New NICE guidance for DPNP: Evidence based and cost effective

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If you would like to read more about DPNP and the new NICE guidance, a copy of the supplement ***Diabetic peripheral neuropathic pain: An update on pharmacological management*** is enclosed in this issue.

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Diabetic peripheral neuropathic pain (DPNP) is a cause of considerable disability and is often under- or misdiagnosed and incorrectly or under-treated. Many pharmacological and non-pharmacological approaches have been suggested for the treatment of DPNP, but in practice achieving a reduction in pain of >50% is rare and side-effects often limit dose titration. Several recent reviews assess current DPNP treatments (Dworkin et al, 2007; 2010).

A recognised but unaddressed issue in clinical trials examining therapies for DPNP is the "placebo effect" (Katz et al, 2008; Wymer et al, 2009). Thus, several recent studies on DPNP have shown a placebo effect that has approached, and even surpassed, the effect of active therapy (Irizarry et al, 2009; Selvarajah et al, 2009). These studies suggest that we need to rethink clinical trial design for DPNP.

While the traditional approaches to DPNP have been to change or substitute treatments, due to lack of efficacy or side-effects, a growing body of evidence suggests that combining lower doses of agents that act on different pain pathways may achieve better efficacy with fewer side-effects (Baron et al, 2009; Zin et al, 2010). The use of combination treatment is, of course, nothing new in the treatment of long-term conditions and their complications, but is quite a new paradigm for the management of DPNP.

NICE (2010) guidance on neuropathic pain was published in March. It provides a comprehensive evidence base for the management of DPNP in non-specialist settings, and an economic rationale (also see Health Technology Assessment Programme, forthcoming). "Non-specialist settings" were defined as primary and secondary care services that did not provide a specialist pain service.

Thirty-four different pharmacological treatments for neuropathic pain (antidepressants, anti-epileptics, opioid analgesics, topical treatments) were considered. Some 23 207 studies were retrieved using systematic searches and reviewed. The analysis not only included 90 randomised placebo-controlled trials but an additional 10 head-to-head comparative trials and four combination therapy trials.

Recommendations were based on evidence of clinical efficacy (determined by percentage pain relief and side-effects) and cost effectiveness, to ensure good use of NHS resources. In the detailed cost-effectiveness analysis, duloxetine – especially in dosages of up to 60 mg per day – was considered to be the most cost-effective treatment. Duloxetine was, in fact, more cost effective than amitriptyline, which was surprisingly similar to pregabalin, which, in turn, was more cost effective than gabapentin.

In addition to the step-wise pharmacological approach to the management of people with DPNP, clear guidance is provided for regular review with assessment of efficacy and adverse effects and timely referral to specialist services. For the first time, combination treatment is advised in the management of DPNP when monotherapy fails due to lack of efficacy or side-effects.

It is important for clinicians to note that this document is only *guidance* and – in the NICE authors' own words – "does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient". ■

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