

Review: Tricyclic and tetracyclic antidepressants are moderately effective for reducing chronic low-back pain

Staiger TO, Gaster B, Sullivan MD, Deyo RA. Systematic review of antidepressants in the treatment of chronic low back pain. *Spine*. 2003;28:2540-5.

QUESTION

In patients with back pain, how do different classes of antidepressants compare for reducing pain and improving functional status?

DATA SOURCES

Studies were identified by searching MEDLINE (1966 to March 2002), PsycINFO (1967 to 2002), and the Cochrane Controlled Trials Register and by scanning the references of identified articles and reviews.

STUDY SELECTION AND ASSESSMENT

Studies in any language were selected if they were randomized controlled trials (RCTs) that compared oral antidepressants with placebo in patients with back pain. Studies with insufficient data to assess treatment response were excluded. Methodological quality was assessed using a 22-point scale based on the 19-point criteria developed by the Cochrane Collaboration Back Review Group.

OUTCOMES

Pain, functional status, and analgesic use.

MAIN RESULTS

7 RCTs ($n = 440$ patients with chronic low-back pain [CLBP]; mean age range 26 to 54 y) met the inclusion criteria. Treatment duration ranged from 1 month to 8 weeks.

The antidepressants studied were nortriptyline, maprotiline, imipramine, amitriptyline, paroxetine, and trazodone. The quality score ranged from 11 to 19 points. The results of the RCTs were not pooled because the designs of the studies were heterogeneous. Of 5 RCTs with antidepressants that inhibit norepinephrine reuptake (NR) (tricyclic or tetracyclic antidepressants), 2 trials (1 of nortriptyline and 1 of maprotiline) showed a moderate reduction in pain (Table). Nortriptyline also showed a borderline improvement in functional status ($P = 0.055$). In 1 RCT, imipramine improved function in work activities ($P = 0.004$). 1 RCT showed that fewer patients who received amitriptyline used analgesics than did those who

received placebo ($P < 0.005$). 3 RCTs that compared antidepressants that do not inhibit NR with placebo showed no difference in pain reduction or functional improvement (Table).

CONCLUSIONS

Tricyclic or tetracyclic antidepressants are moderately effective for reducing pain in patients with chronic low-back pain. Antidepressants that do not inhibit norepinephrine reuptake show no benefit for pain relief or functional status.

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Antidepressants vs placebo for reducing chronic low-back pain at up to 8 weeks*

Antidepressant class	Comparisons	Number of trials (number of patients)	Effect size†	P value
Antidepressants that inhibit NR (tricyclics and tetracyclics)	Nortriptyline vs placebo	1 (78)	0.43	0.05
	Maprotiline vs placebo	1 (103)	0.69	0.023
Antidepressants that do not inhibit NR (SSRIs and trazodone)	Paroxetine vs placebo	1 (103)	-0.13	0.648
	Paroxetine vs placebo	1 (92)	-0.05	0.35‡
	Trazodone vs placebo	1 (42)	0.32	0.618‡

*NR = norepinephrine reuptake; SSRIs = selective serotonin-reuptake inhibitors.

†Magnitude of effect size: 0.20 = small; 0.50 = moderate; > 0.80 = large.

‡Information provided by author.

COMMENTARY

Although antidepressants are helpful for several painful conditions, their effectiveness for CLBP has been unclear (1). Unlike previous reviews, Staiger and colleagues considered the effects of tricyclic and tetracyclic antidepressants (NR inhibitors) separately from selective serotonin-reuptake inhibitors (SSRIs). Separating the 2 drug classes explains why previous reviews have found contradictory evidence on the use of antidepressants for CLBP.

No data exist to support the use of SSRIs for CLBP. The finding that NR inhibitors are moderately effective for CLBP is important. However, the number, size, and quality of the studies in this review limit the strength of its conclusion. It was only possible to calculate an effect size for pain reduction from 2 relatively recent, high-quality studies, which compared nortriptyline and maprotiline with placebo. Data to calculate numbers needed to treat were also not available. The mean duration of CLBP in these 2 studies was 16 and 14.5 years, respectively, and follow-up was only 8 weeks. Because both of these studies excluded patients with depression and recruited patients from a mix of primary care, orthopedic clinics, and local advertising, the findings should be

generalizable to routine practice. Only 1 of the studies included a measure of functional status, which showed a small benefit of borderline significance.

Thus, we have some evidence that 2 NR inhibitors have an analgesic effect for CLBP independent of any antidepressant effect at 8 weeks, and insufficient data to comment on their effect on functional status. We have no long-term follow-up data and no data to do a risk-benefit analysis of NR inhibitors. We have no robust information on amitriptyline, which is a common first-line NR inhibitor for pain relief (2).

For patients with CLBP, tricyclic or tetracyclic antidepressants, but not SSRIs, are worth trying for their analgesic effect.

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References

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