Long-term pharmacological treatment of generalized anxiety disorder

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Authors' objectives
To identify any pharmacological treatment that has been proven to benefit patients with generalised anxiety disorder (GAD).

Searching
MEDLINE, BIOSIS Previews and EMBASE (1963 to 1998) were searched for trials using the terms, 'generalized anxiety disorder', 'anxiety neurosis' or 'anxiety'.

Study selection
Study designs of evaluations included in the review
Clinical trials. Seven out of fourteen were double blind, three were placebo controlled and six were open label trials. Studies had to be of at least two months duration and ranged from 2.5 months to 12 months.

Specific interventions included in the review
Any pharmacological interventions. Interventions evaluated in the included studies were kava-kava (70mg); clonazepam (10mg); diazepam (5mg-33mg), ketazolam (50mg-60mg) and lorazepam (1mg-6mg), alprazolam (3.3mg), buspirone (5mg-75mg), clorazepate (15mg-60mg), and alpidem (50mg-100mg).

Participants included in the review
Patients with conditions described as generalised anxiety disorder, anxiety neurosis or anxiety symptoms. One study also included chronic psychoneurotic patients. GAD was diagnosed according to American Psychiatric Association (APA) DSM criteria in 9 of the 14 studies.

Outcomes assessed in the review
Reduction in symptoms using Hamilton Anxiety Rating Scale (HAM-A scores).

How were decisions on the relevance of primary studies made?
All papers were read and individually selected by two authors and subsequently compared.

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. Data were extracted on: inclusion criteria, diagnosis criteria, duration of study, drug and dosage, sample size, drop-outs, baseline rating of generalised anxiety disorder, and results.

Methods of synthesis
How were the studies combined?
A narrative synthesis of the studies was undertaken.

How were differences between studies investigated?
Studies were grouped by study design (placebo-controlled, double-blind studies without placebo control, and open label studies). Studies were also grouped by diagnostic criteria, and type of treatment.
Results of the review
Fourteen studies with a total of 2,966 participants were included.

1. Studies involving heterogeneous groups of patients where diagnosis was not well defined (n=5).

Kava-kava was significantly superior to placebo from the second month up until the end of the trial (6 months). Benzodiazepines improved the scores on the Hamilton Anxiety Rating Score.

2. Studies involving patients diagnosed using the APA DSM criteria (n=9) In one study, alprazolam was significantly superior to placebo from the second month until the end of the study (at four months). Lorazepam was significantly superior to placebo from the third month until the end of the study. In another study there was no significant difference between diazepam and placebo. Buspirone was found to be superior to diazepam from first month to end of study (at three months) in a third study. In the fourth study there was no significant difference between clorazepate and buspirone.

In the open label studies (n=4), diazepam, buspirone, and alpidem all significantly improved Hamilton Anxiety Rating Scores from baseline.

Authors' conclusions
The results are inconclusive and no reference drug could be identified. In addition, an adequate evaluation of the long-term treatment of GAD has not yet been performed.

CRD commentary
This review attempts to evaluate pharmacological treatments of generalised anxiety disorder. The search for trials is fair, but no attempts to locate unpublished trials were made, which may have resulted in publication bias. There were scant details provided on the methodology of the review, and no assessment of validity of the included studies was performed. Details of the included studies were fair, but the summary of the results from the included studies was poor. The authors’ conclusions appear to follow on from the results of the review, but readers should bear in mind the limitations of the review.

Implications of the review for practice and research
Practice: The results are inconclusive and no reference drug could be identified.

Research: Studies should be conducted in homogeneous groups of patients, preferably using more standard diagnostic criteria, and adequate trials must include a placebo arm in a double-blind design in order to differentiate drug effect from spontaneous improvement.

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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.