

treatment is ineffective or not tolerated, then expert advice ought to be sought.

Nonpharmacological treatment

It is important to bear in mind that these guidelines are specifically for pharmacological treatment of neuropathic pain. Other forms of treatment such as acupuncture, transcutaneous electrical nerve stimulation (TENS), physiotherapy, psychology, osteopathy or chiropractic treatment are not considered.

The multidisciplinary approach to managing neuropathic pain is now well established and clinicians should always consider nonpharmacological treatment on top of drugs recommended in this guideline.

Which drugs to use

These guidelines do not recommend which drug to start first. My practice is to use amitriptyline or gabapentin as initial choice as they have lower acquisition cost.

The guideline does not separate out specific pain syndromes either, such as central or peripheral neuropathic pain. This differentiation can be relevant. Pregabalin is licensed for central neuropathic pain and there is some evidence that amitriptyline may be effective. The evidence is less so for gabapentin or duloxetine.

There is also evidence that some drugs are more efficacious for different neuropathic pain syndromes. For example, in painful peripheral neuropathy secondary to cancer chemotherapy, there is better evidence that duloxetine is effective compared to pregabalin, gabapentin or amitriptyline.

For patients with painful peripheral neuropathy secondary to HIV treatment, none of the recommended drugs have been shown to be effective in placebo-controlled studies. Therefore, capsaicin may be the treatment of choice.

These small differences are difficult to separate out in broadly produced guidelines. However, they are important to guide clinicians in choosing the best initial treatment or to seek early referral for specialist care.

The guideline does not mention the use of the lidocaine (Versatis) local anaesthetic patch because efficacy data derive mainly from open-labelled studies. Similarly, other tricyclic drugs such as imipramine or nortriptyline (unlicensed indications) were not mentioned.

In my clinical practice, I continue to offer the lidocaine patch as it is well tolerated and effective for localised peripheral pain, particularly when allodynia or hyperalgesia is present. Similarly, although most published studies used amitriptyline as the main

tricyclic drug, I continue to prescribe imipramine or nortriptyline, which causes less sedation and is better tolerated.

The guidelines only mention carbamazepine as the initial treatment for patients with trigeminal neuralgia. Although a very useful drug, it has many side-effects and allergic reactions can be severe, particularly in those with southern Chinese ancestry. The recommendation to seek expert help early on would also be justified. There are a number of other drugs that are as effective and associated with less side-effects.

These guidelines do not make any recommendations on combination therapy. They do, however, call for more research to be carried out. Combination therapy is obviously very important as most single treatments have a number needed to treat of between two and five. This means that you will have to prescribe a medication for between two and five patients for one to achieve 50 per cent pain relief. In the practical setting, it is combination therapy that offers the best choice for patients between pain relief and side-effects.

Conclusions

In my opinion, these guidelines offer clarity for the initial treatment of neuropathic pain in nonspecialist settings. Although four drugs are recommended as initial therapy, side-effects may decide which drug to choose.

The recommendation to avoid long-term use of opioids is also important. It is common to see patients referred to pain clinics prescribed large doses of opioids, especially via the transcutaneous route. For example, a 12µg per hour patch of fentanyl is equivalent to 50mg of morphine a day. This is a very large dose when one considers that 2.5–5mg of morphine is the recommended dose for alleviating pain of myocardial infarction. Large doses of opioids suppress endocrine and immunological function and can lead to paradoxical hyperalgesia.

Even milder opioids such as tramadol can induce medication overuse headaches.

The implementation of these guidelines should be coupled with a good education programme, both for clinicians and the public. It is important for patients to understand why they develop neuropathic pain and what can be done to alleviate the symptoms. To that end, it is important that colleagues in a nonspecialist setting have a clear understanding and be able to use simple analogies to help patients understand the pathogenesis of their very unpleasant and commonly distressing symptoms.

Declaration of interests

Dr Chong has worked with NICE and was a member of the Guideline Development Group for neuropathic pain published in 2013. He was also specialist advisor to the Standards Committee as well as the Health Technology Assessment Group at NICE.

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