Statins for everyone?

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Cardiovascular disease is responsible for one in three deaths globally.[1] It is estimated that by the end of 2010, it will be the leading cause of death in developing countries.[2] NICE guidelines state that those already established with coronary heart disease (CHD), cerebrovascular disease and those with established risk factors such as diabetes mellitus should be considered for treatment with a statin.

But what, if any, is the role of statin therapy for patients at low cardiovascular risk? Would any benefit be clinically efficacious, safe and cost-effective? The key question is: should GPs be prescribing statins for 'healthy' patients at low cardiovascular risk?

This controversial topic was in part answered by the recent published JUPITER (Justification for the Use of Statins in Primary Prevention: an Interventional Trial Evaluating Rosuvastatin) study.[3]

JUPITER was a large placebo-controlled RCT that included 17 802 'healthy' individuals from 26 countries. The study recruited healthy people with normal LDL levels (<3.4 mmol/l) but with elevated levels of C-reactive protein (C-RP) (>2 mg/l). The mean age of the study population was 66 years. Those with definitive cardiovascular risk factors were excluded as well as those with inflammatory conditions (eg, arthritis). Study participants were given rosuvastatin 20 mg daily or placebo. The primary endpoint was a composite of myocardial infarction, stroke, arterial revascularisation, hospitalisation for unstable angina or death from cardiovascular causes. The study was supported by AstraZeneca.

C-RP is an inflammatory marker reflecting active inflammation. Elevated C-RP levels are associated with an increased risk of myocardial infarction,[4] thus supporting the possible relationship between inflammation and atherosclerosis.

The study was stopped after 1.9 years, because of a clear benefit seen in the rosuvastatin group. Rosuvastatin decreased the relative risk of the primary end point by 44% (95% CI 0.46 to 0.69). Those with a family history of premature CHD had an even greater relative risk reduction in the primary end point of about 65%.

Similar results were obtained from a substudy of the AFCAPS/TexCAPS trial; a 5-year study of 5742 participants compared lovastatin with placebo and demonstrated reduced coronary events in a population with a normal lipid profile and elevated C-RP.[5]

From the evidence, advantages of giving statins to all include:

- JUPITER found that rosuvastatin reduced LDL-cholesterol levels by 50%, decreasing from a median 108 mg/dl at baseline to 55 mg/dl at 12 months. CRP levels were also significantly reduced, declining from 4.2 mg/l at baseline to 2.2 mg/l at 12 months.
- Rosuvastatin significantly reduced the incidence of major cardiovascular events, a population that were mostly below the threshold for treatment according to current prevention guidelines.
- Despite previous concerns regarding the side-effect profile of potent statin therapy, JUPITER found that the side-effects for rosuvastatin were no higher than placebo, thus suggesting that the rate of side-effect occurrence was low.
- The study included populations that had not been previously well represented in studies; therefore there is no doubt that all these populations share the benefit of cholesterol lowering.

But the reasons why giving statins to all is questionable include:

- The population studied in JUPITER needs careful evaluation. They were elderly, at least 40% had the metabolic syndrome (but none were overtly diabetic); 16% were taking aspirin prior to entry into the study, and at least 10% have a family history of premature cardiovascular disease.
- Compliance with taking statins may be a problem due to the side effects of myalgia: GPs often report a higher prevalence than clinical trials.
- Not all 'healthy' individuals have elevated C-RP levels.
- There are many ways to decrease the risk of coronary events. Modifiable risk factors such as obesity and smoking should be addressed. By prescribing a statin, individuals may not appreciate the need to address lifestyle changes.
- From JUPITER, 25 people would have to take a rosuvastatin over 5 years to prevent one new major cardiovascular event. This needs to be balanced against the cost of drug therapy and monitoring.

The use of statins is ubiquitous and has proven benefit for secondary prevention and primary prevention for patients at high cardiovascular risk (defined as a 20% risk of an event over 10 years). The data from JUPITER are exciting but do not provide a convincing reason to prescribe statins to the worried well, even those with an elevated C-RP. Although C-RP level may be a future determinant in deciding statin therapy, the population under study were mostly elderly, and a significant number had soft markers of cardiovascular risk.

In terms of cost-effectiveness, the cost needs to consider the potential risks and subsequent monitoring.

Finally, the danger of statin therapy might be to lower patients' acceptance to undertake lifestyle advice. Although strict dieting has only a small reducing effect on LDL-cholesterol, lifestyle measures, if taken as a whole significantly reduce cardiovascular events.[6]

Competing interests None.

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