Efficacy and tolerability of mirtazapine versus paroxetine in the treatment of major depressive disorder

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CRD summary
The authors concluded that mirtazapine was effective earlier, but at six to eight weeks, paroxetine was equally effective for the treatment of major depressive disorder. There were some methodological limitations, and no validity assessment, leaving the reliability of the conclusions uncertain.

Authors’ objectives
To compare the efficacy and tolerability of paroxetine with those of mirtazapine for the treatment of major depressive disorder.

Searching
PubMed and PsycINFO were searched for articles from 1980 to June 2011; search terms were reported. It appears that published systematic reviews were checked for relevant trials.

Study selection
Studies of any design that compared paroxetine with mirtazapine, in patients of any age, who had major depressive disorder, were included in the review. It appears that any trials had to include patients who met Diagnostic and Statistical Manual of Mental Disorders IV Text Revision (DSM-IV-TR) criteria for a single or recurrent major depressive episode, and have a score of at least 18 on the Hamilton Rating Scale for Depression (HRSD). The outcomes of interest were response (50% reduction in HRSD score, from baseline), remission (score of 7 or less on the HRSD), symptom reduction, mean time to response, adverse events, and drop-outs due to adverse events.

In the included studies, the mean age of the patients ranged from 40 to 72 years, and the percentage of women ranged from 50 to 76. All studies were conducted in out-patient settings. The paroxetine dose ranged from 10mg to 40mg, and the mirtazapine dose ranged from 15mg to 45mg. The treatments lasted from to six weeks to 24 weeks.

The authors did not state how many reviewers selected studies for inclusion.

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

Data extraction
The outcome data were extracted for all time periods reported in the studies; comparisons were made using data at six or eight weeks. Two reviewers independently extracted the data, which were reviewed by a senior researcher.

Methods of synthesis
The studies were described in a narrative synthesis.

Results of the review
Five randomised controlled trials (in seven reports; 831 patients) were included in the review. Sample sizes ranged from 58 to 250. One trial was open label, and the rest were double blind.

The results appeared to vary between trials depending on the time of analysis. When all trials were compared at six or eight weeks, no significant differences in response or remission were observed between the treatment groups.

Discontinuation due to adverse events was reported in four trials: one found that discontinuation was less frequent in patients receiving mirtazapine (15%) than those receiving paroxetine (26%); two found similar rates between groups; and the fourth found that only one patient discontinued paroxetine.

Patients on mirtazapine more frequently reported somnolence, dizziness and weight gain, while those on paroxetine
more frequently reported gastrointestinal discomfort and headache. Other outcomes were not reported.

**Authors' conclusions**
At six to eight weeks of treatment, mirtazapine was as effective as paroxetine for the treatment of major depressive disorder. Differences in effectiveness were only observed in the first or second week of treatment, when mirtazapine was more effective.

**CRD commentary**
The review question and inclusion criteria were clear. The search was limited to two databases, and it was not clear if unpublished data were sought, so it is possible that some studies may have been missed. Some aspects of the review process were conducted by more than one reviewer, reducing the potential for reviewer error and bias. The absence of any formal quality assessment of the included trials limits the interpretation of the reliability of the findings. It was not clear if all the available data were reported, making it difficult to assess if the results were based on a complete review of the data.

Due to some methodological limitations, and the absence of a validity assessment, the reliability of the conclusions is uncertain.

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

*Research:* The authors stated that further studies on patients with suicide ideation or behaviour were needed.

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