Guidelines Ease Up on Glycemic Control for Some Patients With Type 2 Diabetes

Mike Mitka

PHYSICIANS ARE BEING TOLD TO loosen up on glycemic control when treating certain patients with type 2 diabetes.

Aggressive glucose management has been a mainstay of diabetes treatment, intended to reduce microvascular risks such as diabetic nephropathy, neuropathy, and retinopathy. Physicians treating patients with diabetes have traditionally set a goal of achieving and keeping glycated hemoglobin (HbA_{1c}) levels below 7.0%. But recent trials have suggested that achieving such a level may put certain patients with diabetes at risk for cardiovascular complications and mortality.

Acknowledging these recent studies, the American Diabetes Association and the European Association for the Study of Diabetes released a consensus report April 19 calling for a more patient-centered treatment approach that takes into account patient needs, preferences, and tolerances (Inzucchi SE et al. *Diabetes Care*. doi:10.2337/dc12-0413 [published online April 19, 2012]).

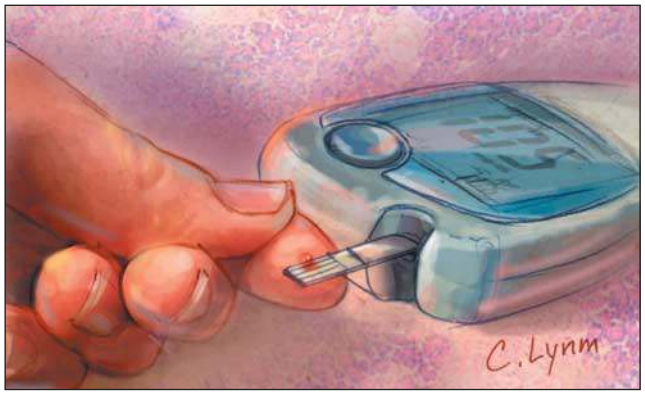
The report notes that lowering HbA_{1c} to less than 7.0% is still recommended for most patients with diabetes. However, less stringent goals of between 7.0% to slightly higher than 8.0% are appropriate for patients with a history of severe hypoglycemia; limited life expectancy; advanced complications; extensive comorbid conditions; or difficulty attaining that 7.0% target despite intensive self-management education, repeated counseling, and effective doses of multiple glucose-lowering agents, including insulin. The report authors added that a goal of 6.5% might be considered in selected patients with short disease duration, long life expectancy, and no significant cardiovascular disease if it can be achieved without significant hypoglycemia or other adverse effects of treatment.

These multiple targets emerged in part because of a 2010 study that found a U-shaped risk curve: those with the lowest rate of all-cause mortality had an HbA_{1c} of 7.5%, while those with higher and lower HbA_{1c} levels saw an increased risk for all-cause mortality and cardiac events (Currie CJ et al. *Lancet*. 2010;375[9713]:481-489). The other study that raised questions about aggressive glucose management for all was the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial of 2008. That trial found that patients randomized to intensive therapy targeting a 6.0% or lower HbA_{1c} level were 22% more likely to experience a nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes when compared with patients randomized to standard therapy with a target HbA_{1c} level of 7.0% to 7.9% (*N Engl J Med*. 2008;358[24]:2545-2559).

"In terms of choosing a target, the studies have been murky; no study says it should be 7% for everybody," said Vivian Fonseca, MD, president of the American Diabetes Association. "The goal of 7% came from a study of patients with type 1 diabetes, and achieving an HbA_{1c} of 7% seemed to balance the benefits and risks of glycemic control."

Beyond suggesting alternative HbA_{1c} levels for various types of patients with diabetes, the consensus report also notes that lifestyle interventions, weight management, diet, and exercise remain key factors for minimizing diabetes complications.

Another important element of the report addresses the growing array of pharmacological agents available for diabetes treatment and their possible adverse effects. Metformin remains the optimal first-line drug for glucose management. If metformin does not enable a patient to achieve or maintain a personalized target HbA_{1c} level, adding another 1 or 2 oral or injectable agents is considered reasonable. But the report authors cannot say with certainty which additional medications are best because of a "distinct paucity of



Age and risk for cardiovascular complications should be considered when setting target levels for glycemic control in patients with type 2 diabetes.

long-term comparative effectiveness trials available."

The report authors emphasized their document is less prescriptive and less algorithmic than earlier guidelines and should serve as one of the tools available to physicians and patients as they discuss treatment options. Fonseca, who is also a professor of medicine at Tulane University's School of Medicine in New Orleans, said moving away from rigid guidelines is probably best for individual patients. "One of the problems with evidence-based medicine, which I support in general, is it can make physicians develop a one-size-fits-all approach to treating patients," he said.

Fonseca added that the less rigid guidelines also allow flexibility to change treatment courses over a patient's lifetime. "You have to recognize that people are different and their perspectives of things change; a continuing dialogue between patients and physician is very important," he said. "So determine goals and tailor therapy, but adjust over time." □

FDA Aims to Curb Farm Use of Antibiotics

Bridget M. Kuehn

NEW GUIDELINES FROM THE US Food and Drug Administration (FDA) aim to curb the large-scale nontherapeutic use of antibiotics by livestock producers, in an effort to reduce the emergence of antibiotic resistance.

A growing body of evidence suggests that large-scale use of antibiotics in livestock production contributes to the emergence in animals of resistant strains of bacteria, which may be transmitted to humans. This has led to increasing calls for the more judicious veterinary use of antibiotics. One practice in particular has been targeted—the long-term use of low-dose antibiotics to promote the growth of healthy food animals.

The new FDA guidelines establish a 3-year time frame for producers to eliminate the use of antibiotics in livestock feed for growth promotion and for drug makers to change the labels of their products to remove such indications. The plan also phases in required veterinary oversight of antibiotic use.

"A public health imperative drives our actions today," said Michael Taylor, JD, the deputy commissioner for foods at the FDA.

Animal growth promotion has been an FDA-approved use of certain antibiotics for decades, and these antibiotics have been available over the counter to animal producers without any veterinary oversight. The new guidelines aim to narrow the use of antibiotics in food production by allowing only therapeutic or preventive use of such medications under the supervision of a veterinarian.

The announcement of the guidelines was greeted with cautious optimism by some groups that have called for changes to such farming practices.

"FDA has taken an important step to help protect the public's health from antibiotic-resistant bacteria linked to the overuse of antibiotics in animal agriculture," said Laura Rogers, director of the Pew Campaign on Human Health and Industrial Farming. "This is the most sweeping action the agency has undertaken in this area, as this covers all antibiotics used in meat and poultry production that are important to human health."

Previously, the agency had targeted agricultural use of specific antibiotics important to human health, such as fluoroquinolones and cephalosporins (Voelker R. *JAMA*. 2011;307[5]:443).

But Rogers noted some gaps in the FDA's approach, such as the fact that the guidelines are voluntary and the need for the FDA to better define acceptable and unacceptable preventive use. Without such definition, she said, some problematic uses may continue under the guise of "preventive use."

"If preventive use in massive numbers is allowed to continue, I don't know if they can say it's a success story," she said.

In one example provided by the FDA, a veterinarian choosing to administer preventive antibiotics to a group of cattle that have endured a lengthy transport in poor weather would be appropriate to prevent the spread of bacterial infection. Rogers said that could be an appropriate use until the production practices that lead to such disease-promoting stressors can be changed. However, preventively dosing entire flocks of birds because their housing

Matt Rourke/APImages

New guidelines may encourage livestock producers to forgo nontherapeutic use of antibiotics, as this turkey farmer has.