Original Article

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Biochemistry Section

Comparability Assessment of Serum Electrolytes on Different Autoanalysers Working on the Same Principle

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ABSTRACT

Introduction: Electrolyte measurement of critically ill patients is frequently requested in emergency central laboratory. These are either obtained from Point of Care (POC) electrolyte analysers on urgent basis or processed on the autoanalysers. Accurate and rapid measurement of electrolyte such as sodium and potassium help in development of focused course of treatment.

Aim: To compare the results of serum electrolytes measured on four different autoanalysers working on the same principle of direct Ion Selective Electrode (ISE) measurement, to determine the extent of agreement amongst them.

Materials and Methods: This prospective comparative study was done using 200 patient samples obtained from the Central Biochemistry Laboratory of Lok Nayak Hospital, New Delhi, India. Serum samples were analysed on four different analysers for electrolytes (Na^+ and K^+), two Roche AVL electrolyte analysers and two Randox Imola autoanalysers working on the same methodology of direct ISE measurement. Means, standard deviations and coefficient of variations were calculated. The Bland-Altman plots were used to compare the results of two different assays and to quantify the limit of agreement. The p-value <0.05 was considered statistically significant.

Results: The mean value for sodium was 135±10.6 mmol/L and 136±10.4 mmol/L for Roche AVL 1 and 2 electrolyte analysers; 140±10.9 mmol/L and 140±10.7 mmol/L for Randox Imola 1 and 2 autoanalysers. Similarly, the mean value for potassium were 4.53±2.86 mmol/L, 4.32±1.03 mmol/L, 4.33±0.97 mmol/L and 4.35±0.94 mmol/L for AVL 1, AVL 2, Imola 1 and Imola 2, respectively. The Bland-Altman plots have shown a good agreement of -0.34 to 0.31 for serum potassium for Imola 1 and AVL 1 however, no such agreement was found for sodium values on inter-analyser comparison. The Bland-Altman plots were used to compare the results of two different assays and to quantify the limit of agreement. The p-value of <0.05 was considered statistically significant.

Conclusion: Serum electrolytes obtained from electrolyte analysers and autoanalysers showed equivalent results for potassium but not for sodium values. Therefore, potassium values can be used interchangeably from these analysers for making critical decisions but same cannot be concluded for the sodium values. The comparability will be useful to minimize analytical bias and allow the results to be used interchangeably. Obtaining equivalent, rapid and reliable results from ready back-up systems will prove to be time-saving and economical in emergency cases irrespective of the analytical system being used.

Keywords: Agreement, Bland and Altman, Ion selective electrode, Potassium, Sodium

INTRODUCTION

Electrolytes plays an essential role in the physiological functioning of the body including regulation of cell membrane potential, water homeostasis, acid-base balance, proper functioning of neurohormonal pathways and energy transformation. Electrolyte measurement by ISE is routinely done in biochemistry laboratories [1]. The two methods of electrolyte assay currently used, are direct and indirect, both employing ion-sensing electrodes [2]. The direct ISE method involves the contact of an undiluted blood sample with the electrode surface. This approach is used in the electrolyte analysers which are Point-Of-Care (POC) testing analysers, both benches top and portable. The indirect ISE method involves pre-dilution step before analysis, and is used in high throughput central laboratory automated analysers [3].

In clinical biochemistry laboratories, routine protocol of batch programming of the samples often causes long delay in estimation of electrolyte levels. In critical cases, where there is the urgent need to obtain the electrolyte values at the earliest possible time, usage of POC testing devices may eliminate several processing steps. The results can be obtained rapidly that help in timely management of the condition and ultimately improve the patient's outcome [4]. It is therefore necessary, to develop rapid and reliable assays that can produce equivalent results, with the least turnaround time. There is no consensus on interchangeability of results of the measured electrolyte levels on these analysers as large differences have been observed across various studies between POC and laboratory autoanalysers [4-7]. There is paucity of data comparing the results of electrolytes using the same sample type (e.g., serum or plasma or whole blood) on the analysers working on the same methodology. Therefore, only equipments working on a common principle (direct ISE) were included in the study.

The aim of the study was to do comparative assessment of the measured serum electrolytes on four different analysers working on the same methodology, to find out the extent of agreement amongst them.

MATERIALS AND METHODS

The prospective comparative study was conducted over a period of two months from June 2018 to July 2018 in the Department of Biochemistry, Lok Nayak Hospital, New Delhi, India. Standard ethical principles were followed for the study. The sample size was calculated as per convenience (confidence interval 95% and power of study 80%). In a total of 200 serum samples, sodium and potassium levels were analysed using four autoanalysers (Roche AVL 1 and AVL 2, electrolyte analysers and Randox Imola 1 and Imola 2 autoanalysers).

Routine samples with sufficient serum volume (>2 mL) were giving a unique lab identification number. Samples which were haemolyzed, highly lipemic or highly icteric were excluded from the study. Serum was obtained after centrifugation for 8-10 minutes at 3500 rpm. The samples were processed as per the manufacturer's instructions and internal quality control was ensured.

STATISTICAL ANALYSIS

The data was analysed using Statistical Package for Social Sciences (SPSS) software. Means, standard deviations and coefficient of variations were calculated. The Bland-Altman plots were used to compare the results of two different assays and to quantify the limit of agreement. The p-value of <0.05 was considered statistically significant.

RESULTS

The Mean±SD of the sodium and potassium in the serum of the patients and in the Quality Control (QC) material observed on all the four autoanalysers is represented in [Table/Fig-1].

	Patient Samples	Quality control 2	Quality Control 3
Sodium (Na^+) mEq/L			
AVL 1 AVL 2 Imola 1 Imola 2	135±10.6 136±10.4 140±10.9 140±10.7	139±1.8 140±2.1 141±2.8 143±1.9	156±3.1 155±2.8 156±2.8 158±2.5
Potassium (K^+) mEq/L			
AVL 1 AVL 2 Imola 1 Imola 2	4.53±2.86 4.32±1.03 4.33±0.97 4.35±0.94	4.07±0.16 4.11±0.16 3.99±0.07 4.06±0.09	6.00±0.19 6.01±0.18 5.84±0.08 5.91±0.11

[Table/Fig-1]: Mean±SD levels of sodium and potassium in serum samples (n=200) and the quality control material.
The difference of the mean sodium and potassium values on the different analysers was not statistically significant (p > 0.05)

The differences between the mean values were observed to be in the acceptable range of that recommended by the Central Laboratory CLIA guidelines i.e., ±4 mmol/L for sodium and ±0.5 mmol/L for potassium values [8]. The correlation coefficient as obtained by comparison of serum sodium and potassium values as on different analysers is depicted in [Table/Fig-2] and the coefficient of variance are depicted in [Table/Fig-3] for all the sets of autoanalysers under study.

	AVL 1	AVL 2
Sodium values (Na^+)		
Imola 1	0.958	0.959
Imola 2	0.955	0.960
Potassium values (K^+)		
Imola 1	0.986	0.985
Imola 2	0.985	0.986

[Table/Fig-2]: Correlation coefficient in sodium and potassium levels as determined on the different analysers.
The correlation values for sodium and potassium were statistically significant (p <0.0001)

Coefficient of Variance (%)				
Sodium (Na^+)				
	AVL 1	AVL 2	IMOLA 1	IMOLA 2
QC 2	1.98 %	1.3 %	1.29 %	1.5 %
QC 3	1.79 %	1.58 %	1.98 %	1.8 %
Potassium (K^+)				
QC 2	1.75 %	2.21 %	3.9 %	3.89 %
QC 3	1.37 %	1.86 %	3.17 %	3.00 %

[Table/Fig-3]: Coefficient of variance (%) of sodium and potassium levels on different analysers.

The average bias (in %) from the target value of the quality control for both levels for each analyser is depicted in [Table/Fig-4]. Bias agreement between reference and back-up analyser is depicted in [Table/Fig-5].

Bland and Altman plots showed 95% limits of agreement for Na^+ and K^+ values in serum [Table/Fig-6]. The graphical scatter plot of difference of the two paired measurements were plotted against the mean of the two measurements for sodium and potassium

	AVL 1	AVL 2	Imola 1	Imola 2
Sodium-Level 2 (143±7 mEq/L)	-2 %	0 %	-4 %	-3 %
Sodium-Level 3 (158±8 mEq/L)	-2 %	0 %	-2 %	-3 %
Potassium-Level 2 (4.15±0.33 mEq/L)	-0.16 %	-0.09 %	-0.08 %	-0.04 %
Potassium-Level 3 (6.03±0.48 mEq/L)	-0.19 %	-0.12 %	-0.03 %	-0.02 %

[Table/Fig-4]: Average bias (in %) of quality control target values.

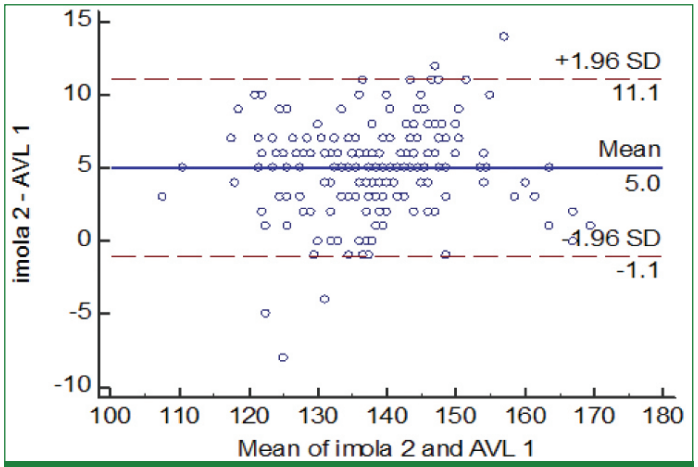
	Quality Control Level 2		Quality Control Level 3	
Bias for Sodium				
	AVL 1	AVL 2	AVL 1	AVL 2
IMOLA 1	-1.43 %	-0.71 %	0 %	-0.65 %
IMOLA 2	-2.80 %	-2.10 %	-1.20 %	-1.94 %
Bias for Potassium				
	AVL 1	AVL 2	AVL 1	AVL 2
IMOLA 1	1.96 %	2.91 %	2.67 %	2.83 %
IMOLA 2	0.2 %	1.21 %	1.5 %	1.66 %

[Table/Fig-5]: Bias agreement between reference quality control and back-up analyser.

	LOA FOR Na^+	p-value	LOA FOR K^+	p-value
AVL 1 vs Imola 1	-1.20 to 10.97	<0.0001	-0.34 to 0.31	0.32
AVL 1 vs Imola 2	-1.06 to 11.1	<0.0001	-0.34 to 0.37	0.24
AVL 2 vs Imola1	-1.45 to 9.90	<0.0001	-0.30 to 0.31	0.89
AVL 2 vs Imola 2	-1.12 to 9.82	<0.0001	-0.29 to 0.35	0.18

[Table/Fig-6]: The limits of agreement from Bland-Altman plots and p-value.
The p-values for sodium and potassium depicts whether significant correlation is present among different analysers for these analytes

respectively [Table/Fig-7,8]. Similar data for the limits of agreement was obtained for other analysers on comparison.

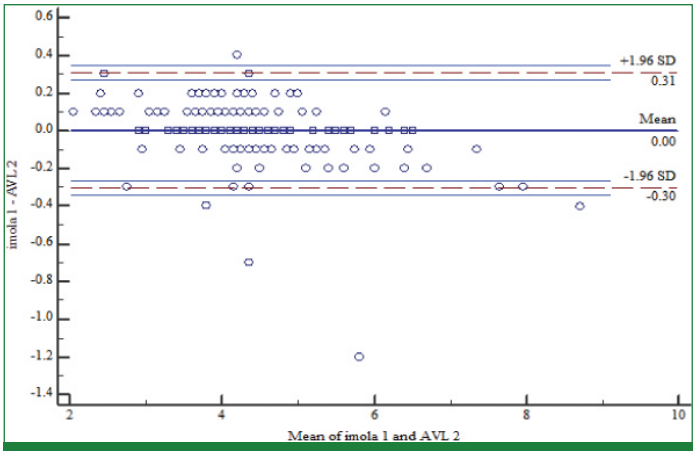


[Table/Fig-7]: Bland and Altman plot showing limits of agreement for sodium between Imola 2 and AVL1.

DISCUSSION

Electrolyte measurement is one of the most frequently ordered tests in the emergency biochemistry laboratory. Rapid results are required by the clinicians to provide timely treatment to the critically ill patients, for which a method/analyser with a shorter turnaround time is essential. Many studies have been done to compare various biochemical parameters across different instruments using same or different methodologies but, conclusions remain debatable [4-7].

The present study compared electrolyte values obtained on different autoanalysers working on the same methodology to analyse if the results were equivalent and can be used interchangeably. The United States Clinical Laboratory Improvement Amendment (US



[Table/Fig-8]: Bland and Altman plot showing limits of agreement for potassium between Imola 1 and AVL2.

CLIA) 2006 accepts an allowable bias of ±0.5 mmol/L in measured potassium, and ± 4 mmol/L in measured sodium [8]. The results of our study were within the set allowable bias standards. The degree of agreement between the autoanalysers was evaluated using Bland-Altman plots and it was observed that the sodium values differ significantly on different analysers while there was a good degree of agreement for potassium values. These findings were similar to Jain A et al., study on ICU patients, where electrolyte comparison on a POC Blood Gas Analyser (BGA) and a central laboratory autoanalyser where significant difference was observed in sodium values [6]. These results were in-line with various other similar studies, which reported that the sodium values obtained from the POC BGA are not completely reliable for making clinical decisions and hence cannot be used interchangeably because of significant differences in the measurement compared to those obtained from laboratory autoanalyser [1,5,9-13]. To compensate for these variations of results between a POC BGA and a laboratory autoanalyser, the usage of correction factor has also been suggested which needs to be further determined individually by each hospital set-up [1,14].

In contrast to our results, Sanakal DB et al., observed no significant difference between the sodium values but a significant difference for potassium values of an ABOTT BGA and a PROLYTE electrolyte autoanalyser, suggesting reliability for sodium values but not for potassium values [15]. It has been shown that even on using identical analysers, identical methods, and the same study population; still POC testing yields different results for sodium and potassium. Zhang JB et al., study concluded that the BGA measured sodium and potassium values had statistical difference compared to those of laboratory measured but the mean biases did not exceed US-CLIA determined acceptable biases [12]. Hence these values can be used in initial stages to guide clinical therapy in critical cases and the results from the autoanalyser can then be used to check or adjust the treatment.

On the contrary, Budak YU et al., observed significant differences between the results of sodium and potassium on BGA and the laboratory autoanalyser [4]. Such differences were also observed in studies by Gupta S et al., Razavi S et al., and Chhapola V et al., thus suggesting that these results cannot be used interchangeably and should be interpreted with caution [3,16,17]. Similarly in 2017, Naz S et al., found statistically significant higher serum sodium and potassium values on Combiline electrolyte analyser compared to Cobas Autoanalyser [18]. Since the values obtained were under acceptable range as per CLIA, so they suggested interchangeable use of these results for critically ill patients where they can prove to be time-saving and life-saving. In the same year similar conclusion was drawn from the study by Allaradet-Servent J et al., where POC siemens RAPID Point 500 BGA was used to compare values of electrolytes, bicarbonate, hematocrit, haemoglobin and glucose from critically ill patients with the values obtained from the central laboratory analyser [19]. Uyanik M et al., also compared results of blood gases, electrolytes and other metabolites measured on two BGA (Nova and Siemens) and an Olympus Autoanalyser, and found comparable results for potassium, lactate and blood gases but poor correlation for sodium, chloride, calcium and glucose values [20]. The study suggested that the clinicians and laboratories should be aware about the limitations of the assay when interpreting the results obtained.

In 2015, an autoanalyser A25 and a semi-autoanalyser BTS-350 were used for comparison of various analytes in a study by Biswas SS et al., [21]. The quality control was run in duplicate for 32 days on both analysers. The CV, Bias, Total Error allowable (TE) were calculated for 10 analytes and most of the analytes were found to be within desirable limits of TE, and thus the study recommended that the semi-autoanalyser can be used as ready back-up analyser for the full Autoanalyser. Furthermore, Amirkhanlou S et al., King R et al., and Nanda SK et al., have also found significant correlation for electrolyte values under similar settings [11,22,23].

With more than 1000 electrolytes being processed and reported per day, achieving higher precision of the measurements will ensure more trust of the clinicians and the users in the reports generated by laboratory. Hence, it is recommended that every laboratory and the hospital set-up at large should conduct such studies, so as to standardize the diagnostic testing and ultimately improve the patient care.

LIMITATION

Our study was based on direct ISE principle based analysers, further studies based on indirect ISE based analysers operational in our laboratory are required to fully determine the interchangeability of results and improve the reliability of the reports.

CONCLUSION

The comparability of different analytical system is useful to minimize analytical bias, and allows the results to be used interchangeably. It can be concluded from our study that the electrolyte analysers and the laboratory autoanalysers may be used interchangeably for the measurement of potassium, while the same cannot be said for the measured sodium values because of the significant difference in the sodium measurements by different analysers using same methodology.

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