

Lipid-lowering drug therapies: the evidence

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Recent clinical trials have proved beyond doubt the benefit of cholesterol-lowering with statins in both primary and secondary prevention. These drugs decrease by 25–45 % the risk of a first or recurrent myocardial infarction, lower cardiovascular mortality and improve overall survival. The magnitude of the relative risk reduction on statin therapy is not modified by lipid phenotype, age, sex or concomitant risk factors; thus, potentially all may benefit from treatment. Current strategies for primary and secondary prevention emphasize that candidates for treatment should be selected on the basis of their absolute risk of a coronary event in the future. This approach targets drug use to those who will receive the greatest benefit and limits the potential strain on resources and budgets.

West of Scotland Coronary Prevention Study (Shepherd *et al.* 1995) was a trial of pravastatin therapy at a single dose of 40 mg/d in men aged 45–64 years who were moderately hypercholesterolaemic but had not had a myocardial infarction. The 6605 recruits to Air Force/Texas Coronary Atherosclerosis Prevention Study (Downs *et al.* 1998) were men and women aged 45–73 years who had no signs or symptoms of ischaemic arterial disease and had average plasma cholesterol but low HDL; here lovastatin was used and titrated to achieve specific lipid goals. Both these primary prevention trials gave very similar results in terms of risk reduction, and advanced greatly our understanding of the potential benefits of statin therapy in CHD prevention in asymptomatic patients across a broad range of plasma lipid levels and coronary risk.

The importance of risk factor modification in general, and lipid lowering in particular, has been accepted for

primary prevention for a long time, but it is only recently that epidemiological data became available to show the strong association between cholesterol levels and risk of a recurrent myocardial infarction.

These observations led to the formulation of trials to test the cholesterol hypothesis in secondary prevention. In 4S (Scandinavian Simvastatin Survival Group, 1994), LDL-cholesterol was decreased 35 % by simvastatin in initially moderately-hypercholesterolaemic patients. This decrease was associated with a 42 % reduction in coronary death and a 30 % decrease in overall mortality. However, most patients who experience a myocardial infarction have unremarkable plasma cholesterol levels, approximately the average seen in the general population. The rationale behind the Cholesterol and Recurrent Events (CARE) study (Sacks *et al.* 1996) was to ask if lipid lowering was of benefit in these individuals also. Pravastatin treatment reduced the risk of the primary end point (CHD death plus non-fatal myocardial infarction) by 25 %, while the need for repeat revascularization was reduced by 27 %. Stroke was a pre-specified outcome, and treatment produced a 31 % reduction. In the Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study (The Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group, 1998), the latest and largest of the statin outcome studies, there was a wide range of plasma cholesterol (4.0–7.0 mmol/l) on entry, and treatment with pravastatin gave ‘highly significant’ risk reductions of 24 % in CHD death and 23 % in total mortality. In the LIPID study, as in the CARE study, stroke was a stated outcome measure and was reduced by 20 % with pravastatin therapy.

Lipid-lowering drug therapies: Statins: Myocardial infarction risk

References

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Abbreviations: CARE, Cholesterol and Recurrent Events; LIPID, Long-term Intervention with Pravastatin in Ischaemic Disease.
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