Efficacy and tolerability of antidepressants for treatment of depression in coronary artery disease: a meta-analysis

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CRD summary
This review assessed the efficacy and tolerability of antidepressants for treatment of depression in people with coronary artery disease. The authors concluded that there were significant therapeutic effects without substantially increased rates of discontinuation. The authors' conclusions are likely to be reliable, although it should be noted that the benefits may be modest.

Authors' objectives
To summarise the data on the efficacy and tolerability of antidepressant treatment for depression in people with coronary artery disease.

Searching
MEDLINE, EMBASE, CINAHL, PsycINFO, The Cochrane Library, AMED and Ageline were searched up to March 2008 for English-language articles. Search terms were provided. Several clinical trials registers and reference lists of retrieved articles were searched.

Study selection
Double-blind placebo-controlled randomised controlled trials (RCTs) that assessed the effectiveness of antidepressants on depression outcomes in patients with coronary artery disease and that met DSM-IV criteria for major or minor depression were eligible for inclusion. The definition of coronary artery disease included patients with histories of myocardial infarction, coronary artery bypass graft, percutaneous coronary intervention or presence of ischaemic heart disease.

The included studies assessed fluoxetine (40 to 60mg/day), sertraline (50 to 200mg/day), citalopram (20 to 40mg/day) and mirtazapine (30mg/day). Treatment duration ranged from 12 to 25 weeks. The outcome measures used were Hamilton Depression Rating Scale (HDRS) and Beck Depression Inventory. Outcomes of interest were treatment response, remission, discontinuation of treatment and adverse events.

Two reviewers independently assessed studies for inclusion. Disagreements were resolved by consensus.

Assessment of study quality
Two reviewers independently assessed study quality using the Jadad scale. Disagreements were resolved by consensus.

Data extraction
Two reviewers independently extracted data that included mean change on outcome measures, number of treatment responders, number who achieved remission, number who reported adverse events, treatment discontinuation and dropout due to adverse events. Response was defined as a 50% or greater reduction on the 21-item HDRS and remission was a score of 8 or less on the scale. Mean difference (MD) and 95% confidence interval (CI) were calculated for continuous outcomes and odds ratio (OR) and 95% CI for dichotomous outcomes.

Methods of synthesis
Studies were pooled using a random-effects meta-analysis. Statistical heterogeneity was assessed using the X^2 and I^2 statistics. Publication bias was assessed using a funnel plot and rank correlation test.

Results of the review
Four double-blind RCTs (n=798) were included. Jadad quality scores were 4 and 5.

Efficacy: Antidepressants showed a statistically significant benefit over placebo in the proportion of treatment
responders (OR 1.72, 95% CI 1.17 to 2.54; three RCTs), proportion that achieved remission (OR 1.80, 95% CI 1.18 to 2.74; three RCTs) and in HDRS (MD 1.41, 95% CI 0.53 to 2.29; four RCTs) and BDI (MD 2.27, 95% CI 0.60 to 3.94; three RCTs) scores.

**Tolerability**: There was no statistically significant difference between antidepressants and placebo in the proportion of patients who dropped out for any reason (OR 0.84, 95% CI 0.42 to 1.68; four RCTs). There was heterogeneity among the studies. There was no statistically significant difference between groups in dropout due to adverse events (OR 1.30, 95% CI 0.75 to 2.25; two RCTs).

The authors reported that publication bias was not identified, based on a funnel plot that used the HDRS.

**Authors’ conclusions**
Treatment with antidepressants for depression in coronary artery disease resulted in significant therapeutic effects without substantially increased rates of discontinuation.

**CRD commentary**
The review had clearly stated inclusion criteria. A number of sources were searched for published and unpublished studies. The language restriction may have resulted in relevant studies being missed. The authors stated that there was no evidence of publication bias, but pointed out that there was a risk that small studies reporting a negative effect of antidepressants may not have been identified. Study quality was assessed and appropriate methods were used to reduce error and bias in quality assessment, study selection and data extraction. The analysis seemed appropriate, heterogeneity was assessed and where found was considered in the discussion.

The authors’ conclusions are likely to be reliable, although it should be noted that the benefits may be modest.

**Implications of the review for practice and research**
**Practice**: The authors stated that the modest benefit must be balanced against possible side-effects and possible drug interactions. Therefore, treatment must be individualised based on patient characteristics.

**Research**: The authors suggested several clinical questions in relation to treatment of depression in patients with coronary artery disease that required investigation: relationship between severity of depression and treatment response; optimal time to begin antidepressant treatment; whether prophylaxis with antidepressants was beneficial compared to the risks; and long-term effects of treatment with antidepressants.

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