Fluvoxamine: a review of the controlled trials in depression

Authors' objectives
To review the safety and efficacy of fluvoxamine in the pharmacotherapy of depression.

Searching
MEDLINE was searched to identify English language trials.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), which were double-blind and placebo- and drug-controlled, were included. Twenty out of the 31 trials had a single-blind placebo washout prior to randomisation.

Specific interventions included in the review
Fluvoxamine compared with placebo, imipramine, clomipramine, tricyclics, mianserin and other antidepressants.

Participants included in the review
Participants with depression. Diagnostic criteria varied amongst studies. All but three trials, however, employed American Psychiatric Association criteria (DSM-III, DSM-III-R), Feighner or Research Diagnostic Criteria. Over 60% of participants enrolled in the included studies were women, typically in their mid-to-late thirties or forties.

Outcomes assessed in the review
The outcome assessed was depression as determined by the Hamilton Rating Scale for Depression (HAM-D) and the Clinical Global Impression (CGI) scales.

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

Assessment of study quality
The author does not report the method used to assess validity, or how the validity assessment was performed.

Data extraction
The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were not combined.

How were differences between studies investigated?
The studies were grouped according to the comparison drugs.

Results of the review
Thirty-one studies with a total of 2,343 participants. Eight trials with 979 participants compared fluvoxamine with imipramine and placebo; five trials with 304 participants compared fluvoxamine with imipramine only (no placebo...
arm); five studies with 211 participants compared fluvoxamine with clomipramine; six studies with 344 participants compared fluvoxamine with tricyclics and placebo; two trials with 113 participants compared fluvoxamine with mianserin; five studies with 392 participants compared fluvoxamine with antidepressants and placebo.

Fluvoxamine compared with imipramine and placebo:

Five of the eight trials found fluvoxamine and imipramine both equally efficacious and better than placebo. Over a four-week period, improvement in depression scores as a result of fluvoxamine ranged from 37.4% to 51.9%, improvement with imipramine was 41%-53.6% and improvement with placebo was 18.7% to 41.7%.

Fluvoxamine compared with imipramine:

HAM-D scores decreased 36.4% to 67% in the fluvoxamine group compared with 30.5% to 62.5% in the imipramine group.

Fluvoxamine compared with clomipramine:

HAM-D scores decreased from 54.1% to 72.9% in the fluvoxamine group compared with 59.1% to 66.3% in the clomipramine group.

Fluvoxamine compared with miscellaneous tricyclics:

HAM-D scores decreased from 39.2% to 60.9% in the fluvoxamine group compared with 28.9% to 59.9% in the tricyclic groups. A placebo group in one study had a decrease in depression scores of 29%.

Fluvoxamine compared with mianserin:

In one study, depression symptoms decreased by 65.5% in the fluvoxamine group compared with 60.8% in the mianserin group.

Fluvoxamine compared with miscellaneous antidepressants:

Overall, fluvoxamine was equivalent to moclobemide, maprotiline and sertraline and superior to placebo. Fluvoxamine was significantly less effective than flupenthixol.

Adverse effects:

Overall, fluvoxamine was associated with inducing a variety of gastrointestinal adverse effects.

**Authors’ conclusions**

Fluvoxamine has been shown to be at least as good, or superior to, placebo and other antidepressant drugs with which it has been compared. It appears safe and well-tolerated in daily doses of 50 to 300 mg. The most common adverse effects are gastrointestinal complaints, particularly nausea. Initiating pharmacotherapy at lower doses and increasing over the period of 1 to 2 weeks minimises this discomfort.

**CRD commentary**

Although the design of the studies included were appropriate to the aim of the review, the search strategy was very limited. The author did assess details of various aspects of study design and outcomes, but it was disappointing that the results of the study were not reported more fully and perhaps combined in a meta-analysis. The author grouped together trials comparing fluvoxamine but grouped separately those with a placebo arm. It would have been more useful to have grouped all those trials with an imipramine arm, and similarly grouped trials with a placebo arm. It appears that there was a significant placebo effect in some of the studies with a placebo arm. There was only one author on the review, so it can be assumed that responsibility for determining studies for inclusion and data extraction was performed by one person which could potentially lead to errors.
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