Articles

Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial

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Summary

Background Although statins reduce coronary and cerebrovascular morbidity and mortality in middle-aged individuals, their efficacy and safety in elderly people is not fully established. Our aim was to test the benefits of pravastatin treatment in an elderly cohort of men and women with, or at high risk of developing, cardiovascular disease and stroke.

Methods We did a randomised controlled trial in which we assigned 5804 men (n=2804) and women (n=3000) aged 70–82 years with a history of, or risk factors for, vascular disease to pravastatin (40 mg per day; n=2891) or placebo (n=2913). Baseline cholesterol concentrations ranged from 4·0 mmol/L to 9·0 mmol/L. Follow-up was 3·2 years on average and our primary endpoint was a composite of coronary death, non-fatal myocardial infarction, and fatal or non-fatal stroke. Analysis was by intention-to-treat.

Findings Pravastatin lowered LDL cholesterol concentrations by 34% and reduced the incidence of the primary endpoint to 408 events compared with 473 on placebo (hazard ratio 0·85, 95% CI 0·74–0·97, p=0·014). Coronary heart disease death and non-fatal myocardial infarction risk was also reduced (0·81, 0·69–0·94, p=0·006). Stroke risk was unaffected (1·03, 0·81–1·31, p=0·8), but the hazard ratio for transient ischaemic attack was 0·75 (0·55–1·00, p=0·051). New cancer diagnoses were more frequent on pravastatin than on placebo (1·25, 1·04–1·51, p=0·020). However, incorporation of this finding in a meta-analysis of all pravastatin and all statin trials showed no overall increase in risk. Mortality from coronary disease fell by 24% (p=0·043) in the pravastatin group. Pravastatin had no significant effect on cognitive function or disability.

Interpretation Pravastatin given for 3 years reduced the risk of coronary disease in elderly individuals. PROSPER therefore extends to elderly individuals the treatment strategy currently used in middle aged people.

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Introduction

Findings of clinical trials[1–6] of 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors (statins) have shown significant benefits in both primary and secondary prevention of coronary and cerebrovascular disease events. Most of this evidence comes from studies done on middle-aged men. The rationale for such treatment in people older than age 70 years, most of whom die of vascular disease, is less clear because the association between plasma cholesterol and risk of coronary artery disease diminishes with increasing age.[7–9] The frequency of stroke, an important manifestation of vascular disease in elderly individuals, is associated with hypertension and seems independent of plasma cholesterol.[10] However, investigators of previous statin trials[11] have reported benefits on stroke, and results of observational studies have raised the possibility that statins could reduce the rate of cognitive decline in elderly people.[12] However, in the oldest old people, low plasma cholesterol is associated with increased mortality.[8,9] In view of these conflicting observations, we concluded that the balance of the efficacy and safety of cholesterol lowering in older people had yet to be established, and we launched the PROspective Study of Pravastatin in the Elderly at Risk (PROSPER). Our aim was to ascertain if treatment with pravastatin reduces the risk of cardiac events, stroke, cognitive decline, and disability in those with existing (secondary prevention) and in those at high risk of developing (primary prevention) vascular disease.[13–15] We chose a treatment period of a minimum of 3 years as a reasonable time frame to test the efficacy of the medication in what for many individuals is the last decade of their life.

Methods

The protocol of PROSPER has been published elsewhere.[13]

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