ABSTRACT
Introduction: Potassium level is measured for patients with high risk of hyperkalemia in the emergency department (ED) using both blood gas analyser (BGA) and biochemistry analyser (BCA). The study was conducted to evaluate the correlation and agreement of potassium measurement between BGA and BCA.

Materials and Methods: This is a prospective cross-sectional study on the data obtained from Hospital Universiti Sains Malaysia (Hospital USM) from Jun 2018 until May 2019. Blood samples were taken via a single prick from venous blood and sent separately using 1ml heparinised syringe and were analysed immediately in ED using BGA (Radiometer, ABL800 FLEX, Denmark) and another sample was sent to the central laboratory of Hospital USM and analysed by BCA (Architect, C8000, USA). Only patients who had potassium levels ≥5.0mmol/L on blood gas results were included. A total of 173 sample pairs were included. The correlation and agreement were evaluated using Passing and Bablok regression, Linear Regression and Bland-Altman test.

Result: Of the 173 sample pairs, the median of potassium level based on BGA and BCA were 5.50mmol/L (IQR: 1.00) and 5.90mmol/L (IQR: 0.95) respectively. There was significant correlation between two measurements (p<0.001, r: 0.36). The agreement between the two measurements showed within acceptable mean difference which was 0.27 mmol/L with 95% limit of agreement were 1.21mmol/L to 1.73mmol/L.

Conclusion: The result of blood gas can be used as a guide for initial treatment of hyperkalaemia in critical cases where time is of the essence. However, BCA result is still the definitive value.

KEYWORDS:
Hyperkalaemia, blood gas analyser, biochemistry analyser, point-of-care, agreement

INTRODUCTION
Hyperkalaemia is a life-threatening electrolyte disorder that may cause cardiac arrest if not treated early. It is commonly seen in patients who present with acute kidney injury and chronic kidney injury in the emergency department (ED). The lethal toxicity of hyperkalaemia is known as it reduces myocardial conduction velocity and accelerates the repolarization phase, producing well described changes on surface electrocardiogram (ECG), including narrow, symmetrical T wave, prolonged PR interval, diminished P-wave amplitude, QRS widening and ultimately sinusoidal QRS that ends in asystole or ventricular fibrillation.

Even though hyperkalaemia may lead to a fatality, it is reversible if the condition is immediately diagnosed and treated by physicians. Therefore, immediate measurement of serum potassium becomes crucial as it may change the treatment approach in hyperkalaemia patients, even during a cardiac arrest. Blood gas analyser (BGA) is used not only to measure blood gas analysis but also electrolytes, especially potassium. This measurement helps in making a clinical decision while waiting for confirmatory results using biochemistry analyser (BCA). BCA is usually located in the main laboratory and is considered as primary reference and accredited by the respective organisation. However, BCA results are always delayed due to the distance from the ED. Therefore, they may compromise the treatment in critically ill patients and affecting their outcome.

There are two methods used to measure the levels of potassium using electrolyte assay either direct or indirect which employing ion-sensing electrodes (ISE). Direct ISE method does not require a diluent solution for samples to interact with the ISE membrane which applies to devices like BGA. The indirect technique requires pre-analytical dilution with fixed volume diluent which takes about 20-30 minutes for the centrifuging which is used in BCA. Comparison between these two methods, direct ISE method measures the actual electrolytes in plasma concentration without being affected by the concentration of solid components in plasma meanwhile indirect ISE method measures mean concentration of electrolytes after dilution in plasma and its measurement is affected by concentration of solid components such as protein or lipid in plasma. Direct ISE method is preferred by clinical chemists as the method of choice as it is free from electrolyte exclusion effects, but the indirect method is still accurate as its widely used in
BGA is one of the bedside point-of-care test (POCT) that many physicians rely on to measure electrolytes and assist in making their clinical decision. It is becoming an important test in the EDs, intensive care units and operation theatres.14,15 Hence, the reliability and validity of BGA should be comparable with the use of BCA that is known to be the gold standard for the measurement of potassium. According to the United States of Clinical Laboratory Improvement Act (USCLIA), the acceptance bias of serum measurement of potassium levels compared to BCA should not exceed ±0.5mmol/L.11

Many previous studies had been done to determine the correlation and agreement between BGA and BCA. Unfortunately, the results of the studies showed inconsistent outcomes. Generalisation of the results of previous studies with our current models in the laboratories may be dangerous as its reliability is controversial.12 The difference probably is due to different types of the analyser models.13 Previous studies had compared a variety of BGA and BCA models such as Radiometer ABL505 versus Hitachi 717, Seimens Rapid Point 500 versus Abbott C8000 Architect, GEM 3000 ABG analyser versus Olympus AU2700 discrete chemistry analyser, ABL825 FLEX analyser versus AU2700 Autoanalyzer, Bayer Rapidlab 865 versus Olympus AU640, Radiometer ABL800 versus AU640, Radiometer ABL90 FLEX versus Vy-S600 automatic biochemical analyser and other different types of analyser models.8,14-20 In Malaysia, majority of laboratories are using the Radiometer models such as ABL800 FLEX, ABL90 FLEX and ABL80 FLEX. In the Universiti Sains Malaysia (USM), BGA model is Radiometer ABL800 in ED and BCA model is Architech C8000 in the main biochemistry laboratory.

The main reason of this study needs to be done because there was no previous study comparing the two types of analysers and the inconsistent outcome evaluating the correlation and agreement between BGA and BCA from the previous studies. Moreover, the outcome of this study may benefit for the centres that use the similar types of machines to evaluate the correlation and agreement between BGA and BCA. Hence, the objective of this study is to evaluate the correlation and agreement of potassium measurement between BGA and BCA.

MATERIALS AND METHODS
This was a comparative cross-sectional study was conducted from 1st June 2018 until 31st May 2019 at ED of USM, Kubang Kerian, Kelantan.

The sampled population were all patients with a potassium levels of 5.0mmol/L or more based on BGA. A total of 173 patients who fulfilled the inclusion and exclusion criteria were included. A single prick of venepuncture provided two blood samples in separate containers were obtained; one was for venous blood gas (VBG) for BGA test and the other one was for BCA test. Exclusion criteria were all patients whose blood samples sent for BGA and BCA tests were taken separately based on the documentation in the folder of the patients. Samples with faulty or machine error results were also excluded. The cut-off potassium level of 5.0mmol/l was chosen because it is the upper limit of the normal value. All data was recorded in ED Hospital USM Hyperkalaemia Checklist Form.

The sample size was calculated by using MedCalc v17.8 Software (Trial version) and a total of 173 blood samples were needed. Decision for potassium measurement by using BGA was exclusively depended on the managing team that consists of specialists, registrars, medical officers and house officers. However, it was also a standard practice that any blood sample that was sent for BGA test would also be sent for BCA test in the main laboratory. BGA test is conducted in the ED, within 10 metres radius and the result is immediately available. On the other hand, BCA test is conducted in the main laboratory and the distance was around 70 meter from the ED. The sample was transported by hospital attendants to the main laboratory. Results from BCA take about five hours to be ready through online system.

All venous blood samples were collected in a sterile environment by trained staff, either by houseman or medical officers. Samples were collected in 1ml blood-gas syringes that were flushed with heparin (1:1000) beforehand and syringed out completely to prevent clotting and dilution that might affect the results. No bubbles inside the blood sample to minimise pre-analytical error. The blood samples were analysed immediately for BGA which was ABL800 FLEX Radiometer from Denmark.

In order to minimise bias or measurement error during sampling, short presentation on how to optimise on sampling of VBG was conducted during weekly department continuous medical education. Regular reminder was done during daily morning pass-over meeting. Since VBG is easier access, less pain and comparable to ABG (except in the partial oxygen pressure result), it has been widely used to measure electrolytes through BGA in the emergency settings for many clinical conditions.26-28 VBG also has been shown to have good clinical positive correlation for sodium, potassium and creatinine.29

Another blood sample was sent to the main laboratory for BCA test using plain tubes and was analysed using Architect C8000 from the United States of America (USA) that was operated under the Pathology Department of Hospital USM. The procedure is considered as the gold standard of test for measurement of potassium levels and the laboratory was accredited by Malaysia Standards of International Organization for Standardization (MS ISO 15189:2007).30 Quality control and assurance are done regularly to ascertain reliability of both test for measurement of potassium levels based on manufacturer recommendation and National Institute of Standards and Technology (NIST).

Statistical analyses were performed via IBM SPSS Statistics version 24 and RStudio software, version 1.2.5019, based on R Language, version 3.6.1. Wilcoxon Signed Rank Test was used to compare the medians of the results from two measurement methods (BGA and BCA). Linear Regression
was used to calculate the correlation coefficient, while Passing and Bablok regression was used to compare slope and intercept between the two methods. Bland-Altman plot was used to assess the agreement between the two potassium measurement methods. A p value of <0.05 was accepted as significant.

**RESULTS**

Of the 173 paired blood samples that were analysed, 88 (50.9%) of the patients were males. The mean (Standard Deviation, SD) age of the patients were 61.0 (12.8) years, in which male patients mean (SD) age was 63.0 (13.4) years and the mean (SD) age of female patients was 58.9 (11.9) years. Majority of the patients (57.8%) were triaged to the yellow zone and 115 patients (66.5%) had background medical illness of chronic kidney disease (CKD). Only 6 hyperkalaemia patients with initial BGA results of ≥5.0mmol/l were eventually discharged, while others were admitted to the general ward, intensive care unit or died in the ED. The range of potassium levels based on BGA were from 5.0mmol/L to 9.2mmol/L. The median of potassium levels measured by BGA was 5.50mmol/L (IQR: 1.00 mmol/l), ranged from 5.00 to 9.20mmol/L. On the other hand, the median of serum potassium level measured by BCA was 5.90mmol/l (IQR: 0.95mmol/L), ranged from 3.80 to 10.00mmol/L.
While there was significant difference in the potassium reading in both methods, as summarised in Table II, there was positive correlation and accepted agreement between the two methods as shown in Table III and Figure 1. Linear regression shows positive correlation, while Passing and Bablok Regression shows that the slope was 1.31 and intercept at -1.42. The agreement between the two methods of potassium measurement with the mean of difference was 0.27±0.75mmol/L with 95% limit of agreement were 1.21mmol/L to 1.73mmol/L. The difference between the two analysers ranged from 0.48 to 1.02mmol/L. Out of 173 sample pairs, 96 blood samples (55.5%) had difference of ±0.5mmol/L or smaller and the rest 77 (49.5%) blood samples had difference of more than 0.5mmol/L between two methods of measurement.

**DISCUSSION**

POCT is a medical bedside diagnostic testing method, provides quicker results and allows for better immediate clinical decision-making of in-patient management. The method includes blood gas analysis, electrolyte analysis, rapid cardiac markers diagnostics, rapid coagulation testing and others. The reliability of BGA as one of the POCT for potassium measurement is important and lifesaving. Even general practitioners in European countries and the USA now use POCT for their clinical practices for managing non-emergency cases. The BGA results have had the most impact for the care of patients compared to other investigations in POCT.

Based on the Table I, the most common cause of hyperkalaemia was CKD that represented 66.5% of the patients. This is comparable with a study from Germany that found among the common cause of hyperkalaemia are kidney failure and hypoaldosteronism. In addition to that, CKD is one of the important predictors for hyperkalaemia due to lower estimated glomerulus filtration rate (eGFR). In fact, BGA is indicated in CKD patients to look for acidosis and hyperkalaemia in emergency settings.

In this study, most of the patients (57.8%) were initially triaged to yellow zone, followed by red zone (39.3%) and green zone (2.9%). Since yellow zone is considered semi-critical zone, most of hyperkalaemia results were in the mild range between 5.0 and 6.0mmol/L. In fact, most of the hyperkalaemia patients were asymptomatic. Symptoms like muscle weakness, ascending paralysis, heart palpitations and paraesthesia may develop at higher level above 6.5mmol/L. Diagnostic uncertainty of hyperkalaemia patients due to a variety of the complaints and unspecific electrocardiogram (ECG) could be the reason for patients to be triaged to yellow zone or green zone. Patients who were triaged to the red zone had presented with acute life-threatening condition such as...
hyperkalaemia and ECG findings. Clinicians are trained not to treat the hyperkalaemia as a stand-alone biomarker, but to manage the patients holistically.

Based on Table II, the median potassium value measured by BGA was 5.50 mmol/L whereas the median of serum potassium measured by BCA was 5.90 mmol/L. In general, the results of potassium from BGA tend to be lower than the levels measured by BCA. Only 12 (6.9%) blood samples had similar readings in the BGA and BCA methods. There were 133 (76.9%) blood samples that had higher reading and 28 blood samples (16.2%) that had lower reading on BCA compared to BGA. This finding is comparable with other studies that BGA has been shown to have lower readings compared to BCA up to 96.6% of the samples.1,3,4,35 Measurement of potassium levels using BGA is underestimated due to pre-analytical bias by negatively charged heparin that binds to positively charged potassium in whole blood and it lowers the potassium measurement.34 However, in the case where the potassium level is much higher, the possible explanation is haemolysis of the whole blood in BGA that lead to the false elevation.35

Based on our results, there is a positive correlation between potassium levels measurement by BGA and BCA in hyperkalaemic patients. Figure 1(a) shows that when the potassium spectrum measured by BGA increases, the difference measured by BCA increases. It may be more than 1.00 mmol/L when potassium levels measured by BGA was more than 7.00 mmol/L. This finding is comparable with a previous study based on the cohort with potassium level more than 6.00 mmol/L.3 The study found that the differences were up to 1.00 mmol/L between two measurement methods for patients who had moderate to severe hyperkalaemia.3 Based on this finding, clinicians should be aware not to underestimate the value of potassium by BGA especially when the level is more than 7.00 mmol/L. This could be the advantage of using BGA result as it could be safety measure to detect early hyperkalaemia as the potassium is possibly higher as expected. However, the clinicians should also be aware of pre-analytical bias as described above as safety issue and diagnosis of hyperkalaemia should be supported by other investigations such as ECG findings and risk factors of the patients.

Several studies assessed the correlation and agreement of BGA and BCA in different spectrum of potassium levels ranging from normal value to abnormal value.36-40 However, most of the studies were based on wider range of potassium level from normal value to hyperkalaemia (abnormal value). Based on study done by LM Quin et al., measurement of potassium at physiological range showed good correlation and agreement between these two analysers but if potassium more than 5mmol/L whilst it had poor correlation and agreement and this may be due to the limitation of the machine to measure the potassium in critically ill patient.37 Nanda et al., found positive correlation indicating agreement between BGA and BCA in managing of critically ill patients.38 Mirzazadeh et al. and Uysal et al., found good agreement and strong correlation between BGA and BCA and can be accepted as a POCT for critically ill patients.39,40 However, Budak et al., revealed that the result of BGA and BCA should not be used interchangeably in clinical practice even though the mean of bias was 0.25 mmol/L due to individual readings on BGA showing wide range of variability.1 All these studies were based on wide range of potassium.

Contrary to other studies, Acikgoz et al., stated their study was the first time to evaluate the agreement between two potassium measurement methods in a cohort where the potassium more than 6mmol/L.1 The result of study showed there was significant difference between these analysers with mean of bias 0.62 mmol/L. Contrarily, our study shows the mean of bias was within an acceptable range of 0.27 mmol/L based on Figure 1(c). The strength of our study is that the samples were collected prospectively from a single source (venous blood) whereas Acikgoz et al., compared retrospectively between venous and arterial blood.

There are some limitations to our study. The results of our study are limited to a single model of BCA and BGA. Even though this result cannot be generalised to other models, these findings are greatly helpful for centres that use similar models. On the other hand, to the best of our knowledge, there are no previous studies that showed that there was concordance between measurement of different types of BGA. Secondly, our practice is by using conventional syringes with pre-flushing heparin which is theoretically may affect the measurement of potassium by BGA.32 We suggest the use of dried heparin syringes in order to optimize the accuracy of the measurement.

In future studies, financial implication may be of interest as the tests are run twice for the same sample. With more clinical data and resources, guidelines can be developed to delineate the clinical needs of BCA compared to BGA in ED. As of now, the focus is more towards immediate and lifesaving decision-making in hyperkalaemia patients.

CONCLUSION

Among hyperkalaemia patients, there is moderate correlation and acceptable agreement in the potassium level between BGA to BCA. However, the BGA results tend to be lower compared to BCA results. Therefore, clinicians should use the BGA results with caution in certain clinical situations where time is of the essence to initiate treatment of patients for hyperkalaemia. For a definitive value, BCA is still considered as a gold standard.

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REFERENCES


