CE

Statins: An Update on Clinical Issues and Selected Adverse Effects

Alev H. Gulum, PharmD, and Anne L. Hume, PharmD, BCPS

ABSTRACT

Statins are among the most extensively studied and commonly prescribed drugs in the United States. In November 2013, new clinical practice guidelines on lipid management were released that emphasized the use of fixed dosages of statins in patients at moderate and high risk of atherosclerotic cardiovascular disease. These new recommendations have decreased the emphasis on the use of nonstatin drugs and routine laboratory monitoring of lipid levels and hepatic transaminases. Although some adverse effects are well-known, statin-induced diabetes, cognitive changes, and acute kidney injury are controversial.

Keywords: acute kidney injury, cognition, diabetes, hyperlipidemia, statins

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All authors are affiliated with the University of Rhode Island in Kingston, RI. Alev H. Gulum, PharmD, is a PGY-1 pharmacy-practice resident and can be reached at alevhg@gmail.com. *Anne L. Hume, PharmD, FCCP, BCPS, is a professor of pharmacy.* *In compliance with national ethical guidelines, the authors report no relationships with business or industry that would pose a conflict of interest.*

Statins are among the most commonly prescribed drugs in the United States, with an estimated 25% of American adults 45 years and older taking one. According to a 2010 report from the Centers for Disease Control and Prevention, statin use has increased 10-fold between 1994 to 1998 and 2005 to 2008 in the United States.[1]

First introduced in 1987, the safety and efficacy of statins have been evaluated in many large randomized controlled trials (RCTs) for the primary and secondary prevention of atherosclerotic cardiovascular disease (ASCVD). Observational studies have continued to explore other aspects of their safety, efficacy, and drug interactions over the intervening years. Emergent concerns with statins have included the development of diabetes, cognitive impairment, and acute kidney injury (AKI). This article presents an update on the clinical use and safety issues with statins.

This CE learning activity is designed to augment the knowledge, skills, and attitudes of nurse practitioners prescribing statins for patients.

At the conclusion of this activity, the participant will be able to:

A. List 2013 ACC/AHA changes for managing elevated LDL cholesterol

B. Describe recent evidence on statin-induced DM and muscle syndromes

C. Discuss controversies of potential cognitive and renal effects of statins

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BRIEF DRUG CLASS REVIEW

Seven statins are available in the US, and 5 are generic drugs. Although statins share a similar mechanism of action, they differ in their potency and ability to achieve either a 30%-50% or over 50% reduction in low-density lipoprotein (LDL) cholesterol values. Based on the guidelines, an individual's risk category should be the major initial consideration in selecting between the available statins.[2]

Several key practice points are that atorvastatin and rosuvastatin may be taken at any time given their long half-life. Lovastatin should be taken with supper to increase its bioavailability and achieve its maximal effects. The use of statins should never supersede the use of intensive nonpharmacologic interventions such as smoking cessation. Recent data from several National Health and Nutrition Examination surveys have raised concerning findings.[3] Between the 1999 to 2000 and the 2009 to 2010 surveys, statin users went from consuming fewer calories and dietary fat than nonusers to ingesting 9.6% more calories and 14.4% more dietary fat than nonusers in the most recent period.[3]

NEW GUIDELINES, MORE STATIN USAGE

In November 2013, new guidelines on lipid management were published by the American College of Cardiology and the American Heart Association.[2] Although not the Adult Treatment Panel IV recommendations that had been anticipated, they will likely guide the decision making on lipid management of many clinicians for the foreseeable future. A brief summary of major changes in the new guidelines is discussed.

Statin Dosing

Two statins, atorvastatin 40 to 80 mg daily and rosuvastatin 20 to 40 mg daily, are recommended for high-risk patients in order to achieve at least a 50% reduction in LDL cholesterol values.[2] The guidelines recommend the use of high-intensity statins as tolerated in individuals with clinical ASCVD under 75 years old, individuals with LDL cholesterol greater than 190 mg/dL, and individuals with type 1 or type 2 diabetes between 40 and 75 years old with a 10-year ASCVD risk of greater than 7.5%.

Atorvastatin 10 mg, rosuvastatin 10 mg, simvastatin 20 to 40 mg, pravastatin 40 mg, lovastatin 40 mg daily, and fluvastatin 40 mg twice daily are recommended to achieve at least a 30%-50% reduction from baseline LDL cholesterol values.[2] The use of these moderate-intensity statins is recommended in individuals with diabetes between 40 and 75 years old with an estimated 10-year ASCVD risk of less than 7.5% and in individuals over the age of 75 with clinical ASCVD or under 75 who are not candidates for high-intensity therapy. The use of a moderate- to high-intensity statin is recommended in individuals 40 to 75 years old with an estimated 10-year cardiovascular risk of greater than 7.5%. When the use of a high-intensity statin is warranted but not tolerated, guidelines recommend the use of a moderate-intensity statin.[2]

Nonstatin Drugs

The new guidelines have downplayed the role of nonstatin therapies because evidence of their benefit in preventing cardiovascular complications is lacking.[2] The practice of adding fenofibrate, niacin, and omega-3 fatty acids to statin therapy has not resulted in better long-term cardiovascular outcomes.[4–6] In the absence of a history of pancreatitis or severely elevated triglyceride concentrations (ie, $>$ 500 mg/dL), the use of these drugs should be reassessed in patients taking statins.[2]

Laboratory Monitoring

Laboratory monitoring before starting statin therapy includes a baseline fasting lipoprotein analysis, hepatic transaminases, and potentially creatine kinase (CK); other measures such as thyroid function tests and A1c should be ordered to assess for potential secondary diseases. Routine measurements of hepatic transaminases and CK are not indicated unless the patient has symptoms suggestive of adverse hepatic or muscle effects. In general, the purpose of lipid monitoring is to document the response to statin therapy and reinforce patient adherence.[2]

ASSESSING PATIENT RISK

The guidelines have identified 4 patient groups in whom the use of statins is clearly beneficial, outweighing the potential for adverse effects. These groups include patients with established clinical ASCVD such as acute coronary syndromes or stroke,