Can we trust change of potassium levels measured by blood gases analyzer in patients who presented to emergency department with hyperkalemia?

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Original Article

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ABSTRACT

Objective: To determine whether the amounts of change in potassium levels (ΔK^+) from pre- and post-treatment differ in hyperkalemia patients depending in whether the measurements were made using blood gases analyzer (BGA) and laboratory auto analyzer (LAA).

Design: Prospective-observational study

Setting: Emergency department of a training and research hospital

Subjects: This study was conducted with hyperkalemia patients between May and December 2016.

Intervention: In this study, several potassium lowering treatments (insulin, salbutamol, etc.) were performed, standardized-controlled intervention was not performed.

Main Outcome Measure: During the study period, change of potassium levels in venous blood gases and routine laboratory results before and after hyperkalemia treatment in patients with hyperkalemia was observed. For amounts of change potassium levels, correlations and agreements between ΔK^+ of BGA and LAA were evaluated Spearmen Correlation test and Bland-Altman test respectively.

Results: Finally, 99 patients' laboratory results were evaluated for statistically analysis. When evaluated correlation between ΔK^+ levels by measured BGA and LAA, we found moderate correlation ($p<0.001$, $r=0.67$). However, when assessed agreements between ΔK^+ levels by measured BGA and LAA, the mean difference was found as (mean±SD) – 0.22±0.7mmol/L and agreement limits were calculated as -1.63 – 1.19mmol/L.

Conclusion: Though most physicians prefer to use BGA test results to manage hyperkalemia patients in the early stages, the present study found that BGA results are not a reliable basis for decision-making when managing hyperkalemia patients, particularly regarding whether post-treatment K^+ levels have decreased sufficiently.

KEY WORDS: Blood gases analysis; hyperkalemia; potassium; venous blood gases

INTRODUCTION

Hyperkalemia can be a life-threatening situation and is a common reason for admission to emergency departments (EDs), especially for patients who have acute or chronic kidney diseases or who are using multiple drugs, including angiotensin-converting-enzyme inhibitors and potassium-sparing diuretics [1-3].

Because hyperkalemia is a potentially life-threatening situation, its diagnosis should be made quickly and reliably. However, in daily practice, potassium (K^+) values are measured using a laboratory auto-analyzer (LAA), which is a time-consuming method. Therefore, many physicians increasingly prefer to use a blood gases analyzer (BGA) in routine clinical practice for several reasons [4,5]. The most important concern when using a BGA is whether its results are reliable. Several studies have addressed whether BGAs are reliable by comparing their results, including those regarding K^+, for venous blood gases (VBG) and biochemistry to those measured using LAA, but the results of these studies have been very contradictory [6-9]. Therefore, many physicians have approached K^+ results obtained using BGA with caution, instead preferring to wait for biochemistry results, which can cause delay in beginning hyperkalemia treatment and may contribute to ED overcrowding.

For these reasons, the present study aimed to determine whether the amounts of change in potassium levels (ΔK^+) from pre- and post-treatment differ in hyperkalemia patients depending in whether the measurements were made using BGA and LAA. In contrast to previous studies, the present study hypothesized that if there is a correlation between the ΔK^+ amounts measured using BGA and LAA after hyperkalemia treatments, then K^+ levels can be predicted quickly by evaluating only the BGA results, without waiting for the LAA results. Thus, the study's results may contribute to more prompt treatment of hyperkalemia shorter waits in EDs.

SUBJECTS AND METHODS

Ethics Committee Approval

The local ethical committee was approved this study. (Kecioren Training and Research Hospital, local ethical committee)**.** This prospective-observational study was conducted using patients admitted to the ED of a training and research hospital and diagnosed with hyperkalemia between May and December 2016. The study was approved by the local ethics committee.

Study Population

The study included all consenting patients with hyperkalemia (> 5.5 mmol/L) who were admitted during the study period and who had had both VBGs and routine laboratory results taken at admission. The study excluded patients younger than 18 or older than 80, those who had received any anti-potassium treatment before venous blood sampling, those whose blood sampling failed in the first three attempts, and those who were diagnosed with cardiopulmonary arrest at admission or during the study period.

Study protocol

This study aimed to observe changes in pre- and post-treatment potassium levels in the VBG and routine laboratory results of hyperkalemia patients. At no time during the study period did the researchers intervene in the hyperkalemia treatment. All decisions on which treatment options to use were made by the physicians responsible for the patients.

When patients were diagnosed with hyperkalemia, their potassium levels as measured using BGA and LAA were recorded on a study form. Then, all patients were treated using anti-potassium treatments, including sodium bicarbonate, insulin-glucose tamponade fluid, diuretics, and hemodialysis, according to the decisions of the patients' physicians. Finally, 30 min after these anti-potassium treatments, venous blood sampling was used to again measure patients' potassium levels using BGA and LAA. Similarly, these second potassium levels were recorded on the study form.

Potassium measurements

To measure VBG, venous blood samples were obtained using heparinized syringes (PICO70 Arterial Blood Sampler; Radiometer Medical ApS; Brønshøj, Denmark) at bedside in the ED and analyzed at bedside using a BGA (GASTAT-1800 series pH/Blood Gas Analyzer; Techno Medica; St. Ingbert, Germany). During the study period, the BGA was calibrated four times daily. The venous blood samples were also sent to the

hospital's core laboratory for analysis using LAA biochemistry tests that relied on an ion-selective electrode-diluted (indirect ISE) method (The ARCHITECT c8000 Clinical Chemistry Analyzer; IL, USA). The material used in this Clinical Chemistry Analyzer was a 2P32 ICT sample diluent [ICTD5] kit. During the study period, the core laboratory determined the calibration time for the biochemistry analyzer at 24-hour intervals, according to the manufacturers' instructions. Two types of controls (normal and abnormal) were to be run every 8 hours and following the calibration. The imprecision of the ICT assays for serum samples was as follows: sodium ≤ 1.5% and potassium ≤ 2.7%. All blood samples were transferred from the ED to the core laboratory within 30 min using a pneumatic system.

Statistical analyses

Statistical analyses were performed using SPSS version 16.0 (Chicago, IL, USA). The Shapiro-Wilk test was used to assess the normal distribution of all parameters. Non-parametric data were expressed as median values and inter-quartile range (IQR) (25–75%). The correlations between ΔK^+ as measured using the BGA and LAA methods were evaluated using the Spearman Correlation test, and an R-value higher than 0.80 was considered a strong correlation. Agreements between the ΔK^+ measurements obtained using the two methods were assessed using the Bland-Altman test, with 95% CI limits of agreement. Finally, to estimate the ΔK^+ level as measured using LAA after anti-potassium treatment, linear regression analysis was performed using the formula y = a + bx, where x = [ΔK^+ in BGA] and y = [ΔK^+ in LAA]. A p value of < 0.05 was considered statistically significant.

RESULTS

During the study period, 121 patients who had been diagnosed with hyperkalemia, whether or not they had any symptoms, had their blood sampled. The study excluded 22 patients who lacked both VBG and routine laboratory results (pre- or post-treatment). Therefore, the laboratory results of 99 patients were evaluated using statistical analysis. The median age of all patients was 72 (IQR 25–75%; 62–80), and 56 patients (56%) were female. Table 1 contains the demographic and clinical characteristics of all patients. The median value of pre-treatment potassium was 6.1 (5.7–6.6) using BGA measurements and 6.5 (6.1–7.1) using LAA measurements. The median values of post-treatment potassium were 4,9 (4.3–5.4) using BGA measurements and 5.3 (4.5–5.7) using LAA measurements. Table 2 shows the results of BGA and LAA measurements for all patients.

The present study's most important finding is that when pre- and post-treatment ΔK^+ was measured using both BGA and routine LAA, the median ΔK^+ value was 1.09 (0.5–1.9) using BGA and 1.35 (0.8–2.1) using LAA. When the correlation between ΔK^+ as measured using BGA and LAA was evaluated, it was found to be moderate ($p < 0.001$, $r = 0.67$) (Figure 1). However, when agreements were assessed between ΔK^+ levels as measured using BGA and LAA, the mean difference was found to be (mean ± SD) -0.22 ± 0.7 mmol/L, and the agreement limits were calculated as being -1.63 to 1.19 mmol/L. The Bland-Altman analyses found poor agreement for ΔK^+ for clinical using (Figure 2). Finally, regression analysis to estimate ΔK^+_{LAA} after anti-potassium treatment found that $\Delta K^+_{LAA} = 0.659 \times (0.644 \times \Delta K^+_{VBG})$ ($p < 0.001$).

DISCUSSION

An evaluation of previous studies found no strong correlations or agreements between the results of BGA and LAA measurements of K^+. Therefore, we hypothesized that there might be a strong correlation or good agreement between pre- and post-treatment amounts of K^+ change as measured using BGA and LAA. However, the present study's main findings indicate that K^+ results measured using the BGA method are not reliable for use in deciding whether K^+ levels have decreased sufficiently in hyperkalemia patients. The results found that although there is a moderate correlation between the results of the BGA and LAA methods of measuring ΔK^+, there is not acceptable agreement between the two methods. In addition, although the study performed regression analyses to estimate ΔK^+_{LAA} by considering ΔK^+_{VBG}, this formula was not found to be reliable for use in daily ED practice because of the lack of a strong correlation between BGA and LAA measurements of ΔK^+.

Quick, reliable measurement of K^+ is crucial in hyperkalemia patients, especially when making decisions regarding hemodialysis and to prevent life-threatening ventricular dysrhythmia. Therefore, most physicians rely on BGA in daily clinical practice, especially to manage hyperkalemia patients [7]. Despite this general use of BGA, several studies in the literature that have addressed its reliability have reached conflicting results.

For example, Budak *et al* used LAA and BGA to evaluate the agreement between Na^+ and K^+ measurements of 1105 test samples, finding wide-ranging agreement limits (mean diff: 0.25, LoA: -0.5 to 1.1) for K^+. The researchers concluded that K^+ results obtained using BGA and LAA cannot be used interchangeably in clinical practice [8]. Acikgoz *et al* analyzed the blood sample results of 118 patients, finding that although there was a strong correlation between the results of a biochemistry analyzer and BGA, the agreement was poor; the mean difference between the two methods was 0.62 ± 0.43 mEq/dL, and the agreement limits ranged from 0.19–1.05 mEq/dL [9]. Similarly, studies conducted Zhang *et al* and Uysal *et al* found wide ranges of agreement limits for K^+ measurements (mean diff: 0.43, LoA:-0.29 to 1.16 and mean diff: -0.46, LoA: -1.34 to 0.42, respectively) [10-11]. In contrast to the results of these studies, others have reported good agreement between these two methods of measuring K^+. For example, Kozacı *et al* analyzed the blood sample results of 100 patients' and found that the mean difference in K^+ values as measured using routine biochemistry and BGA was 0,5 and that the agreement limits ranged from 0.36–0.62 [12]. Similarly, Mirzazadeh *et al* reported that the mean difference for K^+ measurements between the two methods was -0.08 mmol/L and that the 95% CI of the agreement limits raged from -0.63 to 0.46 mmol/L [13].

Because of the conflicting results in the literature, the present study did not plan to evaluate the agreement of K^+ measurements made using the two methods. Instead, the study evaluated the agreement between the BGA and LAA methods regarding the amount of change in K^+ between pre- and post-treatment measurements. We believed that if there is strong correlation and agreement between the ΔK^+ amounts measured using BGA and LAA, then after hyperkalemia treatment, K^+ levels can be predicted quickly by evaluating only the BGA results, without waiting for the LAA results, leading to more prompt treatment of hyperkalemia by shorter wait times in EDs. However, it is our opinion that the results of the present study do not support this hypothesis because of the relatively poor agreement limits.

Limitations

The present study has some limitations. First, its sample size was relatively small; however, we believe that this is permissible because the probability of a type-2 error is low. Second, although BGA devices are calibrated daily in routine practice, in the present study, standardization of the daily calibration may not have been sufficient. However, we believe that the results obtained because of this limitation may better compare to those in real clinical practice. Finally, the study analyzed only venous blood samples, not arterial samples.

CONCLUSION

Although most physicians prefer to use BGA test results to manage hyperkalemia patients in the early stages, the present study found that BGA results are not a reliable basis for decision-making when managing hyperkalemia patients, particularly regarding whether post-treatment K^+ levels have decreased sufficiently.

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Informed Consent: Not applicable.

Author Contributions:

1) conceived and designed the experiments; ŞKÇ, SD, OLD
2) performed the experiments; OLD, ŞKÇ, SD
3) analyzed and interpreted the data; ŞKÇ, SD, YÇ, OLD
4) contributed reagents, materials, analysis tools or data; ŞKÇ, YÇ
5) wrote the paper ŞKÇ, OLD

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FIGURE LEGENDS

Figure-1: Scatter plots for the correlation between ΔK^+ levels by measured BGA and LAA **BGA:** Blood gases analyzer **LAA:** Laboratory auto-analyzer

Figure-2: Agreements limits of ΔK^+ levels by measured BGA and LAA according to Bland-Altman analysis. Flat lines showed the mean differences of ΔK^+ levels in blood gases analyzer and laboratory auto-analyzer; dotted lines showed agreements limits with 95%CI. **BGA:** Blood gases analyzer **LAA:** Laboratory auto-analyzer

Table 1: Demographic and clinical characteristics of patients

Type of Characteristics	**Value**
Age (years) median (IQR25%-75%)	72 (62-80)
Sex	
• Male	56 (56%)
• Female	43 (44%)
Comorbidities n (%)	
• Ischemic heart disease	13 (13%)
• Diabetes mellitus	26 (26%)
• Hypertension	36 (36%)
• Chronic obstructive pulmonary disease	5 (5%)
• Congestive heart failure	18 (18%)
• Chronic kidney disease	31 (31%)
Vital signs	
• Mean arterial pressure mmHg	90 (73 – 103)
• Respiratory rate rate/min	18 (16 – 20)
• Heart rate beat/min	94 (81 – 108)
• SO_2 %	92 (90 – 95)
Hyperkalaemia treatment n (%)	
• Insulin and dextrose infusion	93 (94%)
• $NaHCO_3$ infusion	6 (6%)
• Inhaler salbutamol	80 (81%)
• Haemodialysis	25 (25%)
• Calcium treatment	25 (25%)

Table 2: Venous blood gases and routine laboratory results of patients

Pretreatment values		**Venous Blood Gases**	**Routine Laboratory Results**
	Sodium (mmol/L)	132 (127 – 137)	135 (129 - 137)
	Potassium (mmol/L)	6,1 (5,7 – 6,6)	6,6 (6,1 – 7,0)
	Creatine (g/dL)	–	2,3 (1,5 – 7,4)
	pH	7,30 (7,23 – 7,35)	–
After-treatment Values		**Venous Blood Gases**	**Routine Laboratory Results**
	Sodium (mmol/L)	133 (128 – 137)	134 (130 – 138)
	Potassium (mmol/L)	4,9 (4,4 – 5,5)	5,3 (4,5 – 5,7)
	Creatine (g/dL)	–	1,9 (1,2 – 5,3)
	pH	7,31 (7,24 – 7,36)	–