

New Methods of Monitoring Glycemia

Standardizing the Reporting of HbA1c Test Results

Average blood glucose may accurately reflect a patient's daily variations in blood glucose, and may be a number that is easier for patients to understand than HbA1c. These findings from an international study support the recent agreement among diabetes organizations worldwide to standardize how HbA1c test results are reported.

The new approach uses a reference method proposed by the International Federation of Clinical Chemistry (IFCC) that measures a single molecular species of glycated HbA1c and is reported in units of mmol/L (or mg/dL) instead of the widely used National Glycohemoglobin Standardization Program (NGSP) method, which gives a percentage value derived from a mixture of glycated hemoglobin.

The IFCC reference number can be translated into the familiar DCCT HbA1c values using simple mathematic formulas, and also into the more patient-friendly average blood glucose number. The adoption of this new approach significantly changes the numerical results provided to clinicians. HbA1c results will be reported worldwide in both IFCC units (mmol/mol) and derived NGSP units (%). For example, an HbA1c value of 5% would become ~33 mmol/mol, and 8% would be ~65 mmol/mol.

The statement was issued in August by the European Association for the Study of Diabetes, (EASD), the American Diabetes Association (ADA), the International Diabetes Federation (IDF), and the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and called for a new standard for measuring and reporting glycosylated hemoglobin. At a press conference, speakers emphasized the need for an internationally recognized reference measurement system (Figure 1).



Figure 1. Consensus on the Worldwide Standardization of the A1c Assay.

<ul style="list-style-type: none"> • The A1c test should be standardized worldwide, including reference system
<ul style="list-style-type: none"> • IFCC reference system is the anchor
<ul style="list-style-type: none"> • A1c assay results are to be reported in <ul style="list-style-type: none"> - IFCC units (mmol/L) - NGSP units (DCCT aligned %) - <i>And</i> if the ADAG study fulfills the prespecified criteria, an A1c derive Average Glucose <ul style="list-style-type: none"> - Criteria: >90% of sample points within +/- 15% of linear estimate



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Different test results from different systems lead to high costs and poor medical reliability, they noted. When universally comparable test results are used instead, there are lower costs and increased clinical reliability. In the case of diabetes, there is a clear need for consistency between the daily self-monitoring of blood glucose and the HbA1c values that clinicians use to monitor and manage chronic glycemia, they said.

ADAG Results Reported

Judith C. Kuenen, MD, VU University Medical Center, the Netherlands, presented the results of the international HbA1c-Derived Average Glucose (ADAG) study, which showed that an estimated average glucose obtained by repeated measurements over 3 months, correlates very closely with HbA1c at the end of those 3 months. The findings support the use of this new method for reporting chronic glycemia. "I hope this is what you remember from your stay in Amsterdam," said JC Kuenen.

The objective of the ADAG study, which was conducted at 10 centers in Europe, North America, and Africa, was to establish the relationship between average blood glucose concentrations and HbA1c values according to the DCCT method in patients with type 1 and type 2 diabetes. This relationship would be used to predict average blood glucose from a measurement of HbA1c in a standardized manner. The study included 643 patients; 323 with type 1 diabetes, 230 with type 2 diabetes, and 90 non-diabetic volunteers. HbA1c levels were measured in a central laboratory using the DCCT standard monthly for 4 months. Glucose values were obtained using a combination of continuous glucose monitoring for 2-3 days for each of the 4 months, plus frequent fingerstick glucose measurements.

JC Kuenen presented the results for the first 427 patients. In a regression analysis, average blood glucose over 3 months compared well with HbA1c at the end of Month 3. The standard deviation of the error was only 0.83 mmol/L, indicating a strong correlation between average blood glucose and HbA1c.

"Not surprisingly, the size of the error increases with higher HbA1c values, however, over the entire HbA1c range, >90% of the values fell within ± 15 ," she added.

Under the previous NGSP assay and nomenclature, the ADA's recommended target was an HbA1c of <7%, and ideally <6%. Using the preliminary results of the proposed

equation between mean blood glucose and HbA1c, a HbA1c of 7% would be converted to an estimated average blood glucose of 8.6 mmol/L (155 mg/dL).

What's Ahead

Robert Heine, MD, also from VU University Medical Center, emphasized that the findings of the ADAG trial fully support the new recommendations for standardized HbA1c reporting. The consensus statement had anticipated favorable findings from ADAG and had tentatively recommended that average glucose be one of the three ways by which chronic glycemia is reported.

"These results are better than we expected and could have hoped for," Prof. Heine commented. "Luckily, there is consensus among the diabetes associations to apply this as the global reference standard. All of the major diabetes organizations are on board."

Patient lab results, as well as the units reported in clinical trials, will therefore be reported in all three ways, giving physicians some degree of choice in how they discuss test results with patients. The transition will not happen overnight, Prof. Heine noted. "Getting used to new numbers requires 2 to 3 years," he said.

At the press conference, representatives from the various diabetes associations emphasized that the HbA1c test itself will not change. Rather, different algorithms will be used to determine test results, and results may be communicated differently to patients. The new method may make more sense to patients, who are accustomed to seeing the results of their self-monitoring of blood glucose expressed in mmol/L or mg/dL, not percentages, said the Executive Director of the ADA, Richard Kahn, MD.

"The diabetes organizations would encourage physicians to use average glucose, but some might decide to use the older methods," he said. However, the hope is that over time the estimated average glucose will eventually become the gold standard for chronic glycemia targets and reporting.