This study randomized 4,126 patients who had been hospitalized for an acute coronary syndrome within the preceding 10 days. The goal of the study was to establish the non-inferiority of pravastatin versus atorvastatin in terms of the time to an end-point event. Standard therapy of pravastatin, 40 mg/day, was compared with intensive therapy of atorvastatin, 80 mg/day.

The primary end point was a composite of death from any cause, myocardial infarction, documented unstable angina requiring rehospitalization, revascularization (performed at least 30 days after randomization) and stroke. Followup lasted 18 to 36 months, with the mean being 24 months.

Patients receiving pravastatin achieved a median low-density lipoprotein cholesterol (LDL-C) of 2.46 mmol/L, compared to an LDL-C level of 1.60 mmol/L achieved in the high-dose atorvastatin group (p < 0.001).

Estimates of the rates of the primary end point at two years were 26.3% and 22.4% in the pravastatin and atorvastatin groups, respectively, reflecting a 16% reduction in the hazard ratio in favour of atorvastatin (p = 0.005).

The authors concluded that an intensive, lipid-lowering statin regimen is superior to a standard regimen in providing protection against death or major cardiovascular events among patients who have recently had an acute coronary syndrome. Furthermore, these findings indicate such patients benefit from early and continued lowering of LDL-C to levels substantially below current targets.
Is lower better? That was the question in treating cholesterol. We knew that based on past trials, there were benefits of treating down to a target LDL of 2.5 mmol/L, but what about going down further? Are there increased risks? What are the benefits?

Many studies involving pravastatin showed it was not necessary to drive down the LDL and that there were other effects of statins on inflammation, C-reactive proteins, etc. that were adding to the protective nature of these medications.

The PROVE-IT trial was designed to look at this exact issue. Does treating to a lower level have any benefit? To this end, pravastatin, 40 mg daily, was compared to atorvastatin, 80 mg daily, in acute coronary patients. If a LDL of 2.5 mmol/L was the lower limit of cholesterol benefit, then as long as both drugs reached that target, the patients should have equal benefit.

In this trial, pravastatin lowered LDL-C to 2.46 mmol/L, which matched our current guideline recommendations. On the other hand, atorvastatin lowered LDL-C to 1.60 mmol/L, which is significantly lower than the target level. The primary end point was in favour of atorvastatin, with an absolute difference of 3.9% (relative reduction of 16%). This would put the number needed to treat around 25.

Future guidelines will be rewritten based on these types of trials, perhaps with new, lower targets. In the end, patients are the ones who will benefit; if this trial has moved us to treat more aggressively, then it has served its purpose.

Perhaps I am not perfect in getting my patients’ LDL down to 1.6 mmol/L, but after this trial, I am going to push it as best I can and ensure my patients know why. My goal isn’t just to hit a target number, but to protect patients from cardiovascular disease.

About the author...
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