Quality assessment of blood glucose monitors in use outside the hospital laboratory

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SUMMARY The quality of analytical results required in clinical practice is generally dictated by analytical rather than clinical criteria. The increasing availability of analytical technology that can be used outside the hospital laboratory challenges this situation. In an attempt to highlight this dilemma one method of glucose analysis outside the laboratory has been assessed using a pilot external quality assessment scheme (EQAS) and the results have been compared with the performance of the same machines in the laboratory.

In the laboratory reliable results were obtained when the Glucometer was used by experienced laboratory personnel giving a good correlation of results ($r = 0.96$) when compared with an automated method. The results of the EQAS revealed that 44% of hospital ward glucose estimations and 63% of general practice estimations would be considered unsatisfactory by conventional laboratory criteria—that is, $> \pm 2$ SD of the mean laboratory result. This level of performance must, however, be considered in relation to the number of times that a clinically misleading result is obtained. No analytical system should be used in clinical practice without a continuous, objective assessment of its performance.

It is claimed that monitoring the blood glucose concentration at frequent intervals may lead to a better control of blood glucose in diabetic patients.¹ This may help to reduce the number of hospital admissions and attendances at the outpatient clinic. Good control of blood glucose concentration aims to reduce the incidence and severity of the microvascular complications of diabetes.

Direct monitoring of blood glucose can be undertaken in the home,² in the hospital laboratory^{3,4} and in the hospital ward or general practice surgery. The problem of delay in the availability of results when using the hospital laboratory has been pointed out by Knight.⁵ Monitoring of blood glucose concentrations (in contrast with indirect measurements such as glycosylated haemoglobin) has the advantage of being a direct measure of a relevant parameter and furthermore employs fairly straightforward methodology. The successful monitoring of blood glucose depends on the way in which existing methodology is used.

Several measurements of blood glucose in diabetics are usually required over a period of time. One

way in which this can be achieved is by using disposable reagent strips and a reflectance meter. The Glucometer (Ames Division, Miles Laboratories Ltd, Slough, UK) is a reflectance photometer designed for use with Dextrostix reagent strips. In evaluating the performance of this meter in the present study, three questions were considered to be of interest: (i) the performance of the system under controlled laboratory conditions; (ii) the assessment of the ability of the system to produce a false result when the manufacturer's instructions were not followed precisely and (iii) the performance of the system outside the laboratory.

An evaluation of the Dextrostix/Glucometer system was undertaken with these three questions in mind initially by studying the system in the laboratory and then by setting up an external quality assessment scheme (EQAS) with users in hospital wards and in general practice.

Material and methods

Portable battery operated instruments were used to measure the light reflectance of the colour produced by the reaction of specimens with Dextrostix reagent

strips. Except where otherwise stated the strips were incubated with blood, and for the one minute indicated by an audible alarm on the instrument. Washing followed using the manufacturer's wash bottle and then the strips were blotted prior to reading. The strips were placed in the test chamber and the result in mmol/l indicated on a digital display to one decimal place. Calibration was carried out by using the two plastic reflectance standards supplied by the manufacturer which substitute in the test chamber for reagent strips; the calibration was checked using a control solution, again supplied by the manufacturer. This gives a glucose concentration with a mean of 5.6 mmol/l and is claimed to react in a similar manner to that of an equivalent amount of glucose in whole blood. When using plastic chips for calibration the manufacturers claim the control test is satisfactory if the result lies between 4.8 mmol/l and 7.8 mmol/l. If a satisfactory control result was obtained the instrument was used for subsequent blood glucose determinations.

Instruction in the use of the system was given by the supplier to one operator in the hospital laboratory and to personnel using the machine in hospital wards (nursing staff) and selected general practices (usually the practice nurse). After further familiarisation the system was investigated in the laboratory with particular reference to variation in the size of the blood sample placed on the reagent strip, variation in incubation time, stability of colour produced and failure to keep the calibration chips clean (the same operator used the machine in all cases). The system was examined with strict adherence to the manufacturer's instructions for precision, accuracy and variations in performance when used by different operators in the laboratory.

Eleven hospital wards and 13 general practices participated in the study. The four hospitals taking part were all in Cambridge and the general practices were volunteer practices participating in a pilot study of diabetic community care in Cambridge Health District.

Over a period of five months, two solutions of glucose in benzoic acid were distributed monthly to the participants. They were asked to treat the samples as specimens of capillary blood and to estimate the glucose concentration within three days using the ward or general practice machine. Samples of the same solutions were also sent by post to the originating laboratory and the glucose concentrations estimated 20 times for each solution using the laboratory Glucometer which had been checked for performance against a laboratory autoanalyser.

Over the same period of time each of the participating practices was asked to send to the laboratory samples of capillary and venous blood (in

fluoride oxalate containers) from two randomly chosen diabetic patients whose capillary blood glucose had been measured at the same time by the participant using the practice Glucometer. The blood glucose concentrations of the capillary and venous samples received were determined in an IL919 analyser employing a modified Trinder method.⁶

Results

LABORATORY TRIAL

Variation of the size of the sample placed on the reagent strip

A sample volume of 120 μ l is required to cover the reagent strip of Dextrostix. The effect of varying the sample size from 20 μ l up to 100 μ l—that is, underloading—was assessed and the results are shown in Table 1 compared with the results for correct loading. Extreme underloading produced a significant reduction in the mean level of blood glucose registered.

Variation of incubation period

The effect of ignoring the one minute audible warning was investigated for a delay of up to 30 s. The results on 20 estimates at each period are shown in Fig. 1. Prolonged incubation produced a significant increase in the concentration of blood glucose registered.

Stability of colour produced

The effect of delay in reading the colour produced after incubation for one minute and washing was investigated up to a delay of five minutes after washing and the results showed no significant differences in the mean glucose values obtained.

Variation of washing time

It was noted, particularly with aqueous control solutions, that some of the colour produced was removed at the washing stage. As this might affect the final result the washing period was varied whilst using the same technique. Two blood samples and one aqueous control sample (DextracheckTM) were

Table 1 *Effect of drop size of heparinised blood on glucose result (p value based on comparison of given volume with 100 μ l)*

No of observations	Volume (μ l)	Mean glucose (mmol/l) $\pm$ SD (and range)	p value
10	20	2.0 $\pm$ 0.58 (1.3–3.1)	<0.001
10	50	3.3 $\pm$ 0.11 (3.0–3.4)	<0.05
10	100	3.4 $\pm$ 0.11 (3.2–3.5)	—
10	120	3.4 $\pm$ 0.10 (3.2–3.5)	—

Fig. 1 Effects of ignoring audible indicator system on glucose result. (Barlines indicate range and points indicate mean for each time delay; p value based on comparison of given time delay with zero time delay.)

analysed with washing times varying from five seconds to 25 seconds under a continuous but mild jet of water.

In the case of the aqueous solution the result fell from 9.5 mmol/l after washing for five seconds down to 5.9 mmol/l when washing for a period greater than 15 s. In the case of the blood samples over the same washing period the results fell from 12.9 to 10.3 and 10.6 to 7.3 mmol/l. In each case where blood was used it was noted that the cells were removed at the washing or blotting stage.

Failure to clean calibration chips

The effect of dirty calibration chips was investigated by smearing the calibration chips with finger prints and household dust. There was little effect on the blood glucose values obtained.

System imprecision (one operator)

This was assessed by repeated measurement over a short time interval of blood glucose in heparinised specimens with a range of values (Table 2). Optimal function was observed with a mean blood glucose of 5.5 ± 0.15 mmol/l. In a separate test daily variations in precision were evaluated by measurements of glucose in aqueous quality control material (Gibcotrol Normal) for 20 consecutive working days (Table 3). The coefficient of a variation observed was 2.4%.

System imprecision (six operators)

Six laboratory personnel were instructed in the use of the equipment and then asked to analyse consecutively aliquots of the same heparinised blood sample 10 times (Table 4). The coefficient of variation of individual operators varied from 2.6%–9.6%. The delay in completing the experiment (approximately 2 h) probably accounts for the change in the mean glucose concentration.

Table 2 Variation in imprecision with differing glucose values (one operator)

Specimen No*	No of observations	Mean glucose (mmol/l) $\pm$ SD	CV (%)
1	10	2.1 ± 0.09	4.3
2	10	5.5 ± 0.15	2.7
3	10	9.2 ± 0.46	5.0
4	10	13.4 ± 0.62	4.6

*Specimens were heparinised capillary blood.

Table 3 Day to day imprecision using quality control material (one operator)

Day	Glucose (mmol/l)
1	6.4
2	6.3
3	6.0
4	6.1
5	6.2
6	6.1
7	6.1
8	6.4
9	6.5
10	6.1
11	6.3
12	6.2
13	6.4
14	6.4
15	6.3
16	6.0
17	6.3
18	6.4
19	6.1
20	6.3

Glucose = 6.2 ± 0.15 mmol/l.
CV = 2.4%.

Table 4 System performance with different operators

Operator	Mean glucose (mmol/l) $\pm$ SD (and range)	CV (%)
1	4.9 ± 0.17 (4.6–5.1)	3.5
2	4.5 ± 0.43 (3.4–5.1)	9.6
3	4.4 ± 0.13 (4.2–4.6)	3.0
4	4.0 ± 0.21 (3.5–4.2)	5.3
5	3.6 ± 0.10 (3.5–3.7)	2.6
6	3.9 ± 0.27 (3.1–4.1)	6.9

System accuracy

The whole blood glucose of a random group of 50 heparinised specimens was measured on the Glucometer immediately prior to plasma glucose estimation using a continuous flow analyser technique based on the Trinder method.⁶ The regression comparing these results (Fig. 2) was estimated using the method of Deming⁷ giving a correlation coefficient of 0.95.

EXTERNAL QUALITY ASSESSMENT

Glucose solution sent to participants

The results obtained for the samples distributed to the hospital wards are shown in Table 5. Table 6 shows the results for general practices. The propor-

Fig. 2 Blood glucose values obtained with Glucometer in laboratory compared with plasma glucose values measured on multichannel analyser. Regression line is $y = 0.92x + 0.09$ (Deming method) and correlation coefficient = 0.95 ($n = 50$).

tion of hospital ward results judged acceptable by usual laboratory criteria—that is, within mean ± 2 SD—was 56%. The proportion of general practice results that would be judged acceptable by these same criteria was 37%. The number of “grossly inaccurate” results ($> \pm 5$ SD) was greater in the hospital ward series, being 26/50 (52%) compared with 40/82 (48%) for the general practice results. In

both cases these figures exclude the results from specimens 2a and 2b.

Capillary and venous blood specimens sent to the laboratory

General practice results are compared with laboratory venous blood and capillary blood measurements in Figs. 3 and 4 respectively. The regression comparing venous blood and capillary results with general practice results yielded correlation coefficients of 0.87 and 0.73 respectively (Deming method).⁷

Discussion

The use of test strips and their associated instrumentation in the monitoring of diabetic control has been the subject of some controversy. Borthwick and Ross⁸ emphasised the need to assess the performance of the meters themselves. Day, Archer and Metcalfe⁹ felt that Legg and Sammons¹⁰ overestimated the performance requirements of home Glucometers. The former make light of the occasional “unusual result” obtained with a home glucose monitor and state without evidence that the use of Dextrostix “probably accounts for most of the variation observed.” No assessment of variation due to the operator was made by these authors. They

Table 5 Comparison of laboratory estimations and hospital ward estimations of aqueous glucose solutions distributed by the laboratory

Specimen	Laboratory mean glucose (mmol/l) $\pm$ SD	No of ward estimations	Range of ward glucose estimations (mmol/l)	Mean ward glucose result	No of ward results acceptable in lab practice
2a	>22.2	11	All >22.2	>22.2	11
2b	>22.2	11	All >22.2	>22.2	11
3a	4.8 ± 0.19	10	2.0–12.5	4.9	2
3b	2.7 ± 0.13	10	1.5–4.1	2.8	4
4a	2.6 ± 0.14	4	1.6–2.7	2.0	3
4b	6.1 ± 0.28	4	1.5–7.3	5.3	4
5a	6.5 ± 0.20	9	3.5–13.4	7.3	2
5b	12.3 ± 0.41	9	5.5–19.1	11.2	1
Total	—	68	—	—	38

Table 6 Comparison of laboratory estimates and general practice estimations of aqueous glucose solutions distributed by the laboratory

Specimen	Laboratory mean glucose (mmol/l) $\pm$ SD	No of GP estimations	Range of GP glucose estimations (mmol/l)	Mean GP glucose result (mmol/l)	No of GP results acceptable in lab practice
1a	7.5 ± 0.23	7	6.9–11.8	9.2	1
1b	17.4 ± 0.68	7	16.2–22.2	18.8	3
2a	>22.2	8	All >22.2	>22.2	8
2b	>22.2	8	All >22.2	>22.2	8
3a	4.8 ± 0.19	10	2.1–4.3	2.9	0
3b	2.7 ± 0.13	10	2.5–5.6	4.2	1
4a	2.6 ± 0.14	13	1.3–4.4	2.8	4
4b	6.1 ± 0.28	13	5.9–8.2	6.7	6
5a	6.5 ± 0.20	11	4.5–8.6	6.2	5
5b	12.3 ± 0.41	11	7.2–19.0	10.2	0
Total	—	98	—	—	36

Fig. 3 Blood glucose values obtained with Glucometer in general practice compared with plasma glucose values measured on IL919 analyser. Regression line is $y = 1.1x + 0.2$ (Deming method) and correlation coefficient = 0.89 ($n = 37$).

Fig. 4 Blood glucose values obtained with Glucometer in general practice compared with capillary blood glucose values measured on IL919 analyser. Regression line is $y = 1.4x - 2.5$ (Deming method) and correlation coefficient = 0.80 ($n = 42$).

also stated that the Hypocount monitors were "certainly accurate enough to provide blood glucose profiles for the more intelligent adjustment of diabetics insulin regimes." Webb *et al*¹¹ studied patient preference, laboratory performance and electronic functioning of four alternative blood glucose monitor systems. Accuracy was stated in an unorthodox fashion and reproducibility tests were unre-

lated to the absolute glucose concentration. Again, errors seen in the use of blood glucose monitor systems were blamed on the test strips without supporting evidence. Comparison of the data produced by a meter system and laboratory analysis was presented graphically without further statistical analysis. The usefulness of their comparisons were limited by the fact that the comparative Autoanalyser method measured total reducing substances.

Worth *et al*¹² suggest that "reagent strips themselves provide an important variable and should not be ignored." Their findings were consistent with those of the present study in stressing the importance of accurate incubation periods, but they found a slight increase in apparent glucose concentration when reading the strip was delayed for up to 20 s.

As in the study of Pantin *et al*,¹³ we were concerned with a more extensive assessment of an individual blood glucose monitoring system than has previously been available. The results of the machine in the laboratory were both accurate and satisfactorily precise. The importance of adequately loading the reagent strip has been demonstrated. The short term stability of stick colour after incubation and washing was also confirmed. Significant variation in precision between laboratory operators was detected. Assessment of accuracy in this experiment was not possible as the concentration of blood glucose in the whole blood specimens would have decreased over the time taken for six operators to each make 10 successive recordings. The results reported here compare favourably with those Pantin *et al* obtained using Glucochek machines.

The study of readings taken on the hospital ward indicated that 56% of results fell within ± 2 SD of the mean laboratory result. However, in this part of the study more grossly inaccurate results were obtained than were seen in the general practices where only 37% of the results were within ± 2 SD of the mean laboratory result. No cases of gross hyperglycaemia was missed, although in several instances inappropriate degrees of hypoglycaemia would have been diagnosed. It was noted during the study that some operators consistently fared better than others. Several participants confirmed the laboratory observation that the spreading characteristics of the glucose solution were not identical to those of blood and tended to give the reagent strip a speckled appearance. This factor should be taken into account in designing a future EQAS for this machine. The larger number of grossly inaccurate hospital results in the hospital series may, at least in part, be due to several junior nursing staff performing analyses whereas in the general practices, one experienced nurse or medical practitioner assumed responsibility for all measurements.

The comparisons of results on specimens sent in by the general practice staff, however, showed a poorer correlation with the laboratory result than that obtained when a similar comparison was undertaken using a Glucometer in the laboratory.

The outcome of this pilot study shows that the results of analyses undertaken outside the laboratory do not meet the performance criteria established and employed on a day to day basis in the laboratory. However, it is not clear whether the degree of accuracy and precision obtained in most laboratory glucose analyses are required for the day to day management of diabetes on the ward or in general practice. Before the performance of the reflectance meter system outside the hospital laboratory can be correctly judged the clinician must indicate what quality of analytical service is required. At the present moment there are very few data on which this decision can be made because previous analyses of blood glucose measurements have been based on the laboratory service. It is vital therefore that the clinical need be defined and the performance of analytical systems outside the laboratory should be reviewed in this light. Any clinician undertaking extra-laboratory glucose analyses should have access to an external quality assessment scheme.

The results of this work have now been reported to and discussed with the general practitioners, nurses and hospital physicians who took part in the study. The general view among the clinicians was that they were reassured about the performance of the system and that an EQAS should be set up on a continuous basis. In the light of experience gained in this study, such a scheme has now been established and will serve to warn general practitioners and others if the results obtained from their practice fall outside accepted standards of accuracy. New technology will inevitably mean that more and more biochemical investigations can be undertaken outside the laboratory and it is important that hospital laboratories cooperate with clinicians practising out-

side hospitals (as well as hospital clinicians) to ensure that acceptable standards of performance are laid down and maintained. In our experience such a service offers an important educational and problem solving facility as well as contributing indirectly to patient care.

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