RESEARCH ARTICLE

Concordance between point-of-care blood gas analysis and laboratory autoanalyzer in measurement of hemoglobin and electrolytes in critically ill patients

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Background: We tested the hypothesis that the results of the same test performed on point-of-care blood gas analysis (BGA) machine and automatic analyzer (AA) machine in central laboratory have high degree of concordance in critical care patients and that the two test methods could be used interchangeably.

Methods: We analyzed 9398 matched pairs of BGA and AA results, obtained from 1765 patients. Concentration pairs of the following analytes were assessed: hemoglobin, glucose, sodium, potassium, chloride, and bicarbonate. We determined the agreement using concordance correlation coefficient (CCC) and Bland-Altman analysis. The difference in results was also assessed against the United States Clinical Laboratory Improvement Amendments (US-CLIA) 88 rules. The test results were considered to be interchangeable if they were within the US-CLIA variability criteria and would not alter the clinical management when compared to each other.

Results: The median time interval between sampling for BGA and AA in each result pair was 5 minutes. The CCC values ranged from 0.89(95% CI 0.89-0.90) for chloride to 0.98(95% CI 0.98-0.99) for hemoglobin. The largest bias was for hemoglobin. The limits of agreement relative to bias were largest for sodium, with 3.4% of readings outside the US-CLIA variation rule. The number of readings outside the US-CLIA acceptable variation was highest for glucose (7.1%) followed by hemoglobin (5.9%) and chloride (5.2%).

Conclusion: We conclude that there is moderate to substantial concordance between AA and BGA machines on tests performed in critically ill patients. However, the two tests methods cannot be used interchangeably, except for potassium.

KEYWORDS

automatic analyzer, blood gas analysis, Electrolytes, hemoglobin

1 | INTRODUCTION

There is a high incidence of electrolyte and acid-base disturbances in critically ill patients.¹ Rapid availability of test results to assess these disturbances is a prerequisite for their management. Conventionally, the blood samples are collected and transported to central laboratory, where serum is separated, diluted, and tested using

auto-analyzers (AA).² The results are then available to the clinician, usually through patient information systems. Even with the latest advancement in bioengineering, the reported turnaround time for serum biochemical analysis results is more than 30 minutes and this is without accounting for the time taken to order the right test and despatching the blood sample to the central laboratory.³ Availability of point-of-care (POC) testing in clinical medicine has dramatically

reduced the turnaround time for results of various tests, facilitating rapid decision-making and possibly better quality of care. The blood gas analysis (BGA) is POC technology that is able to provide crucial information such as electrolytes, acid-base status, and hemoglobin, within 10–12 minutes.⁴ Besides the advantage of rapid turnaround time, the BGA also minimizes the number of pre-analytic steps and involves significantly less volume of blood. However, there are key differences in how the blood sample is processed and analyzed in BGA machines as compared to the AA in central biochemistry laboratories, for instance, the separation of serum and pre-analytic dilution in AA.² An understanding of differences, if any, in results of the same test performed on these machines and their clinical relevance, would be crucial to ascertain the implications in clinical decision-making. The existing literature comparing these tests yielded mixed results and use of small sample sizes, study population, and method of sampling may have contributed to the discrepancy.^{5–9}

We tested the hypothesis that results of the same test performed on BGA machine and AA machine have high degree of concordance in an unselected population of critical care patients and that the two test methods could be used interchangeably. To test this hypothesis, we retrospectively analyzed the concordance between the electrolyte and hemoglobin values obtained from these two test methods using the largest sample size reported to date.

2 | MATERIALS AND METHODS

The study was a retrospective observational study, conducted on patients admitted to mixed medical and surgical intensive care unit (ICU) in a tertiary level hospital in year 2015. The study was approved by Southern Adelaide Clinical Human Research Ethics Committee (SAC HREC EC00188).

Test results from the two methods (POC BGA and AA in central laboratory) were included for analysis if they were performed within 30 minutes of each other. Simultaneously measured (<30 minutes) concentration pairs of the following analytes were extracted from the two test methods: hemoglobin, glucose, sodium, potassium, chloride, and bicarbonate.

The tests were performed on POC BGA machine (ABL Flex 800, Radiometer Medical A/S, Bronshøj, Denmark) and AA machine (Roche/Hitachi Modular Analyzer; Hitachi High-Technologies, Tokyo, Japan) in the central biochemistry laboratory. Hemoglobin was measured in the central laboratory spectrophotometrically using the Cyan-Met (CM) hemoglobin method (Cyan-Met Hemoglobin, UniCel DxH 800; Beckman Coulter, Brea, CA).

To ensure the accuracy of test results, the central laboratory participates in an external quality assessment program. BGA machines perform one-point calibration every two hours and two-point calibration every eight hours. All blood samples were collected by trained ICU nurses using existing arterial access. In the absence of arterial access, central venous access was used. The sample for BGA was collected in an electrolyte balanced heparin 1.7-mL syringe (safePICO Aspirator®, Radiometer Medical ApS, Denmark), and

sample for AA was collected in lithium heparin and gel 2.5-mL vial (VACUETTE® Tubes, Greiner Bio-One, Austria) and potassium EDTA 2-mL vial (VACUETTE® Tubes, Greiner Bio-One, Austria) for electrolyte and hemoglobin measurement, respectively.

2.1 | Analysis

Study sample size was primarily based on sodium concentrations, as our previous study revealed the significance of this electrolyte in morbidity and mortality in critically ill patients.¹⁰ A sample of 100 paired specimens was analyzed. The mean (SD) of sodium in BGA and AA was 138.23 (5.33) and 138.02 (5.25), respectively, with average difference (bias) of 0.22. The sample size based on these differences at α of 0.05 and β of 0.20 was 9078 paired specimens.

We determined the agreement between the results obtained by the AA and BGA methods using concordance correlation coefficient (CCC)¹¹ and Bland-Altman analysis.¹² It is customary in such agreement analyses to use paired *t* tests (to test significant differences between means), Pitman's test (to test significant differences between variances), and Bradley-Blackwood *F* test (to simultaneously test for significant differences between means and variances). However, these tests are sensitive to large sample sizes and yield significant differences due to small standard errors resulting from large sample sizes. We therefore did not conduct these tests of significance and, instead, reported the results as 95% confidence intervals (CI) for the CCC. Multivariate outlier detection method¹³ was used to limit the analyses to meaningful numbers.

Additionally, result pairs with at least one hemoglobin result less than 70 g/L were analyzed for agreement between the two test methods. A test result of less than 70 g/L was regarded as an indication for blood transfusion.¹⁴

The difference in results from the two test methods was also assessed against the United States Clinical Laboratory Improvement Amendments (US-CLIA) 88 rules,¹⁵ according to which the following variations are considered as acceptable: chloride $\pm 5\%$; glucose $\pm 10\%$; sodium ± 4.0 mmol/L; hemoglobin $\pm 7\%$; potassium ± 0.5 mmol/L. There were no available performance criteria on bicarbonate.

The test results were considered to be interchangeable if they were within the US-CLIA variability criteria and would not alter the clinical management when compared to each other. All analyses were performed using SPSS version 21 (IBM Corp., Armonk, NY, USA).

3 | RESULTS

A total of 9398 matched pairs of BGA and AA results were obtained for analysis from 1765 patients. The median (IQR) time interval between sampling for BGA and AA in each result pair was 5 (3–10) minutes.

Table 1 reveals the analysis of the electrolytes and metabolites performed by the BGA and AA machines. The number of outliers for all analytes was below 2%, therefore minimizing any

influence on the fit of statistical models. The CCC values were moderate to substantial for all assays. The bias was generally small. The largest bias was for hemoglobin. The limits of agreement (LOA) relative to bias were largest for sodium (Figure 1), with 3.4% of readings outside the US-CLIA variation rule. The number of readings outside the US-CLIA acceptable variation was highest for glucose (7.1%) followed by hemoglobin (5.9%) and chloride (5.2%).

There were 245 result pairs where at least one hemoglobin result was ≤ 70 gm/L, indicating the need for blood transfusion.¹⁴ Of these, only in 115 (47%) pairs, both the test results were less than 70 gm/L. Of the remaining 130 pairs, where there was discrepancy, the laboratory-based hemoglobin measurement more frequently indicated the need for transfusion (101 pairs [77%]) as compared to BGA (29 pairs [23%]). Upon analyzing the result pairs where the time interval was less than 10 minutes, similar results were obtained. The laboratory-based hemoglobin measurement more frequently indicated the need for transfusion (74 pairs [82%]) as compared to BGA (16 pairs [18%]).

4 | DISCUSSION

There was good concordance between the two test methods, with low bias. The LOA relative to bias was relatively large for sodium and chloride, with 3.4% and 5.2% readings lying outside the US-CLIA variability limits, respectively. Also the bias for hemoglobin was largest with 5.9% readings outside the US-CLIA limits. Only for potassium concentration, the two tests yielded similar, interchangeable results. The LOA and bias were concerning for sodium and hemoglobin, respectively, and this may have implications for clinical practice.

Sodium levels if outside the normal range are associated with high morbidity and mortality.¹⁰ Furthermore, if they are not corrected gradually and carefully, the associated morbidity is significant.¹⁶ This necessitates repeated sodium measurements during correction. Given the wide limits of agreement relative to the small bias, it will be a safer practice to either follow BGA alone or AA alone to guide treatment and they should not be used interchangeably. Although only 3.4% of pairs were outside the US-CLIA limit of 4 mmol/L, this limit appears to be clinically significant as this limit approximates the

safe maximum acceptable change per day in sodium concentrations in high-risk patients.¹⁶ Also varying sodium levels may distort the calculated anion gap, a measure frequently used in critically ill patients.⁵ The findings are similar to previous studies.^{5,7,9,17,18} Similar to sodium, the limits of agreement were large relative to the bias for chloride; however, the impact of such degree of discrepancy on clinical practice is not clear.

The bias for potassium was only 0.09, which is the lowest reported in literature (0.1–0.7 mmol/L).² Also only 1.6% of the readings were outside the US-CLIA variability limits. The bias is well acknowledged as the potassium is released from platelets during clotting.² This small degree of bias and the fact that majority of readings were within the acceptable variation, suggests that for practical purposes, the two tests yield similar results.

The bias was largest for hemoglobin levels. Such differences may be mistaken as evidence of bleeding or may lead to treatment dilemma as the results from these machines could lie on different sides of the transfusion threshold for a given clinical situation. A frequently recognized transfusion threshold for critically ill patients is 70 gm/L.¹⁴ Transfusion threshold was met by at least one of the two test results in 245 pairs. The clinical dilemma is likely to be a frequent occurrence, as there was discrepancy between the two tests, in terms of meeting transfusion threshold, in nearly half of these result pairs. In these result pairs, the laboratory-based Hb measurement tends to indicate blood transfusion 3–4 times more frequently than BGA. This overestimation by BGA has been observed in previous studies.¹⁹

The blood glucose had small bias and limits of agreement; however, there were two observations of concern. Firstly, 7.1% of readings by the two methods were outside the US-CLIA variability limits, and secondly, the difference between the BGA and AA increased above 10 mmol, with BGA tending to overestimate blood glucose levels. In critically ill patient, blood glucose levels are generally controlled to less than 10 mmol/L. The reason behind this differential agreement between the two tests is not clear.

The above observations in sodium and hemoglobin levels may be explained by number of factors. High proportion of critically ill patients have protein levels outside normal range.²⁰ The indirect ion-specific electrode employed in AA has been shown to be more susceptible to effects of protein levels, thereby altering the

TABLE 1 Agreement analyses between AA and BGA as continuous data

Analyte	N	Mean (SD)		Concordance correlation coefficient		Limits of agreement	Bias	No. of pairs outside US-CLIA limits
		BGA	AA	Point	95% CI			
Hemoglobin (g/L)	9198	98.29 (18.99)	100.28 (19.57)	0.98	0.984–0.985	−7.471–3.486	−2.19	554 (5.9%)
Glucose (mmol/L)	9192	7.85 (2.26)	7.75 (2.15)	0.98	0.980–0.982	−0.711–0.923	0.10	662 (7.1%)
Sodium (mmol/L)	9342	138.34 (5.17)	138.05 (5.12)	0.92	0.916–0.922	−3.751–4.316	0.29	322 (3.4%)
Potassium (mmol/L)	9293	3.97 (0.55)	3.87 (0.52)	0.95	0.947–0.951	−0.199–0.378	0.09	148 (1.6%)
Chloride (mmol/L)	9345	103.75 (5.58)	105.11 (5.65)	0.89	0.887–0.895	−5.831–3.119	−1.35	486 (5.2%)
Bicarbonate (mmol/L)	9362	24.45 (5.10)	24.87 (5.20)	0.95	0.952–0.955	−3.386–2.553	−0.42	N/A

FIGURE 1 Bland-Altman plot of AA and BGA for (A) hemoglobin, (B) glucose, (C) sodium, (D) potassium, (E) chloride, and (F) bicarbonate; showing the 95% limits of agreement

measured levels of sodium.¹⁸ It is possible this may contribute to wide LOA observed in our patient population. The syringes used for BGA have heparin, type of which may differ between brands and such syringes can thereby introduce different degrees of bias when the levels of positively charged ions are being measured.^{21,22} Other factors that may contribute to differences include sample transport, dilution of serum samples prior to testing, and variations

in instrument calibration.² For hemoglobin concentration measurement, the difference in dilution from heparin-based or EDTA-based anticoagulation may have contributed. Also there is some suggestion in literature of difference in hemoglobin concentration in venous vs arterial blood. As this was not controlled for in our study, this may have also contributed to observed bias. The other differences such as error from high leukocyte counts in Cyanmethemoglobin coulter

method²³ and induced hemolysis in the BGA machine may have also contributed to the bias observed.

Although the bicarbonate levels are *calculated* in the BGA machine as opposed to *measured* in the central laboratory, there was acceptable bias although with relatively large limits of agreement. This may have implications while calculating anion gap in critically ill patients.⁵

There are some notable limitations of this study. Firstly, our study did not explore the pre-analytical process of using POCT machine which would impact on the quality of results as previously reported.²⁴ The analysis of factors, such as plasma proteins, leukocyte count, arterial vs venous sample, sample collection, and handling, may help explain the observed biases and limits of agreement. Another limitation which is present in several other studies is unavoidable due to retrospective design, and due to pragmatic reasons, is the time difference between the sampling for the two tests. Treatment interventions such as fluid resuscitation or blood transfusion may alter the agreement between the two tests. The median time interval was only 5 minutes in our study, and the large sample size to certain extent would have diluted this error. However, this should be controlled for in future study, with ideally the tests performed on the same blood sample procured from the patient.

We conclude that there is moderate to substantial concordance between the central laboratory AA and BGA machines on tests performed in critically ill patients. However, the two tests methods cannot be used interchangeably, except for potassium. For clinical practice such as following analyte trends and measuring before-after concentrations during clinical intervention, using the same test method is important.

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