NICE National Institute for Health and Care Excellence

Medicines Evidence Commentary

commentary on important new evidence from Medicines Awareness Weekly

Published: May 2014

Fibromyalgia: limited evidence suggests that duloxetine may help reduce pain and other symptoms for some people

Document as included in MAW

A Cochrane review of 6 trials of duloxetine suggests that the drug may have beneficial effects on several symptoms of fibromyalgia, but the average benefits are limited and more trials are required to make convincing determinations of efficacy. Adverse effects were common in both the placebo and duloxetine groups, but people taking duloxetine were considerably more likely to stop treatment because of adverse effects than those taking placebo.

Overview and current advice

The main symptoms of fibromyalgia are chronic, widespread pain associated with cognitive dysfunction, sleep disturbances and physical fatigue. It is about 7 times more common in women than in men. People with fibromyalgia often report high disability levels and poor quality of life, along with extensive use of medical care. There is no NICE or NICE-accredited guidance on the management of fibromyalgia. The 2007 European League Against Rheumatism (EULAR) guidelines state that it should be recognised as a complex and heterogeneous condition in which there is abnormal pain processing and other secondary features. The guidelines recommend a multidisciplinary approach with a combination of non-pharmacological and pharmacological treatment options. In discussion with the person, these should be tailored according to pain intensity, function and associated features, such as depression, fatigue and sleep disturbance. The guidelines suggest that heated pool treatment with or without exercise, individually tailored exercise programmes, cognitive behavioural therapy and other approaches such as relaxation, rehabilitation, physiotherapy and psychological support may be helpful non-drug therapies. However, in the absence of good quality research studies, these recommendations are based largely on expert opinion.

No drug is licensed in the UK for treating fibromyalgia. The EULAR guidelines suggest a wide range of drugs may be helpful in fibromyalgia including pramipexole, pregabalin, some analgesics and some antidepressants, including duloxetine. Duloxetine is licensed for treating major depression, generalised anxiety disorder and diabetic peripheral neuropathic pain. It is recommended as an option for treating all types of neuropathic pain except trigeminal neuralgia in the NICE clinical guideline on pharmacological management of neuropathic pain.

New evidence

This Cochrane review (Lunn et al. 2014) assessed the benefits and harms of duloxetine for treating painful neuropathy and different types of chronic pain[1]. This medicines evidence commentary discusses only the results relating to fibromyalgia, because use of the drug in neuropathic pain is covered in the NICE clinical guideline.

The review considered only double-blind randomised controlled trials of duloxetine that lasted at least 8 weeks. Six trials (n=2249) that tested duloxetine for fibromyalgia were included. Of these, 4 trials lasted 12 weeks and 2 trials lasted 6 months; all compared duloxetine with placebo. One trial included only women (n=354) and more than 90% of participants in the other 5 trials were female, despite being open to men and women. The high proportions of women in the studies reflects the epidemiology of fibromyalgia.

The pooled risk ratio (RR) for a 50% or greater improvement in pain at 12 weeks for duloxetine 20–120 mg daily compared with placebo was 1.50 (95% confidence interval [CI] 1.29 to 1.75, p<0.00001; 5 trials, n=1887). When taking individual doses into account, the difference in this outcome was statistically significant for duloxetine 60 mg and 120 mg daily, but not for lower doses. The pooled number needed to treat for 50% or greater improvement in pain at 12 weeks with duloxetine 60 mg daily was 8 (95% CI 4 to 21), but only about 37% of people taking duloxetine obtained this level of pain relief (2 trials, n=528). A daily dose of 120 mg was no more effective than 60 mg.

Trials also reported effects on subscores of the SF-36 scale. For the mental component summary score, the 30 mg, 60 mg and 120 mg daily doses had a statistically significant increasing effect compared with placebo. The effect on the physical component summary score was statistically significant only at 120 mg daily, whereas for the bodily pain subscale there was a statistically significant benefit at both the 60 mg and 120 mg daily doses compared with placebo. However, the absolute differences for all these outcomes were only about 2–8 points on these 100 point scales.

The Cochrane authors considered the risk of adverse events across all studies in the review (painful peripheral neuropathy, fibromyalgia and pain in major depressive disorder). Serious adverse events were uncommon and were no more frequent with duloxetine than placebo at any dose or when combining all doses together. However, the rate of any adverse event was high in both the treatment and placebo arms of all studies. Adverse events were statistically significantly more common with duloxetine than with placebo especially at 60 mg and 120 mg doses, and people taking these doses were also statistically significantly more likely to stop treatment than those taking placebo (RR for adverse events leading to discontinuation with duloxetine 60 mg daily 1.95, 95% CI 1.6 to 2.37; number needed to harm 18, 95% CI 13 to 30, 14 trials, n=4837). The most common individual adverse events were nausea, dry mouth, dizziness, somnolence, fatigue, insomnia, constipation, decreased appetite, sweating and rhinitis.

The authors conclude that there is lower quality evidence for the efficacy of duloxetine in fibromyalgia than in diabetic peripheral neuropathy, and the effects in fibromyalgia may be achieved through a greater improvement in mental symptoms than in somatic physical pain. They say that more trials in this indication are required to make convincing determinations of efficacy.

Commentary

Fibromyalgia is a disabling condition that is difficult to treat, with little high quality evidence to guide practice. The results of this Cochrane review suggest that a minority of people may benefit from duloxetine, although average benefits were limited and must be weighed against the person's risk of adverse events. Other antidepressants that the EULAR guideline suggests may be useful in the care of people with fibromyalgia were not assessed in the Cochrane review.

This would be an off-label use. Therefore, in line with advice from the Medicines and Healthcare products Regulatory Agency (MHRA), it is the responsibility of the prescriber to be satisfied that such use would better serve the person's needs than an appropriately licensed alternative, to be satisfied that there is a sufficient evidence base or experience of using duloxetine in this context to show its safety and efficacy, to take responsibility for prescribing it and for overseeing the person's care including monitoring and follow-up, and to make appropriate records. The prescriber should give the person sufficient information to enable them to make an informed decision.

The evidence base for management of pain is often limited, especially in complex, chronic conditions such as fibromyalgia, because of the many, highly individual factors that determine a person's perception of pain and pain relief. The EULAR recommendation for a multidisciplinary approach with a combination of non-pharmacological and pharmacological treatments tailored according to the person's particular needs seems sensible. It would also seem prudent to adopt a 'therapeutic trial' approach to treatment, even using simple self-assessment scales such as 100 mm visual analogue scales to assess and record symptom response over an agreed period of time.

Study sponsorship

This Cochrane review was supported by the Institute of Neurology, University College London and the National Institute for Health Research University College London Biomedical Research Centre.

References

1. Lunn MPT, Hughes RAC, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD007115.

About this Medicines Evidence Commentary

Medicines Evidence Commentaries form part of NICE's Medicines Awareness Service and help contextualise important new evidence, highlighting areas that could signal a change in clinical practice. They do not constitute formal NICE guidance. The opinions of contributors do not necessarily reflect the views of NICE.

Visit Evidence Search