Original Article

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# Application of Sigma Metrics and Performance Comparison Between Two Biochemistry Analyser and A Blood Gas Analyser for the Determination of Electrolytes

YASEMIN USTUNDAG-BUDAK[1], KAGAN HUYSAL[2]

## ABSTRACT

**Introduction:** Electrolytes have a narrow range of biological variation and small changes are clinically significant. It is important to select the best method for clinical decision making and patient monitoring in the emergency room.

The sigma metrics model provides an objective method to evaluate the performance of a method.

**Aim:** To calculate sigma metrics for electrolytes measured with one arterial blood gas analyser including two auto-analysers that use different technologies. To identify the best approach for electrolyte monitoring in an emergency setting and the context of routine emergency room workflow.

**Materials and Methods:** The Coefficient of Variation (CV) was determined from Internal Quality Control (IQC). Data was measured from July 2015 to January 2016 for all three analysers. The records of KBUD external quality data (Association of Clinical Biochemists, Istanbul, Turkey) for both Mindray BS-2000M analyser (Mindray, Shenzhen, China) and Architect C16000 (Abbott Diagnostics, Abbott Park, IL) and MLE clinical laboratory evaluation program (Washington, DC, USA) for Radiometer ABL 700 (Radiometer Trading, Copenhagen, Denmark) during the study period were used to determine the bias.

**Results:** The calculated average sigma values for sodium (-1.1), potassium (3.3), and chloride (0.06) were with the Radiometer ABL700. All calculated sigma values were better than the auto-analysers.

**Conclusion:** The sigma values obtained from all analysers suggest that running more controls and increasing the calibration frequency for electrolytes is necessary for quality assurance.

**Keywords:** Chloride, Potassium, Quality improvement, Quality control, Sodium

## INTRODUCTION

Electrolytes are electrically charged elements that are essential for the normal functioning of human body and for maintaining cellular integrity. Electrolyte disturbances can lead to serious and critical events and represent significant risks to life with a prevalence of about 15% among emergency patients [1,2]. They are one of the most common causes of morbidity and mortality in critically ill patients [3]. Patients' problems are complex and invasive interventions are frequent in emergency units. Thus, monitoring electrolytes is critical. At the same time, it is important to obtain data quickly to an efficient and fast triage of the patients [4]. Electrolytes with a narrow biological variation and small changes are likely to be clinically significant. Therefore, accurate test results are very important [5]. It is important to select the best method for clinical decision-making and patient monitoring in Emergency Room (ER).

Analysis of electrolytes such as sodium, potassium and chloride are performed by two different technologies; direct Ion-Selective Electrode (ISE) and indirect ISE. Indirect ISE is typically used in the large chemistry analysers in the centralized laboratory. The sample is first diluted with diluent before the concentrations of the electrolytes are measured. Direct ISE technology is used in Blood Gas Analysers (ABG) and measures electrolytes in the undiluted sample types [6]. Most hospitals use these two methods interchangeably.

Sigma metrics are a model in laboratory applications that provides an objective method for evaluating the quality of the analytic phase [7-12]. Sigma metrics combine bias, precision, and allowable Total Error (TEa) and the exact number of errors made can be quantified [7-12]. The TEa is based on the biological variation of the measured analyte and is readily available in the literature. Here, Coefficient of Variation (CV) stands for the analytical standard deviation [5,7,8]. With the help of sigma metrics, the quality of the test results can be compared in a standardized way. Thus, some laboratories find the most appropriate method for their clinical needs [9].

Our object was to calculate the sigma metrics for electrolytes measured with one ABG analyser and two autoanalysers Mindray BS-2000M analyser (Mindray, Shenzhen, China) and Architect C16000 (Abbott Diagnostics, Abbott Park, IL). The goal was to identify the best approach for electrolyte monitoring in emergency settings in the context of a routine ER workflow.

## MATERIALS AND METHODS

We conducted a retrospective study on data contained in the Saglik Bilimleri University, Bursa Yuksek Ihtisas Training and Research Hospital that provides service to a 1150-bed tertiary care hospital. A centralized data repository integrates information in several databases including the Internal Quality Control (IQC) database of our hospital.

We analysed IQC data for imprecision and External Quality Control (EQC) data for inaccuracy of sodium, potassium and chloride for 6 months from July 2015 to January 2016 with Radiometer ABL 700 ABG analyser (Radiometer Trading, Copenhagen, Denmark) and on a Mindray BS-2000M analyser (Mindray, Shenzhen, China) and Architect C16000 (Abbott Diagnostics, Abbott Park, IL).

In the ABG analyser, one-point automatic calibrations were performed every four hours and two-point calibrations every eight hours. All tests were done according to instructions by the manufacturer. During the study period, all reagents, calibrators, and controls used were provided by the manufacturers (solution S7735; Lot 623, 633, 654, 628 Radiometer Trading, Copenhagen, Denmark). The internal quality control material was Qualicheck+ Quality Control (QC) ampoules that are specifically designed for the radiometer's blood gas analysers. The CV (%) was calculated with the mean of six months (n=168) of internal QC data.

For ABG analyser, our laboratory participated in the MLE clinical laboratory evaluation program (American Collage of Physicians Medical Laboratory Evaluation, Washington, DC, USA)

The Mindray BS-2000M analyser (Mindray Bio-Medical. Electronics Co., Ltd, Shenzhen, China) employs an ISE method. The auto-analyser was calibrated routinely every 24hours by linear calibration. We used internal quality control material Multi Control Sera N (BS-800, BS-5002 Mindray Bio-Medical. Electronics Co., Ltd, Schenzhen, China) for calculation of CV. We participated in the KBUD (Klinik Biyokimya Uzmanları Dernegi, Istanbul, Turkey) external QC program for Mindray BS-2000M analyser.

The Architect C16000 (Abbott Diagnostics, Abbott Park, IL) employs an ion-selective electrode. The auto-analyser was routinely calibrated every 24hours by linear calibration. We used internal QC material Multichem plus technopath (Abbott Diagnostics, Abbott Park, IL) for calculation of the CV. We also participated in in the KBUD (Klinik Biyokimya Uzmanları Dernegi, Istanbul, Turkey) external QC program for Architect C16000 analyser.

## STATISTICAL ANALYSIS

Data were evaluated using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). Means, standard deviations, and CVs were calculated. The CV was calculated from the IQC data over the six-month period using the following equation:

CV (%) = (standard deviation x 100)/laboratory mean(IQC)

Bias was calculated from the external quality assessment records using the following formula:

Bias (%) = (mean of all laboratories using the same instrument and method - our laboratory's mean)/ (mean of all laboratories using the same instrument and method) x 100

Sigma levels were calculated using the formula as follows:

Process sigma = (% TEA - % "biasEQC")/% CVIQC [7,8].

Assessment of the quality on the sigma scale of six provides an objective assessment of the analytical performance.

## RESULTS

[Table/Fig-1] shows the recommended total allowable goal values for electrolytes; sodium has a relatively smaller TEa.

[Table/Fig-2] shows the internal quality control evaluation data for the different parameters obtained from 3 different analysers during the study periods.

The mean calculated CVs were for 0.61, 1.23, 1.82 for sodium, potassium, chloride with ABL700 analyser. The calculated CVs were better with the ABG analyser than both analysers [Table/Fig-2]. The calculated mean CV for Na was worst with the Mindray BS-2000M analyser.

| Test | TEa $_{Ricos\ BV}$ [a] | TEa $_{RILIBAK}$ [b] | TEa $_{RCPA}$ [c] | TEa $_{SC}$ [d] | TEa $_{SEKK}$ [e] |
|---|---|---|---|---|---|
| Sodium | 0.73% | 3% | 2% | 5% | 5% |
| Potassium | 5.6% | 4.5% | 5% | 8% | 8% |
| Chloride | 1.5% | 4.5% | 3% | 9 % | 9 % |

**[Table/Fig-1]:** Recommended total allowable goal values for electrolytes.
TEa, allowable total error; TEa sources were reference 15.
a 2014 Ricos BV (biological variability) data-base; b RILIBAK (German Medical Council for the Quality Assessment of Quantitative Analysis in Medical Laboratories); cRCPA (Royal College of Pathologists of Australasia); dSC (Spanish Consensus); eSEKK(Czech Republic EQA programme)

| Instrument | Parameter | Mean | SD | CV |
|---|---|---|---|---|
| ABL700 analyser | Na | 159 | 0.95 | 0.59 |
| | | 140 | 0.9 | 0.64 |
| | K | 1.79 | 0.03 | 1.67 |
| | | 3.79 | 0.03 | 0.79 |
| | Cl | 121 | 2.0 | 1.65 |
| | | 98 | 2.0 | 2.0 |
| Mindray BS-2000M | Na | 113 | 7,3 | 6.4 |
| | | 140 | 12,3 | 8.7 |
| | K | 3,5 | 0,2 | 5.7 |
| | | 6,3 | 0.3 | 4.7 |
| | Cl | 83± | 4,4 | 5.3 |
| | | 111 | 8,8 | 7.9 |
| Architect C 16000 | Na | 141 | 4.7 | 3.2 |
| | | 143 | 1.4 | 0.97 |
| | K | 3.6 | 0.08 | 2.2 |
| | | 5.9 | 0.2 | 3.3 |
| | Cl | 97 | 3.2 | 3.2 |
| | | 83 | 2.1 | 2.5 |

**[Table/Fig-2]:** Internal quality control evaluation data for the different parameters obtained from July 2015 to January 2016 for 3 different analysers.
Arithmetic mean; SD, Standard deviation; CV, coefficient of variation; Na+, sodium; K+, potassium; Cl-, chloride.

Bias was derived from the EQC reports [Table/Fig-3]. The bias values ranged from 0% to 5.7% for sodium and 0.2% to 5.7% for K, 0% to 5.6% chloride ABG analyser. The bias values ranged from 0.3% to 3.9% for sodium and 0.6% to 1.2% for K, 4.4% to 12.8% chloride with Mindray. The bias values were acceptable with Architect C16000, but we could get only one external quality control data during the period.

[Table/Fig-4] highlights sigma values for each electrolyte with all analysers. Sigma values <1 were achieved with all the analysers, while the ABG analyser was the best. Sigma values > 3 were recorded with Radiometer ABL700 using. Using TEa targets from Spanish consensus [Table/Fig-1], the best sigma value for Na was 5.8 with the Radiometer ABL700.

## DISCUSSION

Assessing quality sigma metrics is increasingly accepted as the best approach for proving objective estimates of analytical quality. The sigma metric summarizes a characteristic of multiple key analytical performance characteristics. As sigma metric value increases, the quality and the consistency of the test improves. Assays above six sigma are all considered ideal, and a sigma level < 3 indicates poor performance [13]. Analytical processes that perform with a sigma value <3 cannot be controlled with Westgard QC rules and might provide serious problems during routine practice [14].

Our finding indicated low sigma levels between -1.1 to 0.12 for the sodium test with both ABG analyser and both autoanalysers using biological variable targets [15]. Sigma levels were acceptable for potassium at 3.3 sigma; chloride had 1.67 sigma on the ABG analyser. None of the parameters achieved a sigma level of >3 for both potassium and chloride. However, biological variability targets are very demanding.

Other studies have also used sigma metrics of electrolytes in laboratory medicine as a quality control indicator [11,12,16,17]. Unsatisfactory sigma values for electrolytes with Mindray BS120 chemistry analyser and Architect C16000 were reported previously [16,17]. In a study by Nanda et al., the sigma metrics value for chloride was found to be 1.4 with a Cobas Integra autoanalyser [12]. A Mindray BS120 chemistry analyser had sodium and chloride sigma values between 1.6 and 2.05 but unlike our study they used internal quality control materials for bias.

| Analyser | Period | Test | Lab's Result | Mean of group | Bias (%) |
|---|---|---|---|---|---|
| Mindray BS-2000M | October | Sodium | 158.6 | 158.0 | 0.3 |
| | November | | 141.8 | 136.4 | 3.9 |
| | December | | 118.7 | 117.9 | 0.6 |
| | October | Potassium | 5.95 | 5.88 | 1,2 |
| | November | | 4.90 | 4.84 | 1.1 |
| | December | | 3.63 | 3.60 | 0.6 |
| | October | Chloride | 122 | 108.1 | 12.8 |
| | November | | 107.5 | 98.05 | 4.47 |
| | December | | 93.7 | 89.7 | 4.4 |
| Architect C16000 | July | Sodium | 115 | 116.3 | 1.01 |
| | | Potassium | 3.60 | 3.59 | 0.99 |
| | | Chloride | 98 | 103 | 1.05 |
| Radiometer ABL 700 | July | Sodium | 139 | 139 | 0 |
| | | | 163 | 163.2 | 0.1 |
| | | | 150 | 150.9 | 0.6 |
| | | | 135 | 134 | 0.7 |
| | | | 110 | 108.9 | 1 |
| | November | | 109 | 108.9 | 0 |
| | | | 123 | 124 | 0.8 |
| | | | 127 | 134.3 | 5.7 |
| | | | 145 | 150.5 | 3.7 |
| | | | 118 | 119.8 | 1.5 |
| | July | Potassium | 4 | 3.99 | 0.2 |
| | | | 6.9 | 6.93 | 0.4 |
| | | | 4.6 | 4.64 | 0.8 |
| | | | 4.6 | 4.61 | 0.2 |
| | | | 2.2 | 2.16 | 1.8 |
| | November | | 2.2 | 2.17 | 1.3 |
| | | | 2.9 | 2.87 | 1 |
| | | | 4.4 | 4.61 | 4.7 |
| | | | 4.5 | 4.66 | 3.5 |
| | | | 3.4 | 3.37 | 0.8 |
| | July | Chloride | 96 | 94.1 | 2 |
| | | | 117 | 116.9 | 0 |
| | | | 107 | 107.1 | 0 |
| | | | 99 | 98.1 | 0.9 |
| | | | 74 | 75.6 | 2.1 |
| | November | | 75 | 74.9 | 0.1 |
| | | | 81 | 80.7 | 0.3 |
| | | | 103 | 97.5 | 5.6 |
| | | | 107 | 106 | 0.9 |
| | | | 98 | 99.9 | 1.9 |

**[Table/Fig-3]:** External quality control data.

| Analyser | Test | Calculated Sigma[a] | Calculated Sigma[b] |
|---|---|---|---|
| Radiometer ABL700 | Sodium | -1.1 | 5.8 |
| Mindray BS-2000M | | -0.12 | 0.43 |
| Architect C16000 | | -0.13 | 1.9 |
| Radiometer ABL700 | Potassium | 3.35 | 5.3 |
| Mindray BS-2000M | | 0.89 | 1.35 |
| Architect C16000 | | 1.67 | 2.54 |
| Radiometer ABL700 | Chloride | 0.06 | 4.1 |
| Mindray BS-2000M | | -0.86 | 0.27 |
| Architect C16000 | | 0.15 | 2.78 |

**[Table/Fig-4]:** Calculated Sigma.
a TEa taken from 2014 Ricos biological variability data-base; b TEa taken from SC (Spanish Consensus) and SEKK(Czech Republic EQA programme).

The TEa is the magnitude of error that is tolerable in a single measurement [18]. The sigma value is dependent on the TEa definition given by various guidelines. Clinical Laboratory Improvment Ammendment (CLIA) sets a unit-based goal, which means there is a variable allowable total error across the range of the assay. The CLIA goal is listed in units, but works out to between 2 and 3% along the reference range and is more pragmatic [19]. Rilibak, Spanish consensus, and Czech Republic External Quality Assessment (EQA) programme set different analytical performance specifications [15]. Using Spanish consensus TEa target sigma values for all electrolyte results were >3.

Choosing a large target may generate better sigma-metrics, but it is rational to demand a tighter level of performance in the ER. The reliability of results is critical in emergency patient care. Electrolyte imbalances present in a wide variety of acute illnesses, and electrolytes are frequently measured in the ER. Reducing the possibility of error during the analytical phase is essential when one is monitoring electrolytes in the ER.

Westgard et al., analysed EQA /proficiency testing programs and identified significant performance differences between manufacturers, instrument models and methods [8]. It is the responsibility of the laboratory to select the most appropriate instrument and to define the level of performance required. A uniform set of objective and measurable indicators will enable each laboratory to monitor, detect and eliminate errors throughout the total testing process [8].

The analytical imprecision, CV, is the measure of stable analytical performance that is within the capability of the laboratory and depends heavily on the performance of the analyser. The measurement of imprecision offers an estimate that reflects the real performance of the method in daily operation as closely as possible. The CLSI C24 [20] guideline recommends three to six months of routine data to calculate the percentage CV. Quality control samples are assumed to have good stability. However, precision can be affected by different operators, different control lots, different reagent lots, and even the differences in operation between weekdays and weekends. Also, calibration is done frequently in routine laboratory practice with ABG analysers but only once a day with autoanalysers. In our study, the CV reflects the performance of true operators in our ER scene.

Currently, electrolyte measurements are done on more than one analyser, but this can increase the variability [21-23]. During instrument selection, it is critical to select methods with acceptable sigma metrics level versus standard reference methods.

## LIMITATION

We determined bias through EQA against the difference between our result and that of the EQA group method mean. Therefore, we cannot be sure if the group method mean is the true value. However, all analysers are used by hundreds of laboratories in our country suggesting that our observations are relevant to medical practice.

We used two different EQC programs and different IQC material for each analyser. This might affect the calculated sigma value. Stored vials of control material can have erroneous results because of environmental factors.

## CONCLUSION

Each analyser operates at a different CV and bias. When monitoring an individual patient, we suggest using only one analyser. This approach offers a better sigma value for arterial blood gas analyses for the ER. If the autoanalyser has more stringent quality rules, then these must be applied. For sodium, potassium and chloride, we need to consider increasing the QC frequency and calibration as corrective action. Upgraded analysers and better methodologies might be needed.

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**PARTICULARS OF CONTRIBUTORS:**
1. Department of Clinical Biochemistry, Saglik Bilimleri University, Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Turkey.
2. Department of Clinical Biochemistry, Saglik Bilimleri University, Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Turkey.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Yasemin Ustundag-Budak,
Bursa Yuksek Ihtisas Egitim ve Arastırma Hastanesi, Biyokimya Laboratuvarı, Yildirim-16330, Bursa.
E-mail: yaseminbudak2000@yahoo.com



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