Comparison of Lactate Values Between Point-of-Care and Central Laboratory Analyzers

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Abstract
Measurement of lactate levels is important in the care of critically ill adult and pediatric patients. We compared 3 whole blood lactate methods (Radiometer ABL 725, Radiometer Medical A/S, Bronshoj, Denmark; i-STAT, i-STAT, East Windsor, NJ; and Nova Lactate Plus, Nova Biomedical, Waltham, MA) with 2 plasma-based methods (Roche Integra, Roche Diagnostics, Indianapolis, IN; and Vitros, Ortho Clinical Diagnostics, Rochester, NY). The Vitros LAC slide assay was used as the reference method. Results were compared by least squares regression and Bland-Altman plots and by comparing concordance within clinically relevant lactate ranges. Correlation between lactate methods was good with slopes between 0.87 and 1.06 and intercepts of 0.9 to 1.8 mg/dL (0.1-0.2 mmol/L) of lactate for all 4 methods compared with the Vitros. At high (>54.1 mg/dL [6 mmol/L]) lactate values, the Radiometer and i-STAT methods reported lower lactate results compared with the Vitros and Integra. The Nova analyzer reported higher lactate results than either the Vitros or Integra. The negative bias in i-STAT and Radiometer results may confound the interpretation of patient condition if multiple methods are used within the same institution.

Measurement of lactate levels is important in the assessment of severely ill adults and children. Recently, more point-of-care platforms and blood gas analyzers have added lactate measurement to allow testing in a stat laboratory or point-of-care application. The National Academy of Clinical Biochemistry draft guidelines on evidence-based practice for point-of-care testing conclude that more rapid turnaround time of lactate results in critically ill patients leads to improved clinical outcomes. Thus, use of point-of-care lactate measurement methods seems to be clinically justified. However, no study has compared lactate values obtained from multiple central laboratory (plasma-based assays) and point-of-care (whole blood) platforms to determine whether clinically relevant discrepancies might occur if testing is performed on both plasma (central laboratory) and whole blood (point-of-care or blood gas analyzer) platforms.

We compared 2 plasma-based lactate assays with 3 whole blood applications. The plasma-based assays were Lactate Gen.2 performed on a Roche Cobas Integra 400 analyzer (Roche Diagnostics, Indianapolis, IN) and the Vitros LAC slide assay performed on a Vitros 250 analyzer (Ortho Clinical Diagnostics, Rochester, NY). Whole blood applications included the i-STAT (i-STAT, East Windsor, NJ), Radiometer ABL 725 blood gas analyzer (Radiometer Medical A/S, Bronshoj, Denmark), and the newly developed Lactate Plus (Nova Biomedical, Waltham, MA). All tests are approved by the Food and Drug Administration for lactate determination except the Nova Lactate Plus Meter, which is currently for investigational use only.

Materials and Methods
Deidentified lithium heparin whole blood specimens obtained from patients in the emergency department and
intensive care units (n = 90) were analyzed on the Radiometer ABL 725, the i-STAT CG4+, and the Nova Lactate Plus within 1 to 2 minutes of each other. Samples were transported to the laboratory at ambient temperature, and all whole blood analysis was completed within 1 hour of draw time. Within 5 minutes of whole blood analysis, the specimens were centrifuged and plasma separated and kept on ice until testing on the Roche Integra and the Vitros 250 analyzers could be completed (within 1 hour of plasma separation). Linearity and precision of each device or assay was also performed using material provided by the individual manufacturers. The study design was approved by the Mayo Clinic Institutional Review Board.

There is currently no reference standard for lactate measurement. The Vitros LAC slide assay, currently the primary method in our laboratory, was originally validated by the manufacturer against an ion exclusion chromatography method. It showed excellent agreement with this nonenzymatic method (slope, 0.99; intercept, 0.18 mg/dL [0.02 mmol/L]; correlation coefficient, 1.00; samples ranged from 9.0-122.5 mg/dL [1.0-13.6 mmol/L]).2 Vitros interassay precision in our laboratory during a 1-month period yields coefficients of variation (CVs) of less than 10% across the range of lactate values typically encountered. The manufacturer of the Lactate Gen2 assay validated its performance on the Integra by comparing results with the same reagent run on a Hitachi 917 analyzer and by comparing with results of a previous generation lactate assay run on the Integra.3 Because there is no single reference method or standard for lactate, evaluation of the point-of-care lactate methods was performed by comparing results with the Vitros assay alone and with the averaged result of the Vitros and Integra methods.

To assess the clinical importance of differences in lactate values observed between methods, the percentage of concordance (compared with the Vitros) within clinically relevant ranges was calculated. Results were classified as low risk (lactate result, ≤19.8 mg/dL [2.2 mmol/L]), intermediate risk (lactate result, 20.7-45.0 mg/dL [2.3-5.0 mmol/L]), or high risk (lactate result, >45.0 mg/dL [5 mmol/L]) based on available literature relating lactate levels to patient outcome.4,6 Among the 90 samples analyzed on the Vitros, there were 29, 30, and 31 samples in the low-, intermediate-, and high-risk categories respectively. The percentage of concordance (percentage of all samples that fell in the same risk category as the Vitros result) was then calculated for each method.

Results

Linearity evaluation for each method using material provided by the individual vendors demonstrated 95% to 105% recovery of the expected values between lactate levels of 9.0 and 126.1 mg/dL (1-14 mmol/L) for all methods tested (the Nova Lactate Plus did not have linearity material available).

Precision experiments on the Radiometer ABL 725, i-STAT, and Integra methods demonstrated that the CV was 3% or less when control material was run 20 times during 7 to 10 days covering ranges of lactate levels of 9.0 to 81.1 mg/dL (1.9 mmol/L). For the Nova meter, precision was assessed by running control samples at 2 levels 20 times during 10 days: CVs were 15.8% at low (15.3 mg/dL [1.7 mmol/L]) and 4.3% at high (63.1 mg/dL [7.0 mmol/L]) levels.

Method correlation by least squares regression (using the Vitros as reference standard) yielded slopes of 0.95 for the Integra 400 Plus, 0.87 for the Radiometer ABL and i-STAT, and 1.06 for the Nova, with $r^2$ of 0.99 or more in each case, indicating strong correlation between the methods. Intercepts were between lactate levels of 0.9 and 1.8 mg/dL (0.1-0.2 mmol/L) for all methods. Because the Vitros and Integra methods correlated extremely well, the averaged result from the 2 plasma methods was also used as a reference method to compare the performance of the 3 whole blood assays. When this was done, the slopes and intercepts of the least squares regression fit for the Radiometer (slope, 0.88; intercept, 0.06), i-STAT (slope, 0.89; intercept, 0.09), and Nova (slope, 1.08; intercept, 0.14) methods changed little. Bland-Altman plots of the 4 assays (vs the Vitros LAC) are shown in Figure 11 and Figure 2. The Roche Integra 400 Lactate Gen2 assay correlated most closely with the Vitros method. The Radiometer and i-STAT assays exhibited negative bias (relative to the Vitros) at high lactate values, whereas the Nova Lactate Plus method exhibited a positive bias relative to the Vitros (Figures 1 and 2).

Sample stability was addressed in 2 separate experiments using whole blood or plasma. Ten whole blood lithium heparin specimens were kept on ice for up to 30 minutes. The mean lactate concentration for the 10 specimens at time 0 was 45.9 mg/dL (5.1 mmol/L; range, 11.7-144.1 mg/dL [1.3-16.0 mmol/L]), and the lactate concentration changed by 1.8 mg/dL (0.2 mmol/L) or less in each specimen during the 30 minutes on ice. In a similar experiment, 10 whole blood specimens were separated into lithium heparin plasma and kept on ice up to 2 hours. The mean lactate concentration at time 0 was 39.6 mg/dL (4.4 mmol/L; range, 8.1-80.2 mg/dL [0.9-8.9 mmol/L]), and lactate values changed by 1.8 mg/dL (0.2 mmol/L) or less in each specimen during 2 hours. Thus, sample stability did not contribute to the differences observed between whole blood and plasma lactate values.

To assess the clinical importance of differences in lactate values observed between methods, the percentage of concordance (compared with the Vitros) within clinically relevant ranges was calculated. For the Integra 400, 89 (99%) of 90 samples fell within the same risk category as the Vitros value. The Radiometer ABL 725 and i-STAT had 85 (94%) of 90 samples concordant with the Vitros result, and the Nova Lactate Plus demonstrated 90% concordance (81/90) with the Vitros Table II.
Point-of-care or stat laboratory (ie, whole blood) lactate testing is increasingly common and increasingly justified based on medical benefits. However, few studies have been published correlating plasma-based with whole blood measurements of lactate levels. One previous study found a strong correlation between the lactate level measured on a Radiometer ABL 700 series instrument and a Vitros but did not include other point-of-care methods or discuss the clinical relevance of any differences. Another recent study found that lactate levels measured on 2 different blood gas analyzers correlated very well, but this study did not compare values with those from a plasma-based method. In this study, we compared 5 different methods for lactate determination—3 whole blood applications and 2 plasma-based laboratory methods. The Integra 400 lactate assay correlates very closely with the Vitros method, such that the 2 methods could be used interchangeably with differences in clinical interpretation of results being uncommon.

The number of samples concordant with Vitros risk category determination for Integra, Radiometer, i-STAT and Nova lactate measurement methods is shown in Table 1.

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Integra</th>
<th>Radiometer</th>
<th>i-STAT</th>
<th>Nova</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low, ≤ 2.2 (n = 29)</td>
<td>29</td>
<td>29</td>
<td>29</td>
<td>27†</td>
</tr>
<tr>
<td>Intermediate, 2.3-5.0 (n = 30)</td>
<td>29§</td>
<td>27‖</td>
<td>27‖</td>
<td>23¶</td>
</tr>
<tr>
<td>High, &gt;5.0 (n = 31)</td>
<td>31</td>
<td>29¶</td>
<td>29¶</td>
<td>31</td>
</tr>
</tbody>
</table>

Lactate values in the risk categories are given in Système International units (mmol/L); to convert to conventional units (mg/dL), divide by 0.1110. 

* Lactate values in the risk categories are given in Système International units (mmol/L); to convert to conventional units (mg/dL), divide by 0.1110. Vitros 250 analyzer, Ortho Clinical Diagnostics, Rochester, NY; Roche Cobas Integra 400 analyzer, Roche Diagnostics, Indianapolis, IN; Radiometer ABL 725 blood gas analyzer, Radiometer Medical A/S, Bronshøj, Denmark; i-STAT, i-STAT, East Windsor, NJ; and Lactate Plus, Nova Biomedical, Waltham, MA.

† Based on the Vitros result.

§ Two samples classified as low risk by Vitros were classified intermediate risk by Nova.

‖ One sample classified as intermediate risk by Vitros was classified low risk by Integra.

¶ Three samples classified as intermediate risk by Vitros were classified as low risk by Radiometer and i-STAT.

Six samples were classified as intermediate risk by Vitros but high risk by Nova, and one sample classified as intermediate risk by Vitros was low risk by Nova.

Two samples classified as high risk by Vitros were classified as intermediate risk by Radiometer and i-STAT.
measurement performed in the central laboratory. Under these conditions, it may seem that the lactate value has increased over time, and the area under the curve of lactate concentration over time may be falsely increased. This would suggest a worse prognosis for the patient. Discrepancies between i-STAT or Radiometer and Vitros were more significant at lactate values of more than 54.1 mg/dL (6 mmol/L; Figure 1). Institutions that use the i-STAT or Radiometer with a central laboratory method should inform clinicians that caution must be used when comparing high lactate values between point-of-care and central laboratory methods. The Nova method, which is not currently approved by the Food and Drug Administration for in vitro diagnostic use, produced lactate values that were higher than values given by any of the other 4 methods.

References