Continuing treatment of depression in the elderly: a systematic review and meta-analysis of double-blinded randomized controlled trials with antidepressants

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CRD summary
This review concluded that continuing antidepressant treatment in elderly patients was efficacious compared with placebo for prevention of relapses/recurrences. There was no difference in efficacy and tolerability of tricyclic antidepressants and selective serotonin reuptake inhibitors. These findings appeared to be supported by the data, but may not be reliable given the limitations of the studies and review methods.

Authors' objectives
To determine the efficacy and tolerability of continuing antidepressant treatment in preventing relapses and recurrences in elderly patients with depression and to assess the differences in effects between tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs).

Searching
PubMed, EMBASE and The Cochrane Library were searched up to June 2009 for studies in any language. Search terms were reported. Reference lists of retrieved studies and reviews were screened for further studies. The authors reported that no specific attempts were made to locate unpublished studies as only one unpublished study in adults had been reported in previous reviews.

Study selection
Double-blind randomised controlled trials (RCTs) that compared the continuation of antidepressant treatment with maintenance treatment of unipolar depression in elderly (>55 years) participants were eligible for inclusion in the review. Eligible patients had to be diagnosed with a major depressive disorder according to the Diagnostic and Statistical Manual of Mental Disorders (DSM), International Classification of Diseases (ICD) or Research Diagnostic Criteria (RDC). Studies only of patients with bipolar depression, psychotic depression or depression associated with specific medical disorders were excluded. Eligible outcomes were number of relapses/recurrences.

The included studies were of nortriptyline, phenelzine, escitalopram, citalopram, dothiepin, paroxetine and sertraline. All studies included patients who had depressive disorders diagnosed according to DSM (DSM-IV or DSM-III-R) or RDC criteria. Specific types of major depression were unipolar non-psychotic, unipolar, recurrent unipolar non-psychotic and non-bipolar non-psychotic. The minimum depression rating scale score at entry ranged from at least 15 to at least 22 points; one study did not use a minimum score. The cutoff cognitive rating scale ranged from a Mini Mental State Examination (MMSE) score of less than 12 to less than 25; one study reported a Geriatric Deterioration Score cutoff of at least 4 and another study did not use a cutoff. Definitions of recurrence/relapse varied between studies. Months to randomisation after remission ranged from zero to four months. Included participants ranged in age from 73 to 77 years.

The authors did not state how many reviewers performed study selection.

Assessment of study quality
The methodological quality of the included studies was assessed using the Jadad criteria of randomisation, blinding and loss to follow-up. Each study was awarded a total score up to a maximum of 5. Studies that scored less than 3 were classified as poor quality.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
Two reviewers extracted intention-to-treat data (ITT) and calculated odds ratios (ORs) or risk differences (RDs) with 95% confidence intervals (CIs); discrepancies were resolved through discussion.
Methods of synthesis
Pooled odds ratios and risk differences, with 95% CIs, were calculated using a random-effects model. The number needed to treat (NNT) was calculated. Statistical heterogeneity was assessed using the $I^2$ statistic. Sensitivity analyses were performed by removing each study individually from the analyses. Publication bias was assessed using a funnel plot.

Results of the review
Eight double-blind RCTs (925 participants) were included in the review. Follow-up varied from 24 weeks to three years. Sample sizes ranged from 43 to 305. The authors reported that none of the studies was of poor quality.

Absolute risk of relapse/remission was significantly reduced in patients treated with depressants in comparison with placebo (28%, 95% CI 21% to 36%, $I^2=37.7$%). The NNT for the effect of continuation or maintenance treatment of all antidepressants was 3.6 (95% CI 2.8 to 4.8) and for TCA was 2.9 (95% CI 2.2 to 4.6) compared with 4.2 (95% CI 3.2 to 5.9) for SSRIs. There was no statistically significant difference in RD for relapse/recurrence between TCAs and SSRIs.

There was no significant difference in drop-outs due to side effects in patients who used TCAs alone or SSRIs alone. Drop-outs due to any reason (seven RCTs) were significantly reduced in the active treatment group (30.3%) compared with placebo (40.7%).

Sensitivity analysis showed that one study that used a substantially lower cutoff on the MMSE was responsible for the heterogeneity. Removing this analysis did not change the significance of the overall efficacy results, but the statistical heterogeneity was eliminated completely ($I^2=0$).

Authors’ conclusions
Continuing antidepressant treatment in elderly patients was efficacious in comparison with placebo for prevention of relapses and recurrences. There was no difference in the efficacy and tolerability of TCAs and SSRIs.

CRD commentary
This review answered a clearly defined review question. The review was at risk of publication bias as no specific attempts were made to locate unpublished studies, although the authors stated that previous reviews included only one unpublished study. The authors reported that publication bias was assessed using a funnel plot but did not report the finding from this analysis, which given the small number of studies may not have been reliable. The risk of language bias was low. Risks of reviewer error and bias were unclear for the assessment of study inclusion; attempts were made to reduce the risk of bias when extracting the study data. The methodological quality of the studies was assessed using relevant criteria, but full details of the quality assessment were not reported. Allocation concealment was not assessed. The authors reported that none of the studies was of poor quality.

There appeared to be significant clinical and statistical heterogeneity between the studies, which suggested that statistical pooling may not have been appropriate. The authors acknowledged this limitation in their discussion of the review findings and particularly highlighted differences in the definition of relapse and recurrence. Some attempt was made to investigate potential sources of statistical heterogeneity and one study was identified as responsible for the heterogeneity. There appeared to be a lack of direct head-to-head trials that compared the two different categories of antidepressants, which would have represented a stronger level of evidence.

The findings of the review appeared to be supported by the data, but may not be reliable given the limitations of the studies and review methods.

Implications of the review for practice and research
Practice: The authors stated that there was data to support the continuation of antidepressant therapy after remission irrespective of patient age. It was not possible to make a recommendation on how long to continue the therapy.

Research: The authors did not state any implications for research.

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