Effect of High-Dose Atorvastatin on Cardiovascular Outcomes in Elderly Coronary Patients

Wenger NK, Lewis SJ, Herrington DM, et al; Treating to New Targets Study Steering Committee and Investigators. Outcomes of using high- or low-dose atorvastatin in patients 65 years of age or older with stable coronary heart disease. Ann Intern Med 2007;147:1–9.

Study Overview

Objective. To assess whether high-dose atorvastatin can improve cardiovascular outcomes in patients aged ≥ 65 years.

Design. Secondary analysis of the Treating to New Targets (TNT) study [1], a multinational, randomized, double-blind trial.

Setting and participants. 3809 patients aged ≥ 65 years with established coronary heart disease (CHD) and low-density lipoprotein (LDL) cholesterol levels < 3.4 mmol/L (< 130 mg/dL). After an 8-week run-in period with 10 mg daily of atorvastatin, patients were randomly assigned to atorvastatin 10 or 80 mg daily and were followed for a median of 4.9 years.

Main outcome measures. The primary outcome measure was the occurrence of a first major cardiovascular event, defined as death from CHD, nonfatal non–procedure-related myocardial infarction, resuscitated cardiac arrest, or fatal or nonfatal stroke. Prespecified secondary outcomes included a major coronary event, a cerebrovascular event, peripheral arterial disease, hospitalization with a diagnosis of congestive heart failure, death from any cause, any cardiovascular event, and any coronary event.

Main results. The absolute risk for the composite major cardiovascular events was reduced by 2.3% and relative risk was reduced by 19% in the high-dose atorvastatin group as compared with low-dose group (hazard ratio, 0.81 [95% confidence interval, 0.67–0.98]; $P = 0.032$). For the primary outcome measure, mortality rates were lower in the high-dose atorvastatin group; however, results were not statistically significant when each component of the primary outcome measure was considered. For secondary outcomes, there were significant reductions in risk in the high-dose atorvastatin group for any coronary event ($P < 0.001$), any cardiovascular event ($P < 0.001$), a cerebrovascular event ($P = 0.01$), and hospitalization with congestive heart failure ($P = 0.008$). No cases of persistent elevations in creatine kinase occurred in the high-dose group. 1.3% of patients in the high-dose group and 0.1% in the low-dose group experienced persistent elevations in alanine aminotransferase or aspartate aminotransferase levels to > 3 times the upper limit of normal.

Conclusion. Aggressively treating older patients with CHD with high-dose atorvastatin to reduce LDL cholesterol levels to < 2.6 mmol/L (< 100 mg/dL) can lower the risk of a major cardiovascular event.

Commentary

Cardiovascular disease is the leading cause of morbidity and mortality in the elderly and is correlated with the level of LDL cholesterol. Previous trials have demonstrated that lowering LDL levels with statins reduces the risk of coronary disease in elderly individuals [2,3]. Consequently, the National Cholesterol Education Program updated and revised the Adult Treatment Panel III guidelines to support intensive LDL-lowering therapy (goal of < 100 mg/dL) in elderly patients with established CHD [4]; based on then-available evidence, an optional goal of LDL cholesterol less than 70 mg/dL could be considered, especially for those at very high risk. Thus, the TNT trial was undertaken to evaluate if lowering LDL to 70 mg/dL using high-dose atorvastatin would improve cardiovascular outcomes [1]. The results of the TNT trial were positive, showing that high-dose atorvastatin (80 mg/day) lowered LDL to a mean of 77 mg/dL in white men (median age, 61 years) and was associated with a 2.2 % absolute and 22% relative risk reduction in major cardiovascular events.

Wenger and colleagues undertook this prespecified subgroup analysis of the TNT study to assess if elderly patients also experience a reduction in cardiovascular risk with high-dose statin therapy. Not surprisingly, the authors found similar absolute and relative major cardiovascular risk reduction in the elderly subgroup. However, unlike this subgroup analysis, the TNT study demonstrated a statistically significant risk reduction in the high-dose atorvastatin group for each individual component of the composite

outcome [1], which is likely due to a sample size difference (10,001 in the TNT study vs. 3809 in this subgroup analysis). In this trial by Wenger et al, the number needed to treat was 35 for patients aged 65 years and older (compared with 26 for patients < 65 years), meaning that 35 elderly patients needed to be treated with high-dose atorvastatin for a mean of 4.9 years in order to prevent 1 more major cardiovascular event than treatment with low-dose therapy.

Applications for Clinical Practice

High-dose atorvastatin significantly reduces the rate of major cardiovascular events in elderly population when compared with low-dose therapy. Whether this reduction is due to the lower LDL levels achieved or other effects of atorvastatin remains unknown.

—Review by Mark S. Horng, MD, MPH

References

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