Effect of selective serotonin reuptake inhibitors on cardiovascular morbidity and mortality

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CRD summary
The authors concluded that there was insufficient evidence to draw definitive conclusions regarding the effect of selective serotonin reuptake inhibitors on cardiovascular morbidity and mortality. The authors' conclusions appear suitably cautious, but their reliability is unclear given the limitations with the included studies and the potential for bias in the review.

Authors' objectives
To investigate the effects of selective serotonin reuptake inhibitors (SSRIs) on cardiovascular morbidity and mortality.

Searching
MEDLINE was searched between 1966 and November 2006 for articles published in English. Search terms were reported. Reference lists of identified studies were searched manually.

Study selection
Studies that investigated the effects of selective serotonin reuptake inhibitors (SSRIs) on cardiovascular morbidity and mortality in patients with depression and coronary artery disease were eligible for inclusion.

The included studies were of patients with first acute myocardial infarction (MI) or first hospitalisation for myocardial infarction, patients with depression or major depressive disorder after myocardial infarction or unstable angina, patients with ischaemic heart disease, patients undergoing coronary artery bypass grafting and patients without psychosis but hospitalised because of a suicide attempt.

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

Assessment of study quality
Although no formal validity assessment was reported, some aspects of study quality were discussed in the review.

Data extraction
The authors did not state how data were extracted.

Methods of synthesis
Data were presented as a narrative synthesis and in tables.

Results of the review
Thirteen studies (n=707,076) were included: one prospective randomised controlled trial (RCT); one retrospective secondary analysis of an RCT; seven case controls; one record linkage study; and three cohort studies.

Four studies (one secondary analysis RCT, two case controls and one cohort study) reported a statistically significant reduction in cardiovascular morbidity or mortality using SSRIs; two studies (one case control and one cohort) reported statistically significantly worse outcomes with SSRIs.

Seven studies (one RCT, four case controls, one record linkage study and one cohort study) found no statistically significant association between SSRIs and cardiovascular morbidity and mortality. However, one of the four case controls reported a significantly lower risk of myocardial infarction using SSRIs with high serotonin transporter affinity (paroxetine, sertraline, fluoxetine): OR 0.59 (95% CI 0.39 to 0.91).

Three of 11 studies that reported findings on antidepressants other than SSRIs reported a statistically significant increase in cardiovascular events associated with at least one type of non-SSRI antidepressant.
Authors' conclusions
There was insufficient evidence to permit definitive conclusions regarding the effect of SSRIs on cardiovascular morbidity and mortality.

CRD commentary
The review question was clear and supported by appropriate criteria for intervention, population and broadly defined outcomes. The search was limited to one electronic database and reference lists, and was restricted to publications in English. Therefore, language and publication biases may have been introduced and potentially relevant data missed. The authors did not perform a validity assessment, but acknowledged the limitations with the study designs. The authors did not state how studies were selected or how data were extracted, so reviewer error and bias could not be ruled out. Details on patient characteristics and treatment types and regimens were limited. A narrative synthesis seemed appropriate.

The authors' conclusions appear suitably cautious, but their reliability is unclear given the limitations with the included studies and potential for bias in the review.

Implications of the review for practice and research
Practice: The authors stated that patients with cardiovascular disease should be screened for symptoms of depression and treated when appropriate.

Research: The authors stated that large randomised controlled studies that included both depressed and non-depressed patients with coronary artery disease were needed to further examine the effect of SSRIs on cardiovascular outcomes.

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