Accuracy of Sensocard Glucose Meter: Comparing with Reference Glucose Oxidase Method

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Abstract

Introduction: Diabetes mellitus is a cause of morbidity, disability and mortality worldwide. Glucose measurement by glucose meter is one of the diagnosing and monitoring tools of diabetes mellitus. However, the accuracy of this instrument is in question. Therefore, the aim of this study was to assess the accuracy of Sensocard glucose meter comparing with reference glucose oxidase method at University of Gondar Hospital, Gondar, Ethiopia.

Methods: A prospective cross-sectional study was conducted in March, 2014. A total of 122 (equal number of type 1 and II) diabetic mellitus patients were selected by consecutive sampling technique. Glucose value was determined by Sensocard glucose meter and reference glucose oxidase method. The data were entered and analyzed using SPSS version 20 and Analyse-it version 3.76.1 softwares. Correlation coefficient and bias were calculated to observe the agreement of the glucose meter result with the comparative method. The minimum accuracy of Sensocard was determined based ISO 15197:2003 and ISO 15197:2013 criteria.

Results: Sixty three (51.6%) participants were females. The mean age was 46.16 ± 15.5. The mean serum glucose value measured by reference method was 164.78 ± 86.33 mg/dl and the mean capillary blood glucose value measured by Sensocard glucose meter was 161.19 ± 78.1 mg/dl. There was no statistically significant difference between the means of Sensocard glucose meter and reference method glucose value (p-value=0.052). The correlation coefficient between the two methods was 0.975. The Sensocard glucose meter underestimated the overall glucose value from the reference method glucose value by a bias of 3.59.

Conclusion: Sensocard did not fulfill the minimum accuracy requirements of ISO 15197:2003 and ISO 15197:2013. Further study should be undertaken including hypoglycemic and normoglycemic individuals to see the accuracy of Sensocard in low and normal levels of blood glucose in addition to high blood glucose level in diabetes mellitus patients.

Keywords: Accuracy; Bias; Diabetes mellitus; Glucose oxidase; Sensocard

Abbreviations: 4-AAP: 4 Amino-antipyrene; BG: Blood glucose; CI: Confidence interval; DM: Diabetes mellitus; FAD: Flavin adenine dinucleotide; FC: Ferrocenecarboxylate; GOD: Glucose oxidase; ISO: International organization for standardization; MDI: Multiple-dose insulin; POC: Point-of-care; POD: Peroxidase; SD: Standard deviation; SMBG: Self-monitoring of blood glucose

Introduction

Diabetes mellitus (DM) is a chronic disease which requires continuing medical care and ongoing patient self-management education and support to prevent acute complications and to reduce the risk of long-term complications. Diabetes care is complex and needs multifactorial risk reduction strategies in addition to glycemic control [1]. Management of blood glucose (BG) in an acceptable range is a major therapy target for diabetes patients in both the hospital and outpatient settings [2]. Patients on Multiple-dose Insulin (MDI) or insulin pump therapy should do self-monitoring of blood glucose (SMBG) at least prior to meals and snacks, occasionally postprandially, prior to exercise, at bedtime, when they suspect low blood glucose, after treating low blood glucose and prior to critical tasks such as driving [1]. Self-monitoring blood glucose systems have the potential to play an important role in the control of diabetes and in the reduction of risk of serious secondary clinical complications [3]. The advantages of these Point-of-Care (POC) testing are reduced therapeutic turnaround time of diagnostic testing, reduced preanalytic and postanalytic testing errors, rapid data availability, self-contained and user-friendly instruments, shorter patient length of stay, small sample volume for a large test menu, convenience for clinicians and ability to test many types of samples [4].

Various POC tests have been found to be non-inferior to laboratory testing for managing chronic conditions in general practice and aboriginal medical services. Maintaining the diagnostic quality of devices and ensuring that staffs are properly trained are critical elements in sustaining a high quality POC testing service [5]. The accuracy of the POC glucose monitor depends on device methodology and other factors, like sample source and collection and patient characteristics. Human parameters capable of influencing measurements include variations in pH, hematocrit, blood oxygen, changes in vasopressor and microcirculation therapy. These elements alone or when combined can significantly impact BG measurement accuracy with POC glucose monitoring devices [2]. Since inaccurate systems bear the risk of false therapeutic decisions, standardized and regular evaluation of BG meters and test strips should be requested in order to ensure adherence.
Materials and Methods

Study design, setting and period

A prospective cross-sectional study was conducted in March, 2014 at University of Gondar Hospital. Diabetic mellitus patients who have come to the hospital for follow up were participated in the study. Equal number of type I and type II DM patients were selected by consecutive sampling technique. Diabetes mellitus patients who were volunteers, who have normal hematocrit value and who were not on medication that affects glucometer measurement like acetaminophen and vitamin C were included in the study.

Data collection

After having received a clear clarification of the aim, risk and confidentiality of the study, participants have signed the informed consent and participated in the study. One hundred twenty two (61 type 1 and 61 type II DM) participants were enrolled. Demographic information including sex, age and type of DM were collected using data abstracting sheet. Blood samples were collected from the ante cubital vein and capillary of finger for the reference glucose oxidase method and SensoCard glucose meter glucose measurement, respectively after an overnight fasting (12-16 h). Tourniquet was applied for less than one minute, for vein puncture and the sites of blood collection were cleaned by 70% alcohol. The venous blood sample was taken to the laboratory and centrifuged at 500 g for 5 minutes to obtain the serum. All measurements were done according to the manufacturer's instructions. Capillary blood glucose was determined by SensoCard glucose meter (77 Elektronika Kft., Budapest, Hungary) and venous blood glucose was measured by BioSystems A25 Chemistry Analyzer (BioSystems S.A, Spain) using glucose oxidase test method. Duplicate measurement of blood glucose was performed by each instrument and the average of each was taken as single glucose value.

Principle of glucose oxidase method: Glucose level was determined by an enzymatic spectrophotometric glucose oxidase method. The basic principle is that, Glucose is oxidized by glucose oxidase (GOD) enzyme to produce gluconate and hydrogen peroxide (H2O2). The H2O2 is then oxidatively coupled with 4 amino-antipyrine (4-AAP) and phenol in the presence of peroxidase (POD) enzyme to yield a red quinoeimine dye that is measured at 505 nm with a spectrophotometer (BioSystems A25 Chemistry analyzer). The absorbance at 505 nm is proportional to concentration of glucose in the sample. The method has linearity from 0.0126 mmol/l (0.23 mg/dl) to 27.5 mmol/l (500 mg/dl).

Glucose +2H2O + O2 GOD Gluconate + H2O2
2H2O2 + 4-AAP+ Phenol POD Quinoeimine Dye + 4H2O
Absorbance of the colored solution is directly proportional to the glucose concentration when measured at 505 nm [8].

Principle of the SensoCard: The SensoCard analysis applies the enzyme glucose oxidase and is based on advanced electrochemical technology that is specific for β-D-glucose measurement. Test strips are designed in such a way that the blood sample absorbs into the reaction area, after blood sample has been applied to the tip of test strip. In the reagent zone, glucose oxidase initiates the oxidation of glucose in blood. Intensity of produced electrons is measured by the meter and correlates well with the concentration of glucose in the blood sample. According to the manufacturer manual, the test is linear up to 33.3 mmol/l (600 mg/dl). This method will accurately measure glucose levels down to 1.1 mmol/l (20 mg/dl) [9].

The SensoCard sensor is constructed on electrodes and uses GOD enzyme and ferrocenecarboxylate (Fc) mediator to carry electrons from GOD to electrode. Flavin adenine dinucleotide (FAD) is used as a coenzyme during the enzymatic reaction. The produced current under the applied electric voltage is measured by amperometer and then converted to glucose concentration. The intensity of formed electrons is directly proportional to glucose concentration [9].

Glucose + GOD(FAD) + 2H+ Gluconolactone + GOD(FADH2)
GOD(FADH2) + 2Fc+ GOD(FAD) + 2Fc + 2H+
Fc Fc+ + 2e (at electrode)

Accuracy evaluation

Accuracy of SensoCard glucose meter for fingertip capillary blood testing was assessed at University of Gondar Hospital. At the study site, we tested the participants’ fingertip blood glucose with the SensoCard and ante cubital vein blood glucose with BioSystems A25 Chemistry Analyzer spectrophotometer, which served as the reference. Accuracy was evaluated using International Organization for Standardization (ISO) 15197:2003 and ISO 15197:2013 requirements by calculating the percentage of meter results falling within ±5%, ±10%, ±15% and ±20% of the reference value for glucose concentrations ≥75 mg/dl and ≥100 mg/dl and within ±5%, ±10% and ±20% of the reference value for glucose concentrations <75 mg/dl and <100 mg/dl. The minimum acceptable accuracy for results produced by SensoCard glucose meter according to ISO 15197:2003, is ≥95% of the individual glucose results shall fall within ±15 mg/dl of the results of the manufacturer's measurement procedure at glucose concentrations <75 mg/dl and within ±20% at glucose concentrations ≥75 mg/dl and according to ISO 15197:2013, is: ≥95% of the individual glucose results shall fall within ±15 mg/dl of the results of the manufacturer’s measurement procedure at glucose concentrations <100 mg/dl and within ±15% at glucose concentrations ≥100 mg/dl [10,11]. In addition, the Bland–Altman plot was used to estimate the difference (bias) limits containing 95% of data because normally distributed differences were needed [12].

Data analysis

The data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 20 (IBM Statistics, USA) and Analyse-it version 3.76.1 (Analyse-it Software, Ltd., UK) softwares. The Bland–Altman analysis was used to see the agreement of SensoCard glucose meter with reference spectrophotometric glucose oxidase method in measuring blood glucose concentration. Correlation coefficient and
Linear regression graph of reference glucose oxidase glucose values between SensoCard glucose meter and reference glucose under estimated glucose concentrations above 134 mg/dl (Figure 1). The SensoCard glucose meter overestimated the glucose concentrations below 134 mg/dl and concentration. According to the equation, the SensoCard glucose meter glucose values were 0.8817 respectively) (Table 2).

The mean difference (bias) between the two methods was not associated with sex, age and DM type. However, the mean bias showed statistically significant association with glucose value. The mean bias increases as glucose value increase in both methods (p-value <0.0001 statistically significant association with glucose value. The mean bias showed

**Ethical consideration**

The study was ethically cleared from the Research and Ethical Committee of School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar. Data were collected after written consent was obtained from the study participants. To keep confidentiality, non-identifier codes were used and unauthorized person could not able to access the data.

**Results**

A total of 122 DM patients were included in this study. Of these, 51.6% (n=63) were females. The mean age was 46.16 ± 15.5 (range 17-77) years. Half (50%) of the study participants were type I DM and the other half were type II DM patients. The mean serum glucose value measured by reference glucose oxidase method was 164.78 ± 86.33 mg/dl (range 42-533) and the mean capillary blood glucose value measured by SensoCard glucose meter was 161.19 ± 78.1 mg/dl (range 65-491). There was no statistically significant difference between the means of SensoCard glucose meter and reference glucose oxidase method glucose value (p-value=0.052). The bias of SensoCard was 3.59 and the strength of association (correlation coefficient) between the two methods was 0.975 (Table 1).

The mean difference (bias) between the two methods was not associated with sex, age and DM type. However, the mean bias showed statistically significant association with glucose value. The mean bias increases as glucose value increase in both methods (p-value <0.0001 and 0.016 for glucose oxidase method and SensoCard method, respectively) (Table 2).

The slope of the regression line for reference glucose oxidase method versus SensoCard glucose meter glucose values was 0.8817 with a positive intercept of 15.9 mg/dl. Under simultaneous equation the Y=X and Y=0.8817X+15.9 graphs meet at 134 mg/dl glucose with a positive intercept of 15.9 mg/dl. Under simultaneous equation method versus SensoCard glucose meter glucose values was 0.8817 statistically significant association with glucose value. The mean bias showed

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The Bland-Altman plot showed that most of the difference (bias) glucose values between SensoCard glucose meter and reference glucose oxidase methods lay within the bias ±1.96SD (95% CI). The 95% limit of agreement was -35.93 to 43.11 (Figure 2).

The percentage of SensoCard blood glucose values within different deviation ranges of glucose oxidase reference method is shown below.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>SensoCard method</th>
<th>Glucose oxidase method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum</td>
<td>65</td>
<td>42</td>
</tr>
<tr>
<td>Percentiles</td>
<td>25</td>
<td>109.875</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>139.5</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>177.375</td>
</tr>
<tr>
<td>Maximum</td>
<td>491</td>
<td>533</td>
</tr>
<tr>
<td>Mean</td>
<td>161.19</td>
<td>164.78</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>78.08</td>
<td>86.33</td>
</tr>
<tr>
<td>Coefficient of variation (%)</td>
<td>48.44</td>
<td>52.39</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Difference between means (bias)</th>
<th>P-value</th>
<th>95% confidence interval</th>
<th>Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.59</td>
<td>-0.02387 to 7.2042</td>
<td>0.975</td>
</tr>
</tbody>
</table>

**Table 1:** General characteristics of the two methods’ glucose value of patients at University of Gondar Hospital, Gondar, Ethiopia, 2014.
According to ISO 15197 standards, SensoCard results within ±20, ±15, ±10, and ±5 mg/dl of the reference results at blood glucose concentrations <75 and <100 mg/dl and SensoCard results within ±20%, ±15%, ±10%, and ±5% of the reference results at blood glucose concentrations ≥75 and ≥100 mg/dl are calculated (Table 3).

<table>
<thead>
<tr>
<th>Cut point of the reference method</th>
<th>Percentage of SensoCard glucose levels within the reference method intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Within ± 5%(5 mg/dl)</td>
</tr>
<tr>
<td>&lt;75 mg/dl</td>
<td>1/9(11.1%)</td>
</tr>
<tr>
<td>≥75 mg/dl</td>
<td>40/113(35.4%)</td>
</tr>
<tr>
<td>Over all</td>
<td>41/122(33.6%)</td>
</tr>
<tr>
<td>&lt; 100 mg/dl</td>
<td>5/22 (22.7%)</td>
</tr>
<tr>
<td>≥100 mg/dl</td>
<td>34/100 (34%)</td>
</tr>
<tr>
<td>Over all</td>
<td>39/122(32%)</td>
</tr>
</tbody>
</table>

For glucose concentrations <75 and <100 mg/dl, the % meter results within ± the specified mg/dl of the reference glucose values are tabulated. For glucose concentrations ≥75 and ≥100 mg/dl, the % meter results within ± the specified % of the reference glucose values are tabulated.

Table 3: Percentage of SensoCard glucose meter results falling within various intervals of the reference glucose oxidase glucose value of DM patients at University of Gondar Hospital, Gondar, Ethiopia, 2014.

Discussion

In this study, the minimum and maximum glucose concentration measured by SensoCard glucose meter and reference glucose oxidase methods were 65 mg/dl and 491 mg/dl and, 42 mg/dl and 533 mg/dl, respectively. The mean capillary blood glucose value measured by SensoCard glucose meter was 161.19 ± 78.1 mg/dl and the mean serum glucose value measured by reference glucose oxidase method was 164.78 ± 86.33 mg/dl and. There was no statistically significant difference between the means of SensoCard glucose meter and reference glucose oxidase method glucose value (p-value=0.052) (Table 1) but the p trend approaches 0.05 and a bigger sample may yield statistically different results. Although the discrepancy between SensoCard and reference glucose oxidase glucose values were not statistically significant from this study, the magnitude of these differences could be considered clinically significant if the glucose values could change treatment decisions in a situation requiring precise glucose measurements.

The mean difference (bias) between the two methods was 3.59. The mean bias was not associated with gender, DM type and age (p-value=0.258, 0.486 and 0.132, respectively). However, the mean bias showed statistically significant association with both reference glucose oxidase method and SensoCard glucose values (p-value <0.001 and 0.016, respectively) (Table 2). The bias between the two methods increases as the concentration of glucose increases. Compared to the reference glucose oxidase method, the SensoCard glucose meter has over estimated and under estimated glucose concentrations in lower and higher concentrations of glucose, respectively. This may be due to the accuracy problem of the SensoCard glucose meter method to determine the lower and especially the higher glucose concentrations.

From the Bland-Altman analysis in Figure 2, when the reference glucose oxidase method was compared to the SensoCard glucose meter, it indicated that the SensoCard was generating glucose results lower than that of the reference method. This is in line with the above observation in Table 1. The bias from this was 3.59 and the 95% limit of agreement was -35.93 to 43.11 (Figure 2). Similarly, another study comparing SensoCard with reference glucose oxidase method found a bias of 3.6 and the 95% limit of agreement was -30 to 37.8 [13].

This study showed that, 55.6% and 90.3% of the SensoCard glucose measurement results fall within ±15 mg/dl and ±20% of the results of the reference glucose oxidase method at glucose concentrations <75 mg/dl and ≥75 mg/dl, respectively. In addition, 59.1% and 86% of the SensoCard glucose measurement results fall within ±15 mg/dl and ±15% of the results of the reference glucose oxidase method at glucose concentrations <100 mg/dl and ≥100 mg/dl, respectively. However, according to ISO 15197 criteria ≥95% the SensoCard glucose measurement results should fall within the above reference glucose value intervals [10,11]. Therefore, SensoCard glucose meter did not fulfill the minimum accuracy requirements of ISO 15197. In spite of our SensoCard result, a study done in other place fulfilled the ISO 15197 criteria. In this study, 97% and 99% of the SensoCard glucose measurement results fall within ±15 mg/dl and ±20% of the results of the reference glucose oxidase method at glucose concentrations <75 mg/dl ≥75 mg/dl, respectively [14].

Limitations of the study

The study was done only on DM patients (majorly hyperglycemic level) and it was not possible to see the accuracy of SensoCard glucose meter at lower glucose (hypoglycemic and normoglycemic) levels.

Conclusion

The SensoCard glucose meter and the reference glucose oxidase methods showed a good correlation of 0.975 in determining blood glucose concentrations. In addition, there was no statistically significant difference between the means of blood glucose values between the two methods. However, SensoCard glucose meter underestimate blood glucose value average by 3.59 from reference glucose oxidase method. Moreover, the SensoCard glucose meter did not fulfill the minimum accuracy requirements of ISO 15197:2003 and ISO 15197:2013. Further study should be undertaken including hypoglycemic and normoglycemic individuals to see the accuracy of SensoCard in low and normal levels of blood glucose in addition to high blood glucose level in diabetes mellitus patients.

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References


