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CONSENSUS STATEMENT

Consensus statement on the worldwide standardisation of the HbA_{1c} measurement

The American Diabetes Association, European Association for the Study of Diabetes, International Federation of Clinical Chemistry and Laboratory Medicine, and the International Diabetes Federation

Consensus Committee

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Abbreviations

ADAG	HbA_{1c}-derived average glucose
IFCC	International Federation of Clinical Chemistry and Laboratory Medicine
NGSP	National Glycohemoglobin Standardization Program

Introduction

The HbA_{1c} assay has become the gold-standard measurement of chronic glycaemia for over two decades. Anchored in the knowledge that elevated HbA_{1c} values increase the likelihood of the microvascular complications of diabetes (and perhaps macrovascular complications as well), clinicians have used the HbA_{1c} test results to guide treatment decisions, and the assay has become the cornerstone for the assessment of diabetes care.

The clinical world has assumed that the HbA_{1c} assay reflects average glycaemia over the preceding few months. However, the data supporting that premise are not exceptionally robust [1–5]; glucose concentrations were not measured frequently enough to compute a true 'average'. To gain a better understanding of the relationship between HbA_{1c} and average blood glucose level, an international study has been initiated to document this relationship, using frequent capillary measurements and continuous glucose monitoring. The results of this study will be known around September 2007. Although some clinicians are already providing patients with their 'average blood glucose', by simply converting the current HbA_{1c} test results [6] to a term more relevant to the values obtained from patient self-monitoring, we hope that the results of the study will provide a more accurate conversion algorithm.

Based on the work of the National Glycohemoglobin Standardization Program (NGSP) in the USA and other similar programmes in other parts of the world, the current HbA_{1c} assay has been harmonised on reference methods that measure a mixture of glycated haemoglobins [7–9]. However, to achieve a more uniform standardisation of HbA_{1c} measurements, it is desirable to have a reference method that measures only a well-defined analyte. Accordingly, after several years of work, the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) developed a new reference method that specifically measures the concentration of only one molecular species of glycated HbA_{1c} [10, 11]. Results by the new reference method have also been compared with the results obtained by current methodologies [12] and the relationship between the assays can be expressed by simple regression equations ('master equations'). Of note, the new reference method is only used to standardise the HbA_{1c} assay, and cannot be used by clinical laboratories in their measurement of HbA_{1c}.

A list of the Consensus Committee members can be found in the Appendix.

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In keeping with the measurement of other analytes, the IFCC has also suggested that the test results be provided in scientifically correct units, i.e. mmol/mol [13]. The impact of both changes proposed by the IFCC would be to significantly change the numerical results provided to clinicians. For example, an HbA_{1c} value of 5% would become ~33 mmol/mol, and 8% would be ~65 mmol/mol.

What are the implications of the above activities?

The advent of a new reference method to standardise the HbA_{1c} results, along with the anticipated documentation that the assay does indeed indicate average blood glucose, has led to a variety of proposed changes in the reporting of HbA_{1c} test results worldwide. To reach agreement on a course of action, a meeting was held in Milan, Italy, on 4 May 2007, at which a consensus agreement emerged. The following statements have been approved by the American Diabetes Association, the European Association for the Study of Diabetes, the International Diabetes Federation and the IFCC:

1. HbA_{1c} test results should be standardised worldwide, including the reference system and results reporting.
2. The new IFCC reference system for HbA_{1c} represents the only valid anchor to implement standardisation of the measurement.
3. HbA_{1c} results are to be reported worldwide in IFCC units (mmol/mol) and derived NGSP units (%), using the IFCC–NGSP master equation.
4. If the ongoing 'average plasma glucose study' fulfils its a priori specified criteria, an HbA_{1c}-derived average glucose (ADAG) value calculated from the HbA_{1c} result will also be reported as an interpretation of the HbA_{1c} results.
5. Glycaemic goals appearing in clinical guidelines should be expressed in IFCC units, derived NGSP units and as ADAG.

All the organisations agreeing with this consensus statement propose that these recommendations be implemented globally as soon as possible. We believe this agreement will further contribute to the worldwide comparability of HbA_{1c} results, paralleling the progress of scientific knowledge related to the analytical and biochemical features of HbA_{1c} testing. Expressing test results in scientifically correct units along with a clinically relevant interpretation of those results is not an uncommon practice (e.g. creatinine and estimated GFR). Consequently, clinicians will have the opportunity to convey the concept of chronic glycaemia in terms and units most suitable to the patients under their care.

Appendix

Consensus Committee

For the IFCC: J. Hicks, M. Muller, M. Panteghini, G. John. For the American Diabetes Association: L. Deeb, J. Buse, D. M. Nathan, R. Kahn. For the European Association for the Study of Diabetes: E. Ferrannini, R. Heine. For the International Diabetes Federation: M. Silink, J.-C. Mbanya.

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