



OTHER PAPERS

Clarithromycin may increase cardiovascular mortality in people with stable heart disease[☆]

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Background

Some studies suggest an association between chlamydia pneumoniae serological markers and cardiovascular events. Previous studies have found variable effects of antibiotics in people with acute or stable coronary heart disease.

Objective

The CLARICOR trial assessed whether the macrolide clarithromycin affects mortality and cardiovascular morbidity in people with stable coronary heart disease. The primary endpoint was a composite of all-cause mortality, myocardial infarction, or unstable angina pectoris during three year follow up. The secondary endpoint was a composite of cardiovascular mortality, myocardial infarction, or unstable angina pectoris.

Method

This double blinded randomised trial took place in five university hospitals in Denmark. Randomisation occurred between October 1999 and April 2000. Follow up was completed in September 2003.

[☆] Abstracted from CLARICOR Trial Group. Randomised placebo controlled multicentre trial to assess short term clarithromycin for patients with stable coronary heart disease: CLARICOR trial. *BMJ* 2006;332:22–4.

Participants

Participants were 4373 people aged 18 to 85 years who were discharged between 1993–9 with myocardial infarction or angina, percutaneous transluminal coronary angioplasty or coronary bypass surgery and were alive in August 1999. Demographic details were not reported.

Intervention

Participants received two weeks' treatment with 500 mg per day clarithromycin or placebo.

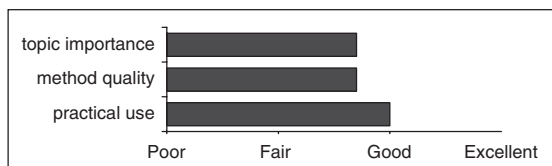
Main results

Clarithromycin had no significant effect on the primary outcome (hazard ratio 1.15, 95% CI 0.99 to 1.34) or secondary outcome (hazard ratio 1.17, 95% CI 0.98 to 1.40). Mortality was significantly higher in those receiving clarithromycin (hazard ratio 1.27, 95% CI 1.03 to 1.54, $p = 0.03$) as a result of significantly higher cardiovascular mortality (hazard ratio 1.45, 95% CI 1.09 to 1.92, $p = 0.01$).

Authors' conclusions

The authors concluded that short-term clarithromycin may be associated with cardiovascular mortality in people with stable coronary heart disease.

Overall quality



Commentary

Various studies suggest an association between infection and atherogenesis. Chlamydia pneumonia has been found within atherosclerotic plaques, suggesting that antibiotic treatment may be a possibility. If atherosclerosis is an inflammatory disease, this offers new opportunities for the prevention and treatment of coronary artery disease.¹ However, recent study results are disappointing.^{2,3}

This study's contribution

The CLARICOR trial investigated the effect of short-term clarithromycin for people with stable heart disease. The methods appear adequate and the results seem reliable and well presented.

Caveats

However, there are some limitations. The study was performed in 1999. It remains uncertain why the authors chose 500 mg oral clarithromycin for two weeks. Heart disease is a chronic infection, so treatment duration of just two weeks appears very short. Other groups have used long-term treatment with 10-day courses every month for one to two years.^{2,3}

It may be that clarithromycin did not reach chlamydia pneumonia in the chronic atherosclerotic lesion.

The key question is whether inflammatory disease is the main cause of coronary artery disease.⁴ The situation is complex. We recently studied the relationship between dental infections and cardiac surgery. We found no correlation between oral health and postoperative infections.⁴

Implications

Initially we thought that there may be some merit in treating heart disease with antibiotics, especially because treating hypercholesterolemia, hypertension and other risk factors may not change cardiovascular morbidity. However, we've now found that this idea was too simple.⁵ Although long-term treatment of chlamydia pneumonia may have a moderate clinical benefit in some people, overall, antibiotics cannot be recommended for treating coronary artery disease.

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Results abstracted by Debbie Singh.

Commentary provided by Torsten Bossert MD, Department of Cardiac Surgery, University of Leipzig-Heart Center, Leipzig, Germany.

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