The effect of antidepressant treatment on chronic back pain: a meta-analysis

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Authors' objectives
To assess the efficacy of antidepressants in treating chronic back pain in adults.

Searching
MEDLINE (from 1966 to August 2000), PsycLIT (from 1987 to August 2000), CINAHL (from 1982 to 2000), EMBASE (from 1974 to August 2000), AIDSLINE, HealthSTAR, Cancerlit and MICROMEDEX were searched using 'antidepressants' as both a textword and keyword (all languages). Another search was performed using the MeSH term 'antidepressive agents' combined with the textwords 'back pain', 'low back pain', 'pain', 'spasm' and 'clinical trial'. In addition, the Cochrane Controlled Trials Register was searched for randomised trials, the Cochrane Database of Systematic Reviews for systematic reviews, and FEDRIP for unpublished literature. The references of reviewed articles were checked for additional articles.

Study selection
Study designs of evaluations included in the review
Studies were included if they were randomised and placebo-controlled.

Specific interventions included in the review
Studies were included if at least one group received an antidepressant medication. The interventions in the included studies were: amitriptyline (25 mg three times daily, or 150 mg once daily), atropine (0.2 mg/day), desipramine (3 mg/kg, schedule not given), doxepine (300 mg/day; or 3 mg/kg, schedule not given), imipramine (150 mg/day), maprotiline (150 mg/day), nortriptyline (100 mg/day), paroxetine (20 to 30 mg/day), trazodone (100 mg four times daily). These were compared with another antidepressant drug, with an inert placebo, or with an active placebo or another drug (diphenhydramine, 37.5 mg on alternative nights).

Participants included in the review
Studies were included if they investigated patients who had had low back discomfort for at least 2 months. All of the studies included patients with chronic back pain; one study also included patients with acute back pain, while another included patients with cervical spine pain. Some studies included only patients with and/or without mood disorders.

Outcomes assessed in the review
Studies were included if they assessed measurable outcomes. The primary outcomes assessed in the included studies were pain severity and activities of daily living (ADL).

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Study quality was assessed using a validated 6-item instrument, which assessed the following criteria: description of randomisation; adequacy of blinding; description of withdrawals and drop-outs; appropriateness of the statistical analysis; description of the inclusion and exclusion criteria; and the method for assessing adverse treatment effects. Two reviewers assessed study quality independently. Any disagreements were resolved by consensus.

Data extraction
Two reviewers extracted the data from the primary studies. The outcomes were extracted as either dichotomous or continuous variables (or both), depending on how they were reported in the studies. The mean outcome scores for the two major outcomes (pain severity and ADL) for the placebo and treatment groups were standardised by dividing the
scores by their standard deviation.

**Methods of synthesis**

How were the studies combined?
The random-effects model of DerSimonian and Laird was used to calculate summary standardised mean differences (SMDs). Publication bias was assessed using the methods of Egger et al. (reference given).

How were differences between studies investigated?
Heterogeneity was assessed visually with Galbraith plots and with Q-statistics using the methods of Mantel-Haenszel.

Sensitivity analyses were conducted to determine the influence of various variables on the results. Sources of heterogeneity such as year and country of publication, study quality scores, and antidepressant type were explored using meta-regression. The authors also tested the relative influence of each individual study on the results by sequentially dropping individual treatment arms and calculating summary measures.

**Results of the review**

Nine studies (504 patients enrolled) were included in the review. One of these studies included two active treatment arms which were considered separately in the review.

The included studies were of moderate quality (mean score: 5.1 +/- 2.2; median 6; range: 6 to 8). Inter-rater agreement for quality was high (kappa 0.89).

The patients had chronic back pain, averaging 10.4 years. The patients treated with antidepressants were more likely to improve in pain severity than those taking placebo (SMD 0.41, 95% confidence interval, CI: 0.22, 0.61; no heterogeneity seen), but not in ADL (SMD 0.24, 95% CI: -0.21, 0.69; effect-size heterogeneity was present, chi-squared=12.76, d.f.=3, P<0.01). Patients treated with antidepressants experienced more adverse effects (22%) than those receiving placebo (14%) (P=0.01).

None of the factors investigated in the sensitivity analyses affected the significance of the results. There was no evidence of publication bias.

**Authors' conclusions**

Antidepressants were more effective than placebo in reducing pain severity, but not functional status, in chronic back pain. The benefits were marginal and must be viewed in conjunction with the marked adverse effects.

**CRD commentary**

This was a well-conducted systematic review and meta-analysis. The question posed was clear, and the methodology of the search and analysis was appropriate. The quality of the studies was assessed in an appropriate manner, and sufficient details of the included studies were provided to allow the reader to assess the validity of the final conclusions of the review. The authors provided a comprehensive assessment of the limitations of the review.

Nearly all of the studies in the review were underpowered, so the benefits of antidepressants may be greater than found.

No firm conclusion could be drawn on whether antidepressant therapy will be effective in the treatment of low back pain in patients without depression, as most included patients had a mood disorder.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that better quality studies using standardised, validated instruments are needed.
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**Other publications of related interest**
This additional published commentary may also be of interest. Ernst E. Antidepressants reduce pain severity but do not improve functional status for people with back pain. Evidence-based Healthcare 2002;6:137.

**Indexing Status**
Subject indexing assigned by NLM

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**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.