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Ramipril reduces mortality in patients at high risk of heart failure

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Keywords

ACE inhibitor, cardiovascular mortality, randomised controlled trial

Comments

This is a well conducted study providing strong level 1 evidence that ramipril is effective at reducing mortality and morbidity in patients with known coronary artery disease or who are at high risk. It broadens the indication for ACE inhibition to many more patients than previous trials.It is worth noting that compliance was less than 70% by four years which implies that the trial probably underestimated the true benefit of ACE inhibition to the compliant patient.However, it is worth bearing in mind that the number needed to treat to save one death from ANY cause is 55. Furthermore, as treatment effects in daily practice are often weaker than in clinical trials, this may underestimate the "real-life" number needed to treat.

Introduction

ACE inhibitors improve outcome in patients with low ejection fraction, heart failure and following myocardial infarction. There has been uncertainty concerning their benefit to patients at high risk of coronary artery disease.

Aims

The aim of this study was to assess the effect of ramipril in a broader group of patients with, or at high risk of, cardiovascular disease but without known heart failure or low ejection fraction.

Methods

The study was a double blind randomised comparison of ramipril (10 mg per day) vs placebo. Patients over 55 years of age with known coronary artery disease, stroke, or peripheral vascular disease or with diabetes and one major risk factor were included. Patients who were taking an ACE inhibitor, or who had impaired left ventricular function or other indication for an ACE inhibitor, were excluded. Primary end-points were the occurrence of myocardial infarction, stroke or death from cardiovascular causes. The secondary end-points included death from any cause and manifestations of worsening coronary artery disease.

Results

Patient groups were well matched at baseline. Follow-up was for up to 4 years. In total, 653 patients (14.1 %) reached a primary end-point in the ramipril group, compared with 824 in the placebo group (17.7 %; relative risk = 0.78; 95% CI 0.70 - 0.86; $p < 0.0001$). There were also highly significant reductions in deaths from cardiovascular causes (6.1 % vs 8.1 %), any cause (10.4 % vs 12.2 %) and in myocardial infarctions, cardiac arrests and a number of other secondary end-points.

Discussion

The magnitude of benefit of ramipril in this broad group of patients is comparable to that from other interventions such as aspirin, beta-blockers and lipid lowering agents. The benefit was not explained by reduction in blood pressure: direct effects of ACE inhibition on the heart and vasculature are possible explanations. The result is unlikely to have been affected by the inclusion of patients with undiagnosed left ventricular dysfunction.

References

1. The Heart Outcomes Prevention Evalutation Study Investigators: Effects of an angiotensin-converting-enzyme inhibitor. N Engl J Med. 1999, 342: 985-990.