Alprazolam and standard antidepressants in the treatment of depression: a meta-analysis of the antidepressant effect
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Authors' objectives
To compare the effectiveness of alprazolam and standard antidepressants in the treatment of depression.

Searching
MEDLINE was searched up to June 1995 using the following headings and terms: 'depressive disorder-drug therapy', 'alprazolam', 'antidepressants' and 'randomised-controlled trial'. Cross-referencing was used to seek out further studies.

Study selection
Study designs of evaluations included in the review
Double-blind, randomised controlled trials (RCTs), which compared the antidepressant effect of alprazolam to that of a standard antidepressant, were included if they measured the severity of depression with a standard scale and presented the means of the end point scores. The duration of the studies was between 4 and 6 weeks.

Specific interventions included in the review
Alprazolam in dosages ranging from 1.80 to 4.60 mg/day (mean dose: 3.15 mg/day). The standard antidepressants were all tricyclic antidepressants (not named) in doses ranging from 63.8 to 229.8 mg/day (mean dose: 147.17 mg/day).

Participants included in the review
Patients with depression (without anxiety disorder) as defined in the studies. Both in- and out-patients were included. The individual studies included patients with minimum scores on the Hamilton Rating Scale for Depression (HRSD) ranging from 6 to 21.

Outcomes assessed in the review
The effect of treatment in each group was determined by the scores on the 17- or 21-item HRSD.

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

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The effect of treatment with alprazolam in each study, compared with standard antidepressants, was calculated by comparing the HRSD scores of the two groups using the method of Rosenthal (see Other Publications of Related Interest). Where the means of the HRSD end point scores were unavailable, the end point scores were calculated by subtracting the mean change scores from the initial scores. The average of the standard deviations of the treatment
groups of the 4 studies reporting such information was applied to the other 7 studies.

The 95% confidence intervals (CIs) of the weighted mean standard normal deviation and the weighted mean drop-out rate were calculated. The weighted mean correlation coefficient and weighted mean effect size were also estimated.

How were differences between studies investigated?
Homogeneity among the studies was assessed with respect to the effect size and drop-out rates using the methods described by Rosenthal (see Other Publications of Related Interest).

**Results of the review**
Eleven RCTs (941 patients) were included.

The weighted mean effect size was 0.06.

The standard normal deviation was 0.03 (95% CI: -0.45, 0.51), and the homogeneity Q test was 0.586 (P<0.05).

The correlation coefficient was 0.03.

For drop-outs, the weighted mean was 0.003 (95% CI: -0.224, 0.230), and the homogeneity Q test was 8.983 (P<0.05).

**Authors' conclusions**
The antidepressant effect of alprazolam was found to be comparable to that of low-dose tricyclic antidepressants. However, these results should be viewed with caution since the benefits and advantages of long-term treatment of alprazolam have not been extensively investigated, and very few studies have investigated severely depressed patients.

**CRD commentary**
This review included clear tables presenting the results and certain characteristics from the included studies. The outcomes were assessed consistently using the HRSD. The heterogeneity of effect size and drop-out rates across studies was assessed. In addition, some of the limitations of the review were discussed.

By limiting the literature search to one database, other relevant studies may have been omitted. Details of the methods used to select the studies for inclusion and to extract the data were not given. The validity of the included studies was not assessed. More comprehensive details of the primary studies, such as the patients' characteristics and the names of the tricyclic antidepressants used, would have been helpful. 'Depression as defined in studies' was used as a criteria for study inclusion, but no information was given of the definitions used in the individual studies. It was unclear whether the analysis was conducted on an intention to treat basis. Examination of the number of drop-outs and the number of patients suggests that some studies had very high drop-out rates, but the reasons for these drop-outs were not given and no mention was made of any adverse reaction encountered.

In view of the uncertainties highlighted, it is not possible to state the patient group for which alprazolam and tricyclic antidepressants may have comparable effects.

**Implications of the review for practice and research**
The authors report that there is a lack of information regarding the following aspects: the use of alprazolam in severely depressed patients; the use of alprazolam compared with higher doses of standard tricyclic antidepressants; evidence of long-term benefit, and the risks of benzodiazepam abuse and dependence.

**Bibliographic details**
Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Alprazolam /therapeutic use; Anti-Anxiety Agents /therapeutic use; Antidepressive Agents /therapeutic use;
Depressive Disorder /drug therapy; Humans; Randomized Controlled Trials as Topic

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.