Guidelines Steer Focus From Glucose to Lifestyle

Endocrinologists say individualized treatment should be emphasized, rather than the 'cookbook approach.'

BY ELIZABETH MECHCATIE
Senior Writer

Diabetes management is becoming less "glucocentric" than it used to be, according to Dr. Helena W. Rodbard.

Dr. Rodbard is the chairperson of the task force that wrote the new clinical practice guidelines on the management of diabetes issued by the American Association of Clinical Endocrinologists. Instead of talking only about how to keep blood glucose at the ideal level, the new guidelines provide more emphasis on lifestyle—in terms of prevention of diabetes—as well as the importance of managing blood pressure and lipids, she said in an interview.

In addition, previous guidelines did not include much information on diabetes complications, particularly microvascular complications, and diabetes management in the hospital setting, both topics of separate sections of the new guidelines. There are also sections on nutrition, screening and diagnosis, glycemic management in type 1 and type 2 diabetes, diabetes and pregnancy, and patient safety in diabetes care.

The guidelines were published in a supplement to Endocrine Practice that was mailed to AACE members and journal subscribers in July (Endocr. Pract. 2007;13[Suppl 1]), and are a result of almost 3 years of work by the task force, which was made up of endocrinologists specializing in diabetes, Dr. Rodbard said.

The final recommendations in the guidelines represent a consensus among the task force members, and were also approved by the AACE board of directors.

These guidelines are distinct from the "Road Maps for the Prevention and Treatment of Type 2 Diabetes" recently released by AACE. The road maps are not guidelines, but instead provide specific treatment algorithms and focus more on glycemic control.

The guidelines include a section on the medical management of diabetes, which contains reviews of the different drugs available, their indications for use, their advantages and disadvantages, and their expected impact on reducing in HbA_{1c} levels.

They do not specifically recommend any one drug or class of drugs as a first-line treatment, but instead, they focus on the importance of individualizing treatment, Dr. Rodbard explained.

"We don't have a cookbook approach because every patient is different, and we list the different medications, the indications for each drug, and which subset of patients can benefit from one versus the other medication," she said.

That approach contrasts with the American Diabetes Association, which last year endorsed a consensus algorithm that recommended metformin along with lifestyle interventions for newly diagnosed type 2 diabetes.

"That may be appropriate for many, perhaps most patients with type 2 diabetes, but definitely not for everybody," Dr. Rodbard noted. "It is up to the judgement of the physician to make a decision about whether metformin would or would not be the right drug for an individual patient."

The task force was able to add a statement close to the publication date regarding a recent meta-analysis reporting an increased risk of myocardial infarction associated with rosiglitazone therapy (N. Engl. J. Med. 2007 [Epub doi:10.1056/NEJMoa072761]). Despite the controversy over the meta-analysis and the unresolved issues, "we felt we had to say something about it, although we tried to keep a very balanced opinion in that regard and are not recommending that patients stop the medication," Dr. Rodbard said.

The statement, which appears in the glycemic management section, says that "definitive resolution regarding the magnitude and statistical and clinical significance of these findings" will require further analyses, including the results of an ongoing phase III study expected to be completed in 2009.

The guidelines also list peripheral fractures in women among the adverse effects of thiazolidinediones (TZDs), a reference to findings showing an increased rate of peripheral fractures in women taking either rosiglitazone or pioglitazone ("Second TZD Connected to Excess Fractures in Women," April 2007, p. 1).

In the section on glycemic management, AACE recommends a glycemic target that includes an HbA_{1c} equal to or below 6.5%, a fasting plasma glucose concentration below 110 mg/dL, and a 2-hour postprandial glucose concentration below 140 mg/dL, values that AACE has advocated in the past. The glycemic goals in the guidelines are consistent with previous AACE consensus conferences and a position statement regarding these targets, said Dr. Paul S. Jellinger, a task force member and a past president of both AACE and the American College of Endocrinology, who is in private practice in Hollywood, Fla.

The guidelines are a "very nice blend of evidence-based and evidence-ranked statements, which also reflect the extensive clinical experience of the task force members," he added. Written with the clinician in mind, "we expect this will be a source of clinically useful information" for any clinician involved in the care of people with diabetes, he said.

AACE last issued diabetes guidelines in 2002. There are plans to release an update of the guidelines next year as new data become available, said Dr. Rodbard. A section on type 2 diabetes in the pediatric population may be included in the updated guidelines, because teenagers are the fastest-growing segment of type 2 diabetes patients. ■

The guidelines are available online at www.aace.com/pub/pdf/guidelines/DMGuidelines2007.pdf.

Lipid Lowering Cuts CV Events in Diabetics With Renal Disease

BY MIRIAM E. TUCKER
Senior Writer

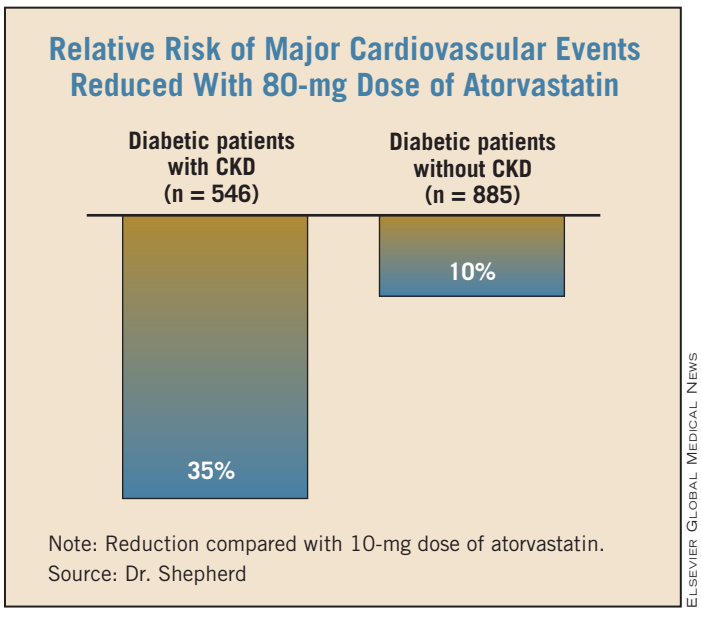
CHICAGO — Intensive lipid lowering with high-dose atorvastatin significantly reduces the incidence of major cardiovascular events in coronary patients who have both type 2 diabetes and chronic kidney disease, Dr. James Shepherd reported at the annual scientific sessions of the American Diabetes Association.

In a new subanalysis of diabetic patients in the Pfizer-funded Treating to New Targets (TNT) study, "Individuals got greater benefit in relative terms and far greater benefit in absolute terms if they had the combination of diabetes and renal disease, because they had much greater risk to begin with," said Dr. Shepherd, professor and head of pathological biochemistry at the Royal Infirmary and the University of Glasgow (Scotland).

The main finding of the TNT study of 10,001 patients with stable coronary heart disease was a 22% reduction in the risk of major cardiovascular events with using 80 mg of atorvastatin per day relative to 10 mg/day at a median follow-up of 5 years (N. Engl. J. Med. 2005;352:1425-35). A subsequent sub-analysis of the 1,501 diabetics in that study showed a 25% event reduction with 80 mg versus 10 mg (Diabetes Care 2006;29:1220-6). However, another study of 1,255 patients who had type 2 diabetes and end-stage renal disease (ESRD) and were undergoing hemodialysis showed no cardiovascular benefit of 20 mg of atorvastatin per day, compared with placebo (N. Engl. J. Med. 2005;353:238-48).

To further investigate the potential role of atorvastatin treatment in patients with both diabetes and kidney disease, Dr. Shepherd and his associates analyzed the TNT outcomes of 1,431 of the diabetic patients in the study for whom renal data were available. There were 546 patients with chronic kidney disease (CKD) — defined as having an estimated glomerular filtration rate (eGFR) of less than 60 mL/min per 1.73 m^2 — and 885 with normal kidney function (eGFR of at least 60 mL/min per 1.73 m^2).

At baseline, those with CKD had greater cardiovascular morbidity than those without, including higher systolic blood pressure (136.1 vs. 133.6 mm Hg); a greater proportion had a history of hypertension (76% vs. 67%), as well as higher rates of peripheral vascular disease, coronary bypass grafting, and congestive heart failure. There were also more women in the CKD group (42% vs. 18%).



ELSEVIER GLOBAL MEDICAL NEWS

The 80-mg dose of atorvastatin lowered LDL equally in both groups, from about 98 mg/dL at baseline to 75 mg/dL at follow-up, Dr. Shepherd reported.

Major cardiovascular events (coronary heart disease death, nonfatal myocardial infarction, resuscitation after cardiac arrest, fatal or nonfatal stroke) occurred in 13.4% of the diabetics with normal GFR and 17.4% for those with both diabetes and CKD. (The rates were 7.8% among those without diabetes or CKD and 10% for the nondiabetics with CKD.) Compared with 10 mg of atorvastatin, the 80-mg dose reduced the relative risk of major cardiovascular events by 35% in the diabetic patients with CKD, compared with just 10% among the diabetics without CKD. "Those patients with the greatest risk got the greatest benefit from intensive intervention with atorvastatin," Dr. Shepherd commented.

The drug was well tolerated overall, with no evidence of myopathy and less than 1% with elevated liver enzymes. "The high dose of atorvastatin created no penalty with regard to side effects," he noted.

Although not an end point in the study, improvements in GFR were seen with both atorvastatin doses over the 5 years of the study, but were greater with 80 mg, he said.

When asked by an audience member why atorvastatin did not benefit the patients with ESRD in the earlier study, Dr. Shepherd responded, "I think it's a function of the degree of kidney compromise. If you have patients with ESRD on dialysis, you're asking far too much of a drug to reverse that. But you can see a reversal if you have compromise but still-viable glomerular filtration rates." ■