Quality-Control Scheme for Blood Glucose Measured Outside the Laboratory
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We propose a quality-control (QC) scheme to evaluate the performance of blood glucose estimates made with a reflectometer in hospital wards or at home. We constructed a chart illustrating the comparison by regression analysis of the results of 254 reflectometer readings (y) and simultaneous capillary blood glucose analyses in the laboratory (x). Arbitrary acceptance limits around the regression line (y = 0.5 + 0.87x; r = 0.97, S_yx = 0.8 mmol/L) were established, based on the mean ±2 SD of the reflectometer readings of a series of classes of 1.1 mmol/L interval, made with the results from the laboratory analyzer. Each ward using a reflectometer is provided with the QC chart, and the first blood glucose estimation with the reflectometer on each working shift is controlled by re-assay in the laboratory. If the reflectometer reading is outside the limits, the next glucose estimation is also re-assayed. If two consecutive readings are outside the limits, the reflectometer procedure is considered to be failing, the instrument’s readings are not used for medical decisions, and remedial action is taken. The chart can also be used as a teaching tool for training the patients or the nurses and to evaluate individual performance.

Additional Keyphrases: reflectance densitometry • physician’s office testing

The last few years have seen a proliferation of analytical equipments specifically designed for use by non-laboratory personnel in clinical areas (1, 2). One of the commonest analytes so estimated is blood glucose. A range of reflectance meters and reagent strips is available. The accuracy of the reagent strips and meters can be evaluated easily in the laboratory but this gives no information about the performance of the individual user—e.g., testing at home—who lacks inherent professional training (2, 3).

Establishing a quality-control program adapted to this new approach of biochemical testing remains an important challenge. Conventional quality-control procedures with lyophilized materials or liquid ethylene glycol-based materials are often inappropriate for many reasons: incompatibility of the control materials, wastage due to unadapted packaging of control serum, lack of pipetting skills to reconstitute the control material reliably, and, in many instances, sporadic testing (4). A quality-control program that is adapted to the concept of testing outside the laboratory is therefore sorely needed.

In the quality-control scheme for blood glucose measurements, we use a chart based on a comparison study between the results from the reflectometers in hospital wards and those for the same samples assayed with a laboratory automated analyzer.

Materials and Methods

The comparison study to generate the chart involved 254 capillary blood samples obtained by finger prick on four different wards by rotating nursing staff over a period of one month. Each sample was immediately tested by the attending nurse, using a reflectometer (Glucometer I, with Dextrostix strips; Ames, Mills Laboratories, Etobicoke, Ontario) according to the manufacturer’s instructions. The nurses participating to the study were specifically instructed by the laboratory staff and a nurse instructor. A second, paired capillary blood sample collected at the same time was sent to the laboratory for glucose determination by the glucose oxidase method with an automated analyzer (Hitachi 705; Boehringer Mannheim Canada, Montréal, Québec).

During the conduct of the comparison study the four reflectometers independently underwent the laboratory assessment of quality control by the laboratory staff.

We assessed the correlation of the results by least-squares linear regression analysis. Glucose results from the Hitachi 705 were grouped in 1.1 mmol/L intervals, and the mean ±2 SD for the results obtained with the reflectometers for the same blood samples was determined for each interval. The limits of acceptance of the reflectometer readings were set arbitrarily at ±2 SD of the mean of each interval, and we drew a chart reflecting those limits.

To validate the chart as part of the quality-control scheme, we sent to the laboratory a paired capillary blood sample for automated analysis during each shift whenever possible. Usually, this was the first glucose determination on each shift. Each chart was used for one month, then sent to the laboratory director for evaluation.

Results and Discussion

The linear-regression equation for the comparison of results from the ward reflectometers (y) and those from the automated analyzer (x) on 254 pairs of specimens was: y = 0.6 + 0.85x (r = 0.91, S_yx = 1.3 mmol/L). We arbitrarily chose as limits of acceptability for the reflectometer readings ±2 SD of the mean of the results obtained with the reflectometers for the specimens in each category of specimens (each 1.1 mmol/L interval of glucose concentration) (Figure 1, left). We rejected 20 reflectometer readings as aberrant, then recalculated the regression equation: y = 0.5 + 0.87x (r = 0.97, S_yx = 0.8 mmol/L) (Figure 1, right).

Fig. 1. Results from the ward reflectometer and from the hospital laboratory compared for 254 pairs of specimens (left) and after rejection of 20 aberrant results (right)

Left: y = 0.6 + 0.85x, r = 0.91, S_yx = 1.3 mmol/L. Right: y = 0.5 + 0.87x, r = 0.97, S_yx = 0.8 mmol/L. Limits of acceptance for reflectometer estimations were arbitrarily drawn as ±2 SD

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Figures 2 and 3 illustrate the use of charts based on these limits of acceptability, and with an upper limit set at 16.5 mmol/L and a lower limit of 2.2 mmol/L. Any reflectometer reading exceeding the upper or lower limit was considered a signal for immediate control by the laboratory.

To assess the general validity of the chart as part of a total quality-control scheme, we ordered paired analyses (reflectometer and laboratory) for the first glucose determination on each shift in the various hospital wards. Figure 2, showing the results obtained by the diabetic ward, where reflectometers were used on a daily basis, illustrates that the chart boundaries are adequate and correspond to the performance attainable by a trained nursing staff. These limits are located at approximately ±25% of the values on the regression line. On wards where the reflectometers were used more sporadically (fewer than two determinations per day), we found that the results were outside these limits in as many as 30% of the cases when chart use was first implemented on those wards (results not shown).

We also used the chart in training patients to use glucose meters and in evaluating their performance (Figure 3). Using the chart as a teaching tool for personnel and patients helped them compare their results obtained with the glucose meter with those obtained in the laboratory. This improved their confidence in the reflectometer readings on one hand and also indicated the necessity for improvement to those who had difficulty following the instructions.

To encourage the use of the chart, we rapidly return results from the laboratory to the ward or to the patient for immediate inscription on the chart. Instructions for results outside of the acceptable limits are kept as simple as possible. When the values for the first glucose determination on a shift are within the limits, the patients' results obtained with the reflectometer are reported during the whole working shift. When the reflectometer value is outside the limits, any decision concerning the patient is based on the laboratory result, and the next blood specimen to be analyzed on the ward is also sent to the laboratory for paired analysis. If the result for the second specimen is within the limits, the analytical procedure is considered to be under control and the patients' results are reported during the whole working shift. If two consecutive control results are outside of the limits, the reflectometer procedure is considered to be failing. The attending nurse must inform the head nurse. If the head nurse cannot correct the situation, the laboratory quality-control agent is informed and no more patients' results from this particular analyst and reflectometer are reported until the controls are back within acceptable limits (e.g., subsequent results are within the limits of the chart).

A similar protocol is used for patients who are using their own charts on the ward during the period of training. Outpatients visiting the diabetic clinic are invited to test their performance at each visit by simultaneous paired analyses. The results are recorded on their chart and discussed with the attending nurse. If necessary, the laboratory staff helps to train patients who have difficulty using their reflectometer.

There is a recent proliferation of analytical equipment and reagents specifically designed for use by non-laboratory personnel either in hospital, in the physician's office, or at home (5, 6). However, the need for quality is no different from that recognized for hospital and independent laboratories (7). Most quality-control schemes and control materials are designed for laboratory use and require specific skills; in many instances, they are not adapted for analytical conditions outside the laboratory. The quality-control chart that we present here minimizes the necessary manipulations for quality assurance by using as a control the blood specimen of the first patient needing blood measurement during any working shift. This approach combines evaluation of accuracy and, indirectly, of imprecision. It has the advantage that fresh blood is used, and it allows evaluation of the personnel on all working shifts. Frequent random errors can be expected when a non-professionally-trained individual analyzes patients' specimens (8). We observed that personnel who used the reflectometer sporadically obtained greater discrepancies between the paired sample. The main problems we identified for this group were improper use of the instrument and the lack of daily maintenance.

The limits of tolerance set in this chart compare well with the precision obtained by others in a multi-users setup (9–11). These limits can be narrowed when the quality of performance increases.

In conclusion, we propose the above scheme for assessing
Differential Assay of Salivary and Pancreatic α-Amylase in Serum and Urine, with Use of Monoclonal Antibody to Human Salivary Amylase Immobilized on Bacterial Cell Wall

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We previously reported (Clin Chim Acta 1986;159:89) that bacterial cell wall chemically coated with a monoclonal antibody specific to human salivary (S) amylase (EC 3.2.1.1) could be successfully used to separate S and pancreatic (P) amylase in solution. We have now applied this method to serum and urine samples and found that the activities of S and P amylases so measured correlated well with those measured by the isoamylase inhibitor method. The present method is simple and reliable for routine clinical tests.

Additional Keyphrases: isoenzymes · enzyme activity · enzyme inhibition assay compared · salivary · pancreatic · cancer

Differential assay of pancreatic (P) and salivary (S) amylase is important in clinical diagnosis, P amylase being increased in sera of patients with acute pancreatitis, S amylase in sera of patients with parotitis or some cancers. Therefore, several methods for differential assay of amylases have been developed based on electrophoresis (1–5), column chromatography (6, 7), radioimmunoassay (8–10), and amylase inhibitor from wheat germ (11–13). All these involve some problems. Electrophoresis and chromatography are time consuming and are inappropriate for prompt assay of many samples. The radioimmunoassay (10) has restrictions for practical use and does not separate the two isoenzymes completely. The amylase inhibitor method (11–13) is easy, but the inhibitor does not totally differentiate the isoenzymes, S amylase and P amylase being inhibited by 80–83% and 12–20%, respectively. Mifflin et al. (14) also have recently described a method for differential assay of the amylases with use of a monoclonal antibody immobilized on poly(vinylidene fluoride), and they showed its good differentiating ability.

In a previous study, we reported establishing a hybridoma that produced a monoclonal antibody specifically reactive with S amylase, but not with P amylase (15). The antibody, immobilized on bacterial cell wall, showed excellent differentiation of S and P amylase isoenzymes. Here we describe further applications of the method to serum or urine from patients or normal subjects. Values for amylase activity as measured by this method are compared with those measured by the amylase inhibitor method.

Materials and Methods

Serum (n = 78) and urine (n = 25) specimens were collected in Kohka Hospital.

Immunized monoclonal antibody was prepared as described previously (15) and used for separating the amylase isoenzymes in these samples as follows: Incubate 40 μL of amylase solution with 20 μL of monoclonal antibody preparation for 6 min at 37 °C and centrifuge for 1 min at 1000 × g. Then add 20 μL more antibody preparation and re-centrifuge. Remove 20 μL of the supernate to another test tube and incubate with 1 mL of amylase substrate solution according to the directions for the amylase assay kit (Hoechst Japan, Tokyo, Japan).

For differential assay of the amylases by the amylase inhibitor method, we used Phadebas Amylase Inhibitor A

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