Research Article

Validity of bedside blood glucose measurement in critically ill patients with intensive insulin therapy

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Abstract

Background and Aims: There have been variable results on the practice of tight glycemic control, and studies have demonstrated that point-of-care (POC) glucometers have variable accuracy. Glucometers must be accurate, and many variables can affect blood glucose levels. The purpose of this study was to determine the difference between blood glucose concentrations obtained from POC glucometers and laboratory results in critically ill patients with intensive insulin therapy. **Materials and Methods:** This was a descriptive study which enrolled 300 critically ill patients. Four samples of arterial blood were collected and analyzed at the bedside with the POC glucometer and also in the central laboratory to obtain the blood glucose level. To define the effect of various factors on this relation, we noted the levels of hemoglobin (Hb), PaO_2, body temperature, bilirubin, history of drug usage, and sepsis. **Results:** There were not any significant differences between blood sugar levels using laboratory and glucometer methods of measurements. There was a good and significant correlation between glucose levels between two methods (r = 0.81, P < 0.001). Among evaluated factors (body temperature, bilirubin level, blood pressure, Hb level, PaO_2, sepsis, and drugs) which added one by one in model, just drugs decreased the correlation more than others (r = 0.78). **Conclusions:** The results of POC glucometer differ from laboratory glucose concentrations, especially in critically ill patients with unstable hemodynamic status while receiving several drugs. This may raise the concern about using POC devices for tight glycemic control in critically ill patients. These results should be interpreted with caution because of the large variation of accuracy among different glucometer devices.

Keywords: Glucometer, Intensive Care Unit, insulin therapy, laboratory, validity

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Introduction

Dysglycemia is common in critically ill patients for many reasons which is closely related to increased mortality.[1-4] NICE-SUGAR trial, a large study of adult critically ill patients, showed that intensive insulin therapy could increase mortality as a result of increase in hypoglycemia, so intermediate level of blood glucose is being recommended.[5] Analysis of their results showed that method of blood glucose measurement, method of acquisition, and blood sampling, all are important factors in reaching good results.[6] Recently, published sepsis guideline-recommended blood glucose level of <150 mg/dl in critically ill patients undergoing

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intensive insulin therapy because of high incidence of hypoglycemia.[7] Although glucose control is very important in treatment of critically ill patients, glucose measurement has some challenges.[8,9] Detection of signs and symptoms of hypoglycemia are difficult in critically ill patients, so repeated and accurate measurement has high priority. There are two types of blood glucose measurement in Intensive Care Unit (ICU); central laboratory and point-of-care (POC) glucometers. Central laboratory delivers glucose levels almost 60 min after blood sampling which is too slow for decision-making in insulin therapy protocol. Factors that physicians should consider for an appropriate and excellent glucose measurement and reporting system should include cost, accuracy, and time to result.[10] Several studies showed that POC blood glucose measurement with fingerstick capillary glucose measurement has high inaccuracy rate and seems to overestimate blood glucose levels[11-16] in critically ill patients, especially those who are hypotensive, anemic, hypoxemic, have erythrocytosis, or receive vasopressors.[17-19] This study compares the results of bedside blood glucose measurement versus laboratory blood glucose measurement in critically ill patients with intensive insulin therapy.

Materials and Methods

This study was performed into two general ICUs of Tabriz University of Medical Sciences in northwest of Iran. Three hundred patients with expected duration of ICU stay of more than 3 days were enrolled in this study from February 2012 to October 2013. Informed consent was taken from patients or their next of kin. All patients, regardless of having diabetes or not, received insulin infusion if their blood glucose levels were more than 140 mg/dl. Septic patients received insulin protocol in blood glucose levels more than 150 mg/dl based on the Society of Critical Care Medicine guideline. Blood sampling was performed every 1 h from upper arm arterial line and if four consecutive samples were in target range, the sampling interval was increased to 2 h. The first sample was taken from patients during the 1st day of ICU admission, and the three consecutive samples were taken during ICU stay. In all patients, 2 ml of blood was withdrawn in a heparinized syringe from an arterial catheter after 2–3 ml of waste blood was discarded. We used glucose oxidase (GO) method for glucose assessment and used Accu-Chek Aviva device (Roche, Switzerland) for capillary glucose assessment. To insure independence between all glucose measurements, four samples were obtained from each patient. Inaccuracy for measurement was defined as >20% difference between the two measurements. Because Accu-Chek was calibrated to give whole blood results, we calculated a correction factor of 1.080 given by Roche Diagnostics. If patients were hypoglycemic, insulin infusion was stopped, patients received DW50% based on the following formula: (100 − blood sugar [BS]) × 0.4 and interval of blood sampling was reduced to 30 min. Patients characteristics consisted of age, sex, ICU admission type and diagnosis, previous history of diabetes, glycated hemoglobin (HbA1c) value, mean arterial pressure, mean bilirubin, PaO_2, hemoglobin (Hb) value, body temperature, sepsis, and drug history (corticosteroids, aspirin, mannitol, acetaminophen, vasopressor, and Vitamin C).

Statistical analysis

Data were presented as mean ± standard deviation. To investigate the relation between laboratory and glucometer measurements, considering the covariance structure of repeated measurement mixed model analysis using first-order autoregressive (AT1) covariance structure and restricted maximum likelihood estimation method was utilized. To access the amount of reduction in relation between laboratory and glucometer measurements, we considered the model containing these variables at reference model and each time we built models by adding body temperature, bilirubin level, blood pressure, Hb level, PaO_2, sepsis, and drugs (dopamine, Vitamin C, mannitol, aspirin, corticosteroids, and acetaminophen) as extra (confounding) factor. The effect size of reduction in relation was the differences between the secondary model comparing to the reference model. Greenhouse-Geisser test was used when Mauchly's test of sphericity was significant to test the significant changes within group. Analysis was performed by SPSS version 16 (SPSS Inc., IL, Chicago, USA). $P < 0.05$ was considered statistically significant.

Results

Three hundred patients with 1200 simultaneous paired samples were enrolled in this prospective study. Demographic characteristics of patients were shown in Table 1. Of all patients, 59.3% were male and 40.7% were female. Of all patients, 22.3% were diabetic. Mean HbA1c was 6.2 ± 1.2. Characteristics of patients in admission are shown in Table 1. As shown, the main reasons for ICU admission are multitrauma, neurosurgical patients and sepsis. Mean value for laboratory and glucometer BS samples during four times measurements were shown in Table 2. There were not any significant differences between BS levels using laboratory and glucometer methods of measurements. There was a good and significant correlation between glucose levels between two methods ($r = 0.81$, $P < 0.001$). Inputting extra (confounding) factor in model, the correlation

between glucose levels in two methods decreased to 0.73. Among evaluated factors (body temperature, bilirubin level, blood pressure, Hb level, PaO_2, sepsis, and drugs) which added one by one in model, drugs and low blood pressure decreased the correlation more than others ($r = 0.78$ and $r = 0.74$, respectively).

Discussion

The results of the current study showed that there was not any significant difference between glucometer and laboratory values. The 2011 American Diabetes Association position statements[20] on self-monitoring of blood glucose has recommended that glucometer values an intermediate goal of limiting total error for 95% of samples to ≤15% at glucose concentrations ≥100 mg/dl and to <15 mg/dl at glucose concentrations <100 mg/dl while the acceptable target is <20% based on Clinical and Laboratory Standards Institute recommendation.[21] The International Organization for Standardization recommendations in 2003[22] proposed that for sample readings >75 mg/dl, the discrepancy between glucometers and an accredited laboratory values should be <20% for glucose readings ≤75 mg/dl, the discrepancy should not exceed 15 mg/dl in 95% of the samples.

After logistic regression analysis, our study showed a good correlation between two methods which could be due to new technology and the fact that the incidence of bizarre blood glucose, which increases the inaccuracy of glucometer, was low in our study. In our study, mean value for both methods was significantly related to PaO_2. Glucose value was increased with decrease in PaO_2 in both groups. In glucose value <110 mg/dl, PaO_2 caused a significant difference between glucometer and laboratory values. In values >180 mg/dl, bilirubin caused this difference between two groups. Based on the results of this study, in glucose level of almost 150 mg/dl, glucometer has good sensitivity and specificity; but for levels lower than 110 mg/dl and higher than 180 mg/dl, the value should be confirmed with laboratory before any intervention.

There are many drugs that could affect the capillary glucose readings. Some of the most important drugs are dopamine, acetaminophen, mannitol, and ascorbic acid. Acetaminophen could increase glucose readings with glucose dehydrogenase (GDH) meters but decreased readings with some, but not all, GO-based meters at therapeutic drug levels. Dopamine at high drug concentrations could increase glucose values on GDH-based meters. Mannitol increased GO-based meter readings, possibly through a nonspecific osmotic effect or by detection by the analyzer. Ascorbic acid at high doses increased GDH-based meter readings but decreased those that used GO.[23,24] Tang *et al*. evaluated the effect of 13 drugs on 7 various glucometers. They proposed that ascorbic acid could interfere with the measurements on all evaluated glucose devices. There is some evidence about the effect of acetaminophen, dopamine, and mannitol with glucose measurements on some devices.[25] Dose-response relationships help evaluation of drug interference in clinical practice. High dosages of these drugs may be given to critically ill patients or self-administered by patients without medical supervision. The effect of mannitol on geometry was similar to the previous studies.[26] Our study showed that bilirubin level did not have a significant effect on the glucose measurement which was similar to the previous study by Kitsommart *et al*.[26]

With such information regarding the various variables which could affect the blood glucose reading in

Table 1: Characteristics of patients in admission

Age, years	53.9±21.2
Sex, Male no (%)	178 (59.3)
Diagnosis on admission, *n* (%)	
Trauma and orthopedic surgery	135 (45)
Neurospinal surgery	128 (43)
Sepsis	17 (6)
CVA	14 (4.5)
Pulmonary Emboli	4 (1)
CVD	2 (0.5)
Diabetes as Past Medical History, *n* (%)	67 (22.3)
HbA1C	6.2±1.3
SOFA score	7.2±5.1
APACHE II score	17.2±9.1

Data is presented as Mean±SD or *n* (%), APACHE II Acute Physiology and Chronic Health Evaluation, CVA: Cerebrovascular Accident; CVD: Cardiovascular Disease, SOFA: Sequential Organ Failure Assessment; BUN: Blood Urea Nitrogen; ESR: Erythrocyte Sedimentation Ratio; PCT: Procalcitonin, Respiratory Index: PO_2/FiO_2, SOFA: Sequential Organ Failure Assessment, Data is presented as Mean±SD or *n* (%), PCT values are presented as median (minimum-maximum)

Table 2: Sequential measurements of blood glucose by laboratory and glucometry

	First	Second	Third	Fourth	*P*
Blood Glucose value measured by laboratory	147.8±20.6	134.4±20.9	119.3±20.6	108.1±25.4	0.001
Blood Glucose value measured by Glucometry	147.2±15.0	133.4±18.9	120.6±21.3	108.8±24.1	0.001
MAP	75.6±6.9	75.7±6.2	75.3±6.1	76.4±6.0	0.08
Hemoglobin	10.6±1.3	10.2±1.0	10.1±1.0	10.1±1.0	0.001
PaO_2	74.7±6.5	75.4±8.9	75.1±8.3	76.3±6.7	0.003
Bilirubin	0.45±0.13	0.51±0.15	0.49±0.15	0.50±0.15	0.001

Data is presented as Mean±SD, MAP: Mean arterial pressure

glucometer, physicians must be alert while interpreting the values during the treatment of a patient. Inoue *et al*., in their review, showed that accuracy of blood glucose measurements with arterial blood gas (ABG) analyzers was significantly higher than values with glucometers using capillary blood and also was higher than values with glucometers using arterial blood.[27] Establishing glucometer accuracy is challenging. Glucometers only use whole blood samples, but existing standards are based on serum samples. As glucose as an analyte is unstable in whole blood, so it needs to be stabilized through glycolysis inhibitors which this process can interfere with some glucometers.[28] Technical accuracy for glucometers is defined by comparing meter results versus clinical laboratory methods that use plasma/serum-based samples. There is no consensus among standard societies and professional organizations regarding acceptable performance criteria. Clinical accuracy establishes how treatment decisions agree between meter results and laboratory glucose results while technical accuracy defines meter performance. All glucometers should be evaluated before use in critically ill patients, and the specific glucometer model selected should be based on technical and clinical performance in the selected patient population. In addition, environmental exposure, operator technique, patient physiologic, and medication effects can affect the accuracy of glucometer results. Our results are similar to the results of Meynaar *et al*., which showed that accuracy of Accu-Chek glucose measurement is acceptable compared to arterial sample as authors corrected measurement with a factor of 1.080 in both studies.[29] Lonjaret *et al*. showed that in critically ill patients arterial glucose and POC capillary glucose measurement are inaccurate which could lead to inappropriate insulin algorithm. Their results are in opposite to ours which could be due to heterogenous nature of patients and wide variation in glucose readings.[30] Inoue *et al*. performed a systematic review about the accuracy of blood glucose measurements using glucose meters and ABG analysis in critically ill adult patients and showed that accuracy of blood glucose measurement was significantly better with ABGs compared to capillary blood samples. They emphasized that the results should be interpreted with caution in hypoglycemic patients, especially patients with unstable hemodynamic.[27] Juneja *et al*. showed similar results and confirmed that capillary geometry in critically ill patients with stable hemodynamic has a good accuracy compared to arterial samples, which is similar to our results.[31] Kanji *et al*. assessed the reliability of POC testing for glucose measurement in critically ill patients and demonstrated that POC glucometer tended to provide higher glucose values, whereas blood gas analysis tended to lower glucose values and this lead to frequent clinical disagreement regarding glucose management.[11]

Limitation of study

This study was conducted in surgical ICUs with and at the same level of care; so, the results of this study should not be generalized to all critically ill patients.

Conclusions

Considering the nonsignificant difference between glucometer and laboratory and the correlation between them, using glucometer could be considered as an alternative to laboratory examination in critically ill patients with stable hemodynamic status not on many drugs. These results should be interpreted with caution because of the large variation of accuracy among different devices, especially in critically ill patients or patients receiving insulin infusion. Physicians should be aware that current blood glucometers have not reached a high enough degree of accuracy and reliability to determine an appropriate blood glucose control in critically ill patients.

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Conflicts of interest

There are no conflicts of interest.

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