



## Management of Dyslipidemia in Patients with Type 2 Diabetes

According to the American Diabetes Association (ADA) *Standards of Medical Care in Diabetes-2010*, patients who have diabetes with clinical cardiovascular disease (CVD) or who are over 40 years of age and have risk factors of CVD, should be treated with a statin in addition to lifestyle changes regardless of baseline lipid levels to prevent CVD events or deaths due to coronary heart disease (CHD).

Patients with diabetes have a two to fourfold increased risk of coronary heart disease<sup>1</sup>, and once the patient develops CHD, their mortality rate is higher than the general population. Controlling the patient's glycemic profile has only modest effects on the reduction of CHD; therefore, controlling all cardiovascular risks is necessary.<sup>2</sup> The American Heart Association identifies the modifiable risk factors for CHD as follows: smoking, hypercholesterolemia, hypertension, physical inactivity, obesity and diabetes.

The DUR Program is responsible for conducting monthly medication reviews and informing providers about their patients' medication use. The most recent review examined patients identified as receiving treatment for diabetes, but not receiving a statin medication. Nebraska Medicaid providers received DUR letters for over 1,500 patients.

According to the ADA, adult patients with diabetes should have a fasting lipid profile monitored at least annually. Patients with low-risk lipid values (LDL <100mg/dl, HDL >50mg/dl and triglycerides below 150mg/dl) should be assessed every two years. Patients

with diabetes tend to have increased triglyceride levels and decreased HDL levels. LDL levels are similar to non-diabetic patients, but in patients with diabetes, the LDL particles are of a different quality, being smaller and denser. Patients with diabetes have an increased level of the small, dense LDL particles which are more atherogenic and easily oxidized.<sup>2</sup>

The first priority in treating diabetic dyslipidemia is lowering LDL levels.<sup>3</sup> The ADA Guidelines note the goal of treatment for all patients with diabetes is an LDL level of less than 100mg/dl, unless the patient has CVD. Patients with diabetes who have CVD should be treated to achieve an LDL goal of < 70mg/dl. Statins are considered first-line therapy for lowering LDL levels in patients with diabetes.<sup>2</sup> Over the past ten years, studies have demonstrated the positive effects of statin therapy on the outcomes for patients with diabetes in the prevention of CVD in patients with CHD as well as primary prevention of CVD<sup>3</sup>. Statin medications also have the added benefits of decreasing fibrinogen levels and viscosity, possessing antioxidant properties, and diminishing smooth-muscle proliferation.<sup>2</sup>

The Collaborative Atorvastatin Diabetes Study examined the use of a statin medication in the primary prevention of CVD in patients with type 2 diabetes. There were 2,838 patients enrolled in the study who had at least one of the following risk factors: hypertension, retinopathy, proteinuria or currently smoking. Results showed that negative cardiovascular outcomes were decreased by 37% for patients taking atorvastatin as compared to placebo. The incidence of acute coronary events was decreased by 36% and stroke

was reduced by 48%. The trial ended two years early, because of the clear benefit of the active treatment.<sup>4</sup>

The most common adverse effects of the statins include gastrointestinal symptoms, headache, and rash, but they are relatively mild and transient. The most important adverse effects of the statin class are myopathy and asymptomatic increases in liver transaminases.<sup>5</sup> Development of myopathy is caused by a combination of the drug, disease, genetics, and concomitant therapy. Myopathy seems to be dose-dependent and increases when statins are prescribed with drugs that are myotoxic or drugs that affect statin metabolism.<sup>6,7</sup> Patients who are elderly, female, debilitated, excessive alcohol users or heavy exercisers, having renal or liver disease, diabetes, hypothyroidism, had surgery or trauma, are at higher risk for myopathy due to statin use.<sup>8</sup> Hepatic enzymes should be evaluated at baseline 6 to 12 weeks after initiation of therapy and after any increase in dosage, as well as every four to six months during therapy. Treatment should be discontinued in patients if serum

transaminase levels exceed three times the upper limit of normal on more than two occasions.<sup>2</sup>

Statins should be avoided in patients who abuse alcohol, have active liver disease, or demonstrate persistent elevations of liver enzymes. Women who are pregnant, lactating, or of child bearing age should not take statin medications.

Medications in the statin class are very selective inhibitors of HMG-CoA reductase and do not interfere with other enzymes or receptors. All statin medications are metabolized by liver enzymes. The drug interactions with statin medications tend to be pharmacokinetic with increases or decreases in the level of the statin drug. Increased levels of statin medications increase the risk of myopathy. It is important to note that grapefruit juice can decrease blood levels of atorvastatin, lovastatin and simvastatin.<sup>5</sup> A few of the most common drugs which interact with the statin medications are listed in the table below.

Drug Interactions with Statin Medications <sup>5</sup>	
Drugs which may increase statin levels	Drugs which may decrease statin levels
clarithromycin, erythromycin	phenobarbital
cyclosporine	phenytoin
fibrates	rifampin
fluconazole, itraconazole, ketoconazole	

**References**

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