The Application of Evidence-Based Principles of Care in Older Persons (Issue 2): Management of Lipid Disorders

Barbara J. Zarowitz, PharmD, FCCP, BCPS, CGP, Wilbert S. Aronow, MD, CMD, Kelly Hollenack, PharmD, CGP, FASCP, and Terry O'Shea, PharmD, CGP, FASCP

DESCRIPTION OF THE PROBLEM

Cardiovascular disease is the leading cause of morbidity and mortality in persons older than 75 years in the United States.[1] Lifestyle and medical management options exist for primary and secondary prevention of cardiovascular disease, yet risk reduction remains elusive because of underuse of therapies proven effective.[2] Despite availability of robust scientific evidence supporting prescription of statin medications, use has been shown to decrease progressively as the baseline cardiovascular risk and future probability of death increases.[3] In a large retrospective cohort of 396,077 patients 66 years of age or older with a history of cardiovascular disease or diabetes, the likelihood of statin prescription was 6.4% lower for each year of increase in age and each percentage increase in predicted 3-year mortality risk.[3] Physician aggressiveness to provide secondary prevention to elderly persons was inversely correlated with baseline cardiovascular risk independent of age.

In another retrospective cohort analysis of 12,106 patients with type 2 diabetes, mean age 64 years, with and without symptomatic atherosclerosis, management of cardiovascular risk was suboptimal.[4] In patients with symptomatic coronary artery disease (CAD), fewer than 37%, 29%, and 60% of patients received an antiplatelet agent, statin, or angiotensin-converting enzyme inhibitor (ACEI), respectively. Undertreatment is prevalent despite well-known strategies to reduce cardiovascular risk in patients with diabetes and established atherosclerotic disease.[4]

There is a great deal of emerging evidence that appropriate lipid management reduces cardiovascular risk in older persons (Table 1).[5–16] Pravastatin in elderly individuals at risk of vascular disease (PROSPER)[8] showed that administering pravastatin for 3 years reduced the risk of coronary disease in elderly individuals, but not all-cause mortality, and therefore extends to elderly individuals the treatment strategy currently used in middle-aged people. In the Heart Protection Study (HPS)[9] with 20,536 adults (aged 40 to 80 years) with coronary disease, other occlusive arterial disease, or diabetes, similar event reductions on simvastatin therapy occurred for men and women and for participants either younger or older than 70 years of age at entry. In the Cholesterol and Recurrent Events (CARE) Trial at 5-year median follow-up in patients aged 65 to 75 years of age, pravastatin significantly decreased coronary artery disease (CAD) death by 45%, CAD death or nonfatal myocardial infarction (MI) by 39%, major coronary events by 32%, coronary revascularization by 32%, and stroke by 40%.[12–16] The Adult Treatment Panel Guidelines III recommended that older persons should not be denied the benefit of low-density lipoprotein (LDL)-lowering therapy on the basis of age alone.[17]

As was discussed in the first issue in this series, the application of evidence-based findings to elderly nursing home residents is challenging.[18] Studies infrequently take into account legitimate goals for nursing home patients such as preservation of physical and cognitive function and comfort. Despite these shortcomings, much can be learned from large randomized trials that include older persons and retrospective analyses in nursing home residents.

There is evidence of the value of cardiovascular risk reduction in older persons in nursing home environments. In 1410 nursing home residents (age 81 ± 9 years) with prior MI and a serum LDL cholesterol of 125 mg/dL or greater, reduction of serum LDL cholesterol by statins to less than 90 mg/dL was associated with a 20% incidence of new coronary events.[19]

Omnicare, Inc., Livonia, MI (B.J.Z., K.H., T.O.); College of Pharmacy and Allied Health Sciences, Wayne State University, Detroit, MI (B.J.Z.); Divisions of Cardiology, Geriatrics, and Pulmonary/Critical Care, New York Medical College, New York, NY (W.S.A); Mount Sinai School of Medicine, New York, NY (W.S.A.).

Address correspondence to Barbara J. Zarowitz, PharmD, FCCP, BCPS, CGP, Omnicare, Inc., 13975 Farmington Road, Livonia, MI 48150. E-mail: Barbara.zarowitz@omnicare.com

DOI: 10.1016/j.jamda.2005.12.009

Table 1. *Evidence Basis for Statins*

Study Design	Patients/# Enrolled	Term	Results	References
Randomized, placebo-controlled, double-blind: Post-hoc subgroup analysis comparing diabetic vs nondiabetic patients Simvastatin (20 mg/d titrated to 40 mg/d) vs placebo	Diabetes (4.5% of study population) or nondiabetes, previous myocardial infarction (MI) or angina pectoris 4444 enrolled Men and women age 35 to 70 years	5.4 years	In participants with diabetes, simvastatin decreased the relative risk reduction (RRR) for total mortality from 43% (simvastatin treated nondiabetic patients) to 29%. In participants with diabetes, simvastatin decreased the RRR for total coronary heart disease from 55% (simvastatin treated nondiabetic patients) to 32%. In participants with diabetes, simvastatin decreased the RRR for any atherosclerotic event from 37% (simvastatin treated nondiabetic patients) to 26%.	Pyorala K, et al.[7]
Randomized, double-blind, placebo-controlled Simvastatin (40 mg/d) vs placebo	Coronary disease, other occlusive arterial disease, or diabetes (19.4% of study population) 20,536 enrolled Men and women age 40 to 80 years	5 years	25% more reduction in incidence rate of first stroke when compared with placebo 24% more reduction in rate of major vascular events when compared with placebo 18% more reduction in coronary death rate when compared with placebo 26% RRR for people with diabetes in the rate of coronary heart disease	Heart Protection Study (HPS) Collaborative Group[9]
Randomized, placebo-controlled Simvastatin (40 mg/d) vs placebo	Diabetes, no diabetes but with occlusive arterial disease 5963 enrolled Men and women age 40 to 80 years	5 years	22% reduction for both participants with and without diabetes in the event rate of major coronary events, strokes, and revascularizations for those diabetic patients treated with simvastatin vs placebo. This reduction rate rose to 33% for those participants with diabetes. Allocation to simvastatin reduced the rate of first major vascular events by ~33.3% in participants with diabetes compared with placebo.	Collins R, et al.[10]
Double-blind, randomized, placebo-controlled Pravastatin (40 mg/d) vs placebo	Type 1 (2.8%) and type 2 diabetes, impaired fasting glucose, nondiabetes, with previous MI 586 enrolled Men and postmenopausal women age 27 to 70 years	6 years	25% of pravastatin-treated diabetic patients suffered recurrent coronary events compared with 37% in the placebo group. Pravastatin (in diabetic patients) reduced the RR of coronary events by 25% when compared with placebo and in nondiabetic patients it was reduced 23%. Pravastatin (in diabetic patients) reduced the RR of revascularization procedures by 32% when compared with placebo.	Goldberg RB, et al.[12]
Double-blind, randomized, placebo-controlled: Pooled analysis of 2 trials (CARE and LIPID) Pravastatin (40 mg/d) vs placebo	Diabetes, coronary heart disease (CHD), hypertension 13,173 enrolled (4159 CARE/9014 LIPID) Men and women age 21 to 75 years (CARE) and 31 to 75 years (LIPID)	5 years for CARE and 6 years for LIPID	In participants with diabetes and low LDL, pravastatin decreased CHD events from 34% (placebo group) to 22%, an RRR of 44%. Pravastatin reduced the event rate of CHD in diabetic patients to that of nondiabetic participants.	Sacks FM, et al.[13]