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Blood Gas Analyzer Accuracy of Glucose Measurements

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Abstract

Objective: To investigate the comparability of glucose levels measured with blood gas analyzers (BGAs) and by central laboratories (CLs).

Material and Methods: Glucose measurements obtained between June 1, 2007, and March 1, 2016, at the Vanderbilt University Medical Center were reviewed. The agreement between CL and BGA results were assessed using Bland-Altman, consensus error grid (CEG), and surveillance error grid (SEG) analyses. We further analyzed the BGAs' performance against the US Food and Drug Administration (FDA) 2014 draft guidance and 2016 final guidance for blood glucose monitoring and the International Organization for Standardization (ISO) 15197:2013 standard.

Results: We analyzed 2671 paired glucose measurements, including 50 pairs of hypoglycemic values (1.9%). Bland-Altman analysis yielded a mean bias of −3.1 mg/dL, with 98.1% of paired values meeting the 95% limits of agreement. In the hypoglycemic range, the mean bias was −0.8 mg/dL, with 100% of paired values meeting the 95% limits of agreement. When using CEG analysis, 99.9% of the paired values fell within the no risk zone. Similar results were found using SEG analysis. For the FDA 2014 draft guidance, our data did not meet the target compliance rate. For the FDA 2016 final guidance, our data partially met the target compliance rate. For the ISO standard, our data met the target compliance rate.

Conclusion: In this study, the agreement for glucose measurement between common BGAs and CL instruments met the ISO 2013 standard. However, BGA accuracy did not meet the stricter requirements of the FDA 2014 draft guidance or 2016 final guidance. Fortunately, plotting these results on either the CEG or the SEG revealed no results in either the great or extreme clinical risk zones.

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Intensive blood glucose control, although controversial, has been found to improve outcomes in several cohorts of hospitalized or nonhospitalized patients.[1-3] Effective control of blood glucose relies on both accurate and timely glucose measurements. Currently, central laboratory (CL) glucose measurement is considered the laboratory comparative method when assessing agreement among glucose measurement devices in a hospital. The obvious drawback to CL measurements is the average turnaround time (TAT) that can be greater than 1 hour,[4] which can be too long for effective glucose control in critically ill and perioperative patients.[5]

Blood glucose meters (BGMs), first introduced in the US market as over-the-counter self-monitoring devices for laypersons in the 1970s, have revolutionized the care of patients with diabetes. These devices have enabled frequent and timely measurement of capillary blood glucose levels, which in turn has improved glucose control[6] and contributed to greatly reduced long-term cardiovascular, renal, and ophthalmic complications.[7] Over time, BGMs have migrated into the hospital environment, where they have become the mainstay for inpatient blood glucose testing in many institutions.[8,9] These devices are problematic because (1) they are inherently not as reliable as CLs, (2) clinical conditions such as impaired perfusion due to hypotension, peripheral edema, or vasopressor support may interfere with accurate capillary (finger stick) blood sampling, and (3) technical limitations and interfering substances may affect the accuracy of these meters, especially in situations such as hypoxia

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(with glucose oxidase-based meters) or anemia and with certain medications such as acetaminophen.[10]

The Centers for Medicare and Medicaid Services (CMS) has proposed enforcing a restriction on BGMs in critically ill patients unless they have been specifically approved by the US Food and Drug Administration (FDA) or waived by Clinical Laboratory Improvement Amendments for these patients[11] based on the draft guidance for professional BGMs written by the FDA in January 2014.[12] This document stated that critically ill patients should not be tested with a glucose meter because the results from capillary finger stick may be inaccurate due to impaired peripheral perfusion. At present, there are only 2 point-of-care (POC) BGMs that are specifically approved for use in critically ill patients (StatStrip Glucose Hospital Glucose Meter and StatStrip Xpress Glucose Hospital meters [Nova Biomedical]),[13] but these meters are not approved for capillary measurements—only for venous and arterial blood—which greatly limits their use.[14] Until BGMs are approved for capillary POC blood glucose monitoring in critically ill patients, enforcement of this FDA guidance by the CMS against off-label use of these products will restrict the widespread availability of this diagnostic tool.

The CMS has recently suggested that blood gas analyzers (BGAs) could be used as an alternative to BGMs.[15] Data regarding the comparability of BGA glucose measurement, however, is limited. Uyanik et al[16] reported 40 BGA glucose measurements, with a large mean bias of 50.2 mg/dL (to convert to mmol/L, multiply by 0.0555) between the Nova Biomedical Critical Care Xpress BGA and the Olympus AU2700 autoanalyzer (Beckman Coulter Inc) (a comparative CL method). No hypoglycemic data points were analyzed in this study. Oliver et al[17] evaluated the performance of the Radiometer ABL90 BGA compared with a CL method and found the estimated bias for glucose was higher than the allowable bias according to local laboratory criteria. However, Leino and Kurvinen[18] reported that blood glucose values measured with 3 types of BGAs were highly correlated (r=0.972-0.985) with CL values in critically ill patients. Luukkonnen et al[19] compared results of blood glucose measurements obtained with a BGA and 2 CLs and found a correlation of 0.982 to 0.987 in an intensive care setting. Uysal et al[20] found a correlation of 0.964 between BGAs and CLs for glucose measurement in emergency department patients. These studies were all limited by relatively small sample sizes, especially in the hypoglycemic range, and none of the studies analyzed performance of the BGA using the latest FDA guidance or International Organization for Standardization (ISO) comparability criteria. Moreover, no study used error grid analysis, which is a tool for evaluating the clinical accuracy of a metric compared with a reference method.

The primary aim of our study was to investigate the agreement of a BGA glucose measurement with a CL glucose measurement in a large retrospective cohort of hospital patients by analyzing paired glucose results available from each patient's electronic medical record. We analyzed the method agreement using metrics of analytical accuracy, including those specified by (1) the FDA 2014 draft guidance,[12] (2) the FDA 2016 final guidance[21] for prescription POC blood glucose monitor systems, (3) the ISO 15197:2013 standard,[22] and (4) a Bland-Altman (BA) analysis. We also analyzed measured BGA results for clinical accuracy against reference methods with the consensus error grid (CEG)[23] and the surveillance error grid (SEG).[24]

MATERIAL AND METHODS

Paired Glucose Values

This study was approved by the Vanderbilt University Institutional Review Board (IRB number 150865). All laboratory glucose measurement results for patients treated at Vanderbilt University Medical Center between June 1, 2007, and March 1, 2016, were reviewed. Paired glucose results, defined as CL glucose collection time within 5 minutes of the BGA glucose collection time for the same patient with numeric results for both, were extracted from our electronic data warehouse for comparison. When a patient had repeated glucose measurement by CL or BGA, whichever one that met the 5-minute pairing criteria was chosen for analysis.