CLINICAL UPDATE

Elderly patients with coronary artery disease: Is pravastatin an answer?

Hunt D, Young P, Simes J, Hague W, Mann S, Owensby D, et al. Benefits of pravastatin on cardiovascular events and mortality in older patients with coronary heart disease are equal to or exceed those seen in younger patients: results from the LIPID trial. *Ann Intern Med* 2001; 134:931-40.

Background: An elevated blood cholesterol level is a significant risk factor for coronary artery disease (CAD). Clinical trials have shown that lipid-lowering treatment with statins is effective in the secondary prevention of coronary events and in preventing death among patients with elevated[1] and average[2,3] cholesterol levels. Whether the benefit observed in the younger patients in these trials extends to elderly patients is uncertain.

Question: In elderly patients with existing CAD, does pravastatin reduce the risk of major cardiovascular events and death?

Design: This study represents a subgroup analysis of data from the LIPID trial, a randomized, double-blind, placebo-controlled trial conducted in 87 centres in Australia and New Zealand.[3] In the original trial, patients aged 31 to 75 years with a history of myocardial infarction or unstable angina were enrolled if their plasma total cholesterol level before randomization was between 4.0 and 7.0 mmol/L following a period of dietary counselling. Exclusion criteria included a recent "clinically significant" medical or surgical event, cardiac failure, renal or hepatic disease, and the concurrent use of any cholesterol-lowering agents. Patients were then randomly assigned to receive either pravastatin (40 mg/d) or placebo. The patients' physicians provided usual care during the study period and could initiate other cholesterol-lowering therapy.

In the current subgroup analysis of patients aged 65 to 75 years, the primary end-point was a composite of death from CAD or nonfatal myocardial infarction. Secondary end-points included death from CAD and death from any cause. All analyses were performed on an intention-to-treat basis.

Results: Of the 9014 patients enrolled in the original trial, 3514 were aged between 65 and 75 years at study entry. Of those, 1741 patients received pravastatin and 1773 placebo. Most (80%) of the patients were men; 60% had a history of myocardial infarction, and 40% unstable angina. ASA was taken by 79%, β-blockers by 45% and angiotensin-converting-enzyme inhibitors by 19%. The initial median lipid levels were as follows: total cholesterol 5.6 mmol/L, low-density lipoprotein (LDL) 3.8 mmol/L, high-density lipoprotein (HDL) 0.9 mmol/L, triglycerides 1.5 mmol/L and total cholesterol:HDL ratio 5.9.

The mean length of follow-up was 6.1 years. Pravastatin was well tolerated and improved the average total cholesterol (–19%), LDL (–28%), HDL (+7%) and triglyceride (–11%) levels. For the primary end-point (death from CAD or nonfatal myocardial infarction), there was an absolute risk reduction with pravastatin of 4.7%, for a number needed to treat (NNT) of 21 (95% confidence interval [CI] 17–31). Pravastatin also reduced the incidence of secondary end-points, with an NNT of 35 (95% CI 24–67) to prevent 1 death from CAD and an NNT of 22 (95% CI 17–36) to prevent 1 death from any cause. Thus, for every 1000 patients with CAD between 65 and 75 years of age, pravastatin treatment is predicted to prevent 45 deaths. The benefit from pravastatin among the elderly patients in this analysis actually appeared greater than that observed among the younger cohort.

Commentary: This elderly subgroup with CAD and average lipid levels likely benefitted from pravastatin therapy because they were at higher risk of major cardiovascular events than the younger cohort. Whether this logic might extend to patients older than 75 years is unknown, given their shorter life expectancy and greater prevalence of other diseases. This study did not include patients without CAD, so the potential role of statins for primary prevention in elderly patients remains unclear.

Practice implications: Lipid-lowering therapy for the secondary prevention of major cardiovascular events and death should not be withheld from elderly patients simply because of their age. Usual precautions need to be followed when using statins, especially in light of recent concerns over rhabdomyolysis and death associated with cerivastatin.[4] — *Benjamin H. Chen*

The Clinical Update section is edited by Dr. Donald Farquhar, head of the Division of Internal Medicine, Queen's University, Kingston, Ont. The updates are written by members of the division.

References

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4. Wooltorton E. Bayer pulls popular cholesterol-lowering drug from market. *eCMAJ Newsdesk* 2001 Aug 8. Available: www.cma.ca/cmaj/cmaj_today/2001/08_08.htm (accessed 2001 Aug 20).