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[Intervention Review]

Milnacipran for neuropathic pain and fibromyalgia in adults

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ABSTRACT

Background

Milnacipran is a serotonin–norepinephrine reuptake inhibitor (SNRI) that is sometimes used to treat chronic neuropathic pain and fibromyalgia.

Objectives

To evaluate the analgesic efficacy and adverse effects of milnacipran in the management of chronic neuropathic pain or fibromyalgia.

Search methods

We searched CENTRAL, MEDLINE, and EMBASE to 4th of January 2012, together with reference lists of retrieved papers and reviews.

Selection criteria

We included randomised, double-blind studies of eight weeks duration or longer, comparing milnacipran with placebo or another active treatment in chronic neuropathic pain or fibromyalgia.

Data collection and analysis

We extracted efficacy and adverse event data, and two study authors examined issues of study quality independently.

Main results

Five studies (4138 participants) were included, all of which were placebo-controlled, involved participants with fibromyalgia, and used titration to a target dose of 100 mg or 200 mg milnacipran. There were no other active comparators or studies in other neuropathic pain conditions. Study quality was generally good, although the imputation method used in analyses of the primary outcomes could overestimate treatment effect.

Both doses of milnacipran provided moderate levels of pain relief to about 40% of those treated, compared to 30% with placebo, giving a number needed to treat of 8 to 10. Adverse events were common in both milnacipran (87%) and placebo (78%) groups, but serious adverse events (< 2%) did not differ between groups. Nausea and constipation were the most common events showing the greatest difference between groups (number needed to treat for an additional harmful outcome of 7 and 13 respectively, compared with placebo).

Withdrawals for any reason were more common with milnacipran than placebo, and more common with 200 mg than 100 mg (NNH of 23 and 8.8 respectively, compared with placebo). This was largely driven by adverse event withdrawals, where the NNH compared with placebo was 14 for 100 mg, and 7.0 for 200 mg). Withdrawals due to lack of efficacy were more common with milnacipran than placebo but did not differ between doses (number needed to treat to prevent an additional unwanted outcome of 45 and 41 respectively).

Authors' conclusions

The evidence available indicates that milnacipran 100 mg or 200 mg is effective for a minority in the treatment of pain due to fibromyalgia, providing moderate levels of pain relief (at least 30%) to about 40% of participants, compared with about 30% with placebo. There were insufficient data to assess substantial levels of pain relief (at least 50%), and the use of last observation carried forward imputation may overestimate drug efficacy. Milnacipran is associated with increased adverse events and adverse event withdrawals, which were significantly greater for the higher dose. There were no data for the use of milnacipran for other chronic neuropathic pain conditions.

PLAIN LANGUAGE SUMMARY

Milnacipran for chronic neuropathic pain and fibromyalgia in adults

The aim of this review was to assess how effective milnacipran is for treating chronic neuropathic pain or fibromyalgia. We identified no studies using milnacipran in neuropathic pain, but five studies in fibromyalgia satisfied the inclusion criteria. Fibromyalgia is a complex pain syndrome, defined as widespread pain for longer than three months; the original diagnostic criteria involved pain on palpation at 11 or more of a number of specified tender points (Wolfe 1990), with later criteria including both widespread pain and symptom severity (Wolfe 2010). The studies included over 4000 participants treated with milnacipran 100 mg or 200 mg, or placebo, for eight to 24 weeks at the target dose. Overall study quality was good, although the method of analysis for our primary outcomes could overestimate treatment effect.

Milnacipran at either dose provided moderate pain relief (at least 30% reduction in pain intensity) to 10% more participants than did placebo. This relatively modest effect may be clinically important in this difficult to treat condition. Adverse events were reported by the majority of participants in all groups, but were more common with milnacipran than placebo, with nausea and constipation showing the greatest differences. Serious adverse events were uncommon (less than 2%) and did not differ between treatment groups. Withdrawals due to adverse events were also more common with milnacipran than placebo, and were more common with 200 mg than 100 mg, while withdrawals due to lack of efficacy were less common with milnacipran, with no difference between doses.

Milnacipran has shown modest effects in a minority of participants with fibromyalgia, and several technical issues indicate that even this modest effect may overstate effectiveness in clinical practice The drug may be a useful option if first-line treatments fail.