



Comparison of POCT and central laboratory blood glucose results using arterial, capillary, and venous samples from MICU patients on a tight glycemic protocol

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ABSTRACT

Background: Point of care (POC) glucose meters are routinely used to monitor glucose levels for patients on tight glycemic control therapy. We determined if glucose values were different for a POC glucose meter as compared to the main clinical laboratory for medical intensive care unit patients on a tight glycemic protocol and whether the site of blood sampling had a significant impact on glucose values.

Methods: Eighty-four patients (114 paired samples) who were on a tight glycemic protocol in the period November 2005 through August 2006 were enrolled. After simultaneous blood draws, we compared the glucose levels for the glucose meter (arterial/venous/capillary), blood gas (arterial/venous), and central clinical laboratory (serum/plasma from arterial/venous samples).

Results: The mean glucose levels of all arterial/venous/fingerstick samples using the glucose meter demonstrated a positive bias of 0.7–0.9 mmol/l (12.6–16.2 mg/dl) ($p < 0.001$) relative to central laboratory venous plasma. There was also a smaller positive (0.1–0.3 mmol/l or 1.8–5.4 mg/dl, $p < 0.05$) bias for arterial/venous blood gas samples and laboratory arterial serum/plasma glucose samples. Using Parkes error grid analysis we were able to show that the bias for arterial or venous POC glucose results would have not impacted clinical care. This was not the case, however, for fingerstick sampling where a high bias could have significantly impacted clinical care. Additionally, in 3 fingerstick samples a severe underestimation (<46% of the central laboratory plasma result) was found.

Conclusion: Glucose meters using arterial/venous whole blood may be utilized in the MICU; however, due to the increased variability of results we do not recommend the routine use of capillary blood sampling for monitoring glucose levels in the MICU setting.

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1. Introduction

Recent research in critical care medicine has provided substantial evidence that maintaining normal or close to normal glucose levels (tight glycemic control) in critically ill patients reduces both morbidity and mortality [1–7]. This has led to the integration of tight glycemic control therapy into the majority of intensive care units. However, this approach has also been associated with increased numbers of hypoglycemic episodes in part because many of the patients in a medical intensive care unit (MICU) setting are unable to communicate and the signs of hypoglycemia are not readily apparent. It is therefore essential that rapid and accurate glucose results are provided to physicians and nurses. For this reason, and to guide insulin dosing, glucose is usually measured at the point of care (POC), in the past using either blood gas

instruments but more recently hand held glucose meters, rather than in the central clinical laboratories.

A number of studies have compared the accuracy of POC glucose meters with other established laboratory methods [8–16]. While the correlation was acceptable in most of the studies, there has been and continues to be a concern about the reproducibility and accuracy of results using POC glucose meter. An additional concern is the use of capillary sampling in critically ill patients with hypotension or edema [8,9,14,16,18]. For these reasons a recent survey of ICU physicians expressed concern about the accuracy of POC glucose meters in critically ill patients [17].

Because of these concerns we designed a QA project to answer the following questions:

1) how do the glucose results for arterial, venous, and capillary whole blood using a POC glucose meter compare with a blood gas and main clinical laboratory instrument for MICU patients on a tight glycemic protocol, and 2) how is the target range for glucose affected by sample

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type (arterial, venous, or capillary whole blood) and testing method (a POC glucose meter, a blood gas instrument, and a main clinical laboratory instrument) for MICU patients on a tight glycemic protocol?

2. Materials and methods

2.1. Study participants

This quality assurance project was approved by the Institutional Review Board. We enrolled 84 patients that had been admitted to our 10-bed university-affiliated MICU from November 2005 through August 2006. All patients had been placed on our institution's tight glycemic protocol and the glucose levels monitored. The insulin infusions were titrated using glucose meters and arterial whole blood glucose test results. If the blood glucose level was less than 2.2 mmol/l (40 mg/dl), or at the discretion of the bedside nurse, 25 ml of 50% dextrose was administered intravenously, and blood glucose measurements were taken every 15 to 30 min until blood glucose reached at least 5.0 mmol/l (90 mg/dl) and then hourly thereafter until stabilization. Those patients without arterial and central venous access were excluded from the study. In addition to the glucose results we also documented blood pressure. Patients that were hypotensive were placed on vasopressors (norepinephrine, dopamine, or a combination of the 2 agents).

2.2. Glucose measurements

A total of 114 paired sets of blood samples from 84 patients were taken for analysis; for the study no patient had more than two sets of glucose measurements during their ICU stay. Samples from the arterial and central venous catheters were collected in serum separator or heparin tubes and capillary whole blood, collected by finger stick. The three sample types were collected within 5 min of each other analysis on the POC meter, blood gas instrument, or the main clinical laboratory. The samples were analyzed as follows: 1) drops of blood from all three sources were analyzed on a POC glucose meter (Accu-Chek® Inform, Roche Diagnostics, Indianapolis, IN) in the MICU, 2) samples for arterial and venous blood gas analyses were collected from a catheter in a syringe containing lithium heparin, capped and tested in the MICU on a blood gas instrument (Rapidpoint® 405, Bayer Diagnostics, Tarrytown, NY) within 5 min of collection, 3) arterial and venous blood samples were collected in lithium heparin and serum separator tubes and sent to the main clinical laboratory for analysis (either Vitros® 950 or 5.1 FS, Ortho-Clinical Diagnostics, Raritan, NJ). The serum and plasma were separated within 45 min of collection. Hypoglycemia was defined as a main clinical laboratory venous plasma glucose <3.9 mmol/l (70 mg/dl) and clinically significant hypoglycemia was defined in our MICU protocol as <2.2 mmol/l (40 mg/dl).

The central clinical laboratory result for central venous plasma was considered the reference standard. The Accu-Chek® Inform uses test strips (Accu-Chek® Comfort Curve test strips) which are calibrated by the manufacture to give agreement with plasma results. The system uses a glucose dehydrogenase-based amperometric biosensor for the measurement of glucose in arterial, venous or capillary whole blood. Two lots of glucose strips were used during the study and the imprecision of the meter for the entire hospital ($N > 9000$ QC data points per lot) during the study was 6.5–8.3% for a level of 3.3 mmol/l (60 mg/dl) and 5.1–5.6% for a level of 18.3 mmol/l (329 mg/dl). As a comparison the imprecision for the blood gas instruments ($N > 2400$ QC data points) was 3.6% and 4.1% for glucose levels of 2.8 mmol/l (50 mg/dl) and 11.2 mmol/l (202 mg/dl), respectively, and the imprecision for the main laboratory ($N > 380$) was 3.0% and 2.6% for glucose levels of 5.0 mmol/l (90 mg/dl) and 15.3 mmol/l (275 mg/dl), respectively. The POC glucose measurements were performed by skilled nursing staff and blood gas measurements were performed by respiratory therapists. Both were trained and educated in the proper use of the instruments. Quality control was performed according to hospital protocols, every 8 and 24 h for blood gas and POC glucose meters, respectively.

2.3. Statistical analysis

All results were expressed as mean \pm SD. The results were analyzed using SAS V9.1 (SAS Institute Inc., Cary, NC) to determine the significance between the groups. A regression model was used to determine the possible impact of blood pressure on the capillary blood glucose levels. Paired *t*-tests were used to determine if there was a significant difference

between the means of the type of specimen based on the methodology of measuring glucose. A 2-tailed $p < 0.05$ was considered the criterion for statistical significance.

Clinical impact of the differences in the glucose measurements was assessed by consensus error grid analysis as described by Parkes et al. [19]. The error grid is divided into 5 risk categories: a) the difference in glucose value has no effect and no clinical action is necessary, b) the difference in glucose value alters or causes a change in the clinical action but has no or minimal impact on the clinical outcome, c) the difference in glucose value causes a change in the clinical action and will likely impact the clinical outcome, d) the difference in glucose value causes a change in the clinical action that will probably place the patient at significant medical risk and e) the difference in glucose value causes a change in the clinical action that will probably have dangerous consequences.

3. Results

Mean values of glucose levels on arterial and central venous catheter samples (plasma and venous) and capillary samples using the glucose meter, blood gas, and main clinical laboratory instruments are displayed in Table 1. The mean glucose levels of all arterial, venous, and capillary samples using the glucose meter were 0.7–0.9 mmol/l (12.6–16.2 mg/dl) higher than the central venous plasma reference standard ($p < 0.001$). Differences were present irrespective of whether patients were fasting, being given a glucose source, or insulin. The mean glucose levels for the arterial and central venous blood gas and main laboratory arterial serum and plasma were only slightly higher (0.1–0.3 mmol/l or 1.8–5.4 mg/dl, $p < 0.05$) than the reference standard glucose concentrations. The glucose concentration for central venous serum was identical to the reference standard ($p = 0.57$). All methods (POC, blood gas, and central laboratory) were highly correlated to each other and to the reference method ($r = 0.97$ – 0.99) except for glucose meter testing using capillary sampling which had significantly lower correlations ($r = 0.87$ – 0.89).

We used error grid analysis as described by Parkes et al. [19] to analyze the differences between the glucose meter results and the reference standard. Using these criteria we observed no instances of glucose overestimation or underestimation for arterial or venous blood gas, arterial or central venous serum, or arterial plasma. However, we did observe overestimation (risk category B) of the POC glucose levels in 13 (11.3%) arterial, 7 (6.1%) venous and 20 (17.4%) fingerstick samples (Figs. 1–3). None of the results for the POC arterial and venous samples would have resulted in a treatment change that would have impacted the outcome of the patients. For the glucose meters the overestimation was due to a bias relative to the central laboratory venous plasma results as indicated by the respective regression equations $y = 1.068x - 0.36$, $y = 1.036x + 0.47$, and $y = 1.11x + 0.04$ for arterial, central venous, and capillary samples, respectively (see Figs. 1–3). However, in 1 (0.9%) capillary sample severe overestimation (risk category C) was observed that would have changed the treatment. In addition we observed significant underestimation (risk category B) of glucose concentrations in 3 (2.6%) capillary samples which were obtained from severely edematous patients.

4. Discussion

The appropriate hypoglycemic cutoff value is extremely important in patients who are on a tight glycemic protocol and at increased risk of hypoglycemic episodes. This is especially true for the MICU population

Table 1
Mean glucose levels of paired samples for patients on a tight glycemic protocol in a MICU

	Accu-Chek® Inform			Blood Gas		Main Laboratory Serum		Main Laboratory Plasma		
	Arterial whole blood glucose (mmol/l)	Central venous whole blood glucose (mmol/l)	Capillary whole blood glucose (mmol/l)	Arterial glucose (mmol/l)	Central venous glucose (mmol/l)	Arterial glucose (mmol/l)	Central venous glucose (mmol/l)	Arterial glucose (mmol/l)	Central venous glucose (mmol/l)	
All samples	Mean	8.0	7.9	7.8	7.4	7.2	7.3	7.1	7.3	7.1
N = 114	Range	4.3–18.0	4.4–16.8	1.7–23.2	4.0–17.8	3.4–17.4	4.1–17.2	3.9–16.4	4.1–17.0	3.9–16.4
	Range 95% C.I.	7.5–8.5	7.4–8.3	7.3–8.4	6.9–7.8	6.8–7.6	6.9–7.7	6.7–7.5	6.9–7.7	6.1–7.5
<i>p</i> -value	<0.0001	<0.0001	<0.0001	<0.0001	0.038	<0.0001	0.57	<0.0001	– ^a	– ^a

^aUsing central venous plasma glucose as the reference the statistical significance of the differences between groups was determined by two-tailed paired *t*-test. A $p < 0.05$ was considered significant.

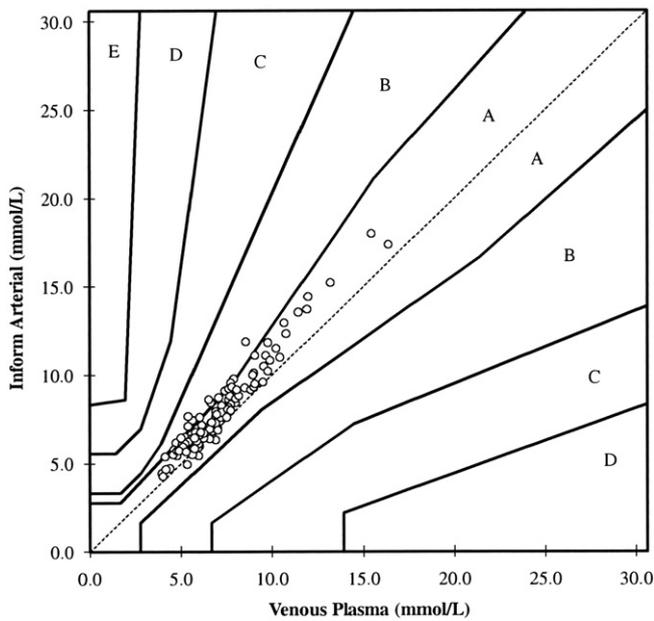


Fig. 1. Comparison of glucose meter using arterial whole blood and the reference standard for all samples. The regression line ($y=1.068x+0.36$, $r=0.97$) of the paired samples is shown for reference.

since many of these patients are not able to communicate with either the physician or nurse and the signs and symptoms of hypoglycemia are not readily apparent. When compared to the reference standard we found that our glucose meters overestimated blood glucose levels in arterial, central venous and capillary samples. These findings are similar to the observations reported by Boyd et al. [16] and Critchell et al. [18]. By using the appropriate regression equations we determined that the lower cutoff value for glucose meter analysis in our institution increased 0.5–0.6 mmol/l (9–11 mg/dl) regardless of the sample type used. Thus for our tight glycemic protocol we established the lower cutoff for samples analyzed by glucose meter to be 4.4 mmol/l (80 mg/dl) for all sample types. The use of the higher cutoff may have reduced the number of episodes where the glucose was <3.9 mmol/l

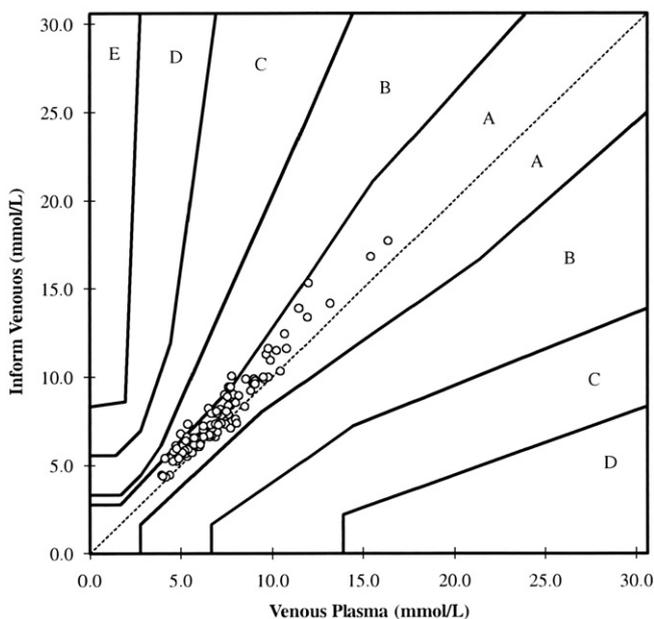


Fig. 2. Comparison of glucose meter using central venous whole blood and the reference standard for all samples. The regression line ($y=1.036x+0.47$, $r=0.97$) of the paired samples is shown for reference.

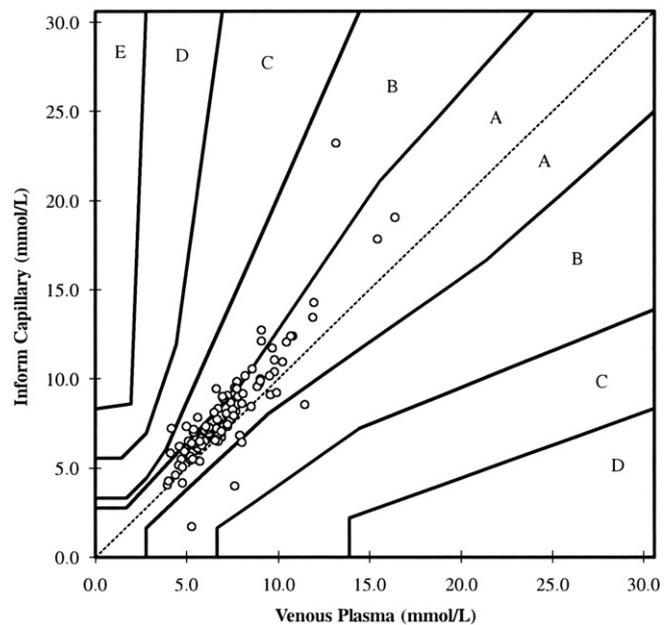


Fig. 3. Comparison of glucose meter using capillary whole blood and the reference standard for all samples. The regression line ($y=1.11x+0.04$, $r=0.88$) of the paired samples is shown for reference.

(70 mg/dl) as measured by the main laboratory. In fact none of our study patients and in $<2\%$ of the total number of glucose results over a 3-month period had glucose values <3.9 mmol/l (70 mg/dl). It is also important to note that as the glucose concentration approached the reference cutoff of 3.9 mmol/l (70 mg/dl) there were no instances of inappropriate treatment (i.e. no change in treatment) with the glucose meter when using either arterial or venous samples. This, however, was not the case for capillary sampling. One sample (0.9%) with a central venous plasma and capillary glucose results of 4.1 mmol/l (75 mg/dl) and 7.2 mmol/l (130 mg/dl), respectively, would have resulted in an error that would likely have impacted the treatment decision (risk category C by Parkes error grid analysis). In this case the use of the capillary glucose result could have placed the patient at significant risk of a hypoglycemic episode.

Interestingly, although hypoperfusion is a known problem in the underestimation of glucose values with capillary sampling [7,9,18], it did not appear to be a major issue in our study. For example, a capillary glucose (9.8 mmol/l or 176 mg/dl) in a patient with blood pressure as low as 74/40 was minimally affected as indicated by a difference of <0.4 mmol/l (7 mg/dl) when compared to either POCT venous or arterial sampling. Additionally, using a regression model blood pressure was shown to have no impact on capillary glucose levels in our study population when compared to the reference standard ($p>0.35$). However, in three patients where severe edema was present there was significant underestimation of the fingerstick glucose results that averaged 46% of the reference standard results (see Fig. 3). This underestimation could have been due to the inability to obtain an adequate capillary sample and may have been more reflective of tissue or interstitial fluid glucose.

There are limitations to our study. First, this study was limited to a single company's glucose meter and may not be reflective of glucose meters from other companies. Second, although our study population included patients who were critically ill and on a tight glycemic protocol, we observed no patients that were hypoglycemic. This was probably due to the low number of patients ($<2\%$ of all samples over a three month time period) with a main laboratory venous plasma glucose value <3.9 mmol/l (70 mg/dl) in our MICU which limited our ability to include such samples in the analysis. Although no patients with glucose levels <3.9 mmol/l (70 mg/dl) were identified in our study, 5 patients were included that had venous plasma glucose concentrations ranging from 3.9–4.4 mmol/l (71–79 mg/dl) that approached the central laboratories

hypoglycemic cutoff of 3.9 mmol/l (70 mg/dl) established for venous plasma samples. Finally, our study was limited to critically ill patients in a MICU and the conclusions about the accuracy of glucose meters may not translate to other populations.

These findings show that the glucose meters are highly correlated with routinely used clinical laboratory instruments and can be utilized in a MICU. However, correlation studies should be performed to assess whether a bias exists between the glucose meter and the reference methodology (venous plasma). With an adequate sample comparison differences between the POCT instrument and the reference method can be used to identify the appropriate cutoff for an institutions tight glycemic protocol for an institutions acutely ill patient population when using a POC glucose device. As shown by our study the overestimation of blood glucose levels using POCT (arterial or venous) glucose meters did not appear to have an impact on treatment decisions as evidenced by the absence of low glucose levels in the study population.

While capillary sampling is useful in non-ICU settings where ischemia and severe edema are rare, we do, however, caution against using capillary sampling to monitor glucose levels in a MICU setting. This is based on the large differences for capillary sampling for four samples when compared to reference standard glucose concentrations (Fig. 3). Although the test strip labeling indicates that capillary testing may be inappropriate in situations of decreased peripheral blood flow which is not uncommon in a MICU setting this can be overlooked as a potential source of error. As indicated by our data and others [12,13,18] the significant underestimation in a limited number of patients could also lead to decreased use of insulin. In addition, since insulin dosing to control the level of glucose in MICUs is usually protocol driven, the overestimation of the glucose value in the one patient (Fig. 3) if capillary sampling was used could have led to the continued administration of insulin, possibility causing an episode of severe hypoglycemia in this patient.

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