Accuracy of Blood Glucose Measurements Using Capillary and Arterial Line of Extracorporeal Circuit of Hemodialysis Among Diabetic Patients Undergoing Outpatient Hemodialysis at The Medical City

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Abstract

Introduction: Accurate and reliable glucose level measurements are essential for ensuring safe and effective glycemic control among diabetic patients undergoing hemodialysis (HD). Capillary blood glucose (CBG) monitoring is the standard of care of glycemic control assessment in patients with diabetes on maintenance HD. In the Philippines, glucose monitoring during HD involves either standard finger stick (CBG) or blood sample from the arterial line (AL) of extracorporeal circuit of HD machine. However, anecdotal observations noted over the years have shown discrepancies in the glucose values from the two sites. This study aimed to determine the accuracy of blood glucose measurements of capillary and AL of extracorporeal circuit of HD machine using point-of-care (POC) glucose meter in comparison to central laboratory venous plasma among diabetic patients undergoing outpatient HD in a private tertiary hospital in the Philippines. Determining the most accurate and reliable method of glucose level measurement is vital in helping patients attain glycemic control. To date, there is limited published data regarding the accuracy of blood glucose values obtained through CBG and AL of extracorporeal circuit of HD machine while patients are undergoing dialysis.

Methods: This is a prospective, cross-sectional, analytical study involving thirty patients. Forty blood samples from 30 patients obtained through CBG, AL and the peripheral venous plasma of the opposite arm were simultaneously analyzed. Specifically, StatStrip was utilized as the POC glucose meter. Accuracy of AL of extracorporeal circuit and CBG were determined and assessed in accordance with International Organization for Standardization (ISO) 15197:2013 minimum accuracy criteria for glucose meters. Regression analysis was used to determine whether AL and CBG significantly predict peripheral venous blood glucose levels.

Results: Analysis showed that there is a statistically significant difference in the glucose values obtained from AL and CBG (*p*-values 0.005 and <0.0001) when compared to venous plasma glucose. However, this may not pose clinical significance in routine practice. It is noteworthy that both AL (concordance rate (CR)=100%) and CBG (CR=96.5%) satisfied the revised ISO 15197:2013 accuracy criteria for glucose value greater than or equal to 100mg/dL.

Conclusion: Both CBG and AL blood glucose measurement significantly predict venous plasma blood glucose level. POC blood glucose value from both AL of extracorporeal circuit during HD and CBG satisfied the accuracy criteria set by ISO 15197: 2013 for glucose value greater than or equal to 100mg/dL. Thus, confirming the glucose level by CBG monitoring is not necessary in patients with arterial glucose value of greater than or equal to 100 mg/dL during HD.

Keywords: accuracy, arterial line, capillary blood glucose, hemodialysis, point of care glucose meter

Introduction

The number of end stage renal disease (ESRD) patients is growing rapidly in developed and developing countries. The increase in incidence of ESRD has been linked to chronic noncommunicable diseases especially diabetes mellitus (DM) and hypertension. Current projections indicate that by 2030, the global population of ESRD patients on dialysis may exceed two million.[1]

In the Philippines, DM is noted to be the most common cause of ESRD leading to dialysis since 2001. The incidence of ESRD secondary to DM comprised 38% of all dialysis cases conducted between 2001 to 2005.[2] Glycemic control is a key predictor of survival among ESRD patients and is therefore a vital consideration in managing these patients.[3] Frequent episodes of hyperglycemia and/or hypoglycaemia during dialysis is associated with long term morbidity and shortened survival.[4,5]

The accuracy of blood glucose measurements is therefore critical in treatment decisions directed towards glycemic control. Erroneously low or high glucose values obtained using point-of-care (POC) glucose meter during dialysis may lead to inappropriate correction resulting in

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hyperglycemia or hypoglycemia.[6] Thus, inaccurate glucose monitoring may negatively impact clinical outcomes.[7]

Different strategies are employed in monitoring blood glucose during hemodialysis (HD). These include blood sample obtained from the standard capillary blood glucose (CBG) or finger stick procedure,[8,9] from the arterial line (AL) of extracorporeal circuit of HD machine.[4,10,11] and continuous glucose monitoring system (CGMS).[12,13] However, CBG monitoring is the standard of care of glycemic control assessment in patients with diabetes on maintenance HD.[14]

Most HD facilities in the Philippines use the standard CBG monitoring during HD. In The Medical City (TMC), where this study was conducted, sample obtained from AL of extracorporeal circuit is used to minimize discomfort caused by finger pricking. Review of charts in the research setting showed a difference of 35mg/dL (1.95 mmol/L) in blood glucose values from two sites. Based on anecdotal observations, when blood glucose value from the AL is low, rechecking with the CBG is done and the value of the latter is considered as the basis of clinical decisions.

Review of literature revealed that there is no published data comparing blood glucose values obtained from AL of extracorporeal circuit versus CBG during HD. Thus, this study was conducted to test the accuracy of blood glucose obtained from two different sites in diabetic patients undergoing HD using POC glucose meter vis-à-vis peripheral venous blood glucose.

General objective

To determine the accuracy of blood glucose measurements of capillary and AL of extracorporeal circuit of HD machine using POC glucose meter vis-à-vis central laboratory venous plasma among diabetic patients undergoing outpatient HD.

Specific objectives

1. To compare the blood glucose levels from AL of extracorporeal circuit of HD machine and CBG using POC glucose meter compared with central laboratory peripheral venous plasma.
2. To determine whether blood glucose measurements of AL of extracorporeal circuit of HD machine and CBG using POC glucose meter can predict the central laboratory peripheral venous plasma.
3. To determine the concordance of the AL and CBG measurement using Statstrip glucose meter with the revised ISO 15197:2013 accuracy criteria.

Methods

This is a prospective cross-sectional, analytical study conducted at TMC hemodialysis unit in December 2016. Patients who were at least 18-years-old with type 1 or type 2 DM, undergoing outpatient HD in TMC. Only patients who freely signified their consent were included in this study. A sample size of 30 was computed at 95% level of confidence and 0.98 reliability coefficient based on the study of Ogawa et al.[9] The present study was able to collect 30 patients with 40 blood samples.

$$n = \frac{(z_\alpha)^2\, pq}{e^2}$$

Where:

n = is the number of subjects needed
p = estimated reliability coefficient = 0.98
q = 1 – p = 1 – 0.98 = 0.02
Zα = 95% confidence level = 1.96

The study was approved by the hospital's Institutional Review Board Ethics Committee. All patients gave informed consents to participate. Patient baseline characteristics including age, sex, duration of diabetes, antidiabetic therapy, and duration of HD were determined through interview and patient records review.

The standard protocol in determining the POC glucose level in the AL of the extracorporeal circuit of HD was measured at the second hour by a well-trained HD nursing staff. An additional determination was done for patients who manifested signs and symptoms of hypoglycemia[15] such as sweating, hunger, shaking, heart pounding, nervousness or anxiety, feeling of warmth, weakness, confusion, drowsiness, dizziness, speech difficulty, and blurring of vision. Simultaneously, CBG from the opposite arm was collected by the same nursing staff and the five milliliter plasma venous blood sample from the peripheral vein was extracted by a skilled medical technologist and sent to the clinical laboratory for analysis.

A total of 40 sets of blood samples from 30 patients were collected for analysis. There were 10 patients who had two sets of glucose measurement because they manifested with hunger symptoms during HD. The blood samples from AL and CBG were analyzed using the same POC glucose meter StatStrip (Nova Biomedical UK) that was calibrated every 24 hours according to manufacturer's instructions.

The POC glucose meter utilized a modified glucose oxidase enzyme method and multilayer-gold, multielectrode, four-well test strip. It provides excellent correlation versus plasma hexokinase reference methods throughout a range of 10 to 600mg/dL (0.5 to 33.3 mmol/L)[16] and has good clinical reliability when used in dialysis setting.[17] This glucose meter eliminates haematocrit interferences, electrochemical interferences such as acetaminophen, uric acid and ascorbic acid; and interferences from maltose

Table I. Demographic characteristics of subjects

	Frequency (n=30)	Percentage
Age (in years)		
Mean ± SD	65.43 ± 14.94	---
Sex		
Male	13	43.3
Female	17	56.7
Duration of hemodialysis (years)	2.56 ± 2.37	---
Duration of diabetes (years)	17.57 ± 8.29	---
Antidiabetic therapy		
Insulin	9	30.0
Insulin+oral hypoglycemic agent	4	13.3
Oral hypoglycemic agent only	5	16.7
None	12	40.0

and galactose, icodextrin and oxygen, thus reducing the likelihood of erroneous results arising from interference factors that influence current conventional glucose meters.[17] This POC blood glucose meter has passed the standards set by the ISO 15197[18] and the Clinical and Laboratory Standards Institute (CLSI) POCT 12-A3 accuracy guidelines.[20]

The peripheral venous samples, on the other hand, were analyzed in the clinical laboratory using the Abbott Architect i2000SR which delivers high quality immunoassays using chemiluminescence detection technology.

Data were encoded and analyzed in SPSS version 10 for windows. Descriptive statistics were generated for all variables. Frequencies and percentages were determined for nominal data. Mean and standard deviation (SD) were generated. Analysis of the different variables was done using the following test statistics:

Paired T-test – used to compare two groups with numerical data that are dependent.

Regression analysis – used to determine predictor/s of an outcome variable.

In accordance to the most recent ISO 15197:2013 criteria for glucose meter accuracy,[18] the acceptable level of accuracy is set at ≥ 95% of POC values within ± 15% of the reference method for glucose values greater than or equal to 100 mg/dL and within ± 15mg/dL of the reference method for POC glucose values less than 100mg/dL. The reading was expressed in proportion of values falling within various intervals following the ISO recommended format.

Results

A total of 30 patients were included in the study,10 of whom manifested symptoms of hypoglycaemia during data collection thus requiring two sets of blood glucose determinations. As shown in Table I, the participants' age ranged from 36 to 88 years with a mean age of 65.43 years.

Table II. Blood glucose levels (mg/dL) by arterial line of the dialysis machine, capillary and peripheral vein blood samples

	n	Mean ± SD
Arterial line (AL)	40	119.85 ± 27.99
Capillary	40	117.38 ± 27.67
Venous†	40	123.95 ± 28.49

†Reference standard

Table III. Predicting central laboratory venous plasma using capillary blood glucose measurement among diabetic patients undergoing outpatient hemodialysis

	Beta coefficient	*p*-value*
Constant	7.848	0.214
Arterial line (AL)	0.969	<0.0001

* $p>0.05$- Not significant; $p\leq0.05$-Significant
Dependent Variable: Venous

More than half (56.67%) of the participants were females. Forty percent were not on maintenance antidiabetic therapy at the time of data collection. The average duration of DM is 17.57 years and an average duration of HD of 2.56 years.

Table II shows the mean values of glucose levels on AL and CBG using POC glucose meter, and venous plasma as reference standard using clinical laboratory instrument. There is a significant difference in the glucose level measurements from blood samples obtained from AL and CBG when compared to venous plasma glucose with *p*-values 0.005 and <0.0001 respectively. However, this difference may not be clinically significant in routine practice.

Table III shows the regression analysis results when AL blood glucose measurement was used in predicting venous plasma blood glucose level. The results showed that AL blood measurement significantly predicts ($p<0.0001$) venous plasma blood glucose level and a regression equation below was derived to compute venous plasma blood glucose levels using AL:

$y = 7.848 + 0.969 (x)$

where y is the venous plasma blood glucose level computed given x, the AL blood glucose level.

Table IV shows the regression analysis results when CBG measurement was used in predicting venous plasma blood glucose level. The results showed that CBG measurement significantly predicts ($p<0.0001$) venous plasma blood glucose level and a regression equation below was derived to compute venous plasma blood glucose levels using capillary blood glucose level:

$y = 7.438 + 0.993 (x)$

where y is the venous plasma blood glucose level computed given x, the CBG level.

The most recent ISO 15197:2013 criteria for glucose meter accuracy sets ≥ 95% of POC values within ±15% of the

Table IV. Predicting central laboratory venous plasma using arterial line blood glucose measurement among diabetic patients undergoing outpatient hemodialysis

	Beta coefficient	*p*-value*
Constant	7.438	0.172
Capillary	0.993	<0.0001

*p>0.05- Not significant; p≤0.05-Significant
Dependent Variable: Venous

Table V. Evaluation of the accuracy of blood glucose level concordance to ISO 15197:2013 criteria

Method	Glucose <100mg/dL	Glucose ≥100mg/dL	Overall concordance
	Within±15mg/dL	Within 15%	
Arterial Line (AL)	70.0% (7/10)	100% (30/30)	92.5%
Capillary	81.8% (9/11)	96.5% (28/29)	92.5%

reference method for glucose values greater than or equal to 100 mg/dL and within ± 15mg/dL of the reference method for glucose values less than 100mg/dL as the acceptable level of accuracy.[18] With this criteria as reference, both AL and CBG satisfied the accuracy criteria for glucose value greater than or equal to 100mg/dL, but neither satisfied the accuracy criteria for glucose values less than 100mg/dL as shown in Table V.

Discussion

Accurate and reliable glucose level measurements are essential for ensuring safe and effective glycemic control among diabetic patients undergoing HD. Accuracy criteria for POC glucose meters set by the ISO 15197 ensures that blood glucose monitors used for patients are reliable on a day to day basis.[18]

Ogawa et al. found that 100% of predialysis capillary glucose sample and 99.3% of post dialysis samples met the ISO 15197:2003 criteria when the glucose levels were more than 75mg/dL. Out of 148 subjects, only three patients were documented to have glucose levels of less than 75mg/dL which satisfy 100% of the accuracy criteria.[9] The recent ISO 15197:2013 criteria sets glucose level of 100mg/dL instead of 75mg/dL as cut off. Out of 40 blood samples in our study, we only documented 11 blood glucose levels of less than 100mg/dL. However, unlike Ogawa's study, our results did not satisfy the accuracy criteria if blood glucose level is less than 100 mg/dL.

In this study, it was found that in accordance with ISO 15197:2013 accuracy criteria, both the AL from extracorporeal circuit of HD machine and CBG were able to meet the accuracy criteria when glucose values are greater than 100 mg/dL but not for glucose values less than 100 mg/dL.

The common practice in our institution in determining blood glucose level during HD is through the arterial line. Burmeister et al reported that glucose levels measured in blood samples from AL of extracorporeal circuit of HD did not differ from those obtained simultaneously from the peripheral vein of the arm opposite to the vascular access.[4] This finding was similar in this study in which blood samples from AL predicts significantly the peripheral venous plasma glucose level.

Limitations

Thirty is the mimimum sample size requirement however increasing the sample size of those glucose values less than 100mg/dL will increase the statistical power of the study. Most patients did not manifest hypoglycemic signs and symptoms because majority of them had no maintenance antidiabetic medications. Furthermore, the presence of hypoglycaemia unawareness, which is commonly found in patients with longstanding diabetes might have contributed.

Conclusion

Both blood samples obtained from AL and CBG are in concordance with venous blood glucose as seen in Table V. Moreover, the results of the study showed that both AL and CBG predict central laboratory venous blood glucose level significantly. With the recent ISO 15197: 2013 accuracy criteria, both AL and CBG satisfied the criteria for glucose value greater than or equal to 100mg/dL but not for glucose value less than 100mg/dL. CBG monitoring is not necessary in patients with arterial glucose value of greater than or equal to 100 mg/dL during HD.

Recommendation

In view of the results of this study, a similar study involving a larger sample size of blood glucose level less than 100mg/dL is recommended.

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