Neuropathic pain

In March this year, the National Institute for Health and Clinical Excellence published a new guideline for the pharmacological management of neuropathic pain. This article outlines four reasons why both primary and secondary care doctors should welcome the guideline.

Dr Mick Serpell Consultant and Senior Lecturer in Anaesthesia and Pain Management, University Department of Anaesthesia, Gartnavel General Hospital, Glasgow G12 0YN
email mgserpell@cheerful.com

The National Institute for Health and Clinical Excellence (NICE) published its guideline for the pharmacological management of neuropathic pain in adults in non-specialist settings in March of this year.[1] It specifically avoids the issue of diagnosis. This was a missed opportunity because the condition is not an easy one to diagnose for the non specialist. There have been several advances over recent years, such as the development of highly sensitive and specific screening tools, that can facilitate this process.[2] Therefore, this guideline makes the mistaken general assumption that diagnosis of neuropathic pain is not part of the problem. However this issue aside, the guideline should be welcomed by both primary and secondary care alike for four basic reasons.

Firstly, the mere fact that NICE has developed a guideline for the management of neuropathic pain gives a level of kudos and public limelight to this condition. This can only benefit the patient and medical services dealing with the problem as now the basic "benchmark" has been set.

The second reason is that the nine key principles of the guideline propose a sensible and holistic approach to the patient with neuropathic pain, which (if followed) will lead to better patient care.

Drugs are not mentioned until the fourth principle. The first three principles deal with onward referral, continuing with previously established effective treatments, and the incorporation of education and psychological components. The remaining six key principles highlight pharmacology issues, such as tailoring of the different drug options to the individual patient needs, advice on drug dose and titration, and promotion of early and regular review of progress.

The third reason is that while the specific order of drug management options will not satisfy everybody, the fact that most of the standard drugs are present (and therefore accessible to the patient) is something that will please all clinicians. Patients will have the opportunity of exposure to all three of the main adjuvant drug classes; antidepressants (amitriptyline, nortriptyline, imipramine, and duloxetine), anticonvulsants (pregabalin), and antiarrhythmics (lidocaine plaster). This principle will prevent the situation that often arose previously, namely that general practitioners (GPs) could only prescribe newer drugs if recommended by the "expert". This practice had the deleterious effect of simply delaying appropriate therapy because of the inevitable delays incumbent while the patient waited to see a specialist.

Algorithms for neuropathic pain have developed considerably over recent years. Historically, all types of neuropathic pain were treated the same — regardless of aetiology. The review by Sindrup was one of the first to collate all the possible treatments for neuropathic pain and give some indication of the strength of their effectiveness.[3] The treatment recommendations from an American expert consensus group were published in 2003.[4] This guidance merely stated the options available and did not indicate a specific prioritisation. The individual drugs were amitriptyline, gabapentin, tramadol, opioids and the lidocaine plaster. Advice was given on which drug might be the best choice in a particular patient, depending on known side effect profiles and contraindications,

speed of action, complexity of titration and type of pain (whether it was pure neuropathic pain or a mix of neuropathic and nociceptive pain). The same group later developed this into more specific advice as further studies materialised and meta-analysis became possible.[5] Specific treatments could be prioritised, based on their "number needed to treat" and "number needed to harm" data. They produced an algorithm, which, because of its simplicity, has helped consolidate the pharmacological treatment of neuropathic pain.[5]

Meanwhile, the European guidelines, first published in 2006, had a slightly different tack.[6] They actually subdivided neuropathic pain into four main categories; painful polyneuropathies, postherpetic neuralgia, trigeminal neuralgia and central pain. They suggested several drugs at each line, and prioritised them into first-, second- or third-line therapies. The latest European version in 2010 has replaced painful polyneuropathies with diabetic neuropathic pain as this pain model, along with postherpetic neuralgia, is one of the most commonly studied forms.[7]

In the present NICE guideline, the first-line therapy for painful diabetic neuropathy is duloxetine. This is based on the recent robust high quality studies completed for the drug in this pain condition. The choice of which drug to use first for all the other types of peripheral neuropathy, either amitriptyline or pregabalin, is left to the clinician's judgement. The NICE group concluded that pregabalin was the most cost effective drug treatment. This was primarily because the pregabalin trials are the most recent trials, which tend to include these kind of data compared with "older" trials of the other drugs. The guideline does mention that the lidocaine plaster is only licensed for postherpetic neuralgia. However, it does not seem to imply restriction of its use to this specific type of neuropathic pain as it does not state that off-label use is not recommended.

The fourth good rationale of this guideline is that there is promotion of drug combinations (amitriptyline and pregabalin) as second-line therapy in resistant neuropathic pain. The evidence for the effectiveness of combination therapy is very recent, though it has been common clinical practice for many years. The recommendation is made with the cautious note of the potential for increased side effects. There is also reassuring advice that combining two drugs that increase serotonin levels (tramadol with amitriptyline, nortriptyline, imipramine or duloxetine) is acceptable as the risk of serotonin toxicity is low. These two facts

are useful to propagate as they are common areas of concern in general practice.

One obvious omission in the NICE guideline is gabapentin, which is not even mentioned as an alternative to pregabalin. Both are equally effective and tolerated, and there are many anecdotes of patients responding to one when they do not tolerate or get benefit from the other. Clinicians find it useful to have several options. Pregabalin is preferred because overall cost effectiveness is better but until the different NHS departments embrace collective budgets, prescribers are always likely to choose to pay for the less expensive gabapentin.

Neuropathic pain is responsive to potent opioids, and they can be as effective as amitriptyline. However the guideline specifically advises not to use them, but tramadol can be considered while the patient is referred. This is probably an acceptable stance to take for non-pain specialists, given the concerns of opioid addiction and abuse. However, if the clinician is knowledgeable in their use, they should be allowed to offer this form of therapy as there is robust evidence and advice in use of potent opioids for non-cancer pain.[8]

This guideline should be actively promoted as it will undoubtedly lead to an improvement in the wider management of peripheral neuropathic pain by the non specialist. It will standardise and speed up the implementation of therapeutic options if adopted. One would expect that a NICE guideline would be common knowledge to both the medical and general population, and that implementation would be taken for granted. However, change in behaviour requires more than just education. Hopefully the impetus of the guideline will help push forward other developments such as Quality Outcome Framework targets to drive activity in general practice. That, and "patient power" in the guise of an informed patient requesting the next line of therapy, will help to secure the widespread adoption of this useful document.

Conflict of interest: Dr Serpell has been involved in clinical trials of analgesic medication for several pharmaceutical companies. He has also received honoraria for speaking at sponsored satellite symposiums.

References

1. NICE Clinical Guideline 96. The pharmacological management of neuropathic pain in adults in non-specialist settings. http://bit.ly/agZ1qu 9accessed 29 September 2010)
2. Bennett MI, Attal N, Backonja M, et al. Using screening tools to identify neuropathic pain. *Pain* 2007; **127**: 199–03
3. Sindrup SH, Jensen TS. Efficacy of pharmacological treatments of neuropathic pain: an update and effect related to mechanism of drug action. *Pain* 1999; **83**: 389–00
4. Dworkin R, Backonja M, Rowbotham M, et al. Advances in Neuropathic Pain. Diagnosis, Mechanisms, and Treatment Recommendations. *Arch Neurol* 2003; **60**: 1524–34
5. Finnerup NB, Otto M, McQuay HJ, et al. Algorithm for neuropathic paintreatment: an evidence based proposal. *Pain* 2005; **118**: 289–05
6. Attal N, Cruccu G, Haanpaa M, et al. EFNS Guidelines on pharmacological treatment of neuropathic pain. *EJN* 2006; **13**: 1153–69
7. Attal N, Cruccu G, Baron R, et al. EFNS Guidelines on pharmacological treatment of neuropathic pain: 2010 revision. *EJN* 2010; **9**: 1113–e88
8. British Pain Society. Opioids for persistent pain: good practice. London: BPS, January 2010. http://bit.ly/c0QMtW (accessed 5 October 2010)