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EVALUATION OF BLOOD GLUCOSE TESTING USING CONTOUR® PLUS GLUCOMETER

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ABSTRACT

The use of glucometers has been widely recommended to help patients in controlling their blood glucose level. This study compared the blood glucose level measured by Contour® Plus glucometer and Cobas c501 chemistry analyzer, as the reference method. The study design was cross-sectional and conducted in the Dr. Cipto Mangunkusumo Hospital in April 2017. Study materials were 120 capillary blood examined by Contour® Plus glucometer and plasma analyzed by Cobas c501 chemistry analyzer. Precision, correlation, accuracy, and clinical accuracy tests were performed based on ISO 15197:2013, using Parkes error grid analysis. Contour® Plus glucometer yielded a CV of 1.56-2.2%, following the recommendation of the American Diabetes Association, of <5%, there was a strong positive correlation between the glucose level of capillary blood and plasma (r=0.997). Accuracy test based on ISO 15197:2013 showed that 100% of capillary blood glucose deviations were within the ±15 mg/dL range for glucose level <100 mg/dL and ±15% range for glucose level ≥ 100 mg/dL. Clinical accuracy test with Parkes error grid showed 100% of results were in zone A. Contour® Plus glucometer test results met the ISO 15197:2013 criteria, so the results were proportional to the reference method' s results and clinically acceptable. Contour® Plus glucometer is safe to be used in blood glucose monitoring, as long as careful attention is given to the device specifications.

Key words: Blood glucose, diabetes mellitus, glucometer

ABSTRACT

Diabetes Mellitus (DM) is a metabolic disease characterized by hyperglycemia due to impaired insulin secretion, insulin action, or both.[1] The World Health Organization (WHO) estimated that there are 422 million people over the age of 18 who have diabetes in 2014, with the highest number in Southeast Asia and the Western Pacific region.2 According to the 2013 Basic Health Research (Riskesdas), the prevalence of DM in Indonesia increased from 1.1% in 2007 to 2.1% in 2013.[3]

To establish the diagnosis of diabetes, a patient must undergo a series of laboratory tests including fasting blood glucose, postprandial blood glucose, or HbA1c. Diabetes can lead to complications in various organs such as the eyes, heart, kidneys, and blood vessels. Preventing complications of diabetes requires early diagnosis so that treatment can be given earlier After therapy, monitoring of blood glucose level should also be performed to determine the success of treatment and prevent complications.[4,5]

The use of tinstruments to monitor blood glucose independently has been widely recommended. The American Diabetes Association (ADA) recommends self-monitoring of blood glucose for people with diabetes who receive insulin or oral hypoglycemic agents.6 Self blood-glucose-monitoring is an essential instrument in diabetes management, especially for people treated with insulin injections.[7] Self-monitoring helps patients to achieve good glycemic control, and reduce the risk of diabetes-related complications. Also, self-monitoring has been reported to be associated with decreased diabetes-related morbidity and mortality in diabetic patients.[8]

There are currently various glucometers available on the market, so data about their performance are needed. One of the glucometers available in Indonesia is Contour® Plus from Bayer, which uses glucose dehydrogenase flavin adenine dinucleotide enzyme (GDH-FAD) which is specific for glucose and does not interact with sugar in another form (maltose, galactose, xylose). Therefore, systems that use GDH-FAD test strip will not give falsely high results in patients treated with drugs that contain or are metabolized to the other forms of sugar.[9]

Contour® Plus glucometer is a glucometer with non-coding technology that has a small size and large screen, making it easier to read the test results. This glucometer determines the blood glucose level from capillary blood with a small sample volume of 0.6 µL and a check range of 10-600 mg/dL. It displays a notice if the glucose results are outside the test range, i.e., "Lo" for a result <10 mg/dL and "Hi" for a result >600 mg/dL. Glucometer Contour® Plus comes with a second chance sampling feature, which is the chance to add blood to the strip of a previous test if the last test has a less sample, as long as it is done within 30 seconds. The test run time is only five seconds since the application of the blood on the test strip. Glucometer Contour® Plus is capable of storing 480 data, and is able to give the mean of stored blood glucose results from 7, 14, and 30 days.[9]

This study compared blood glucose level measured by Contour® Plus glucometer and Cobas c501 chemistry analyzer, as the reference method. Cobas c501 uses hexokinase enzyme and kinetic spectrophotometry. Measurement of serum glucose concentration by spectrophotometric technique using hexokinase has more accurate results and better reproducibility compared to glucose oxidase or glucose dehydrogenase methods.[5]

METHODS

The study design was cross-sectional and was conducted in the Inpatient Clinical Pathology Laboratory of the Dr. Cipto Mangunkusumo Hospital in April 2017, comprising 120 study subjects. Inclusion criteria were age ≥ 18 years old, hematocrit value <70% on the same day and willingness to participate in this study by signing informed consent. Exclusion criteria were blood glucose level >600 mg/dL, and hemolytic, lipemic, or icteric sample.

Materials used in this study were control, capillary blood, and venous blood with lithium heparin. For the comparison study, 120 capillary blood and venous blood samples were collected with blood glucose level <50 mg/dL in 6 samples, 50-80 mg/dL in 18 samples, 81-120 mg/dL in 24 samples, 121-200 mg/dL in 36 samples, 201-300 mg/dL in 18 samples, 301-400 mg/dL in 12 samples and >400 mg/dL in 6 samples. Determination of sample size was based on the provision in ISO 15197:2013 for glucometer evaluation, which stated a minimum of 100 samples.[10] For groups with blood glucose level <50 mg/dL, venous blood with lithium heparin were kept at room temperature until glucose level decreased due to glycolysis.

Contour® Plus glucometer uses GDH-FAD enzyme, glucose in the sample will react with GDH-FAD enzyme and potassium ferricyanide in the strip. This reaction produces an electric current which is then measured by the glucometer, generating a number that corresponds to the glucose concentration in sample.[9,11]

Cobas c501 uses hexokinase enzyme and kinetic spectrophotometry. Glucose in the sample will be phosphorylated by ATP with the help of hexokinase enzyme, generating glucose-6-phosphate, which in the presence of $NADP^+$ will be oxidized by glucose-6-phosphate dehydrogenase to form gluconate-6-phosphate and NADPH. The NADPH is measured by a photometer at a wavelength of 340 nm. Its formation rate is proportional to the glucose concentration in sample.[5,12]

Three Contour® Plus strip lots were used. The expiration date ranged between July and September 2018. The glucose control materials used were Precinorm U, with an expiration date of May 2018 and a range of 85-115 mg/dL and Precipath U, with the same expiration date and a range of 198-270 mg/dL.

Contour® Plus glucometer precision test was performed by examining venous blood with three different glucose levels, using three glucose test strips with different lot numbers for each level. The glucose levels were 54-108 mg/dL (low), 126-180 mg/dL (normal) and 198-360 mg/dL (high). The samples were randomly selected from valid subjects with known normal, low, or high blood glucose concentration measured by the reference method. The measurement was performed according to the protocol of the manufacturer to minimize errors. Each venous blood was examined 20 times consecutively for each lot, the examination was done consecutively on the same day and the precision testing was carried out in less than half an hour for each level.

Within-run precision test and accuracy test of Cobas c501 were done by testing Precinorm U, and Precipath U control materials from Roche 10 times consecutively in one day. The between-day precision test was done by testing Precinorm U and Precipath U control materials once a day for 10 days. Comparisons were made between the results of capillary blood tested with Contour® Plus and venous blood tested with Cobas c501.

A statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) ver. 20.0. This research has been approved by the Ethics Committee of the Faculty of Medicine, University of Indonesia, number 1097/UN2.FI/ETIK/2016.

RESULT AND DISCUSSION

Contour® Plus glucometer precision test used venous blood with low, normal, and high glucose level. Examination for each blood glucose level was performed 20 times for each lot, and was done consecutively on the same day. The result of the Contour® Plus glucometer precision test showed CVs for low, normal, and high blood glucose level is 1.86%, 1.56% and 2.2% respectively. Variation of results between the three lots used were 0.9% for low blood glucose, 1.6% for normal and 1.2% for high.

Within-run precision test and accuracy test of Cobas c501 were performed ten times in a row on the same day using Precinorm U and Precipath U control materials for blood glucose. The Cobas c501 within-run precision and accuracy test, which used Precinorm U, the CV was 0.79% with a deviation of -3–2.1%, while in the one which used Precipath U, the CV was 0.7% with a deviation of 1.5–3.76%. The Cobas c501 between-days precision test, obtained a CV of 0.76% for Precinorm U and 0.96% for Precipath U.

For the examination of the blood glucose level of the 120 samples, Kolmogorov-Smirnov test showed abnormal data distribution for capillary blood samples ($p < 0.001$) and plasma samples ($p < 0.001$). Median blood glucose for capillary blood samples was 138 mg/dL and for plasma samples was 132.2 mg/dL. Data transformation was performed, but the distribution remained abnormal.

Mann-Whitney test result found no significant differences in blood glucose level between the capillary blood and plasma blood ($p=0.871$). Spearman correlation test between the blood glucose results of capillary blood and plasma blood obtained a correlation coefficient (r) of 0.997. The Parkes error grid showed 100% of results being in zone A and can be seen in Figure 1.

System accuracy evaluation based on ISO 15197:2013 showed 100% of blood glucose deviations were within

the ±15 mg/dL range for blood glucose level <100 mg/dL and ±15% range for blood glucose level ≥ 100 mg/dL, as can be seen in Figure 2.

In the Contour® Plus glucometer precision test, which used venous blood with three different glucose levels (low, normal, high), the CVs ranged between 1.56 and 2.20%. According to the ADA, the recommended CV for glucometer is less than 5%.[13] The CVs of Contour® Plus glucometer fulfilled the ADA recommendation. Variations between the three lots used in this study were 0.9%, 1.6% and 1.2% for low, normal, and high blood glucose, respectively. These variations were consistent with the factory variation, which was ≤ 15% for different lots.[9]

For the Cobas c501 within-run precision and accuracy test which used Precinorm U, the CV was 0.79% with a deviation of -3–2.1%, while in the one which used Precipath U, the CV was 0.7% with a deviation of 1.5–3.76%. The Cobas c501 between-days precision test obtained a CV of 0.76% for Precinorm U and 0.96% for Precipath U. The factory within-run CV was 1% for Precinorm U and 0.9% for Precipath U.11 The Cobas c501 within-run CVs were consistent with the factory CVs.

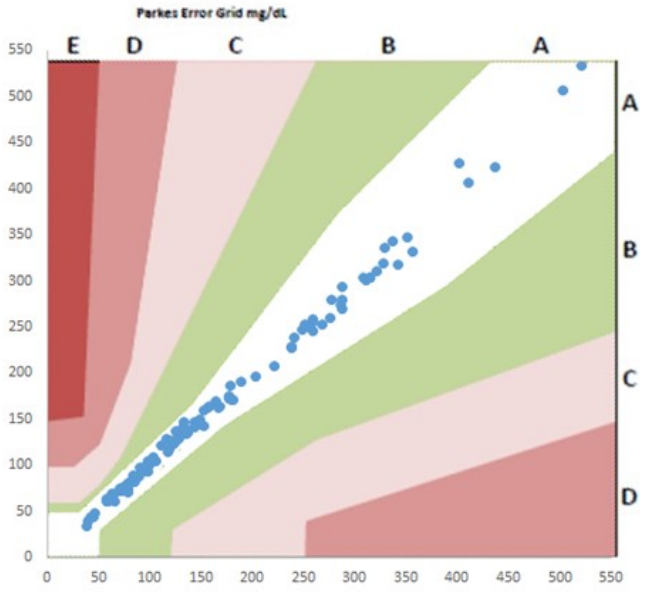

Figure 1. The Parkes error grid of capillary blood glucose analyzed by Contour® Plus and plasma glucose examined by Cobas c501

The inclusion criteria were subjects ≥ 18 years old and hematocrit value <70% on the same day. Hematocrit values greater than 70% may interfere with Contour® Plus glucometer testing and lead to falsely low results. The exclusion criteria of this study were blood glucose level >600 mg/dL and hemolytic, lipemic, or icteric samples. Blood glucose levels greater than 600 mg/dL cannot be read by Contour® Plus glucometer and it will only display "high" in the result. Hemolytic, lipemic, or icteric samples may interfere with Cobas c501 testing.

The statistical analysis using Mann-Whitney test

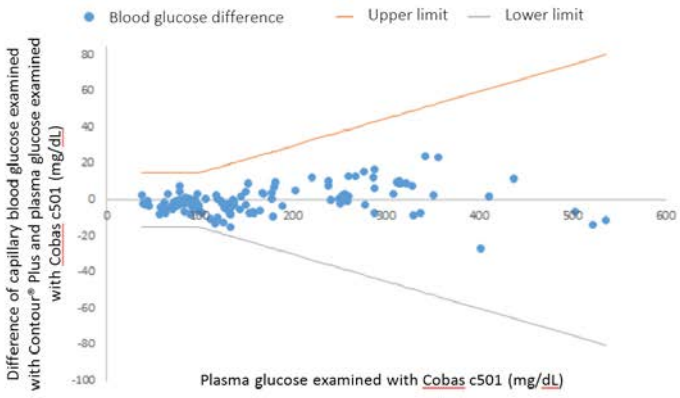

Figure 2. Blood glucose accuracy evaluation of Contour® Plus using capillary blood against Cobas c501 using plasma based on ISO 15197:2013

showed no significant difference in blood glucose results between capillary blood and venous plasma ($p>0.05$). Spearman correlation test showed very robust positive correlation.

Under ISO 15197:2013, the glucometer accuracy must meet two conditions. The first condition is 99% of measured results must lie in zone A and B according to Parkes error grid analysis. The second condition is 95% of measured results must have a <15 mg/dL difference for blood glucose level <100 mg/dL, or <15% difference for blood glucose level ≥ 100 mg/dL compared to the reference method.[10]

The Parkes error grid analysis for clinical accuracy classified the results in five zones based on clinical risk, which are zone A, B, C, D, and E. Zone A is considered to be the safest zone for clinical treatment (the Contour® Plus glucometer results are considered proportional to the Cobas c501 results, as the reference method). Zone B is a zone with a deviation of >20% of the reference method but has a none to small potential to cause a therapeutic error, so the data are still acceptable. Zone C is a zone where there is a tendency to influence clinical outcomes. Zone D is a zone that can lead to significant medical risks. Zone E is a zone that can have dangerous consequences.[10]

Hundred percent of Contour® Plus glucometer results were in zone A (Figure 1). This finding showed that measurement of capillary blood glucose with Contour® Plus glucometer was proportional to the reference method and clinically acceptable.

Under ISO 15197:2013, at least 95% of results must have <15 mg/dL difference for blood glucose level <100 mg/dL, or <15% difference for blood glucose level ≥ 100 mg/dL compared to the reference method. In this study, 100% of Contour® Plus glucometer results were well within the range (Figure 2). This showed that blood glucose examination using Contour® Plus glucometer met the criteria of ISO 15197:2013. The research by Kapusta *et al*., compared Contour® Plus glucometer with Maxmat PLII analyzer which used the hexokinase method as the reference method

The study showed that 99.5% of the results were in zone A of Parkes error grid analysis, hence meeting the accuracy requirements of the ISO 15197;2013.[14] Another research by Dunne *et al*. showed that 100% of Contour® Plus glucometer results were in zone A and B of Parkes error grid.[15]

CONCLUSION AND SUGGESTION

In the evaluation of Contour® Plus glucometer for testing blood glucose, compared to Cobas c501 automatic chemistry analyzer as the reference method, the results showed good precision. Contour® Plus glucometer system accuracy met the criteria in ISO:15197:2013. In the Parkes error grid analysis, 100% of results were in zone A.

Contour® Plus glucometer is safe to be used for blood glucose monitoring, as long as careful attention is given to the device specifications.

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