Glycated haemoglobin values

Standardisation is essential

EDITOR,—Eric S Kilpatrick and colleagues' observations regarding the problems of assessing control of blood glucose concentrations in diabetes mellitus are important.[1] We agree that standardisation of assessment of glycated haemoglobin concentration is essential for appropriate interpretation of this test. Not only should haemoglobin A_{1c} be specifically measured but normal ranges need to be standardised nationally.

Important developments in diabetes care include the development of local and national registers comprising data conforming to an agreed national dataset. Such registers will be important for comparative analysis to assess success in achieving the objectives of improving metabolic control and monitoring the rates of development or progression of complications of diabetes. Measurement of glycated haemoglobin is essential to assess metabolic control, and its standardisation is therefore essential to permit meaningful comparisons.

We must remember that it is the person with diabetes to whom the result is of primary importance. Different methods in use around Britain, substantially different normal ranges for different assays, and changing assays within a locality may confuse and demotivate both patients and professionals.

In recognition of these considerations the British Diabetic Association is currently working with the Royal College of Pathologists towards the standardisation of assessment of haemoglobin A_{1c} concentration. There is not a simple solution to the present confused situation, but efforts are being made on several fronts.

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1 Kilpatrick ES, Rumley AG, Dominiczak MH, Small M. Glycated haemoglobin values: problems in assessing blood glucose control in diabetes mellitus. *BMJ* 1994;309:983-6. (15 October.)

Methodological discrepancies are not important

EDITOR,—The article on glycated haemoglobin values by Eric S Kilpatrick and colleagues fails to add anything to diabetic care and misses the most important point.[1] It is well known that there is no standardisation in increasing glycated haemoglobin concentration; primary standards do not exist, secondary reference standards are not applicable to different methods, and there is no agreement about which method most accurately mirrors diabetic control.[2-4] The most important clinical factor is the trend of glycated haemoglobin concentration with treatment and the approximate relation of trend in glycated haemoglobin concentration and the results recorded on a patient's diabetic control card. This gives clinicians information on whether patients are compliant and well trained in monitoring glucose concentrations in their own blood or urine and gives some indication of the previous three months' trend in control.

The discrepancies between methods are well characterised through the different quality control and external quality assurance schemes for each type of glycated haemoglobin analyser and are not important unless a laboratory changes its method of analysis, a patient moves districts, or a general practitioner changes laboratory service. Reference ranges for individual instruments are defined from sampled populations, so discrepancies are to be expected between laboratories that use their own sample populations for standardisation. The high labour intensity and slowness of electrophoretic methods may be a major consideration in the choice of method for laboratories with large numbers of samples given the pressure for quick reporting.

The effects of numerical derivation of results by subtraction from initial results which have a significant variance can clearly be seen in figure 2 of Kilpatrick and colleagues' article and cast doubt on the value of such secondary results. Any method comparisons involving significant imprecision on both axes should be compared with Deming's regression analysis and not linear regression. There is also no mention of the common confounder of glycated haemoglobin analysis, haemoglobin variants (especially haemoglobin S and fetal haemoglobin),[5] and no mention of their incidence in the study population. The most interesting analysis that could have come from this study would have been a comparison of patients' glycated haemoglobin fractions with their own capillary glucose records over four months and regular plasma analyses in the laboratory, but unfortunately the relevant data were not presented.

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Derive reference range locally

EDITOR,—During the past decade measurement of the glycated haemoglobin concentration has become the gold standard for assessing glucose control in diabetes.[1] Eric S Kilpatrick and colleagues identified a discrepancy between measurements of total haemoglobin A_1 and haemoglobin A_{1c}, but our experience indicates that this may not apply to other laboratories.

When we changed our analytical method to automated ion exchange chromatography (Glycomat, Ciba-Corning) we established our own reference range for a healthy population (n=100). The mean (SD) concentrations for this group were 5·9 (0·6)% and 4·8 (0·5)% for haemoglobin A_1 and haemoglobin A_{1c} respectively. We subsequently categorised 360 diabetic patients as having good, borderline, or poor control by the criterion of a concentration <3, 3-5, or >5 SD from the mean in the healthy population.[3] When categorised by haemoglobin A_1 concentration 82, 107, and 171 fell into each group respectively, which was in close agreement with the classification by haemoglobin A_{1c} concentration (91, 120, and 149 respectively). Furthermore, 313 patients fell into the same category whichever variable was used, and of the 47 who were classified differently, none were classified as having good control by one method and poor by the other. Thus, in contrast with the conclusions of Kilpatrick and colleagues, the risk of developing microvascular complications would not have been assessed differently by either method.

Haemoglobin A_{1c} is the only specific adduct of glucose to haemoglobin A. Our results showed, however, that levels of non-glucose haemoglobin adducts (haemoglobin A_{1a1}, haemoglobin A_{1a2}, haemoglobin A_{1b}) were well correlated with haemoglobin A_{1c} ($r=0·742$, $P<0·0001$); consequently the former could provide an index of diabetic control in their own right. At present there is no consensus on whether haemoglobin A_1 or haemoglobin A_{1c} is preferred in diabetic care. While Kilpatrick and colleagues' call for more uniformity in measurements of glycated haemoglobin echoes widely held views,[4] in practice the consistency between haemoglobin A and haemoglobin A_{1c} seen in our results suggests that either measurement would suffice. Clinicians should not be dissuaded from using this valuable tool for assessing glycaemic control provided that results are interpreted in relation to a reference range derived locally. Efforts towards universal standardisation would ensure comparability among laboratories, simplify the audit procedure when several hospitals are involved, and ease the interpretation of results when patients' care is transferred.

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1 Diabetes Control and Complications Research Group. The effect of intensive treatment of diabetes on the development and