LETTER TO THE EDITOR
Statins and Diabetes Mellitus: What’s the Answer?

The number of people living with diabetes mellitus in the U.S. has crossed the 20 million mark, with 1.5 million cases having been diagnosed in 2005 alone.1 Because nearly 65% of this population will suffer from heart disease or stroke, it is crucial for health care professionals to continually investigate the efficacy of current diabetes treatment regimens.

The “glucocentric” focus of diabetic care may be leading to suboptimal treatment of our diabetic population. Current therapies emphasize and possibly rely on antidiabetic drugs to reduce the morbidity and mortality associated with the disease. However, macrovascular complications continue to be the leading cause of morbidity and direct costs, even in patients who use antidiabetic medications.2,3

New standards of care are being promoted and further studied in order to optimize our current approach to diabetes treatment. There is a movement toward the consistent inclusion of initial therapy with medications that are known to reduce cardiovascular risks, such as the HMG–CoA reductase inhibitors [statins]. At this point, it is still debatable whether or not all diabetic patients, with and without abnormal lipid profiles, can benefit from additional therapy with a statin. However, many trials have shown clinical benefits in both populations with the use of statins.

To understand the need for statin therapy in diabetic patients, it is first important to understand how lipid abnormalities differ in diabetic and nondiabetic patients and why statins are the lipid-lowering therapy of choice.

The diagnosis of diabetes places patients in a higher risk category for coronary heart disease. Diabetes is a “risk equivalent” for a coronary event such as a myocardial infarction (MI) or stroke. Diabetic patients appear to have poor endothelial function and increased platelet aggregation, which lead to macrovascular complications despite normal lipid concentrations.4 When lipid abnormalities are present, diabetic patients have been shown to have higher triglyceride levels and lower HDL levels than the nondiabetic population.

The Framingham Offspring Study demonstrated this difference in its study. Lower HDL was present in 43.9% of the diabetic patients versus 20.5% of the nondiabetic patients; the percentages were similar for elevations in triglycerides.

LDL clearance also differs in diabetic patients. Insulin is needed for regulation of LDL receptors and its clearance from the blood; as a result, insulin resistance leads to elevated LDL levels.

HDL also seems to be more quickly hydrolyzed in patients with insulin resistance, leading to lower HDL levels.5 Statins can reduce LDL levels by 18% to 55% and triglycerides by 7% to 30%; they can also increase HDL levels by 5% to 15%.4

Although few studies have been directed solely toward statin use in the diabetic population, many studies have included a sufficient number of diabetic patients to extrapolate relevant information. One of the largest diabetic populations was involved in the Heart Protection Study (HPS). Baseline requirements included a total cholesterol level of at least 135 mg/dl, which implies possible inclusion of diabetic patients with and without dyslipidemia prior to intervention.

The study found that diabetic patients taking simvastatin 40 mg daily (Zocor, Merck) had a highly significant reduction in the incidence of a first nonfatal MI or coronary death (95% CI 15–38; P < .0001) compared with placebo. The incidence of stroke was similarly reduced (95% CI 6–39; P = .01). Both percentages of reductions were similar to those of high-risk patients who were enrolled in the study who did not have diabetes. The study concluded that in initiating statin therapy as the standard of care for diabetic patients, physicians should evaluate a patient’s overall risk of having a major coronary event.2,4

The Collaborative Atorvastatin Diabetes Study (CARDS) included only patients with type-2 diabetes mellitus; these patients were required to have a diagnosis of type-2 diabetes, at least one other risk factor for coronary heart disease, and normal LDL concentrations. The study found a reduction in MI by 36%, stroke by 48%, and the need for revascularization by 31%. The trial was terminated two years earlier than expected because of significant positive outcomes in the treatment group.2,4

Now that these two large trials, along with several other trials, have shown data to support the use of statins in diabetic patients with and without dyslipidemia, the question is: Are we adequately managing our diabetic patients?

A study in 2004 claimed that patients are not being optimally treated.7 The HPS and CARDS announced their findings in 2003, but not much has changed in the past three years. We have reached a point where it is important for us to re-examine our standard of care for diabetic patients. Currently, the recommendations state that a goal of below 100 mg/dl for LDL is beneficial in preventing coronary events and that a goal of less than 70 mg/dl should be considered in diabetic patients with additional risk factors. Controversy still remains as to whether the LDL goal for all diabetic patients should be below 70 mg/dl.

The American Diabetes Association currently recommends the use of statins in all diabetic patients over 40 years of age with a total cholesterol level of more than 135 mg/dl, regardless of baseline LDL levels or the presence of coronary heart disease.1

There is evidence supporting the routine use of simvastatin or atorvastatin (Lipitor, Pfizer) in these patients. However, high-dose simvastatin raises some concerns about adverse events. Physicians must exercise caution and weigh the risks and benefits when considering statins, especially high doses of simvastatin, as the standard of care in diabetic patients.

An article by Dr. Steve Nissen highlights the safety concerns that were addressed in the famous A to Z [Aggrastat to Zocor] trial.8 Published in 2004, this trial compared the safety and efficacy of high-dose simvastatin versus low-dose therapy. The study concluded that there was no difference

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in the primary endpoint of cardiovascular death, MI, stroke, or acute coronary syndrome; however, it noted an alarming increased risk of myopathy at doses of simvastatin 80 mg.8

Statins are known to reduce the cardiovascular risks in patients with dyslipidemia; now they are predicted to have just as much benefit in patients with type-2 diabetes mellitus. The risks and the benefits of statins should always be evaluated on a case-by-case basis. However, good data suggest that statins should be routinely used in our diabetic population to decrease morbidity and mortality because of their ability to reduce LDL levels by 30% to 40% regardless of baseline values. The next big step 

REFERENCES


Sincerely,

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