Comparison of the HemoCue β-Glucose Photometer and Reflotron for Open Heart Surgery

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The HemoCue β-glucose photometer (Angelholm, Sweden) was evaluated for use in monitoring blood glucose in both diabetic and nondiabetic patients undergoing open heart surgery. Because occasional discrepancies were noted in patients with low total proteins when the Reflotron (Boehringer Mannheim, Indianapolis, IN) was used for this purpose, the effects of protein and hematocrit on glucose results from both instruments were investigated and compared with plasma values from a Paramax 720 ZX (Baxter Healthcare, Irvine, CA). Linear-regression analysis of the HemoCue results (y) versus Paramax (x) yielded $y = 0.956x + 0.35$, $r^2 = 0.980$, with $Sy/x = 0.57$ mmol/L (10.3 mg/dL). Results from the Reflotron (y) versus Paramax (x) yielded $y = 1.075x - 0.10$, $r^2 = 0.964$, with $Sy/x = 0.99$ mmol/L (17.8 mg/dL). Bias plots of (HemoCue - Paramax) or (Reflotron - Paramax) versus glucose, hematocrit, or protein showed no effect of glucose on the results from either instrument and no effect of protein or hematocrit on the HemoCue findings. The Reflotron, however, showed a positive bias of up to 3.5 mmol/L (63 mg/dL) at protein concentrations between 30-40 g/L (3.0-4.0 g/dL) and a possible positive bias at low hematocrit levels. (Key words: Glucose assay; Protein effect; Hematocrit effect; HemoCue β-Glucose Photometer; Reflotron) Am J Clin Pathol 1993;100:130–134.

The need for a rapid turnaround of glucose results in critical care settings involving diabetic patients is widely accepted. Patients in diabetic ketoacidosis or undergoing surgery can experience rapid and dramatic changes in blood glucose levels. Proper maintenance of blood glucose in these patients, through intravenous insulin administration, requires frequent measurements with minimal delay in reporting results.

The introduction of small, whole blood glucose analyzers allowed many laboratories to decrease their turnaround time and improve care by moving testing closer to the patient in these situations.1 Test strips, read visually or by reflectance meters, however, have been fraught with problems when implemented in the critical care unit in a hospital. Some meters do not have adequate accuracy, particularly in the hypoglycemic range, and are susceptible to errors associated with the use of finger-stick, capillary samples. The capillary sample itself has been shown to introduce error in patients who are hypotensive or who have increased or decreased hematocrits. Severe anoxia or unstable oxygenation may also cause errors in glucose measured amperometrically. Additional variability can be introduced when testing is done infrequently by multiple individuals with varying degrees of training.10

A previous report describes our use of the Reflotron (Boehringer Mannheim, Indianapolis, IN) for bedside testing on patients with diabetic ketoacidosis and diabetic patients undergoing transplant or open heart surgery. The Reflotron provides significant improvement in accuracy over the reflectance meters originally designed for home monitoring. However, we have noted occasional discrepancies in Reflotron results from patients undergoing open heart surgery compared with Beckman Glucose Analyzer 2 (Beckman Instruments, Brea, CA) values. Because the HemoCue β-Glucose (HemoCue AB, Angelholm, Sweden) Photometer has demonstrated good analytic performance characteristics,11 we evaluated it as an alternative for these applications. The results were compared with laboratory-determined plasma values, and the influence of hematocrit and plasma protein concentration on both the HemoCue and the Reflotron findings was investigated.

MATERIALS AND METHODS

The HemoCue β-glucose photometer (Angelholm, Sweden) is a hand-held, battery-powered photometer that measures glucose in whole blood after lysing red cells with saponin or in plasma using any of the common anticoagulants. A 5-μL specimen is drawn by capillary action into the measurement cuvette and mixed with dried reagents. The cuvette is then placed in the photometer, and the sample is measured undiluted at wavelengths of 660 and 840 nm. Measurement, using a modified glucose dehydrogenase method,12 is made at an end point that varies, depending on the glucose concentration, from less than 90 to 240 seconds.

Heparinized arterial blood gas samples from 50 open heart surgical cases were obtained while the patients were undergoing cardiopulmonary bypass and measured within 10 minutes of receipt on both the HemoCue and the Reflotron. After sampling for these two instruments, the remaining specimen was...
immediately centrifuged, and the plasma was assayed for glucose and total protein on a Paramax 720 ZX (Baxter Healthcare, Irvine, CA). All measurements were completed within 30 minutes of receipt of the sample.

Within-run imprecision of the HemoCue was determined at two levels by assaying 10 replicates of two different heparinized blood gas specimens. All measurements were completed within 15 minutes. Hematocrits were determined on a Heraeus Haemo-Fuge (Osterode, FRG).

The results were subjected to linear-regression analysis with their correlation determined by the method of Pearson. Bias between the results from the HemoCue or the Reflotron and the Paramax was evaluated using the bias plot described by Bland and Altman. Mean values were compared using the paired Student’s t-test.

RESULTS

Imprecision Study

The within-run imprecision of the HemoCue photometer, obtained for 10 replicates of two different heparinized arterial whole blood samples, yielded standard deviations of 0.112 mmol/L (2.0 mg/dL) or 2.22% coefficient of variation at 5.02 mmol/L (90.4 mg/dL) glucose and 0.128 mmol/L (2.3 mg/dL) or 1.40% coefficient of variation at 9.12 mmol/L (164.2 mg/dL) glucose.

The within-run standard deviation obtained for the Reflotron in a previous study was 0.13 mmol/L (2.3 mg/dL) or 2.4% coefficient of variation at 5.5 mmol/L (99 mg/dL) glucose, and the comparable figure for the Paramax was 0.05 mmol/L (0.9 mg/dL) or 0.97% coefficient of variation at 5.1 mmol/L (91.8 mg/dL) glucose.

Correlation Study

Of the 60 samples selected for comparison, one result fell outside the measurement range of the HemoCue. The remaining 59 results covered a range of 1.67 mmol/L (30.1 mg/dL) to 21.61 mmol/L (389 mg/dL). Linear regression of HemoCue results (y) on those from the Paramax 720 ZX (x) yielded a linear relationship with $y = 0.956x + 0.35$, $r^2$ of 0.980, and a standard error of the estimate of 0.57 mmol/L (10.3 mg/dL).
Paramax values ranged between 0.89 mmol/L (16 mg/dL) and 22.61 mmol/L (407 mg/dL). The mean difference between HemoCue and Paramax results was −0.014 mmol/L (0.31 mg/dL) (HemoCue − Paramax) and was not significant by the paired t-test.

All 60 samples fell within the measurement range of the Reflotron and yielded values between 1.67 mmol/L (30 mg/dL) and 30.22 mmol/L (544 mg/dL). A linear relationship was again obtained on the regression of Reflotron results (y) on those from the Paramax (x), with \( y = 1.075x - 0.10 \), \( r^2 \) of 0.964, and a standard error of the estimate of 0.99 mmol/L (17.8 mg/dL). The mean difference (Reflotron − Paramax) of +0.548 mmol/L (9.9 mg/dL) was significant by the t-test, with \( P < 0.0001 \).

**Bias Plots**

Figures 1 and 2 illustrate the effect of hematocrit on the difference between paired results from either the HemoCue or the Reflotron and the Paramax, respectively. In each case, Paramax values were subtracted from those from the evaluation analyzer so the differences would have the same sign as the apparent bias. Figures 3 and 4 illustrate the effect of plasma total protein on the same paired differences. Plots of the differences versus Paramax glucose values revealed no evident bias in the results from either the HemoCue or the Reflotron as a function of the glucose level (data not shown).

Figure 5 illustrates the differences between the Reflotron and the Paramax as a function of the hematocrit after adjusting the values for the effect of protein according to the following formula:\(^\text{15}\)

\[
d_{\text{adj}} = d - b (p - \overline{p})
\]

Eq. 1

In this equation \( d_{\text{adj}} \) is the adjusted difference, \( d \) is the observed difference, \( p \) is the protein level, \( \overline{p} \) is the average protein level, and \( b \) is the regression slope of the difference (Reflotron − Paramax) versus the protein level (Fig. 4).

**DISCUSSION**

Because of its ability to determine glucose quickly in whole blood, we have used the Reflotron analyzer to monitor glucose
in diabetic patients undergoing renal transplant or open heart surgery, or for bedside testing of patients experiencing diabetic ketoacidosis. On several occasions, when Reflotron values exceeded our imposed upper limit of 500 mg/dL (27.8 mmol/L), the results for the same sample, measured on a Beckman Glucose Analyzer 2, fell below 500 mg/dL. Patients undergoing open heart surgery commonly receive plasma-expanding agents, and it has been shown that these agents and others given during the use of extracorporeal circulation may lower the hematocrit and total protein concentration of the plasma within 10 minutes of the time they are started. Further investigation of samples with both low and high total proteins indicated an apparent effect on the Reflotron that varied with the total protein concentration (data not shown).

The HemoCue analyzer provides an alternative with a comparable turnaround time and specimen requirements, which does not use a test strip for measurement. Both the HemoCue and the Reflotron were, therefore, evaluated for the effects of hematocrit and total protein and for general analytic agreement with plasma glucose values determined on a Paramax 720 ZX. The levels of within-run imprecision observed with the HemoCue were analytically acceptable and compared favorably with values reported by Rundell and associates. Because the HemoCue reagent system incorporates saponin to lyse red cells, it measures true whole blood glucose. The Reflotron, in contrast, restricts red cells from the measurement area of its test pad and measures plasma glucose. Both analyzers correlated well with the Paramax, but the HemoCue showed a slightly higher r² value (0.980) than the Reflotron (0.964). Both regression slope values are significantly different from unity with P < 0.0001.

The results from the HemoCue do not show the expected 10−15% lower values of whole blood compared with plasma, and because the negative 4% proportional bias is offset by a positive constant bias in the regression data, the values are not significantly different from those of the Paramax by paired t-tests. This effect is also evident in the bias plots of Figures 1 and 3 in which the points center around the zero-difference line. Because the actual difference observed between whole blood and plasma depends on the hematocrit, this finding may be partially explained by the low hematocrit values obtained for most of the samples in this study.

Reflotron results show a statistically significant difference by paired t-test (P < 0.0001) as a result of the fact that the positive proportional bias of 7.5% is not completely offset by the negative constant bias in these data. This effect is also evident in the bias plots of Figures 2 and 4, in which the points center above the zero-difference line. These biases may also be caused, in part, by differences in the calibration approach applied to the analyzers, something that cannot be altered with either the Reflotron or the HemoCue, because they are factory set.

The bias plots also indicate no apparent bias in the HemoCue as a result of variations in hematocrit (Fig. 1), at least up to the level of 50%. The two elevated points labeled 1 and 2 were from samples with total protein concentrations of 47 g/L (4.7 g/dL) and 63 g/L (6.3 g/dL), respectively, and glucose concentrations of 4.55 mmol/L (81.9 mg/dL) and 0.89 mmol/L (16 mg/dL), respectively. The low point labeled 3 was from a sample with a protein of 79 g/L (7.9 g/dL) and a glucose of 19.05 mmol/L (342.9 mg/dL). These same three samples appear in the plot of HemoCue differences versus total protein (Fig. 3) as the two highest and lowest points again. The lack of consistency in the hematocrit, protein, and glucose levels associated with these points makes it difficult to ascribe these deviations to any particular cause. There appears, therefore, to be no significant effect of protein level on the HemoCue results in Figure 3.

Figures 2 and 4 illustrate more noticeable effects in the results from the Reflotron. These plots show a positive bias in glucose results at low levels of hematocrit or protein. Because the apparent effect of hematocrit evident in Figure 2 could be caused by the protein concentration, these differences were adjusted to remove the effects of protein according to Equation 1. In fact, the six most positive points between 20–35% hematocrit all have protein concentrations between 30–40 g/L (3.0–4 g/dL); the one low point at 47% has a protein of 79 g/L (7.9 g/dL). A similar distribution of higher differences at lower hematocrits remains evident in Figure 5, however, indicating a slight effect of hematocrit on the Reflotron results. The effect of protein on the Reflotron is clearly seen in Figure 4, where the points below 40 g/L (4.0 g/dL) are almost all above the zero-difference line, with increasing positivity at lower protein levels. A negative effect of high protein values is less pronounced but also may exist.
The change in plasma matrix introduced by a low total protein concentration or hematocrit may increase the amount of plasma available for analysis in the Reflotron glucose test strip. The effect observed in this study could produce misleading glucose results in patients with low protein levels, causing values to be artificially elevated by as much as 3.5 mmol/L (63 mg/dL).

In conclusion, we evaluated the HemoCue β-glucose photometer and the Reflotron for the effects of hematocrit and total protein on the measured glucose values. The HemoCue shows no effect of either and appears to be well suited to use in open heart surgery or other critical care applications. The Reflotron is affected by the protein concentration and, to a lesser extent, by the hematocrit, with glucose values artificially elevated in samples with low total proteins.

REFERENCES