The Use of Glycosylated Haemoglobin Measurements in the Control of the Diabetic Patient

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SUMMARY

Glycosylated haemoglobin (HbA1c) has recently been used as an indicator of long-term diabetic control. This study compares the efficacy of HbA1c measurements and post-prandial blood glucose estimations in assessing diabetic control in 51 diabetic patients. It was found that the HbA1c levels reflected overall diabetic control significantly better than did a single post-prandial blood glucose estimation. HbA1c measurements give considerable aid in the assessment of the longitudinal blood sugar control in the diabetic, and may be a useful indicator of the efficacy of diabetic treatment.


Until recently there has been no simple way to ascertain whether the blood sugar of an individual diabetic has been well controlled in the long or medium term. Urine sugars, 'spot' specimens of fasting or postprandial blood sugars, or multiple blood sugar estimations over a single day have all been used. Unfortunately, all these measurements are subject to day-by-day and even hour-by-hour fluctuations, dependent upon variations in the patient's diet and activity on the day of measurement.

Over the past few years it has been suggested that the measurement of haemoglobin A1c (HbA1c) can be used as an indicator of diabetic control.2-3 HbA1c is formed by the post-transcriptional glycosylation of haemoglobin A at the amino terminal of the β-chain.4-5 This chemical reaction occurs slowly throughout the lifespan of the erythrocyte, and the most important factor governing the quantity of HbA1c formed is the prevailing plasma glucose concentration.6 It is therefore probable that a single HbA1c estimation will reflect the average blood glucose concentration over the preceding few weeks.

We have tried to evaluate the usefulness of the estimation of the HbA1c concentration in the assessment of overall diabetic control.

PATIENTS AND METHODS

Fifty-one patients of both sexes were admitted to the study, all having confirmed overt diabetes. Their ages ranged from 14 to 74 years. Thirty-seven were controlled on insulin, 6 on oral antidiabetic agents, and 8 on diet alone. All these patients had normal renal function with a normal renal threshold for glucose, and all had a complete record of at least twice daily urine glucose estimation for the preceding 2 weeks.

The degree of diabetic control was rated according to the degree of glycosuria, as listed in Table I. A random postprandial plasma glucose estimation using a glucose oxidase method was performed on each patient, and simultaneously heparinized venous blood was obtained for HbA1c estimation. The HbA1c was measured exactly as described by Kynoch and Lehmann1 using a two-stage elution of a dilute haemolysate from a Bio-rex 70 cation exchange resin. The measured glycosylated haemoglobin included HbA1c and HbA1c(a and b). A normal range for HbA1c was determined in 25 healthy non-diabetic individuals and was found to be 7·13% of the total haemoglobin. This range was somewhat higher than that found in the literature.7 Therefore the presence of any contamination with non-glycosylated haemoglobin was assessed by electrophoresis on cellulose acetate strips,8 for 8 hours at 150 volts in a system consisting of 6.0M urea in 0.04M phosphate buffer, pH 6.6, containing 0.05M mercaptoethanol. This showed no contaminating haemoglobin fractions, so that the reason for our higher normal range is not apparent.

RESULTS

A highly significant correlation (P<0.001) was found between the clinical rating based on the degree of glycosuria and the HbA1c level, as seen in Fig. 1. It is of interest that all patients assessed as having very good diabetic control (rating scale 1) had HbA1c levels in the normal range. This association was significantly better (P<0.001) than that found between the clinical rating and postprandial
Fig. 1. Correlation between the clinical assessment of diabetic control and the HbA₁c levels in 51 diabetic patients.

Fig. 2. Correlation between the clinical assessment of diabetic control and postprandial blood glucose estimations in 51 diabetic patients.

Fig. 3. Correlation between HbA₁c levels and a simultaneous postprandial blood glucose estimation in 51 diabetic patients.

Fig. 4. Comparison between HbA₁c levels in diabetic patients on different forms of therapy. There is no significant difference between the groups.
blood sugar estimations (Fig. 2). While the correlation between HbA\textsubscript{c1} levels and the postprandial blood glucose levels was significant (Fig. 3), there was a marked discrepancy between the HbA\textsubscript{c1} and the plasma glucose estimations in several patients. In 1 patient, in particular, the HbA\textsubscript{c1} was low at 11.1\%, with a postprandial blood glucose of 345 mg/100 ml, and this patient was subsequently found to have reactive hyperglycaemia (Somogyi effect).

Comparisons were made between the HbA\textsubscript{c1} levels in patients on different forms of therapy for their diabetes (Fig. 4), and no significant difference was found. One patient on diet alone and 1 patient on treatment with oral hypoglycaemic agents were on all counts poorly controlled, and were seen with a view to converting them to insulin therapy.

**DISCUSSION**

Since the purpose of this study was to ascertain the practical value of a single HbA\textsubscript{c1} estimation in the assessment of overall diabetic control, we decided to compare its usefulness to that of a postprandial blood glucose level. Because of patient convenience, the single random blood sugar is the estimation most commonly used by many clinicians, particularly those dealing with a large number of diabetics on an outpatient basis. Previous studies have shown good correlation between HbA\textsubscript{c1} levels and the response to oral glucose tolerance tests, as well as between fasting plasma glucose levels and mean plasma glucose levels. Outpatient studies in juvenile diabetics have shown good correlation between HbA\textsubscript{c1} levels and 24-hour urinary glucose determinations measured 1, 2 and 3 months before the haemoglobin determinations. Cholesterol and triglyceride levels in diabetic patients have also been shown to be directly correlated with HbA\textsubscript{c1} levels,

This study has demonstrated that although the HbA\textsubscript{c1} level correlates significantly with a single random postprandial blood glucose estimation, it appears to reflect diabetic control more accurately than a single blood glucose estimation.

The HbA\textsubscript{c1} concentration does not reflect the simultaneous blood glucose concentration, nor is it influenced by short-term fluctuations in blood glucose. Rather, a single HbA\textsubscript{c1} measurement reflects the average blood glucose level of the patient for the preceding few weeks. For this reason, it may have considerable advantages both in accuracy and in convenience in assessing overall diabetic control. In addition to being a useful measurement in the longitudinal follow-up of any individual diabetic patient, the HbA\textsubscript{c1} level is of particular use in follow-up of patients with renal glycosuria or a raised renal threshold for glucose. We also find it particularly useful in confirming good control in the pregnant diabetic and for detecting patients with reactive hyperglycaemia. In time, the measurement may help to determine the answer to the relationship between diabetic control and the vascular complications of diabetes.

**REFERENCES**


Books Received: Boeke Ontvang


