HbA_{1c} Expressed as 'Estimated Average Glucose'

BY MIRIAM E. TUCKER
Senior Writer

SAN FRANCISCO — Hemoglobin A_{1c} levels can now be accurately expressed as estimated average glucose for most patients with type 1 and type 2 diabetes.

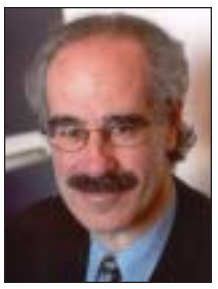
In a multinational study presented at the annual scientific sessions of the American Diabetes Association, data from both continuous glucose monitoring and fingerstick monitoring over 3 months in 507 individuals with and without diabetes were compared with hemoglobin A_{1c} values to derive a formula that relates average glucose levels to HbA_{1c}.

The finding means that laboratories will now report both numbers (as well as the actual value in mmol/mol), and physicians can begin discussing glucose control with their patients in the same units that patients are familiar with from their home blood-glucose monitoring. "Right now, patients hear that their glucose control is some percentage, and are asked to adjust their therapy to achieve results in another unit. We thought it made sense to have both the day-to-day monitoring and the [HbA_{1c}] in the same units," lead author Dr. David M. Nathan said at a press briefing during the meeting.

The shift to what is now being called the "estimated average glucose," or "eAG," began in 2002, when the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) published a new reference method that measures the concentration of only one molecular species of glycated hemoglobins (the A_{1c}), as opposed to the mixture that had previously been measured. Recognizing that the IFCC's adoption of the new reference method would cause confusion in the clinical setting, an international working group decided in 2004 to launch the study for which final results are now being reported. The study will also appear in the August issue of Diabetes Care (2008; 31:1-6).

Although previous data had provided a rough estimate of average glucose from HbA_{1c}—and indeed, many labs have long reported those numbers—they were generated from old studies using infrequent fingerstick monitoring. In contrast, the participants in this study, who were recruited from 11 centers in the United States, Europe, Africa, and Asia, generated approximately 2,400 glucose measurements each by wearing the continuous glucose meter for at least 2 days at baseline and then every 4 weeks during the next 12 weeks, and another 300 values by performing eight fingerstick glucose measurements per day for at least 3 days per week. Hemoglobin A_{1c} values were measured at baseline and monthly for 3 months, Dr. Edward S. Horton, professor of medicine at Harvard Medical School, Boston, explained during the briefing.

Of the 507 analyzed study participants, 268 had type 1 diabetes, 159 had type 2, and 80 were not diabetic. Of the initial 661 patients recruited into the study, 18% had baseline hemoglobin A_{1c} values greater than 8.5%; 44% had values of 6.6%-8.5%; and 38% had values of 4.0%-6.5%. These levels generally remained stable with 96% of the subjects maintaining values within 1 percentage point of their baseline value.



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DR. NATHAN

At the end of 3 months, the relationship between the HbA_{1c} level and the calculated average glucose (AG) during the preceding 3 months could be expressed in the following formula: AG (in mg/dL) = 28.7 X HbA_{1c} – 46.7. That translates to an eAG of 97 mg/dL for an HbA_{1c} of 5%; 126 mg/dL for 6%; 154 mg/dL for 7%; 183 mg/dL for 8%; 212 mg/dL for 9%; 240 mg/dL for 10%; 269 mg/dL for 11%; and 298 mg/dL for 12%, Dr. Horton said.

For the overall study results to be considered acceptable, it had been decided a priori that at least 90% of the individual patients' calculated AG would have to fall within 15% of the studywide calculated AG. The actual percentage was 89.95%, and was considered to have met the requirement.

There was no effect of gender, age, ethnicity, diabetes type, or cigarette smoking on the results. However, the number of ethnic minority patients was small, which is a limitation of the study. Other limitations include the lack of data on children, pregnant women, or people with impaired renal function, Dr. Horton noted.

In the fall of 2007, a joint consensus statement from the American Diabetes Association (ADA), the European Association for the Study of Diabetes, the IFCC, and the International Diabetes Federation had called for labs to begin reporting HbA_{1c} in the familiar percentage, in the new eAG, and in the actual values in mmol/mol, pending the results of this study (Diabetes Care 2007;30:2399-400).

At the briefing, study coauthor Dr. Robert Heine, now with Eli Lilly & Co., noted that although lab reports will now contain three different numbers expressing the same value instead of two, the "whole idea behind the study is to simplify education in clinical practice. Now three numbers will be reported, but we really hope that just one number will be applied in clinical practice, and that's the eAG. … The advantage of having this eAG is that we can now educate our patients in a way that they can understand the relationship between long-term glycemic control and what they're doing at home, making it much easier for them to appreciate what blood glucose control means."

To anyone who might object to this move, Dr. Nathan reminded the audience that the decision to move to a new standard for HbA_{1c} measurement and its reporting had come from the IFCC and was not going to change. "We were faced with a change in the units and the reporting that was out of our control. [The IFCC's] new standard is a fine thing, but they were going to report it in a way we thought would be confusing." Indeed, he noted, a study in Sweden had shown that when laboratories there made a change in units, diabetes control among patients suffered (Diabetes Care 2002;25:2110-1).

The timetable for the new reporting standard is not clear. Manufacturers will need to upgrade laboratory machines with new software, which may not necessarily happen all at once, and some upgrades could take a year or two. New point-of-care machines will come with the new standard, but the machines that some physicians already have in their offices will be "more of a challenge" to upgrade, said Dr. Nathan, professor of medicine at Harvard Medical School. In the meantime, the ADA has an online calculator (www.diabetes.org/ag) that can be used to make the conversion, an ADA official commented.

When asked whether the HbA_{1c} percentage value eventually will be eliminated from the physician-patient conversation in favor of the eAG alone, Dr. Nathan replied, "I think that many of us think [eAG] may ultimately replace [HbA_{1c}]. Why present two numbers when you can present just one?" ■

Increased Diabetes Risk Seen With Androgen Deprivation

BY DAMIAN McNAMARA
Miami Bureau

ORLANDO — With increasing use of androgen deprivation hormone therapy for men with prostate cancer come growing concerns about an increased risk of diabetes, cardiovascular morbidity, and other adverse treatment effects.

Consider these risks when prescribing gonadotropin-releasing hormone agonist therapy for men with prostate cancer, and screen for comorbidities, Dr. Matthew Smith advised. Educate patients about adverse treatment effects and counsel them on lifestyle modifications that could ultimately decrease these risks, he added.

A gradual improvement in prostate cancer–specific mortality since the early 1990s has been accompanied by the rising use of GnRH agonists in the United States, so physicians might start seeing more patients with adverse effects from these agents. About 3% of the entire male Medicare population and one-third of approximately 2 million prostate cancer survivors now take GnRH agonists, Dr. Smith said at the annual meeting of the American Urological Association.

Loss of libido, vasomotor flushing, fatigue, anemia, and increased risk of osteoporosis are among the adverse events associated with androgen deprivation, said Dr. Smith, director of genitourinary medical oncology at Massachusetts General Hospital in Boston.

"GnRH agonists also make a common problem—obesity—worse," Dr. Smith said. These agents decrease muscle mass and increase fat mass, according to a previous study by Dr. Smith and his associates (J. Clin. Endocrinol. Metab. 2002;87:599-603).

Changes can become apparent as soon as 12 weeks after initiating therapy, Dr. Smith said. Also, 2- to 3-kg muscle loss and 3-kg fat accumulation can occur in 1 year, he and his associates reported (Cancer 2008;112:2188-94). These agents selectively increase subcutaneous fat mass, with approximately 94% of the fat accumulation occurring in the abdomen. Because accumulation of abdominal fat is often associated with adverse health outcomes, "it's not just a cosmetic issue."

Lipid changes are more prevalent among men treated with GnRH agonists, compared with those not treated with these agents, according to a cross-sectional study by other researchers (Int. J. Impot. Res. 2006;18:494-8).

Dr. Smith said lipid changes can occur rapidly, in as little as 3 months after initiation of GnRH agonist therapy. However, overall cardiovascular risk is less clear because patients can experience increases in total cholesterol, LDL cholesterol, and triglyceride levels as well as increases in HDL cholesterol. "Overall cardiovascular risk effect warrants further study."

Also consider monitoring patients for changes in insulin sensitivity during GnRH agonist therapy, Dr. Smith said. In one study, there was a "fairly dramatic rise in compensatory insulin levels in nondiabetic men—changes consistent with nondiabetic insulin resistance" (J. Clin. Endocrinol. Metab. 2006;91:1305-8).

A 44% excess risk for diabetes and 16% excess risk for coronary heart disease were among the findings of another study by Dr. Smith and colleagues (J. Clin. Oncol. 2006;24:4448-56). More than one-third of 73,196 Medicare enrollees aged 66 years and older received androgen deprivation therapy in this Surveillance Epidemiology and End Results (SEER) database study. After controlling for baseline covariates, GnRH agonist exposure was associated with a greater risk for diagnosis of incident diabetes (hazard ratio, 1.44), coronary heart disease (HR, 1.16), myocardial infarction (HR, 1.11), and sudden death (HR, 1.16), Dr. Smith said.

Even slightly elevated risks associated with GnRH agonist treatment are clinically relevant given the increased risks already associated with advanced age in the prostate cancer population, Dr. Smith said.

What is less clear is whether GnRH agonists alter cardiovascular mortality. Dr. Smith said, "It's premature to conclude that GnRH agonists increase cardiovascular disease mortality. More studies are needed." ■