Effects of antibiotic therapy on outcomes of patients with coronary artery disease: a meta-analysis of randomized controlled trials

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CRD summary
This review evaluated the efficacy of antichlamydial antibiotic therapy in patients with coronary artery disease. The authors concluded that there was no benefit of antibiotic therapy in reducing mortality or cardiovascular events in these patients. As the potential for error and bias could not be ruled out, the conclusions may not be reliable and should be treated with caution.

Authors' objectives
To evaluate the efficacy of antichlamydial antibiotic therapy in patients with coronary artery disease (CAD).

Searching
MEDLINE (1966 to April 2005) and the Cochrane CENTRAL Register (April 2005) were searched; the search terms were reported. Bibliographies of retrieved articles and proceedings from scientific meetings were also searched.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. The duration of follow-up of the included studies ranged from 3 months to 4 years.

Specific interventions included in the review
Studies of antichlamydial antibiotic treatment as an adjunct to standard medical care, compared with placebo, were eligible for inclusion. The antibiotic treatments evaluated in the included studies were azithromycin, roxithromycin, clarithromycin or gatifloxacin; details of the dosages were given.

Participants included in the review
Studies of patients with established CAD were eligible for inclusion. The participants in the included studies had either stable CAD or acute coronary syndromes (ACS). The mean age of the participants ranged from 58 to 66 years, and the percentage of males ranged from 71 to 100%. A large proportion of the participants in the included studies had additional risk factors such as hypertension, previous myocardial infarction (MI), diabetes, hyperlipidaemia, prior coronary artery bypass graft or angioplasty, or current or previous smoker.

Outcomes assessed in the review
Studies reporting all-cause mortality, MI or unstable angina (UA) were eligible for inclusion.

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

Assessment of study quality
The criteria used to assess study quality were blinding of randomisation, allocation concealment, follow-up and objectivity of the outcome assessment. The authors did not state how the papers were assessed for quality, or how many reviewers performed the quality assessment.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data
extraction. Data on the occurrence of all-cause mortality, MI and UA were extracted from the individual studies and used to calculate an odds ratio (OR) with 95% confidence intervals (CIs), using an intention-to-treat analysis.

**Methods of synthesis**

How were the studies combined?
Summary ORs and 95% CIs were calculated for each outcome, as well as for MI and UA combined, using a random-effects meta-analysis. The studies were weighted by the square root of the sample size. Publication bias was investigated using a funnel plot.

How were differences between studies investigated?
Heterogeneity was assessed statistically using the Q statistic. Sensitivity analyses were performed to investigate the effect of each study on the summary results; each study was excluded each study in turn from the analysis.

**Results of the review**

Eleven double-blind RCTs (n=19,217: 9,613 treated and 9,604 placebo) were included in the review.

The authors reported that none of the analyses showed statistical heterogeneity.

All 11 RCTs included in the review were double-blinded and used an intention-to-treat analysis. Nine RCTs reported the use of a blinded endpoints committee for the adjudication of outcome events. The drop-out rate was 2% or less in all included RCTs, with 6 RCTs having 100% follow-up.

All-cause mortality (11 RCTs, n=19,217).
There was no statistically significant reduction in mortality with antichlamydial antibiotic treatment in comparison with placebo (OR 1.02, 95% CI: 0.89, 1.16, P=0.83). The exclusion of any single study, or restriction of the analysis to studies where participants had positive serology, did not alter the overall result of the analysis.

MI (9 RCTs, n=18,939). There was no statistically significant reduction in the rate of MI with antichlamydial antibiotic treatment in comparison with placebo (OR 0.92, 95% CI: 0.81, 1.04, P=0.19). The exclusion of any single study did not alter the overall result of the analysis.

ACS (10 RCTs, n=17,778).
There was no statistically significant reduction in ACS event rates with antichlamydial antibiotic treatment in comparison with placebo (OR 0.91, 95% CI: 0.76, 1.07, P=0.09). The exclusion of any single study, or restriction of the analysis to studies where participants had positive antichlamydial titres, did not alter the overall result of the analysis.

Funnel plots found no evidence of publication bias.

**Authors' conclusions**

There was no overall benefit of antibiotic therapy in reducing mortality or cardiovascular events in patients with CAD.

**CRD commentary**

The review question and the inclusion criteria were clearly reported. The authors undertook a limited search to identify published and unpublished studies. However, they reported that the funnel plot showed no evidence of publication bias. No details of the methods used to select the studies for inclusion, assess quality, or extract the data were reported; therefore, the possibility of error and bias could not be ruled out. Adequate details of the characteristics and results of the included studies were given. The methods used to combine the studies were appropriate, although limitations in the reporting of the review process mean that the conclusions and implications for practice may not be reliable and should be treated with caution.
Implications of the review for practice and research
Practice: The authors stated that the management of patients with CAD should focus on lifestyle interventions and medical therapies (aspirin, beta-blockers and statins). The effectiveness of the regimens recommended were not evaluated in detail in the review.

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

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