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Editorial

Use of Statins in the Treatment of Chronic Kidney Disease

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Chronic kidney disease (CKD) is associated with cardiovascular disease [1-9]. Efforts need to be made to treat and to prevent cardiovascular events and mortality in patients with CKD [9-13]. The 2011 European Society of Cardiology /European Atherosclerosis Society guidelines state that patients with CKD should be treated as patients at very high risk for cardiovascular disease who need active management of all risk factors [14].

A meta-analysis of 16 randomized controlled trials including 3,594 patients found that stains significantly improved serum lipids in patients with CKD not on dialysis with a trend to be more effective with longer duration of therapy and had less beneficial effect in patients on dialysis with the trend to be less effective with longer duration of therapy [15]. The beneficial effect of statins in preventing the development of renal dysfunction appears to be independent of their lipid-lowering effect [11]. A meta-analysis of 20 clinical trials of 6,452 patients with CKD randomized to statins or placebo showed that statins might exert significant renoprotective effects in CKD patients depending on the duration of treatment but only in patients not receiving dialysis therapy [16]. A meta-analysis of 11 randomized controlled clinical trials included 21, 295 patients with CKD, 6,857 receiving dialysis [17]. In patients with CKD not on dialysis, treatment with statins reduced all-cause mortality 34% ($p < 0.0001$), cardiovascular mortality 31% ($p = 0.0012$), cardiovascular events 45% ($p = 0.0001$), and stroke 34% ($p = 0.0022$) [17]. In patients receiving dialysis, treatment with statins had no effect on all-cause mortality and stroke but reduced cardiovascular mortality 21% ($p<0.05$) and cardiovascular events 19% ($p<0.05$) [17].

High-dose statins reduce serum low-density lipoprotein (LDL) cholesterol ≥50% and include atorvastatin 40 mg to 80 mg daily and rosuvastatin 20 mg to 40 mg daily [18]. Moderate-dose statins reduce serum LDL cholesterol 30% to 49% and include atorvastatin 10 mg to 20 mg daily, rosuvastatin 5 mg to 10 mg daily, simvastatin 20 mg to 40 mg daily, pravastatin 40 mg to 80 mg daily, lovastatin 40 mg daily, fluvastatin XL 80 mg daily, fluvastatin 40 mg twice daily, and pitavastatin 2mg to 4 mg daily [18]. Low-dose statins reduce serum LDL cholesterol less than 30% and include simvastatin 10 mg daily, pravastatin 10 mg to 20 mg daily, lovastatin 20 mg daily, fluvastatin 20 mg to 40 mg daily, and pitavastatin 1 mg daily [18].

The 2013 American College of Cardiology (ACC)/ American Heart Association (AHA) guidelines on therapy of hypercholesterolemia state that lifestyle modification must be used both prior to cholesterol-lowering drug therapy and together with use of cholesterol-lowering drug therapy [18]. Lifestyle modification includes a heart healthy diet, regular exercise, avoidance of tobacco products, and an ideal body weight [18].

These guidelines support the use of statins in patients with clinical evidence of atherosclerotic cardiovascular disease (ASCVD). ASCVD includes acute coronary syndromes, a history of myocardial infarction, stable or unstable angina pectoris, coronary or other arterial revascularization, stroke, transient ischemic attack, or atherosclerotic peripheral arterial disease [18]. These guidelines recommend use of high-dose statins in men and in women aged 75 years and younger with evidence of ASCVD with a class I indication. If high-dose statins are associated with adverse effects in patients with ASCVD, moderate-dose statins are recommended if tolerated with a class I indication. In patients older than 75 years with clinical ASCVD, use of high-dose or moderate-dose statins has a class IIa indication [18].

Patients with New York Heart Association class II, III, or IV heart failure and patients undergoing maintenance hemodialysis are unlikely to benefit from treatment from statins. No recommendation was made regarding initiation or continuation of statin therapy in these patients [18].

The ACC/AHA guidelines also recommend treating persons aged 21 years and older with a serum LDL cholesterol ≥190 mg/dL (group 2) with high-dose statins with a class I indication. For persons unable to tolerate high-dose statins, use the maximum tolerated dose of statin [18].

The ACC/AHA guidelines recommend for primary prevention in persons with diabetes mellitus and a serum LDL cholesterol between 70 to 189 mg/dL moderate-dose statins in adults aged 40 to 75 years of age with a class I indication [18]. If the 10-year risk of ASCVD is ≥ 7.5% using the Pooled Cohort Equations [19,20], high-dose statins is reasonable in diabetics aged 40 to 75 years with a class IIa indication [18]. In diabetics younger than 40 years and older than 75 years, moderate-dose statins or high-dose statins is reasonable to use with a class IIa indication [18].

Patients aged 40 to 75 years with serum LDL cholesterol of 70 to 189 mg/dL without ASCVD or diabetes mellitus and an estimated 10-year ASCVD risk of ≥7.5% should be treated with high-dose or moderate-dose statins with a class I indication [18]. It is reasonable to treat persons aged 40 to 75 years with a seum LDL cholesterol of 70 to 189 mg/dL without ASCVD or diabetes mellitus and an estimated 10-year ASCVD risk of 5% to 7.4% with moderate-dose statins [18].

Bile acid sequestrants should not be used in persons with fasting serum triglycerides ≥300 mg/dL or type III hyperlipoproteinemia because severe triglyceride increases may occur (class III indication harm) [18]. Gemfibrozil is contraindicated in patients treated with statins (class III indication harm). Fenofibrate may be considered in patients on low-dose statins or moderate-dose statins with serum triglycerides ≥ 500 mg/dL with a class IIb indication [18]. Fenofibrate is contraindicated in these patients if the estimated glomerular filtration rate is less than 30 mL/minute/1.73 m^2 (class III indication harm) [18]. If the the estimated glomerular filtration rate is between 30 and 59 mL/minute/1.73 m^2, the fenofibrate dose should not exceed 54 mg/day [18]. If omega-3 fatty acids are used for the treatment of serum triglycerides ≥500 mg/dL, the patient should be evaluated for gastrointestinal disturbances, skin changes, and bleeding [18].

The ACC/AHA guidelines committee also found no evidence that titration of statins or combination drug therapy to achieve specific LDL cholesterol levels or non-HDL cholesterol levels or percent decrease improved ASCVD outcomes. Therefore, the guidelines do not recommend their use [18].

The Kidney Disease: Improving Global Outcomes (KDIGO) 2013 guidelines recommend use of statins in patients aged 50 years and older with an estimated glomerular filtration rate less than 60 ml/min/1.73 m^2 but not treated with chronic dialysis or kidney transplantation [21]. In patients aged 18 to 49 years with CKD but not treated with chronic dialysis or kidney transplantation, these guidelines recommend treatment with statins in patients with one or more of the following: known coronary artery disease, diabetes mellitus, prior ischemic stroke, or an estimated 10-year incidence of coronary death or non-fatal myocardial infarction >10% [21]. These guidelines suggest not starting statins in patients receiving chronic dialysis but continuing statins in these patients if they are already being treated with statins [21]. These guidelines suggest treatment with statins in adult kidney transplant recipients [21]. In adults with CKD, follow-up measurements of serum lipids are not needed for the majority of patients [21].

On the basis of the available data, I favor the ACC/AHA 2013 guidelines for the management of patients with CKD not being treated with chronic dialysis or kidney transplantation [18]. However, I favor the KDIGO 2013 guidelines in patients who are being treated with chronic dialysis or kidney transplantation [21].

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