Efficacy of venlafaxine compared with tricyclic antidepressants in depressive disorder: a meta-analysis
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CRD summary
This review compared the efficacy and tolerability of venlafaxine with tricyclic antidepressants in depressive disorder, concluding that there was no difference in treatment effect between them. Although the findings appear to represent the evidence, uncertainty over the review process and methodology suggest that the authors' conclusions should be interpreted with caution.

Authors' objectives
To compare the efficacy and tolerability of venlafaxine with tricyclic antidepressants in depressive disorder.

Searching
PubMed, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL) and DARE were searched. Search dates were not given, but search terms were reported. Reference lists of included studies were manually searched to identify additional articles.

Study selection
Double-blind randomised controlled trials (RCTs) that compared venlafaxine with tricyclic antidepressants for the treatment of depression were eligible for inclusion; single-blind comparisons were excluded.

The primary outcome was a response rate of 50% or greater based upon a decrease in depression rating scale from baseline using the Hamilton Rating Scale for Depression (HRSD) or Montgomery and Asberg Rating Scale; where more than one scale was used the HRSD took precedent. Tolerability was assessed through 'all-cause' and 'side-effects' withdrawals.

In the included trials, tricyclic antidepressants used included imipramine (range 116 to 176mg/day), clomipramine (range 61.5 to 105mg/day) and amitriptyline (range 75 to 103.1mg/day). The mean daily dose of venlafaxine ranged from 75 to 233mg. Just under half of the trials excluded psychotic-depressed and suicidal patients. The majority of trials were undertaken in an outpatient setting. Trial duration ranged from six to 13 weeks, with an average duration of 7.4 weeks.

Four reviewers independently selected studies for inclusion in the review, with disagreements resolved through discussion.

Assessment of study quality
Study quality was assessed using criteria from the Dutch Institute for Healthcare Improvement based on criteria for: randomisation, allocation concealment, loss to follow-up, intention-to-treat analysis, comparability of treatment, relevant clinical outcomes and length of follow-up.

It appeared that six reviewers assessed study quality.

Data extraction
Odds ratios (ORs) with 95% confidence intervals (CI) were calculated using intention-to-treat data based on 2x2 tables for differences between response and withdrawal. Where necessary, authors were contacted for unpublished/missing data.

The authors did not state how many reviewers extracted the data.

Methods of synthesis
The studies were pooled in a meta-analysis and heterogeneity was assessed; methods were not reported.
Results of the review
A total of seven RCTs were included in the review (n=947 patients, range 102 to 167; 476 patients received venlafaxine and 471 patients received tricyclic antidepressants).

There was no significant difference in treatment effect between venlafaxine and tricyclic antidepressants (OR 0.88, 95% CI 0.66 to 1.16; seven RCTs). Significant heterogeneity was present (p=0.021).

Tolerability, assessed by overall withdrawals, or withdrawals due to side-effects, did not significantly differ between tricyclic antidepressants and venlafaxine. No significant heterogeneity was present.

Authors' conclusions
No significant difference in treatment effect between low doses of both venlafaxine and the tricyclic antidepressants could be found.

CRD commentary
The review question and inclusion criteria were clear. A thorough search for studies was undertaken, but search dates were not reported and it was unclear whether language restrictions were placed on the search or unpublished studies were sought; this meant that language bias could have been present and that some studies may have been missed. Stages of the review process appear to have been conducted by multiple reviewers, but it was unclear whether this extended to data extraction.

Appropriate criteria were used to assess the quality of the included trials, but the results of the assessment were not reported. It was unclear whether suitable methods were used for the meta-analysis as the methods were not clearly reported. Heterogeneity was assessed and found to be present.

Although the findings appear to represent the evidence presented, uncertainty over the review process and methodology suggest that the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further study with slower titration or plasma control of venlafaxine compared with tricyclic antidepressants is worthy of investigation.

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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.