Comparative Testing for Better Glycemic Control

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Abstract

Objective: We compared 2 hospital-based glucose meter technologies for accuracy and compared them with a laboratory chemistry analyzer as a reference.

Methods: This study was done on 213 samples at 3 locations to compare our currently used LifeScan Flexx glucose meter with the newer StatStrip Nova glucose meter and we compared them with the laboratory-based Vitros Fusion analyzer.

Results: Regression analysis demonstrated lower intercept and a better bias plot along with meeting the total allowable error limit in 100% of the runs for the StatStrip Nova Glucose meter. The analytical superiority was further complimented by improved satisfaction by the nonspecialist users.

Discussion: Better accuracy from the newer technology ensures improved patient care for critically ill patients on tight glycemic protocol.

Maintaining tight glycemic control (TGC) in critically ill patients is a big challenge. The challenge involves not just rapid turnaround time but also reliability of the methodology giving best accuracy. Point-of-care (POC) glucometers are the standard of care in bedside glucose management in most critical care units. The Food and Drug Administration standard for POC glucose analyzer accuracy recommends that average error be no more than 15% of reference values; however, the American Diabetic Association 1996 consensus statement suggests the error in glycemic measurement should be no more than 5%. A major concern for accuracy in the analytical methods is the interference caused by various factors like abnormal hematocrit levels or the electrochemical abnormalities seen in the specimens of these hospitalized patients. Besides this, various medications used in the critical care setting and patient hematocrit have also been found to affect the performance of almost all glucose meter technologies available. Many studies have shown that low hematocrit gives a high bias to glucose and, conversely, high hematocrit causes a low bias in glucose levels, regardless of the meter technology used.

In addition, the degree of correlation between hypoglycemic and hyperglycemic ranges is also quite variable with currently available meters.

Last but not least is the user friendliness of the technology, which determines the confidence in the technology adding to the analytical accuracy.

The objective of the current study was to compare 2 hospital-based glucose meter technologies for accuracy compared with a laboratory chemistry analyzer as a reference.

Materials and Methods

This study compared our currently used LifeScan Flexx meters and the newly introduced Nova StatStrip meters against the laboratory-based reference method to determine the methodology that has an edge over the other in terms of correlating to the laboratory reference method. Ortho Clinical Diagnostics Fusion 5.1 analyzer (Ortho Clinical, Raritan, NJ) was used as a reference assay to measure plasma glucose based on the glucose oxidase methodology. The 2 glucose meters used for comparison were LifeScan Flexx (LifeScan, Milpitas, CA), which uses a photometric glucose oxidase detection system and Nova StatStrip (Nova Biomedical, Waltham, MA), which uses a modified glucose oxidase based amperometric test system with hematocrit and interference correction.

A validation study was done before performing the comparative analysis by using 100 samples spiked with glucose spiking solution and obtaining different target glucose concentrations ranging from 10 mg/dL to 500 mg/dL. The samples were then tested parallel on both meters and then spun for obtaining plasma used for analysis on the reference analyzer.

After the completion of the validation study, the critical care nurses were trained and their competency was assessed by direct observation of quality control testing, patient testing, and maintenance checks.

A regression analysis study was then run by the Kaiser Permanente San Francisco laboratory for comparing data between Fusion and LifeScan, Fusion and Nova Stat Strip, and LifeScan and Nova Stat Strip. The data was obtained from patients in the cardiovascular intensive care unit (CVICU) transferred from the cardiovascular operating room (CVOR) after open heart surgery following their existing protocol of sending an arterial sample in lithium heparin tubes every 4 hours to the laboratory for immediate testing. A parallel bedside testing was also performed every hour using the glucose meters as per the TGC protocol. One to 4 samples per patient were obtained for analysis. There were 41 samples on which correlations were performed by registered nurses (RNs) on 2 Nova Stat Strip and 2 LifeScan Flexx meters and by the clinical laboratory scientists on the reference Fusion instrument. Another 86 samples were tested by the RNs on both the Nova Stat Strip and LifeScan Flexx meters.

A similar study was also conducted at the Kaiser Permanente Redwood City laboratory using 2 meters and also by Kaiser Permanente South Sacramento laboratory using 4 meters by the RNs on a total of 172 patients in the intensive care unit and comparing the Nova Stat Strip and LifeScan Flexx with Vitros Fusion.

In addition, a precision study was performed to study the within-run precision of the Nova Stat Strip meter and comparing it with the currently used LifeScan Flexx meter. Two lots of Nova Stat Strip test strips and 1 lot of LifeScan test strips were used for testing. Ten replicates on 3 levels of whole blood dosed with glucose stock solution were tested on both meters.
Results

Results from both the meters across all 3 sites are shown in Table 1. Combined data from all 3 sites was used based on the results of analysis of variance (ANOVA): single factor analysis showed a lower F ratio (1.131 for Nova StatStrip and 0.062 for LifeScan Flexx) than the F critical value (3.038 for Nova StatStrip and 3.038 for Life Scan Flexx) for both meters. A lower F ratio than the F critical value suggests no difference in the regression equation variance between all 3 sites and statistically supports the consolidation of data in one large group. The mean reference glucose value was 113 mg/dL and the range of glucose covered was 68 to 153 mg/dL.

Linear regression analysis for all 213 samples by Deming’s method (Table 2) demonstrated a slope of 0.972 and an intercept of 5.3 mg/dL for the Nova StatStrip and Fusion meters (Figure 1). The values were noted to be consistently closer to the slope of 1.

The LifeScan and Fusion meters demonstrated almost the same slope (0.864) but with a much higher intercept of 22.5 (Figure 2). The values were noted to be lower for higher concentrations of glucose and higher for lower concentrations of glucose.

The Nova StatStrip and LifeScan Flexx meters had a slope of 0.890 and an intercept of 17.7 (Figure 3).

Table 1. Regression Analysis (Deming’s Method) Performed at 3 Different Facilities Using Laboratory-Based Fusion as Reference Method

<table>
<thead>
<tr>
<th>Name of Meter</th>
<th>Kaiser San Francisco</th>
<th></th>
<th></th>
<th></th>
<th>Kaiser South Sacramento</th>
<th></th>
<th></th>
<th></th>
<th>Kaiser Redwood City</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Slope</td>
<td>Intercept</td>
<td>Slope</td>
<td>Intercept</td>
<td>Slope</td>
<td>Intercept</td>
<td>Slope</td>
<td>Intercept</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LifeScan Flexx</td>
<td>0.935</td>
<td>27.3</td>
<td>1.028</td>
<td>10.188</td>
<td>0.859</td>
<td>16.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>StatStrip Nova</td>
<td>0.957</td>
<td>4.0</td>
<td>1.016</td>
<td>1.988</td>
<td>0.968</td>
<td>5.4</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Table 2. Consolidated Analysis from all 3 Sites Based on Results of Analysis of Variance (ANOVA)

<table>
<thead>
<tr>
<th>Comparison Method</th>
<th>N</th>
<th>Slope</th>
<th>Intercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nova StatStrip and Fusion</td>
<td>213</td>
<td>0.972 (0.962–0.982)</td>
<td>5.3 (3.8–6.9)</td>
</tr>
<tr>
<td>LifeScan and Fusion</td>
<td>213</td>
<td>0.864 (0.840–0.888)</td>
<td>22.5 (18.8–26.2)</td>
</tr>
<tr>
<td>Nova StatStrip and LifeScan</td>
<td>213</td>
<td>0.890 (0.865–0.914)</td>
<td>17.7 (13.9–21.5)</td>
</tr>
</tbody>
</table>

Both meters were also assessed for the total allowable error limits based on CLIA (Clinical Laboratory Improvement Amendment) guidelines as shown in Figure 4. Nova StatStrip was found to meet total allowable error limits in 100% of the runs.

Comparative analysis of the percent bias also shows good bias between the Vitros Fusion and Nova StatStrip (1.8) as compared with the percent bias between the Vitros Fusion and the LifeScan Flexx (5.3) and between the Nova StatStrip and the LifeScan Flexx (3.5) as shown in Figure 5.

The within-run precision study gave acceptable results for the coefficient of variation (CV) as less than 5% on both meters when tested with controls. Results with both analyzers at 3...
levels of controls are shown in Table 3. Although not used as a major monitor for achieving TGC, a lower CV was observed with the Nova StatStrip meter.

Accuracy of the analyzers was also determined based on the fact that significantly more samples on the Nova StatStrip (29 of 41) fell within 10% of the reference method compared with the LifeScan Flexx (7 of 41). In addition, significantly fewer values on the Nova StatStrip differed by more than 15% from the reference method (1 of 41) compared with the LifeScan Flexx (26 of 41) meters.

Besides doing all analytical correlation and comparisons, a survey was also performed for CVICU nurses who were actually using the meter to analyze the user choice and reasons. One-hundred percent of the nurses concurred on the preference of Nova StatStrip over LifeScan Flexx meter. Faster results and higher reliability because of the values falling closer to the laboratory analyzer were the main drivers for building confidence.

Discussion

Regarding the differences in the CVs noticed with the precision study for both meters along with the extent to which the glucose meters correlated with the laboratory Fusion method, significant differences were noticed between the 2 meters. The Nova StatStrip technology demonstrated closest correlation with the laboratory Fusion method based on the assessment of the slope and intercept calculated by Deming’s regression analysis. Nova StatStrip was also able to meet the CLIA proficiency testing criteria for acceptable analytical performance by meeting the total allowable error limits 100% of the time.

Analytical performance has many ramifications on clinical decision making, both in diagnosis and monitoring. Assessment of such an effect is influenced by various recommendations and numerical quality specifications set by expert groups. These numerical quality specifications include imprecision, bias, or total allowable error as major analytical monitors to achieve TGC.10

Modeling of errors in insulin dosing showed that to provide the intended insulin dosage 95% of the time, the
bias and CV needed to be <1% to 2%. Using a Monte Carlo simulation, Boyd and Bruns previously demonstrated that at 10% total error, 16% to 45% of sliding scale insulin doses would be an error, though small dosing errors would predominate. Larger dosing errors were common when total error exceeded 10% to 15%.7

In conclusion, the improved performance on the Nova StatStrip as measured by regression analysis with the reference Fusion method, low bias, good precision, and a total allowable error of less than 10%, 100% of the time should result in fewer insulin dosing errors for patients. Along with the analytical edge, end-user satisfaction also ensures better compliance with enhanced acceptability. Together, this should allow for better management of critically ill patients on TGC protocols. LM

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<table>
<thead>
<tr>
<th>Level of Controls</th>
<th>LifeScan Flexx, CV%</th>
<th>StatStrip Nova, CV%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>3.83</td>
<td>2.25</td>
</tr>
<tr>
<td>Level 2</td>
<td>1.72</td>
<td>1.03</td>
</tr>
<tr>
<td>Level 3</td>
<td>1.75</td>
<td>0.75</td>
</tr>
</tbody>
</table>

9. CLIA Requirements for Analytical Quality. Available at: www.westgard.com/clia.htm