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ORIGINAL ARTICLE

Interchangeability of Electrolyte and Metabolite Testing on Blood Gas and Core Laboratory Analyzers

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SUMMARY

Background: **Using blood gas (BG) analyzers as backups for core laboratory analyzers has the potential to greatly reduce turnaround times and costs.**
Methods: **One venous blood gas syringe, one plasma separator tube (PST), and one serum separator tube (SST) were drawn from 42 healthy individuals. All samples were run on the GEM4000 BG analyzer whereas the PST and SST samples were also run on the Roche Modular chemistry analyzer. Blood electrolyte and metabolite parameters were compared for paired measurements, and their differences were assessed for statistical and clinical significance.**
Results: **Whole blood on GEM4000 and plasma/serum on Roche Modular produced incomparable results for Na^+ in plasma and serum (2.5 percentile difference, GEM4000 - Modular: -4.975 and -4.95 mmol/L, respectively) and K^+ in serum (2.5 percentile difference, GEM4000 - Modular: -0.7975 mmol/L). When comparing whole blood to plasma/serum samples, all from the GEM4000, incomparable parameters were also found for Cl^- in plasma and serum (97.5 percentile difference, plasma or serum - whole blood: 6 and 5 mmol/L, respectively), and K^+ in serum (97.5 percentile difference, serum - whole blood: 0.7 mmol/L). None of the parameter differences when comparing plasma/serum results on the GEM4000 to those on the Roche Modular were found to be clinically significant.**
Conclusions: **The off-label use of plasma/serum on a BG analyzer produced electrolyte and metabolite measurements that were more interchangeable with standard core laboratory analyzer results than with its designated whole blood samples. The interchangeability of results, therefore, seems to be affected more by different sample types than by different measurement methods.**
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KEY WORDS

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INTRODUCTION

The demand for more rapid feedback of accurate blood test results has been highlighted by the increasing prevalence of point of care (POC) testing in healthcare internationally [1,2]. Receiving faster test results can optimize therapies, improve patient compliance, reduce both short and long-term costs by facilitating faster decision-making, decrease the length of hospital stays and number of clinic visits, delay the onset of health complications, and lower the overall cost of therapies [3].

The most prominent benefactors of this rapid service in a clinical setting, include patients in life-threatening crises, those undergoing surgery, and those with chronic diseases that require regular modifications to long-term therapeutic intervention strategies such as diabetes [4-7]. In response to these findings, central laboratories have undergone increasing automation in the past half-century in an attempt to become more efficient at routine testing [1,2].

Core laboratory chemical analyzers are generally considered the gold standard in terms of electrolyte and metabolite testing. However, due to budget, many hospitals - especially in more rural areas - have had to resort to cabbing samples off to regional centers, an expensive process itself with long turnaround times. As hospitals will generally have multiple blood gas (BG) analyzers, one solution would be to use those as backups for core lab analyzers. BG analyzers can help meet local demands and provide clinical and economic benefits by producing results faster than lab chemistry analyzers [8].

Results obtained from more rapid methods may not necessarily translate into faster, better clinical outcomes if not acted upon in a timely fashion [6,9]. Electrolyte and metabolite values from blood gas analysis are traditionally rarely trusted for clinical decision-making because of a lack of research [8], and concerns have been raised about small differences in results compared to accepted reference methods that could cause clinical misdiagnoses [10]. In our hospital setting, lab analyzers are designed for plasma or serum samples whereas BG analyzers are designed for whole blood [8]. This leads to two factors that could impact the interchangeability of values: different sampling methods and different analyzers used. Small differences have been demonstrated when comparing whole blood BG analyzers to plasma core laboratory analyzers for sodium [11], however, there is a lack of studies comparing BG plasma/serum specimens to core laboratory analyzer measurements. To determine whether interchanging results from different analyzers is possible, we compared analyte values reported by a BG analyzer on whole blood to lab analyzer plasma and serum reference samples. We also looked at the individual effects of having A) different sample types by comparing BG plasma/serum to BG whole blood and B) different analyzers by comparing BG plasma/serum to lab plasma/serum.

MATERIALS AND METHODS

Heparin ABG syringes were used to collect whole blood samples from 42 healthy individuals at the Dr. Everett Chalmers Regional Hospital, Horizon Health Network (Fredericton, New Brunswick, Canada). Plasma (PST) and serum separator tubes (SST) were then used to obtain paired plasma and serum samples. The analytes measured in each case were sodium (Na^+), potassium (K^+), chloride (Cl^-), total carbon dioxide (TCO_2), and glucose (Glu). All three sample types were run on the GEM4000 (Instrumentation Laboratory, Bedford, MA, USA) blood gas analyzer and plasma and serum samples were run on the Roche Modular P800 (Indianapolis, IN, USA) laboratory chemistry analyzer. This study was approved by the Horizon Health Network Research Ethics Board as part of a continuous laboratory quality improvement study and participants provided informed consent.

R Studio (version 3.3.2) and Excel 2016 were used for data analyses and manipulations. The Shapiro-Wilk and Levene's tests were used to assess normality and equal variance (p-value < 0.05). The Wilcoxon signed-rank test without Bonferroni correction was used to compare all parameters ($p < 0.05$) because false negative differences would be more costly in a clinical setting [12]. Data used in the Wilcoxon test were summarized as medians with interquartile ranges (IQR).

When comparing BG analyzer results against lab analyzer results, or BG analyzer plasma/serum results against BG whole blood results, the latter in both cases was considered the reference. Pearson's product-moment correlation and Deming's linear regression were used to evaluate relationships between blood parameters from the same individual measured using different methods. Good correlation does not necessarily translate into good agreement between the two measuring methods [13], but it can highlight some important systematic biases. Difference plots were constructed, which along with clinically-defined acceptance limits, were then used to determine whether the parameter results from the methods were interchangeable. Given that we have defined reference methods, we plot differences as a function of the reference measurement instead of the mean of the two measurements [14]. Clinical acceptance limits (CAL) were considered to be 4 mmol/L for Na^+, 0.5 mmol/L for K^+, 4 mmol/L for Cl^-, 6 mmol/L for TCO_2, and 0.5 mmol/L for Glu following the Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulation requirements [15] and the College of American Pathologists Chemistry/Therapeutic Drug Monitoring survey evaluation criteria [16].

RESULTS

Not all whole blood analyte values from GEM4000 are interchangeable with Modular P plasma and serum values

The statistics evaluating differences between GEM4000 whole blood samples compared to Modular P plasma and serum samples are summarized in Table 1. All parameters were seen to differ by a statistically significant amount except for Glu between BG whole blood and lab plasma samples which had a median difference of 0. Difference plots for comparisons showing limits of agreement that exceeded CAL (Na^+ for lab plasma and lab serum; K^+ in lab serum) are shown in Figure 1. Large intercepts that exceeded CAL were observed for

Table 1. Correlation and parameter difference statistics between GEM4000 whole blood and Modular P plasma and serum samples. Differences are calculated as y - x.

	GEM4000 whole blood (y) vs. Modular P plasma (x)							GEM4000 whole blood (y) vs. Modular P serum (x)							Clinical acceptance limits (mmol/L)
	Slope (95% CI)	Intercept (95% CI)	Correlation coefficient (95% CI)	GEM-4000 median (IQR)	Modular median (IQR)	Median difference (95% CI)	p-value	Slope (95% CI)	Intercept (95% CI)	Correlation coefficient (95% CI)	GEM-4000 median (IQR)	Modular median (IQR)	Median difference (95% CI)	p-value	
Na^+	0.68 (0.49 - 0.88)	42.4 (14.7 - 70.1)	0.7919 (0.6427 - 0.8833)	139 (2)	141 (3.8)	-2 (-5.0 - 1.0)	< 0.05	0.73 (0.53 - 0.94)	35.8 (6.7 - 64.9)	0.7884 (0.6372 - 0.8812)	139 (2)	141 (3)	-2 (-5.0 -1.0)	< 0.05	4
K^+	0.97 (0.90 - 1.04)	0 (-0.3 - -0.2)	0.9780 (0.9591 - 0.9882)	3.8 (0.5)	4 (0.6)	-0.2 (-0.2 - 0)	< 0.05	0.86 (0.74 - 0.99)	0.1 (-0.4 - 0.7)	0.9032 (0.8260 - 0.9471)	3.8 (0.5)	4.4 (0.6)	-0.5 (-0.8 - -0.2)	< 0.05	0.5
Cl^-	0.86 (0.74 - 0.97)	12.3 (0.8- 23.8)	0.8953 (0.8125 - 0.9427)	102 (3)	105 (2)	-3 (-4 - -1)	< 0.05	0.82 (0.71 - 0.92)	16.5 (5.7 - 27.4)	0.9029 (0.8254 - 0.9469)	102 (3)	105 (2.8)	-3 (-4 - 0)	< 0.05	4
TCO_2	1.02 (0.81 - 1.23)	1.2 (-5.1 - 7.5)	0.8056 (0.6643 - 0.8913)	31.5 (4)	29.5 (4)	2 (-1 - 6.0)	< 0.05	1.13 (0.88 - 1.37)	-2.8 (-10.4 - 4.8)	0.7762 (0.6180 - 0.8739)	32 (4)	30 (3)	2 (-3 - 5)	< 0.05	6
Glu	0.98 (0.95 - 1.01)	0 (0 - 0)	0.9960 (0.9925 - 0.9979)	5.1 (1.4)	5.2 (1.4)	0 (-0.3 - 0.1)	0.1703	0.99 (0.94 - 1.04)	0 (-0.3 - 0.3)	0.9888 (0.9791 - 0.9940)	5.1 (1.4)	5.1 (1.3)	-0.1 (-0.4 - 0.3)	< 0.05	0.5

Cl - confidence interval, IQR - interquartile ranges.

Table 2. Correlation and parameter difference statistics for GEM4000 measurements between plasma/serum and the prescribed whole blood samples. Differences are calculated as y - x.

	GEM4000 plasma (y) vs. GEM4000 whole blood (x)							GEM4000 serum (y) vs. GEM4000 whole blood (x)							Clinical acceptance limits (mmol/L)
	Slope (95% CI)	Intercept (95% CI)	Correlation coefficient (95% CI)	GEM-4000 plasma median (IQR)	GEM-4000 whole blood median (IQR)	Median difference (95% CI)	p-value	Slope (95% CI)	Intercept (95% CI)	Correlation coefficient (95% CI)	GEM-4000 serum median (IQR)	GEM-4000 whole blood median (IQR)	Median difference (95% CI)	p-value	
Na^+	0.94 (0.78 - 1.11)	10.3 (-12.9 - 33.5)	0.9087 (0.8356 - 0.9502)	141 (2.8)	139 (2)	2 (1 - 4)	< 0.05	0.84 (0.63 - 1.04)	24.2 (-4.1 - 52.4)	0.8551 (0.7447 - 0.9200)	140.5 (1.8)	139 (2)	2 (-1 - 2)	< 0.05	4
K^+	1.08 (1.02 - 1.14)	-0.3 (-0.6 -- 0.1)	09838 (0.9698 - 0.9913)	3.8 (0.5)	3.8 (0.5)	0 (-0.1 - 0.1)	0.2002	1.24 (1.07 - 1.42)	-0.5 (-1.2 - 0.1)	0.9070 (0.8326 - 0.9492)	4.3 (0.5)	3.8 (0.5)	0.4 (0.1 - 0.7)	< 0.05	0.5
Cl^-	0.96 (0.81 - 1.10)	9.0 (-5.5 - 23.4)	0.9193 (0.8539 - 0.9561)	107 (2)	102 (3)	5 (3 - 6)	< 0.05	1.04 (0.90 - 1.19)	0 (-14.8 - 14.7)	0.9314 (0.8752 - 0.9628)	107 (1.8)	102 (3)	4 (3 - 5)	< 0.05	4
TCO_2	1.10 (0.97 - 1.23)	-3.4 (-7.5 - 0.8)	0.9413 (0.8928 - 0.9682)	31 (4.8)	31.5 (4)	0 (-2 - 1)	0.2706	0.97 (0.82 - 1.11)	1.8 (-2.8 - 6.4)	0.9045 (0.8283 - 0.9479)	32 (3)	31.5 (4)	1 (-2 - 3)	< 0.05	6
Glu	1.09 (1.06 - 1.12)	-0.3 (-0.5 - 0.1)	0.9959 (0.9923 - 0.9978)	5.3 (1.5)	5.1 (1.4)	0.2 (-0.1 - 0.4)	< 0.05	1.12 (1.04 - 1.20)	-0.4 (-0.9 - 0)	0.9895 (0.9805 - 0.9944)	5.3 (1.4)	5.1 (1.4)	0.2 (-0.1 - 0.7)	< 0.05	0.5

Cl - confidence interval, IQR - interquartile ranges.

Table 3. Correlation and parameter difference statistics for plasma and serum measurements between GEM4000 and Modular P. Differences are calculated as y - x.

	GEM4000 plasma (y) vs. Modular P plasma (x)							GEM4000 serum (y) vs. Modular P serum (x)							Clinical acceptance limits (mmol/L)
	Slope (95% CI)	Intercept (95% CI)	Correlation coefficient (95% CI)	GEM-4000 median (IQR)	Modular median (IQR)	Median difference (95% CI)	p-value	Slope (95% CI)	Intercept (95% CI)	Correlation coefficient (95% CI)	GEM-4000 median (IQR)	Modular median (IQR)	Median difference (95% CI)	p-value	
Na^+	0.64 (0.47 - 0.81)	51.6 (27.8 - 75.4)	0.7858 (0.6331 - 0.8796)	141 (2.8)	141 (3.8)	0.5 (-2 - 3)	0.1393	0.61 (0.47 - 0.76)	54.2 (33.3 - 75.1)	0.8088 (0.6694 - 0.8932)	140.5 (1.8)	141 (3)	0 (-3 - 2)	0.7762	4
K^+	1.05 (0.99 - 1.11)	-0.4 (-0.6 - -0.1)	0.9889 (0.9792 - 0.9940)	3.8 (0.5)	4 (0.6)	-0.2 (-0.2 – -0.1)	< 0.05	1.07 (1.02 - 1.11)	-0.4 (-0.6 - -0.1)	0.9906 (0.9825 - 0.9950)	4.3 (0.5)	4.4 (0.6)	-0.1 (-0.2 - 0)	< 0.05	0.5
Cl^-	0.83 (0.74 - 0.92)	19.8 (10.9 - 28.7)	0.9522 (0.9123 - 0.9742)	107 (2)	105 (2)	2 (1 - 4)	< 0.05	0.86 (0.75 - 0.97)	16.4 (5.2 - 27.6)	0.9467 (0.9025 - 0.9712)	107 (1.8)	105 (2.8)	2 (0 - 3)	< 0.05	4
TCO_2	1.14 (0.92 - 1.37)	-2.5 (-9.3 - 4.3)	0.8402 (0.7202 - 0.9114)	31 (5)	29.5 (4)	2 (-1 - 4)	< 0.05	1.07 (0.79 - 1.35)	-0.5 (-9.2 - 8.1)	0.8007 (0.6566 - 0.8884)	32 (3)	30 (3)	2 (-1 - 5)	< 0.05	6
Glu	1.07 (1.03 - 1.11)	-0.2 (-0.4 - 0.0)	0.9959 (0.9923 - 0.9978)	5.3 (1.5)	5.2 (1.4)	0.1 (-0.1 - 0.3)	< 0.05	1.11 (1.07 - 1.15)	-0.5 (-0.7 - -0.2)	0.9974 (0.9952 - 0.9986)	5.3 (1.4)	5.1 (1.3)	0.2 (-0.1 - 0.4)	< 0.05	0.5

Cl - confidence interval, IQR - interquartile ranges.

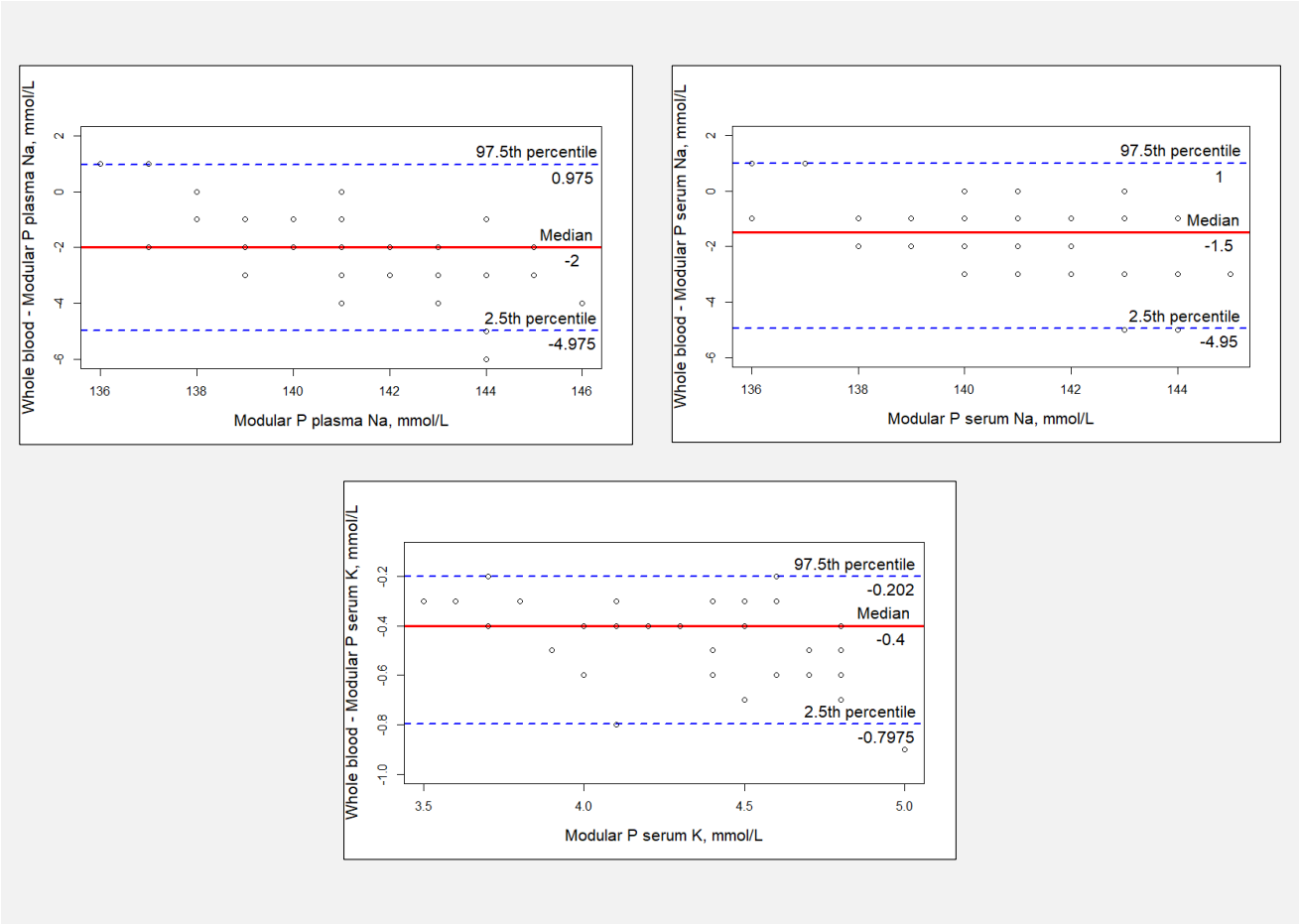

Figure 1. Median difference plots for GEM4000 analyzer whole blood test samples compared to Modular P plasma and serum reference samples.

Limits of agreement are given in terms of 2.5th and 97.5th percentile values, and measurement differences are plotted against the reference Modular P samples.

BG whole blood Na^+ comparisons to lab plasma and serum samples (42.4 and 35.8 mmol/L respectively) as well as large deviations in slope from 1 (0.68 and 0.73 respectively). Weaker correlation coefficients were also observed for these two comparisons (0.7919 plasma, 0.7884 serum). The limits of agreement for Cl^- differences were found to be at CAL in both comparisons (2.5 percentile = -4 mmol/L). BG whole blood samples produced interchangeable results with lab plasma and serum samples for Cl^-, TCO_2, Glu, and lab plasma K^+, but not for Na^+ or lab serum K^+.

Not all GEM4000 plasma and serum analyte values are interchangeable with GEM4000 whole blood values

The statistics evaluating differences between the use of GEM4000 on plasma and serum test samples compared to reference whole blood samples are summarized in Table 2. All parameters were seen to differ by a statistically significant amount except for K^+ and TCO_2 between plasma and whole blood samples - these two comparisons had median difference values of 0. Difference plots for specific comparisons against reference whole blood samples which had limits of agreement that exceeded CAL (Cl^- in plasma; Cl^- and K^+ in serum) are shown in Figure 2. Within these clinically significant differences, Cl^- and K^+ levels were consistently higher in the non-reference measurements. Relatively large intercepts that exceeded CAL were observed for Cl^- in plasma, and K^+ in serum (9.0 and -0.5 mmol/L, respectively). A large deviation in slope was also seen for K^+ in serum (1.24). The correlation coefficients for all three comparisons were > 0.85. The use of GEM-4000 on plasma or serum samples, produced results comparable with BG whole blood samples for Na^+, TCO_2, and Glu levels, and plasma K^+ but not for Cl^- or serum K^+.

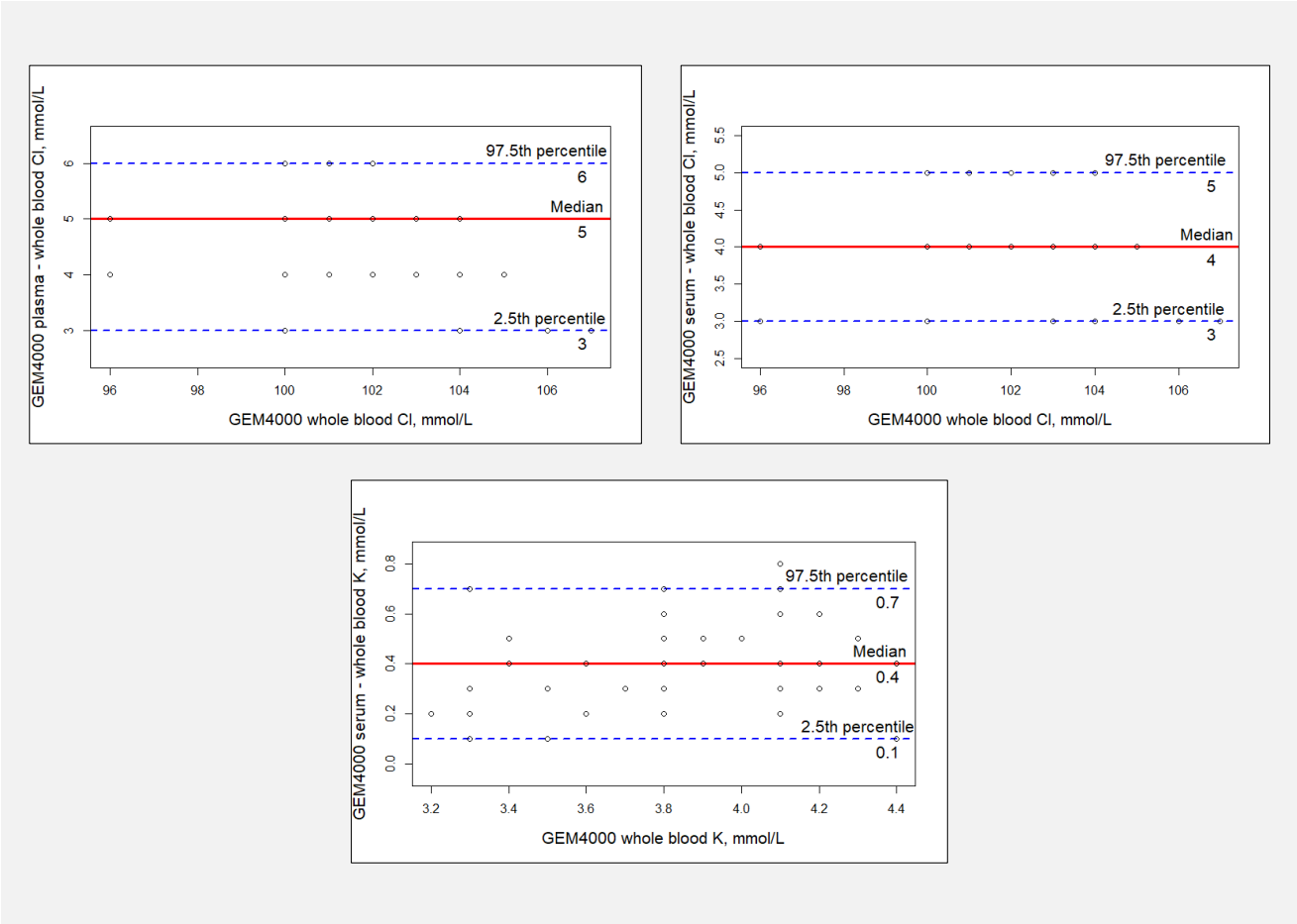

Figure 2. Median difference plots for GEM4000 plasma and serum test samples compared to GEM4000 whole blood reference samples.

Limits of agreement are given in terms of 2.5th and 97.5th percentile values, and measurement differences are plotted against the reference whole blood samples.

GEM4000 values can be used as a backup for Modular P values

Plasma and serum test samples from the GEM4000 BG analyzer were compared to Modular P lab analyzer reference results (Table 3). The Wilcoxon signed-rank test showed that all parameters differed significantly within plasma and serum except for Na^+. No parameters showed limits of agreement that exceeded CAL, but the difference plots for parameters Na^+, Cl^-, and TCO_2 are shown in Figure 3 as these had limits of agreement that were > 50% of CAL. Correlation analysis showed that all comparisons of electrolytes and metabolites between sample types showed good correlation (> 0.7 correlation coefficient, p-value < 0.05), but we observed relatively large intercepts that exceeded CAL for Na^+ and Cl^- (plasma: 51.6 mmol/L Na^+, 19.8 mmol/L Cl^-; serum: 54.2 mmol/L Na^+, 16.4 mmol/L Cl^-), along with lower slopes (plasma: 0.64 Na^+, 0.83 Cl^-; serum: 0.61 Na^+, 0.86 Cl^-). Comparisons also showed relatively lower correlation coefficients in Na^+ (0.7858 and 0.8088) and TCO_2 (0.8402 and 0.8007); the other parameters all had correlation coefficients > 0.9. The limits of agreement for all parameters were all within CAL, supporting the use of GEM4000 as a backup for Modular P in measuring plasma and serum electrolyte and metabolite concentrations.

DISCUSSION

The potential for local use of BG analyzers as backups for core lab chemistry analyzers in measuring electrolyte and metabolite concentrations stands to be both more efficient and economical, especially in more rural areas where access to the more expensive lab analyzers could have turnaround times upwards of days.

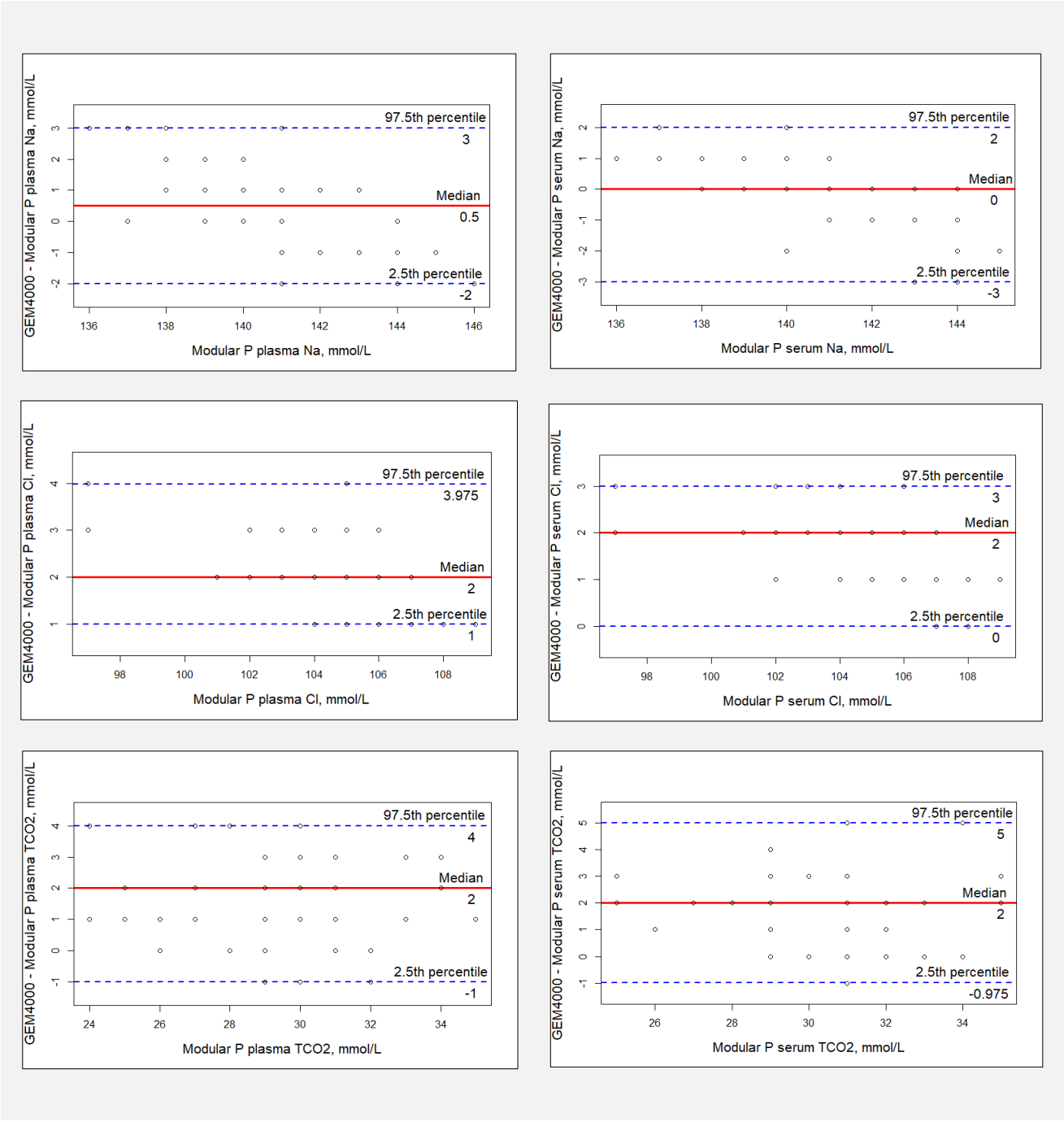

Figure 3. Median difference plots for GEM4000 analyzer plasma and serum test samples compared to their respective plasma and serum Modular P reference samples.

Limits of agreement are given in terms of 2.5th and 97.5th percentile values, and measurement differences are plotted against the reference Modular P samples.

GEM4000 underestimates electrolyte levels in whole blood compared to Modular P plasma and serum samples

Multiple studies have shown that BG analyzers will tend to underestimate ions like Na^+ and K^+ levels in whole blood samples compared to lab analyzer plasma and serum samples [17-19]. These observed differences would have been due to the combined effects of two independent variables: different sample types and different analytical measurement techniques. Some potential

confounders that fall into the sampling category include an underestimation of ion levels in whole blood due to varying heparin volumes present in the ABG syringes or inadequate blood volumes drawn which can lead to dilution of whole blood samples [17]. The different methods used by BG analyzers (direct ion selective electrodes) and lab analyzers (indirect ion selective electrodes) to take measurements has also been shown to cause differences in reported ion concentrations [20, 21].

Our results from comparisons of BG whole blood to lab plasma/serum show that many electrolyte levels are underestimated in whole blood. The elevated K^+ observed in serum but not in plasma is known as pseudohyperkalemia whereby the degranulation of platelets during the process of blood coagulation releases K^+ into the surrounding serum [17,22]. The magnitude of K^+ increase is thus directly proportional to the platelet count [23], so the relatively wide range of K^+ difference values between the 2.5 and 97.5 percentile marks we saw in Table 1 can be attributed to platelet count variance among normal individuals. We also observed Na^+ levels in whole blood to be underestimated by a clinically significant degree, and Cl^- levels to be underestimated with 2.5 percentile limits of agreement at CAL (-4 mmol/L) when compared to both lab plasma and lab serum.

GEM4000 underestimation appears to be caused by the different sample types used

Our comparisons of BG whole blood and BG plasma/serum samples isolated the effects of different sample types on parameter values from its combined effect with different types of analyzers. Again, we saw a highly variant, elevated serum K^+ compared to whole blood, which supports the notion of pseudohyperkalemia [17, 22,23]. Paired values for K^+ were higher in serum than in whole blood to a clinically significant degree, and the difference plot in Figure 2 showed a large range between the limits of agreement with no obvious trends. Contrastingly, the difference in K^+ between plasma and whole blood was not even statistically significant. We still found Na^+ and Cl^- levels to be underestimated in whole blood samples; therefore, the underestimation we saw between BG whole blood and lab plasma/serum for these two parameters looks to be due to different sample types and not because of different measuring technologies used. More studies with larger sample sizes are needed to confirm this proposal.

No clinically significant differences when looking only at the effect of different analyzers used but biased trends may be important to consider for more stringent CAL standards

We looked at the isolated effects of different analyzers being used on electrolyte and metabolite measurements. Story et al. [24] compared Na^+ and Cl^- plasma concentrations measured using a benchtop BG analyzer and a central laboratory analyzer and found limits of agreement for difference values that exceeded our CAL; however, their sample consisted of 300 critically ill patients. In our study of 42 healthy patients, none of the limits of agreement for any parameter differences exceeded CAL in the analyses of paired plasma or serum samples measured on the GEM4000 and Modular P. We note that there are some biases highlighted by the regression calculations and correlation coefficient values; these may become important for more stringent CAL standards. Systematic biases can be highlighted by deviant intercept and slope values, and the level of agreement can be inferred based on the correlation coefficient, as weaker correlation is associated with larger individual differences in parameter measurements between sample types.

Trends present for a parameter in plasma samples were also present in serum samples. The large intercept values for Na^+ that we saw can be explained by a trend in our difference plots shown in Figure 3. GEM4000 tends to overestimate lower Na^+ levels and underestimate higher Na^+ levels compared to the lab analyzer standard, thus producing very large positive intercepts, and slopes much lower than 1 in our regression analyses. GEM4000 also tends to overestimate Cl^- in plasma and serum samples, but to a lesser degree as Cl^- levels increase - this leads to large intercepts but less severe deviations in slope compared to Na^+. Finally, we saw large variations between TCO_2 measurements expressed by the wide ranges in the limits of agreement for plasma and serum TCO_2 (5 mmol/L plasma, 5.975 mmol/L serum; CAL = 6 mmol/L), which explains why we saw weaker correlations in those comparisons.

Our data showed that the GEM4000 tends to slightly underestimate K^+ measurements and generally overestimate Glu measurements. We saw that in both plasma and serum, K^+ and Glu showed intercepts and slopes much closer to 0 and 1, respectively, as well as very strong correlation. The difference plots for these parameters were not shown because their limits of agreement were very narrow and were well within CAL. So, although good correlation and regression calculations do not automatically imply good agreement, the reverse looks to stand true.

All things considered, despite the biased trends that we saw for certain parameters, clinically, they are not significant enough to warrant rejecting the use of the GEM4000 as a backup for plasma and serum measurements taken on the Modular P. Often in studies, mean or median difference values will be compared to CAL to determine whether two methods are interchangeable, but to avoid falsely finding no difference between methods, we used more stringent criteria for assessing interchangeability by evaluating the 2.5 and 97.5 percentile limits of agreement for deviance. Plasma and serum values of all five parameters from GEM4000 and Modular P were still found to differ by clinically insignificant amounts.

CONCLUSION

We conclude for our purposes that the GEM4000, when used off-label on plasma and serum samples, produces results that are more interchangeable with the gold standard lab chemistry analyzer, than with the whole blood sample types for which it was designed for. This is likely due to the larger impact of different sample types on parameter values compared to the minimal effects of different measurement methods.

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Declaration of Interest:
No potential conflict of interest relevant to this manuscript was reported.

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