Brief Communications

Patient-Determined Glycosylated Hemoglobin Measurements: An Aid to Patient Education

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The feasibility of patient determination of fast fraction hemoglobin (HbA_1) was evaluated. In the laboratory, the fast fraction method correlated well with known mixed standards of between 0 and 40% hemoglobin A_{1c} ($r^2 = 0.97$, slope 1.19) and reasonably well with radioimmunoassay ($r^2 = 0.78$, slope 1.09), although prepackaged columns performed poorly about 18% of the time. Sixteen patients practicing home blood monitoring performed the determination of HbA_1 on their own blood obtained from fingerstick. Two hours of patient training were required for the procedure. The correlation of patient determination of HbA_1 with the results obtained by the laboratory on venous blood was reasonable ($r^2 = 0.81$ with a slope of 0.88). Patient performance of HbA_1 was useful in (1) providing enhanced reinforcement for self-monitoring programs, (2) engaging patients in groups in the monitoring process, and (3) providing an educational tool with which to teach pathophysiologic principles involved in diabetes mellitus. DIABETES CARE 4: 480–483, JULY–AUGUST 1981.

Patient monitoring of blood glucose has become a component of diabetes management programs in a number of centers. In a high percentage of cases, patients accept the responsibility of documenting their own blood glucose concentrations and modify their insulin regimens appropriately. The psychological effects of this type of patient involvement have in general been beneficial, and are associated with an increase in patient compliance.[1–4]

The recent observation that glycosylated hemoglobin (HbA_{1c}) levels correlate with average glucose concentration over time (4–8 wk) has been useful in documenting patient "control" of blood glucose.[5,6] Patients involved in management programs have become increasingly interested in their glycosylated hemoglobin measurements as a positive feedback for the extra work necessary to achieve good control. The present study was undertaken to determine whether patients could accurately measure their own glycosylated hemoglobin in the outpatient department using available techniques. We are able to show a high feasibility of patient determination of HbA_{1c} and can report that involving the patient in the monitoring process has several theoretical and practical advantages regarding patient education and motivation.

MATERIALS AND METHODS

Patients. Sixteen patients were chosen from the outpatient department of The Rockefeller University Hospital to participate in the study. All the patients had insulin-dependent diabetes (type I) and were between the ages of 18 and 46 yr. They had all mastered the technique of self-monitored blood glucose determinations and had used home blood glucose monitoring for periods ranging from 1 mo to 4 yr.

Laboratory evaluation. Patient-performed fast fraction determinations used a mini-column method. The system chosen included prepackaged columns, hemolyzing solution, and preprogrammed spectrophotometers ordered directly from the company (Helena Laboratories, Beaumont, Texas). Two spectrophotometers were used, and a comparison test showed that their measurements correlated well with each other over a range of 2–15% fast hemoglobin ($r^2 = 0.99$, slope 0.96). One spectrophotometer was left in the laboratory, and assays were performed on patient venous bloods. Temperature corrections were performed according to a monogram supplied by the company. For the laboratory evaluations, patients' venous blood was handled according to the company's directions, except that all the samples were washed three times in normal saline[7] and measured in dupli-

cate. The interassay coefficient of variation was 15.3% (r = 16). Therefore, those duplicate measurements with a coeffcient of variation greater than 10% were repeated. Patient self-measurements were performed on venous blood drawn from a capillary fingerstick in a clinical setting. These determinations were done once rather than in duplicate.

A radioimmunoassay for HbA_{1c}[8] was used to test the reliability of the fast fraction determinations made by the mini-column system and the preprogrammed spectrophotometer. HbA_0 and HbA_{1c} standards were obtained by the method of Trivelli et al.[8] and verified by isoelectric focusing on polyacrylamide gels with a pH gradient of 6–8.[10] These were diluted to a uniform concentration of 2 mg/ml using phosphate-buffered glycerol. Standards of 0–40% HbA_{1c} were then prepared in HbA_0, and tested in the mini-columns and the preprogrammed spectrophotometers.

Statistical evaluations were obtained using a prepackaged program for linear regression using the method of least squares (Hewlett-Packard).

RESULTS

Evaluation of the column performance in the laboratory by persons not practiced in column chromatography revealed a failure rate of approximately 18%. These failures were usually caused by inadequate filtration of the hemolysate, resulting in spuriously low fast fraction levels. Careful resin suspension and avoidance of air bubbles would eliminate this error. Because of the column failure rate, it was decided that optimum laboratory use of the prepackaged column system should employ duplicate determinations. Those duplicates that did not agree to within 10% would then be repeated.

The correlation of the mini-columns system with the radioimmunoassay was reasonable ($r^2 = 0.78$, slope 1.09), considering that the radioimmunoassay is specific for HbA_{1c}, while the total fast fraction includes HbA_{1a} and HbA_{1b} as well. Using the HbA_{1c} standards described above, the mini-columns were found to perform adequately; a plot of the known values versus the spectrophotometric results showed a correlation coefficient of 0.97 with a slope of 1.19.

The patients were enthusiastic about performing their own fast hemoglobin determinations. It was found that about 2 h of teaching was required before patients could perform the measurement. Teaching was effectively performed in small groups of 3–5 persons. Table 1 summarizes the protocol developed for teaching patients the measurements. Since patients were accustomed to measuring insulin in units, it was decided to use the unit nomenclature instead of microliters. In Figure 1, patient-monitored fast fraction values are compared with fast fraction values from the same patients determined by a technician in the laboratory. The correlation is reasonable, with an r^2 of 0.81 and a slope of 0.88.

Following performance of the assay, the patients were asked whether they felt that learning the glycosylated hemoglobin measurement was more or less difficult than learning to monitor their own blood glucose using a reflectance

TABLE 1
Protocol for glycosylated hemoglobin measurements by patients

I. Practice—using micropipettes and tips
Practice A. Mixing the column
B. Shake, remove top carefully
C. Use long (pasteur) pipette to mix contents
Avoid air bubbles
Mix all contents off filter

II. Collecting blood
A. Add 300 milliunits HEMOSYLATE to your small tube
B. Notice the NUMBER on your tube
C. PIPETTE 20 milliunits exactly of blood from your finger
D. ADD IT to your small tube and throw PIPETTE TIP away
E. SHAKE GENTLY to mix
F. Let this tube stand at least 5 MINUTES

III. Prepare columns
A. SHAKE column
B. REMOVE TOP GENTLY (from here on, wash hands before eating or touching food or face)
C. Mix contents with pasteur pipette
CAREFUL—feel for filter at bottom, do not press
—clean off filter and avoid air bubbles
D. REMOVE small bottom cap
E. PLACE COLUMN IN RACK to drain

IV. Watch your column (do not allow to dry out)
A. When no more liquid on top of column, place column into *small test tube* with YOUR NUMBER in the next rack
B. IMMEDIATELY add 100 milliunits of BLOOD SOLUTION onto column with correct pipette, by dropping blood near top of resin, but allow to run down the side of plastic column—do not disturb the resin
C. ADD *some* water to the large tube with your number
D. ALSO ADD 100 milliunits of your blood solution to the large tube

V. Watch your column (do not allow surface of column to dry out)
IMMEDIATELY when surface of column has no more blood
ADD FAST FRACTION DEVELOPER 1.5 ml with correct pipette
ADD CAREFULLY TO COLUMN as before—Do not disturb resin
ADD SLOWLY

VI. Wait for column to empty out
No more drops should be coming out of the column

VII. FILL small tube and large tube with DISTILLED WATER so that the center of the water surface (MENISCUS) is even with RED LINE. Mix well

VIII. PLACE large and small tubes in the machine
Press each tube down
CLOSE DOOR
Record value which remains on the screen
CORRECT this from the chart for the temperature in the room
RECORD THIS VALUE as your fast fraction
NORMAL VALUES: 5.4–8.9%

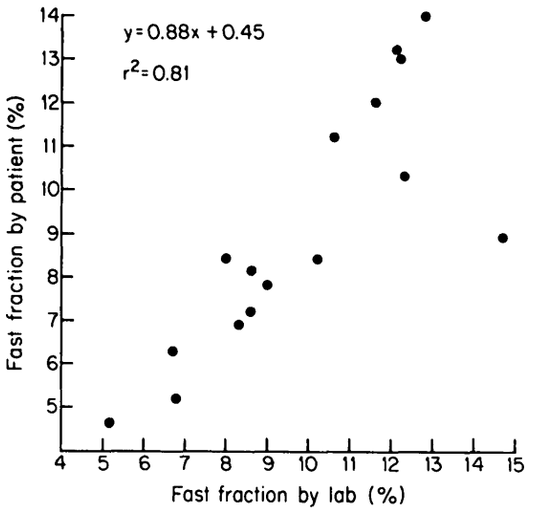

FIG. 1. Patient-determined fast fraction by finger stick compared with laboratory determination from washed venous blood.

meter. All patients felt that performance of the fast fraction determinations was no more difficult than learning home glucose monitoring.

DISCUSSION

The present study demonstrates that patients with diabetes mellitus who have participated in a program of home glucose monitoring can be taught to measure their own fast hemoglobin fractions, and that their measurement correlates reasonably well with the measurement performed in the laboratory by a technician. Having patients measure their own fast hemoglobin fractions at home, in a physician's office, or a hospital outpatient clinic has the important advantage of immediately confirming the level of glucose control over the previous 4–6 wk.[5]

The high failure rate of the prepackaged columns, when evaluated by persons not familiar with column chromatography in the laboratory, probably explains why the patient data correlated with the laboratory data with a slope of less than 1. The samples determined in the laboratory were washed, and therefore would be expected to have an even lower reading than those performed by the patients, due to the removal of the labile adduct.[7] It thus seems likely that the patients' samples included a number of column failures which led to spuriously low results. This appears to be due to poor resin suspension with subsequent erratic buffer flow. Nevertheless, repeated glycosylated hemoglobin evaluations over time, in conjunction with patient-monitored glucose determinations, should facilitate recognition of this type of error.

There are three ways in which the results represent an advance in patient self-monitoring programs. One is that the new capability gives the patient immediate reinforcement for the effort put into other measures (i.e., urine and blood glucose monitoring). The glycosylated hemoglobin level documents long-term developments in the patient's disease control process. Laboratory measurements offer the same results, but with a longer time delay.

A second advantage is that the procedure engages the patient in the monitoring process. This is especially true for the way we organized the experiment, namely, with people in groups. Working on their measurements together, the patients served as what Vygotsky[11] has called "zones of proximal development" for each other. That is to say, the patients used each other's behavior, concern, and evaluation to focus attention on the development and maintenance of their disease control program.

The third and most important advance is in the use of the technique as an educational tool. The physical system used to measure the glycosylated hemoglobin models the conceptual terrain the patients must master to understand the pathophysiology of their disease. Learning and memory tend to be enhanced by manipulation of physical models of complex ideas.[12,13] The fact that all patients completed the task indicated that the 2-h session was worth the effort even if the technique is not used as a recurrent aid in monitoring.

Programs of home glucose monitoring have stimulated reevaluation of the traditional approach to patients with diabetes mellitus. Didactic approaches to patient education and management are being increasingly replaced by programs designed to provide the patient with the skills and tools required to manage his own disease. Glycosylated hemoglobin determinations have been shown to be a useful measurement of outpatient glucose control.[1–7] The present study demonstrates that patient monitoring of fast hemoglobin fractions is possible with technologies now available and has definite potential as a new educational tool for programs using principles of self-management.

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