Algorithm Can Guide Prescribing for Diabetes

BY MIRIAM E. TUCKER

A new one-page treatment algorithm for type 2 diabetes from the American Association of Clinical Endocrinologists is aimed at assisting physicians in choosing appropriate therapy from among all the approved classes of glucose-lowering medications.

The algorithm stratifies treatment based on hemoglobin A_{1c} values, with separate treatment pathways for patients with levels of 6.5%-7.5%, 7.6%-9.0%, and greater than 9.0% (Endocrine Practice 2009;15:541-59).

In general, patients with HbA_{1c} values of 7.5% or lower can start with monotherapy, with metformin considered the "cornerstone" but with three other drug classes included as alternatives. Patients with values of 7.6%-9.0% typically require dual therapy. The algorithm advises insulin for patients with values higher than 9% who already are receiving other treatments or who are drug-naive and symptomatic. For patients with levels higher than 9% who are drug-naive but asymptomatic, dual or triple combination therapies can be used.

"This is an authoritative, up-to-date, practical, and simple algorithm which should provide meaningful guidance to physicians as they make their therapeutic decisions," said Dr. Helena W. Rodbard, cochair of the consensus panel that developed the algorithm, which is officially a publication of both AACE and its educational branch, the American College of Endocrinology (ACE).

"It's an easily readable clinical point-of-care tool designed to assist endocrinologists, primary care physicians, and others involved in the care of patients with type 2 diabetes," said Dr. Paul S. Jellinger, panel cochair who, like Dr. Rodbard, is a former president of both AACE and ACE.

Both Dr. Jellinger and Dr. Rodbard emphasized that the algorithm—written by a panel of 14 practicing endocrinologists—accurately represents the way a majority of experienced endocrinologists approach the treatment of type 2 diabetes.

In contrast to a recently revised algorithm from the American Diabetes Association and the European Association

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for the Study of Diabetes (Diabetes Care 2009;32:193-203), the AACE/ACE algorithm fully incorporates all classes of drugs approved to treat type 2 diabetes and places less emphasis on the drug costs.

"Most previous algorithms placed an undue emphasis on the cost of medications. Drugs can be expensive, but the cost of medications is only about 11% of the total cost of care of the population with diabetes. We need to consider the total cost of care, which is overwhelmingly driven by the cost of complications," said Dr. Rodbard, an endocrinologist in Rockville, Md.

Dr. Jellinger, who practices endocrinology in Hollywood, Fla., added: "We placed a big emphasis on safety, particularly in terms of hypoglycemia. We included GLP-1 mimetics, DPP4 inhibitors and TZDs, along with metformin, since those classes have no potential for hypoglycemia. At the same time, we have downgraded the use of sulfonylureas due to their increased risk for hypoglycemia. By avoiding hypoglycemia, you avoid hospitalizations, which are far more expensive than the medicine."

But Dr. David M. Nathan, chair of the ADA/EASD consensus panel, said he doesn't believe it makes sense to include the additional agents as alternatives to metformin for first-line therapy or to list so many drug classes at every level. "The ADA/EASD guidelines were specifically formulated to help busy nonspecialists make informed choices from the large number of treatments that have become available in the last decade. With that in mind, the ADA/EASD consensus committee tried to narrow the choices based on effectiveness, safety, tolerability, acceptability, and cost."

In contrast, "AACE has taken a different tack and included all approved medications. Their more complex algorithm offers more choices but, in our opinion, doesn't help the busy clinician make the best choices," said Dr. Nathan, professor of medicine at Harvard University and director of the diabetes center at Massachusetts General Hospital, Boston.

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"The TZD, DPP-4, and AGI they recommend are manyfold more expensive than metformin, have far less clinical experience than with metformin, are no safer—and probably less safe for TZD—and have the same frequency or far more side effects," he added.

Accompanying the AACE algorithm is a text document that explains the rationale for each treatment option and other issues, which include the following:

- Lifestyle (diet and exercise) modifications are essential for all patients with diabetes, but delaying pharmacotherapy to allow for lifestyle modifications to take effect is likely to be inadequate. Counseling regarding lifestyle changes should be initiated along with diabetes self-management education and medications.
- Achieving an HbA_{1c} of 6.5% is the primary goal, but this goal must be individualized based on factors such as comorbid conditions, hypoglycemia history, and life expectancy.
- Effectiveness of therapy must be evaluated frequently, typically every 2-3 months.
- Safety and efficacy should be given greater priority than cost of medications because the cost of drugs is only a small part of the total cost of diabetes care.
- Rapid-acting insulin analogs are a better alternative to "regular human insulin." Similarly, long-acting synthetic analogs glargine and insulin detemir yield better reproducibility and consistency as basal insulins than does NPH, which is not recommended.

Also included is a one-page summary of the major risks and benefits of each of the classes of drugs, described further in an appendix.

Dr. Rodbard has received consultant honoraria, speakers honoraria, and research grant support from several pharmaceutical companies. Dr. Jellinger has received consultant and speaker honoraria from several pharmaceutical companies. Dr. Nathan has received a research grant and support for educational programs from two pharmaceutical companies. ■

The diabetes care algorithm can be accessed at www.aace.com/pub/pdf/GlycemicControlAlgorithmPPT.pdf.

Metformin, Sulfonylureas, and Insulin May Be Sufficient

BY MIRIAM E. TUCKER

VIENNA — Glycemic control was maintained over 5 years using metformin, sulfonylureas, and insulin almost exclusively in a longitudinal study of cholesterol lowering in 4,900 patients with type 2 diabetes.

The findings call into question the need for new diabetes drugs, especially now that increased emphasis is being placed on the safety of these agents, Dr. James Best said at the annual meeting of the European Association for the Study of Diabetes.

The finding comes from the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study, which investigated whether fenofibrate could reduce the risk of cardiovascular disease in patients with type 2 diabetes in Finland, Australia, and New Zealand (Lancet 2005;366:1849-61). FIELD failed in its primary end point, but because its design did not involve modifying any aspect of glycemic management, it offered a real-world opportunity to see what happened over time with standard care for diabetes, mainly in primary care settings.

The results suggest that diabetes control can be effectively maintained using the three oldest and least expensive classes of diabetes drugs, and challenges the prevailing belief that new types of glucose-lowering drugs are needed. "There's this background subtext that diabetes control inexorably deteriorates despite optimal therapy and therefore we need to find new drugs to treat this disease. My message is that we don't," Dr. Best, professor of medicine and head of the school of medicine at the University of Melbourne, said in an interview.

At baseline, the study population had a mean age of 62 years and diabetes duration of 5 years. Just over a third were women. They were reasonably well controlled at baseline, with a median hemoglobin A_{1c} of 6.9%, even though 26% were on no diabetes medications, 60% were on oral agents only, and just 14% were using insulin. Median body weight was 86.3 kg.

Over the subsequent 5 years, the median HbA_{1c} rose slightly (0.22 percentage points), to just over 7.0%, while body weight fell slightly, to 85.0 kg. Oral hypoglycemic medication—nearly all metformin, sulfonylureas, or both—was initiated in 56% of the 1,287 who had been taking no medications at baseline, and insulin was started in 25% of the 2,917 who had not been taking it at baseline. Thus, at 5 years, 77% of patients were on oral agents and 28% were on insulin, but only 4% were on oral agents other than sulfonylureas or metformin, Dr. Best reported.

The 0.22 percentage-point increase in HbA_{1c} seen in FIELD is in contrast to the 1.0 percentage-point rise that occurred in the landmark U.K. Prospective Diabetes Study (UKPDS), which is often cited as evidence for the inevitable decline in glucose control in patients with type 2 diabetes (Lancet 1998;352:837-53).

The findings support the new emphasis on cardiovascular safety that regulatory bodies are now imposing on all glucose-lowering drugs, following reports of adverse cardiovascular outcomes with the thiazolidinedione (TZD) rosiglitazone, Dr. Best said.

"I see much less urgency for new therapies. We need safety outcomes for new treatments, rather than just efficacy. The TZDs are a good example. They got to market before there was really safety data, on the grounds that glycemic control deteriorates with standard treatment and therefore we needed them. Now that we've seen the safety outcomes, their use should be much more limited than was thought initially."

Dr. Best stated that he did not have any relevant financial disclosures. ■