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International Journal of Clinical Biochemistry and Research

Journal homepage: https://www.ijcbr.in/

Original Research Article

A comparison of serum sodium levels measured using a colorimetric kit approach and those determined using direct and indirect ion selective electrode techniques- in a Hospital Central Lab

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ARTICLE INFO

Article history:
Received 02-06-2023
Accepted 20-06-2023
Available online 14-07-2023

Keywords:
Hyponatremia
Serum sodium levels
Colorimetric kit
Direct and indirect ion selective electrode
Hospital central lab

ABSTRACT

Background: When electrolyte imbalances are not recognized, they are known to cause severe morbidity and mortality. Dyselectrolytemia is frequently curable. Hyponatremia is a common symptom seen in the elderly. Laboratory equipment may be lacking in rural healthcare settings. As a result, the purpose of this study was to investigate the feasibility of developing a screening technique that can aid in the detection of hyponatremia in such facilities.

Materials and Methods: Serum sodium levels in 120 samples were determined by direct, indirect, and colorimetric ISE. SPSS version 17, NCSS 11, and MINITAB 18 software were used for statistical analysis. Statistical significance was defined as a p-value of 0.05.

Results: While comparing the instruments, a basic linear regression analysis was performed, and a regression equation for sodium levels was established. The Bland-Altman analysis yielded a 95% agreement limit between the instruments, which is well within the CLIA-recommended target value of 4 mmol/L in the hyponatremic and normonatremic ranges.

Conclusion: The resulting regression equation computes a predicted value for direct and indirect ISE using the colorimeter readings, making it similar to all three instruments in the hyponatremic and normonatremic ranges. The colorimetric method can be used as a low-cost screening technique to identify hyponatremic elderly people for whom a tertiary hospital may be inaccessible, allowing for early care.

1. Introduction

The principal extracellular cation in the extracellular fluid, sodium, is essential for the preservation of tissue hydration, acid-base balance, and osmotic pressure. Serum sodium levels are crucial markers in critical care management that direct clinical choices for patient care. It is crucial to measure salt levels accurately. Newer, more effective techniques for calculating sodium levels in blood and serum have been developed over time.[1]

The creation of salt with zinc uranyl acetate and subsequent gravimetric, titrimetric, or colorimetric quantification were early procedures for determining serum sodium levels. To measure low sodium concentrations in solution, Barnes, Richardson, Berry & Hood later developed the flame photometer. R.W. Bunsen, Gustav, and R. Kirchhoff developed atomic absorption spectrometry, which was used to calculate the electrolytes present in various bodily fluids. However, these procedures frequently required lengthy turnaround times, had little sample throughput, and were difficult to use.[2]

The Ion Selective Electrode (ISE) evolved as the current standard reference method for quick and accurate

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https://doi.org/10.18231/j.ijcbr.2023.027

monitoring of sodium levels with the development of improved techniques. Numerous research has examined various electrolyte estimate techniques. One study established ISE as the reference method by showing that the colorimetric approach had an adequate analytical performance for sodium and potassium while flame photometry did not fulfill the criteria. These investigations examined the sodium readings from the flame photometer with both the direct and indirect ISE methods, finding a good agreement between the two and arguing that they may be used interchangeably. Comparing electrolyte measurements made with an auto-analyzer and arterial blood gas equipment, it was also suggested to use caution when comparing these measurements.[3]

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2. Material and Methods

2.1. Study design

Prospective study.

2.2. Inclusion & exclusion criteria

The study comprised 120 serum samples from patients with ages ranging from 18 to 80, of either gender, that were given to the lab with a request for electrolyte calculation. Excluded samples included those that were haemolyzed, turbid, lipemic, or hyperbilirubinemia.

2.3. Ethical approval & informed consent

Every patient or his family member who requested electrolytes was asked to sign a written informed consent form after the Ethics Committee of the Medical College granted its approval. (Enclosed).

2.4. Methods

Indirect ISE on the Roche Cobas c501 chemistry analyzer (Roche Diagnostics GmbH, Mannheim, Germany) or direct ISE on the Roche AVL 9180 (9180) electrolyte analyzer (Roche Diagnostics) were used to analyze the samples that were collected in response to a request for electrolytes. The same serum sample was subsequently used to detect sodium using a sodium electrolyte colorimetric test kit within two hours.

3. Results

A total of 120 serum samples were collected through simple random sampling and analyzed for sodium (Na+) using two different instruments: Roche Cobas (c501) and Roche AVL 9180 (9180) by Indirect ISE and Direct ISE methods, respectively. Statistical analysis was conducted using SPSS, NCSS, and MINITAB software, with a significance level of $p<0.05$. Descriptive statistics, correlation analysis, scatter plots, and linear regression were performed to assess the relationship between the instruments. The comparison of sodium values was primarily focused on the hyponatremic and normonatremic ranges due to limited samples in the hypernatremia range.

Table 1: Classification of sodium (Na+) levels and reference ranges in different groups

S. No.	Analyte	Reference Ranges (mmol/L)	Groups
1.	Sodium (Na^+)	134 – 147	Normonatremia
2.	Sodium (Na^+)	<134	Hyponatremia
3.	Sodium (Na^+)	>147	Hypernatremia

The sodium (Na+) values obtained from the C501 instrument and the 9180 instruments were further classified into three groups based on the reference ranges (Table 1).

Table 2: Mean, S.D and CV% for sodium levels between C501, 9180 and colorimetry

	N	Mean	Std. Deviation	CV%
Na^+ c501	100	134.32	11.21	8.57
Na^+ Colorimetry	100	145.89	17.96	11.41
Na^+9180	35	132.01	9.79	6.64
Na^+ Colorimetry	35	139.13	15.27	12.04

Descriptive statistics, including the mean, standard deviation (S.D), and coefficient of variation (CV), were calculated for the sodium values (Table 2).

Table 3: Pearson's correlation between Na^+ c501 vs colorimetry & Na^+ 9180 vs colorimetry

	N	Na^+ on Colorimetry	P value
Na^+ on c501	100	0.495	<0.001
Na^+ on 9180	35	0.487	<0.001

Correlation analysis was performed using Pearson's correlation coefficient for the sodium values obtained from

Table 4: Simple linear regression between instruments and ANOVA for unstandardized predicted values

	R	R^2	Prediction Equation	ANOVA forUnstandardized Predicted Values
Na^+C501 vs Colorimeter	0.487 P<0.001	32.57% P<0.001	Na^+ on C501 = 84.22 + 0.3426 Na^+ by colorimetry	F=168.47, P<0.001
Na^+ 9180 vs Colorimeter	0.547 P<0.001	30.01% P<0.001	Na^+ on 9180 = 84.89 + 0.3871 Na^+ by colorimetry	F=41.89, P<0.001

Table 5: Na+ levels between the instruments in hyponatremia & normonatremia

Na^+ Levels	**Na^+ C501 vs Na^+ Colorimetry <135 mmol/L**	**Na^+ 9180 vs Na^+ Colorimetry <135 mmol/L**	**Na^+ C501 vs Na^+ Colorimetry 135-145 mmol/L**	**Na^+ 9180 vs Na^+ Colorimetry 135-145 mmol/L**
Total % of samples	41.99%	56.17%	47.89%	38.00%
% of Comparable samples	68.87%	69.94%	57.22%	91.98%
R (P<0.001)	0.743	0.74	0.487	0.37
R^2 (P<0.001)	55.64%	74%	27.96%	16.02%
Prediction Equation	Na^+ on C501 = 54.62+0.49 Na^+ by colorimetry	Na^+ on 9180 = 18.76+0.72 Na^+ by colorimetry	Na^+ on C501 = 109.3+0.14 Na^+ by colorimetry	Na^+ on 9180 = 112.4+0.14 Na^+ by colorimetry
Bland Altman Analysis (Mean Difference)	-2.99	-1.84	-3.14	-2.55
Limits of Agreement [defined as Difference ± 1.96 * standard deviation (SD)] by Bland Altman analysis	-14.96 to 8.72 mmol/L	-10.82 to 7.62 mmol/L	-14.54 to 8.28 mmol/L	-9.72 to 4.74 mmol/L

different instruments (Table 3). Scatter plots were also generated to visualize the correlation.

A simple linear regression analysis was conducted to establish a linear regression equation between the sodium values obtained from the C501 instrument and colorimetry, as well as between the sodium values obtained from the 9180 instruments and colorimetry. This analysis aimed to determine good fit.

A comparison of sodium values was performed only within the hyponatremic and normonatremic ranges (Table 5) due to the study's sampling method, which involved simple random sampling. Reference ranges for serum sodium were used to determine the classification of the samples.

4. Discussion

A vital analyte frequently measured in intensive care units and annual physicals are serum sodium. Although ion-selective electrodes (ISEs) are frequently employed in tertiary care institutions for salt estimation, they are expensive and logistically impractical for basic health centers, which could result in the underdiagnosis of hyponatremia in rural regions. To solve this problem, this study compared serum sodium measurements made with the colorimeter, a low-cost tool, to those made using ISEs.[5]

It was determined that a sample size of 10 would be adequate for statistical significance and a power of 99% based on a prior study comparing various sodium measurement techniques. However, greater sample size was suggested to account for manual mistakes related to the colorimetric approach and to attain desirable precision amongst equipment.[6]

Table 3 shows a moderately positive linear connection for sodium readings between the C501 and the colorimeter as well as between the 9180 and the colorimeter. To evaluate the comparability of sodium readings across the methods/instruments (indirect ISE/C501 vs.colorimetry and direct ISE/9180 vs. colorimetry), a straightforward linear regression analysis was conducted.[7] The sodium levels were similar between the instruments, according to the ANOVA for unstandardized predicted values (Table 4), and the regression models offered a reasonable fit for the data. Significant F values (169.429 and 42.85, both with P<0.001) were shown by the ANOVA for unstandardized predicted values. The sodium levels on the C501 instrument and the 9180 instruments may be predicted based on the findings of the colorimetry using the regression equations created using the R2 value.[8]

The mean difference in sodium readings surpassed the proposed target value by 4 mmol/L, according to Bland-Altman analysis (Table 5).[9] As a result, additional research was done primarily in the hyponatremic and normonatremic areas. In the hyponatremic range, the instruments had a significant positive connection, and in the normonatremic range, they had a moderately positive association. The prediction of sodium values on the C501 instrument and the 9180 instruments using the regression equations indicated better prediction accuracy in the hyponatremic range. The bland-Altman analysis confirmed that the mean difference for sodium levels fell within the suggested ±4 mmol/L range.[10]

Early-stage hypo and hypernatremia can be asymptomatic and show symptoms that resemble conditions of the central nervous system, including irritability, nausea, weakness, confusion, and seizures.[11] Dysnatremia must be identified early since it raises the risk of mortality and morbidity. A low-cost tool like the colorimeter can be used in rural healthcare settings to help detect hyponatremia in its early stages, allowing for early intervention and enhancing the quality of life.

5. Limitations of our Study

It is well-established that quantities of glucose, protein, and lipids influence serum sodium levels. A significant flaw in our study is the inability to estimate the aforementioned components. Except for roughly 15 samples, the same sample was not analyzed for sodium on both the c501 and the 9180 because it is well-known that the results of direct and indirect ISE are equivalent. A bigger sample size estimate would have allowed for the evaluation of the Sodium colorimetric kit's sensitivity and specificity. Due to random sampling, the study also lacked a statistically significant number of hypernatremic samples.

6. Merits of the Study

This pilot project aims to highlight the value of a low-cost, straightforward tool for diagnosing hyponatremia in rural healthcare facilities, enabling prompt medical intervention and reducing the incidence of morbidity and mortality that would otherwise be associated with it.

7. Conclusion

The sodium values calculated by the Direct & Indirect ISE instruments are comparable to those determined by a colorimeter in the hyponatremic and normonatremic ranges. When the samples are analyzed using a colorimeter, the regression equations were developed to forecast the Na+ values on C501 and 9180. Using a low-cost colorimeter to screen for a curable ailment like hyponatremia in rural regions will give patients the chance to receive early interventional therapy, especially in the geriatric age groups.

8. Source of Funding

None.

9. Conflict of Interest

None.

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Cite this article: Saraladevi T. A comparison of serum sodium levels measured using a colorimetric kit approach and those determined using direct and indirect ion selective electrode techniques- in a Hospital Central Lab. *Int J Clin Biochem Res* 2023;10(2):159-162.