LETTERS

Statin doses after acute coronary syndrome

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Drs Eng-Frost and Chew address the diagnosis and management of acute coronary syndromes in their helpful review.[1] However, we question the need for the maximum tolerated statin dose in secondary prevention.

Significant toxicities are not always symptomatic and can be difficult to ascertain particularly in older patients or patients with comorbidities. Higher statin doses have not been shown to improve overall survival nor coronary mortality.[2,3] Safety and quality of life are important and toxicities increase with increasing drug doses.[4]

The greatest absolute risk reductions in mortality in randomised placebo-controlled clinical trials were seen with 40 mg of simvastatin or pravastatin in the 4S, HPS and LIPID studies.[3] Although some reductions in coronary events have been reported with higher statin doses, there is plateauing efficacy, as seen with all drugs at the top of their dose-response curves. This makes it likely that a greater reduction in coronary events will be achieved with statins in combination with other therapies such as antithrombotics, antihypertensive drugs, weight reduction and smoking cessation.

Specific target cholesterol concentrations have never been established in any appropriately designed randomised clinical trial. Epidemiology shows that reductions in coronary event rates plateau with lower cholesterol concentrations. There is no reduction, and in several analyses an increase, in mortality with total cholesterol concentrations below 5 mmol/L[5,6] (low-density lipoprotein cholesterols below 3.5 mmol/L).

In addition to plateauing efficacy, the failure of higher doses of statins to reduce mortality is likely to be related to the often non-plateauing increases in potentially serious toxicities, such as liver dysfunction,[3,7,8] diabetes,[9] cerebral haemorrhage[10] and renal impairment.[7,8] We suggest that for many patients it may be neither necessary nor prudent to increase doses, especially if the statin is used with other therapies known to reduce mortality.

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Joanne Eng-Frost and Derek Chew, the authors of the article, comment:

The recommendation that statins should be up-titrated to the highest tolerated doses is not solely intended to reduce mortality. It also aims to reduce the broader array of future coronary events, specifically recurrent myocardial infarction and revascularisation. There is a significant burden of recurrent events in patients who have symptomatic coronary artery disease.

The practice of encouraging the use of higher statin doses, to achieve lower concentrations of low-density lipoprotein in patients with symptomatic coronary artery disease to reduce recurrent cardiac events, is recommended in several guidelines. This provides greater benefit than the other therapies mentioned in the letter. However, clinical judgement and individualisation of therapy for each patient should always prevail when selecting statin doses.

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