Formula Links HbA_{1c} to Average Plasma Glucose

BY MIRIAM E. TUCKER
Senior Writer

AMSTERDAM — Data from an international trial have yielded a formula that accurately converts hemoglobin A_{1c} values to an estimated average blood glucose.

The results of the A_{1c}-Derived Average Glucose (ADAG) study, comprising 4 months' worth of glucose data from 643 diabetic and nondiabetic subjects from 10 centers around the world, provided this "simple, linear" equation to obtain glucose values in mmol/L: $(1.583 \times HbA_{1c}) - 2.52$. Thus, when multiplied by 18 to get the value in the American units mg/dL, a hemoglobin A_{1c} of 6% is converted to approximately 126 mg/dL, 7% is converted to 155 mg/dL, and 8% is converted to 182 mg/dL.

"The results are even better than we expected or could have hoped for. There's a linear correlation between the HbA_{1c} and the calculated mean glucose over a wide range of A_{1c} values. … The results should apply to the majority of patients with diabetes," study leader Dr. Robert Heine of Vrije University, Amsterdam, said at a press briefing held during the annual meeting of the European Association for the Study of Diabetes (EASD), where the study results were presented later that day at a special symposium.

No need to pull out your calculator for every diabetic patient, though. In August, a joint consensus statement from the EASD, the American Diabetes Association (ADA), the International Diabetes Federation, the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the International Diabetes Federation advised that—pending the results from the ADAG study—clinical laboratories begin reporting both the HbA_{1c} percentage and the ADAG, along with a third number, the "true" HbA_{1c} value expressed in mmol/mol (Clin Chem. 2007;53:1562-4 and Diabetes Care 2007;30:2399-400).

Clinically, these developments provide an opportunity for physicians to begin shifting discussions with diabetic patients away from hemoglobin A_{1c} and toward average glucose, two representatives from the ADA said at the briefing. "The clinician has the choice to use one, two, or three values when communicating with the patient. The diabetes organizations would encourage physicians to use the estimated average glucose," said Richard Kahn, Ph.D., ADA's chief scientific officer.

The reason, explained ADA president Dr. John Buse, is that "[The HbA_{1c}] has always been kind of confusing for patients. At home they measure their glucose, then every 3 months they visit the doctor and get something that has the word 'hemoglobin' in it … There's always been a disconnect." In contrast, "The estimated average glucose is expressed in numbers that people are used to looking at all day every day," said Dr. Buse, director of the Diabetes Care Center of the division of general medicine and clinical epidemiology at the University of North Carolina at Chapel Hill.

It's not yet clear what will happen with point-of-care HbA_{1c} machines that many physicians currently have in their offices, but it's likely that the manufacturers can provide some sort of simple software adjustment or Internet link that won't be excessively burdensome or costly, Dr. Kahn noted at the briefing.

These developments provide an opportunity for physicians to begin shifting discussions away from hemoglobin A_{1c} and toward average glucose.

The shift to ADAG was initially spurred by the 2002 IFCC publication of 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 ADAG study. Although there already were data that provided a rough estimate of average glucose from HbA_{1c}—and indeed, many labs currently report those numbers—they were generated from old studies using infrequent fingerstick monitoring. The ADAG study, in contrast, utilized both frequent fingerstick and continuous glucose monitoring (CGM) to gather "thousands of data points" in order to derive a precise average, Dr. Heine explained.

Dr. Judith Kuenen, who works with Dr. Heine at Vrije University, presented the study data at the symposium. The entire group of 643 patients was about half men and half women. Half had type 1 diabetes, 36% had type 2 diabetes, and the other 14% did not have diabetes. Three-fourths were Caucasian. A total of 38% of participants, including all the nondiabetics, had hemoglobin A_{1c} values of 4%-6.5%. Another 44% had values between 6.6% and 8.5%, while 18% had HbA_{1c} levels about 8.5%.

A total of 427 patients had completed the study at the time of the meeting; the addition of the other 216 subjects is not expected to change the results. Of the 427 patients, 224 had type 1 diabetes and 125 had type 2 diabetes; the rest did not have diabetes. They had a mean age of 46 years; 53 were women, and 82% were white.(More minority subjects are among the other 216 patients who had not yet completed the study.) Approximately 2,400 CGM and 300 fingerstick glucose measurements were collected per subject, "an enormous amount of data," Dr. Kuenen remarked.

Despite such frequent monitoring, HbA_{1c} levels remained stable in most patients during the course of the study, with only 4% showing improvement of more than 1 percentage point.

The study was supported by grants from several pharmaceutical and glucose monitoring device manufacturers. Among its limitations were the inclusion of only small numbers from various ethnic minority groups, and the lack of any data on children, pregnant women, or patients with renal impairment, Dr. Kuenen noted.

Independent commentator Dr. Philip Home, professor of diabetes medicine at the University of Newcastle-upon-Tyne (England), cautioned that it will take time to transition to using new numbers that don't correlate with a huge amount of published literature on data using the HbA_{1c} measurement to predict diabetes complications and other important clinical values. "The problem we have as a result of all this is that we have to re-standardize all our guidelines to align with this [ADAG], and that means a bit of re-education." ■

Carbs Often Undercounted by Diabetic Patients

BY MIRIAM E. TUCKER
Senior Writer

AMSTERDAM — Patients with type 1 diabetes often underestimate the amount of carbohydrates in their meals, Dr. Guido Freckmann reported at the annual meeting of the European Association for the Study of Diabetes.

The ability to accurately estimate the carbohydrate content is key to a patient's efficacy in making appropriate therapy decisions with insulin pump or basal-bolus insulin injection regimens. It is therefore of concern that underestimation by about 25% was typical in this study of 74 such patients, with warm meals and large meals presenting even greater potential for error, said Dr. Freckmann, of the Institute for Diabetes Technology in Ulm, Germany.

The study included 38 men and 36 women with a mean age of 44 years and mean diabetes duration of 21 years. Their mean hemoglobin A_{1c} level was 7.2%. Twenty-six were on multiple daily injections and 48 were on insulin pump therapy.

Patients were given 24 different test meals—11 warm and 13 cold—in random order, including 8 breakfasts, 8 lunches, and 8 dinners ranging in carbohydrate content from 55 g to 164 g. Among the meals were a breakfast of rye bread, roll, margarine, ham sausage, Camembert, and yogurt containing 82 g of carbohydrate; a pizza lunch including mozzarella, basil, olive oil, and fruit, adding up to 138 g of carbs; and a dinner of baguette, tomato, mozzarella, and olive oil totaling 101 g of carbs.

Patients estimated the carbohydrate content of the meals to be a median of 75% compared with the actual content; estimates ranged from 53% to 127%. Warm meals prompted even more carb underestimation than cold (72% vs. 77%), and large meals were underestimated to a greater degree than were smaller meals, Dr. Freckmann reported.

Possible reasons include the fact that patients often don't count the carbs of vegetables and other low-carb items. It's also possible that some patients might compensate for the underestimate by adapting their individual insulin-to-carb ratio, thereby giving themselves sufficient insulin doses despite the carb underestimate, he said.

On the positive side, the degree of correct estimation was significantly improved—from 73% to 83%—among 35 patients who received training in carb counting. ■