Original Article

http://dx.doi.org/10.3349/ymj.2014.55.5.1348
pISSN: 0513-5796, eISSN: 1976-2437

Yonsei Med J 55(5):1348-1353, 2014

YMJ

Evaluating the Utility of Rapid Point-of-Care Potassium Testing for the Early Identification of Hyperkalemia in Patients with Chronic Kidney Disease in the Emergency Department

Je Sung You,[1,2] Yoo Seok Park,[1] Hyun Soo Chung,[1] Hye Sun Lee,[3] Youngseon Joo,[1] Jong Woo Park,[4] Sung Phil Chung,[1] Shin Ho Lee,[5] and Hahn Shick Lee[1]

[1]Department of Emergency Medicine, Yonsei University College of Medicine, Seoul;
[2]Department of Emergency Medicine, Graduate School of Medicine, Kangwon National University, Chuncheon;
[3]Department of Research Affairs, Biostatistics Collaboration Unit, Yonsei University College of Medicine, Seoul;
[4]Department of Emergency Medicine, Changwon Fatima Hospital, Changwon;
[5]Department of Emergency Medicine, National Health Insurance Corporation Ilsan Hospital, Goyang, Korea.

Received: November 6, 2013
Revised: January 4, 2014
Accepted: January 20, 2014
Corresponding author: Dr. Sung Phil Chung, Department of Emergency Medicine, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 135-720, Korea.
Tel: 82-2-2019-3030, Fax: 82-2-2019-4820
E-mail: emstar@yuhs.ac

· The authors have no financial conflicts of interest.

Purpose: Severe hyperkalemia leads to significant morbidity and mortality if it is not immediately recognized and treated. The concentration of potassium (K^+) in the serum increases along with deteriorating renal function. The use of point-of-care K^+ (POC-K^+) in chronic kidney disease (CKD) could reduce the time for an accurate diagnosis and treatment, saving lives. We hypothesized that POC-K^+ would accurately report K^+ serum level without significant differences compared to reference testing, regardless of the renal function of the patient. **Materials and Methods:** The retrospective study was performed between January 2008 and September 2011 at an urban hospital in Seoul. The screening program using POC was conducted as a critical pathway for rapid evaluation and treatment of hyperkalemia since 2008. When a patient with CKD had at least one warning symptom or sign of hyperkalemia, both POC-K^+ and routine laboratory tests were simultaneously ordered. The reliability of the two assays for serum-creatinine was assessed by intra-class correlation coefficient (ICC) analysis using absolute agreement of two-way mixed model. **Results:** High levels of reliability were found between POC and the laboratory reference tests for K^+ (ICC=0.913, 95% CI 0.903–0.922) and between two tests for K^+ according to changes in the serum-creatinine levels in CKD patients. **Conclusion:** The results of POC-K^+ correlate well with values obtained from reference laboratory tests and coincide with changes in serum-creatinine of patients with CKD.

Key Words: Point-of-care testing, hyperkalemia, chronic kidney disease

INTRODUCTION

Hyperkalemia is defined as serum potassium (K^+) concentrations >5.5 mmol/L. Hyperkalemia can be classified according to serum K^+ into mild (5.5–6.5 mmol/L), moderate (6.5–7.5 mmol/L) and severe (>7.5 mmol/L).[1] Although it is a life-

threatening condition, hyperkalemia presents non-specific symptoms such as heart palpitation, nausea, general weakness, and muscle pain. If left untreated, hyperkalemia can lead to an alteration of cardiac electrophysiology, which can be fatal.[1,2] Severe hyperkalemia usually leads to significant morbidity and mortality if it is not immediately recognized and treated.[3,4]

Serum K^+ levels are maintained within a very narrow range. The important part of K^+ regulation depends on K^+ excretion.[2] Serum K^+ levels have been shown to positively correlate with deteriorating renal function.[2] In fact, chronic renal disease (CKD) was the most common underlying medical condition for hyperkalemia.[3]

The use of a rapid point-of-care K^+ test (POC-K^+) to quickly detect hyperkalemia in patients with CKD could reduce the time needed to achieve an accurate diagnosis and initiate treatment in the emergency department (ED) of hospitals. Such an improved diagnostic has the potential to save lives and improve turnaround time in the ED. The aim of our study was to determine the ability of POC-K^+ testing to accurately detect serum K^+ levels by comparing the results with those of traditional reference laboratory tests.

We hypothesized that POC-K^+ would accurately report K^+ serum level without significant differences compared to reference testing, regardless of the renal function of the patient, thereby justifying their use in emergency departments in the future.

MATERIALS AND METHODS

This retrospective study was approved by the Institutional Review Board and performed between January 2008 and September 2011 at an Severance Hospital affiliated with our institution. This hospital has an ED census of 50000 patients per year. In this hospital, an effective screening program using POC has been conducted for the rapid evaluation and treatment of hyperkalemia since 2008. Upon the arrival of a patient with chronic renal failure (CRF) or end stage renal disease (ESRD) at the ED, emergency physicians identified patients with hyperkalemia according to the predetermined protocol E-DASH: Emergency-Detection and Acquisition of Suspicious Hyperkalemia. The protocol directed diagnosis of hyperkalemia using known warning symptoms (palpitation, nausea, vomiting, diarrhea, weakness, and muscle pain) and signs (shock, dehydration, and EKG abnormality-peaked T, QRS widening, and disturbance of cardiac rhythm).[5]

When a patient with CRF or ESRD had at least one warning symptom or sign listed above, the emergency physician ordered both a POC-K^+ test and routine laboratory tests including the reference laboratory serum-K^+ test. POC-K^+ was performed on whole blood with the NOVA Stat Profile CCX (Nova Biomedical, Waltham, MA, USA). The quality of assay have been assessed quality by auto-function in equipment and trained technicians of laboratory medicine on eight-hour shifts. Reference laboratory tests usually used in the clinical setting were performed on serum obtained from whole blood in the central laboratory with the Hidachi 7600 (Hidachi, Tokyo, Japan). The interval times from patient arrival at the ED to the beginning of testing and from the beginning of testing to the reporting of the results of an assay were tracked by the computerized physician order entry, which is set as a universal time throughout the hospital.

Statistical analysis

Comparison of K^+ measurements between POC-K^+ and the reference laboratory tests was performed by Passing-Bablock linear regression analysis. The reliability of each of these outcome measures was assessed by intra-class correlation coefficient (ICC) analysis. The ICC ranges from 0 to 1, with 0 indicating no agreement and 1 indicating perfect agreement. The ICCs were interpreted as follows; excellent: 0.75–1, modest: 0.40–0.74, and poor: 0–0.39.[6,7] A Bland-Altman plot was constructed for serum K^+ levels; this scatter plot reveals the differences between the measurements obtained by the two tests and the mean of the measurements for each subject in the study. The mean difference of zero indicates perfect agreement, while the 95% limits of agreement are the intervals within which 95% of the data lie. A serum K^+ level of 5.5 mmol/L is usually considered as the cut-off concentration for hyperkalemia. This cut-off was applied to the population to explore the accuracy of the POC-K^+ in detecting hyperkalemia, and patients received actual emergency treatment (medications or emergency dialysis) accurately at this concentration. The proportion of hyperkalemia between the two groups was compared by McNemar test. Comparison of area under the curves (AUCs) was performed using the Delong method. The results of serum-creatinine (Cr) were divided into five categories according to interquartile ranges, and the reliability of each POC-K^+ for serum Cr was assessed by ICC analysis using absolute agreement with a two-way mixed model. All analyses were performed on SPSS software package (ver-

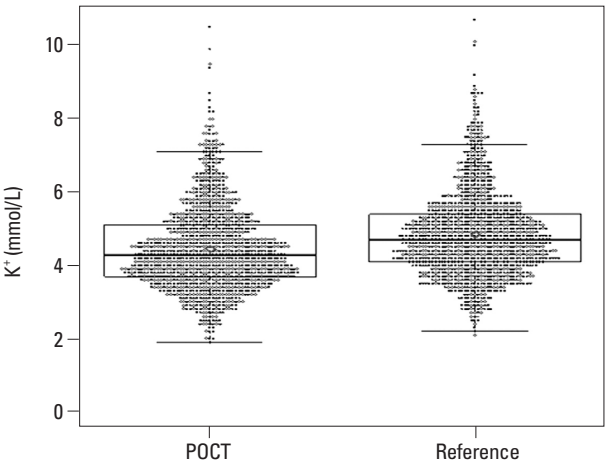


Fig. 1. Box-and-whisker plot. Serum concentrations of potassium detected by POC-K^+ and reference tests. Although a significant difference in the mean of 0.39 mmol/L was found between the two groups (p<0.001). The propensity of data for K^+ showed a high degree of concordance between POC and the reference test. POC, point-of-care; POCT, point of care testing.

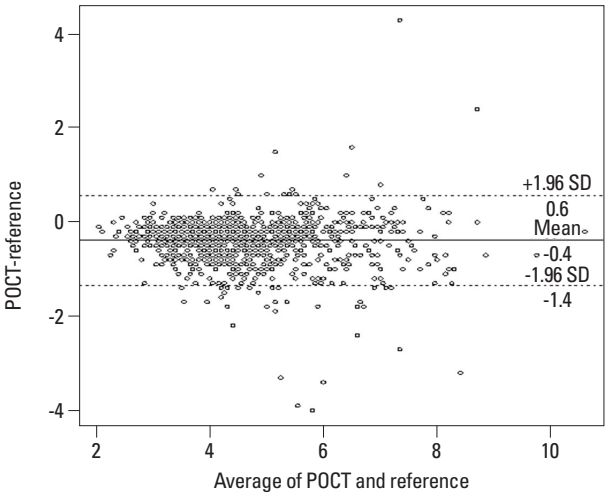


Fig. 2. Bland-Altman plot showing the mean differences (solid line) and 95% limits of agreement (dot line) for K^+ serum levels. POCT, point of care testing.

sion 20; SPSS Inc., Chicago, IL, USA), R version 2.13.1 (R foundation for statistical Computing, Vienna, Austria), or SAS 9.2 (SAS Institute Inc., Cary, NC, USA).

RESULTS

A total of 1188 patients with suspected hyperkalemia were included in this study. The median interval from arrival at the ED to the reporting of the results was 24 [16, 17] minutes for point of care testing (POCT) and 61 [53, 74] minutes for the serum reference laboratory tests (p<0.001). The intervals from arrival at the ED to beginning of test and from beginning of test to the reporting of the results were 18 [10, 31] and 4 [3, 6] minutes for POCT-K and 15 [9, 23] (p<0.001) and 44 [38, 51] minutes (p<0.001) for the serum reference laboratory tests. Although there was a significant difference (0.39 mmol/L) between two groups (p<0.001) for the mean value, the propensity of data showed a high degree of concordance between K^+ serum levels measured by POC-K^+ and the reference test (Fig. 1). Analysis by Passing-Bablock regression demonstrated the relationship of Y=1.00×-0.30 (Y: results obtained using the reference test, and X: results obtained using POC-K^+). At the threshold value of 5.5 mmol/L, the total allowable error of potassium analysis was 5.8%, as derived from recent biological variation data.[8] The calculated total error at the cut-off value (5.5 mmol/L) was within total allowable error recommendations. All observations were displayed in dot plot and box-and-whisker plot.

The intra-class correlation coefficients (ICC) were determined to measure the agreement between the two methods in this study. High levels of reliability (the consistency agreement) were found between POC and the laboratory reference tests for K^+ [ICC=0.913, 95% confidence interval (CI) 0.903–0.922]. Additionally, the agreement between the two tests was evaluated using the Bland-Altman method. The Bland-Altman plots demonstrate the mean differences and 95% limits of agreement between the two methods for K^+ serum concentrations (Fig. 2).

The sensitivity and specificity of the POC-K^+ test was evaluated. When the 5.5 mmol/L threshold was applied to the population, the sensitivity was 66.4% (95% CI 61.0–71.9) and specificity was 98.9% (95% CI 98.2–99.6) in POC-K^+ (Fig. 3). However, if a value of 0.4 was added to the results of POC-K^+ [a correction based upon difference (0.39 mmol/L) for the mean value], the sensitivity was 85.5% (95% CI 81.4–89.5) and specificity was 93.9% (95% CI 92.3–95.5). The sensitivity was also evaluated for patients that received actually emergency treatment of hyperkalemia based on results of the POC-K^+ assay. The sensitivities were 92.9 (95% CI 87.1–96.2) between 5.5 mmol/L and 6.4 mmol/L, 100.0 (95% CI 93.5–100) between 6.5 mmol/L and 7.4 mmol/L, and 100.0 (95% CI 83.9–100) for more than 7.5 mmol/L. The AUC was compared for each test. The AUC of POC-K^+ could be improved from 82.7 (95% CI 79.9–85.4) to 89.7 (95% CI 87.5–91.9) (p<0.001) (Table 1).

Finally, the level of reliability was compared between the two tests. Reliability was determined by comparing each K^+ test result with the Cr levels measured for each sample. Table 2 shows that high levels of reliability were found between the two tests according to the change in serum Cr. If

results of POC-K^+ were corrected based on the findings of difference for the mean value (adding 0.4 mmol/L), the reliability of the results increased in agreement between the two methods by ICC and outstandingly narrowed the 95% CIs.

DISCUSSION

In most cases of hyperkalemia, the delay caused by waiting for a K^+ result is not critical. However, in situations where patients may have life-threatening and time-sensitive conditions, such a delay may affect patients' outcomes in a deleterious manner. The use of rapid POC-K^+ to determine hyperkalemia could potentially reduce the time needed to achieve an accurate diagnosis and administer early treatments. It may also reduce the turnaround times in the ED. POC-K^+ has several clear advantages. First, it can be directly conducted on scene outside a central laboratory in hospital.[9] Second, the test may be performed on whole blood; it is not necessary to obtain plasma for analysis by centrifugation for 30 minutes. Finally, POC-K^+ takes only 2–3 minutes, while the reference laboratory test usually takes at least 40 minutes, including the centrifugation time of 30 minutes.[10]

There have been several attempts to find a rapid-detection test for hyperkalemia. Chhapola, et al.[11] revealed that blood gas analyzers underestimated K^+ levels and revealed a significant, systematic bias and wider limits of agreement for K^+ levels. The reliability of POC-K^+ estimation in a pediatric intensive care unit on this comparative study was not clinically acceptable. José and Preller[10] showed that most clinicians want to confirm results obtained from POC-K^+ by central laboratory assay. Although the agreement of potassium concentrations determined by two different assays is controversial, there is sufficient agreement between POC-K^+ and the general laboratory assay to make a clinically effective decision to use POC-K^+ in the setting of intensive care unit (ICU).[10,12] The US Clinical Laboratory Improvement Amendment recommended that the acceptable criteria for potassium performance is the target value ±0.5 mmol/L[13] and our study also demonstrated that calculated total error for cut-off of hyperkalemia (5.5 mmol/L) was within the total allowable error recommendations. The propensity of data for K^+ showed a high degree of concordance between POC and the reference test in ED. As shown in the results of ICU, there was a significant difference (0.39 mmol/L) between the two groups (p<0.001) for the mean value. The value of POC-K^+ was lower than laboratory value in ED.

If the threshold value of 5.5 mmol/L was applied in this analysis, the sensitivity was 66.4% and specificity was 98.9% for the POC-K^+ detection method. However, if a val-

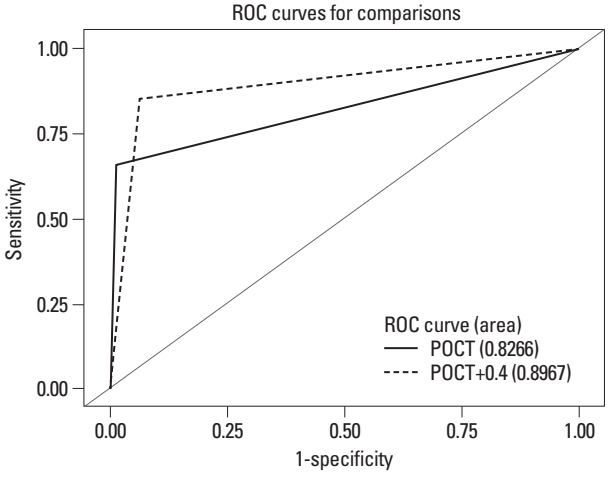


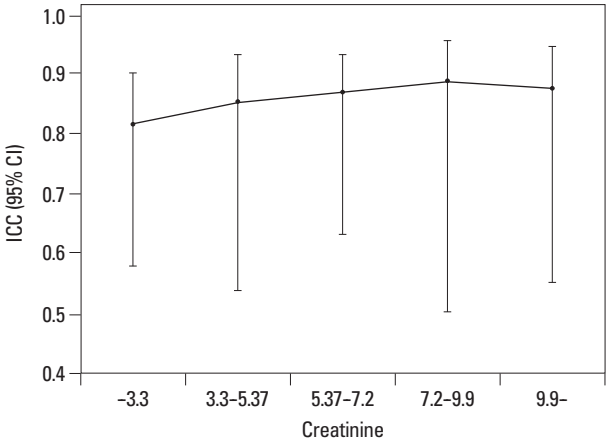
Fig. 3. ROC curves of POC-K^+ and reference tests of K^+ serum levels. The AUC of POC-K^+ can be improved from 82.7 (95% CI 79.9–85.4) to 89.7 (95% CI 87.5–91.9) (p<0.001) if a value of 0.4 mmol/L was added to the mean value result of POC- K^+. POC-K^+, point-of-care K^+; AUC, area under the curve; CI, confidence interval; POCT, point of care testing.

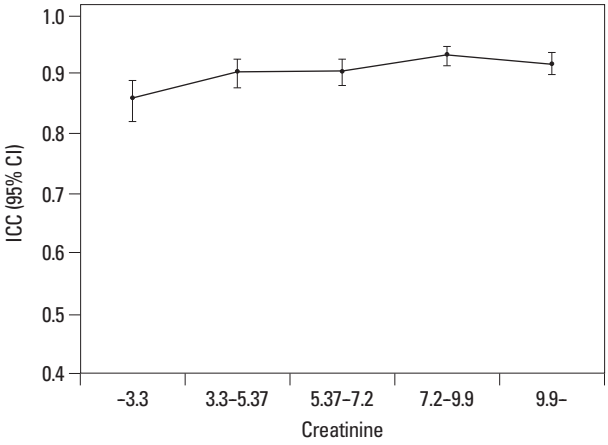
Table 1. Sensitivity and Specificity Analysis of POC-K^+ and Reference Tests of K^+ Levels

POC-K^+ vs. Reference					
Reference	POC-K^+		Sensitivity	Specificity	AUC
	Yes	No			
Yes	192	97	66.44 (60.99–71.88)	98.89 (98.20–99.57)	82.66 (79.91–85.41)
No	10	889			
POC-K^++0.4 mmol/L vs. Reference					
Reference	POC-K^+		Sensitivity	Specificity	AUC
	Yes	No			
Yes	247	42	85.47 (81.40–89.53)	93.88 (92.32–95.45)	89.67 (87.49–91.86)
No	55	844			

POC-K^+, point-of-care K^+; AUC, area under the curve.
A cut-off of 5.5 mmol/L was applied to the population.

Table 2. The Correlation of Creatinine Levels with K^+ Serum Levels Resulting from POC-K^+ and Reference Tests





Percentile	POC-K^+ & Reference			POC-K^++0.4 mmol/L & Reference		
	Point estimate	Lower bound	Upper bound	Point estimate	Lower bound	Upper bound
0–20% (Cr<3.3)	0.816	0.577	0.903	0.866	0.830	0.895
20–40% (3.3≤Cr<5.37)	0.856	0.535	0.935	0.908	0.883	0.928
40–60% (5.37≤Cr<7.2)	0.872	0.630	0.939	0.913	0.889	0.932
60–80% (7.2≤Cr<9.9)	0.890	0.502	0.957	0.939	0.922	0.952
80–100% (Cr≥9.9)	0.877	0.545	0.948	0.926	0.905	0.942

POC-K^+, point-of-care K^+; ICC, intra-class correlation coefficient; CI, confidence interval; Cr, creatinine.

ue of 0.4 mmol/L was added to the results of POC-K^+, the sensitivity and specificity were improved to 85.5% and 93.9%, respectively. Additionally, the difference in estimation of hyperkalemia between the two assays disappeared when this correction was applied. Several studies have reported underestimation in potassium values measured by POC-K^+.[11] Our results, with large paired samples, offer a mathematical formula to increase accuracy of the POC-K^+, enabling clinicians to make effective clinical decisions.

There are a number of possible reasons for the observed bias in the POC-K^+ results, including the hemolysis of blood samples and the dilution effect of liquid heparin.[11,12] First, our study did not consider whether the tests were performed using venous or arterial samples, because the POC-K^+ assay can be performed on both venous and arterial samples. POC-K^+ cannot recognize hemolysis and reports K^+ values regardless of hemolysis.[10] In a separate study, arterial samples were collected with larger-bore needles without tourniquets. These samples may have lower hemolysis than venous samples.[10] The occurrence of hemolysis can be confirmed by obtaining plasma through centrifugation. In our study, hemolysis occurred only 6.23% of the whole blood samples. Second, arterial blood samples were collected in heparinized syringes. Clinicians may collect variable volumes of arterial blood or liquid heparin in the syringes under the emergency circumstances in the ED. A relatively high volume of heparin or low volume of arterial blood may underestimate the value of K^+ on POC.[12,13] Despite having arterial blood samples for our study, the use of liquid heparin may be a limitation in our results. In many of the institutions providing samples to our study, dried balanced heparin syringes were used and could improve the accuracy of K^+ values measured on POC by decreasing the dilution effect.[11] The difference of 0.4 in the mean value between the two tests compared in this study may be explained by the conventional arterial sampling and liquid heparin. For clinical decision based on our study, consideration of the difference (0.4) for mean value can compensate underestimation of the POC-K^+ by conventional arterial sampling with liquid heparin. In a future, prospective study with a larger number of patients, the dilution effect of hemolysis and liquid heparin could be evaluated to improve the protocol for POC-K^+.

Hyperkalemia is more relevant in emergency situations. For example, rapid changes of K^+ are associated with ESRD, as well as acute and chronic kidney diseases. To date, there have been no studies investigating the reliability of POC-K^+ and traditional laboratory K^+ tests as a function of changes in serum Cr. However, our study revealed that high levels of reliability were found between the two tests for potassi-

um according to change in serum Cr levels.

In the ED, other rapid diagnostic tests are beneficial when making clinical decisions. For example, electrolyte and blood gas analysis can be simultaneously identified in unstable or fatal patients. As this study was a retrospective study and included patients of different severity, the influences on clinical outcomes could not be considered for rapid detection of hyperkalemia. These values are useful when making clinical decisions for critical patients like septic shock, severe trauma, and sudden cardiac arrest. The addition of the POC-K^+ diagnostic to this set of rapid tests would help to identify hyperkalemia in both the ED and the ICU.

In conclusion, this study suggests that the results of POC-K^+ correlate well with values obtained from reference laboratory tests according to the change for serum Cr of patients with chronic kidney disease. If the POC-K^+ can be implemented as a standard rapid diagnostic for the early detection of hyperkalemia in the ED, it has the potential to reduce mortality and morbidity by hyperkalemia, the time needed to achieve an accurate diagnosis and treatment, and the turnaround time in ED.

ACKNOWLEDGEMENTS

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2013R1A1A2009391).

REFERENCES

1. Lehnhardt A, Kemper MJ. Pathogenesis, diagnosis and management of hyperkalemia. Pediatr Nephrol 2011;26:377-84.
2. Hsieh MF, Wu IW, Lee CC, Wang SY, Wu MS. Higher serum potassium level associated with late stage chronic kidney disease. Chang Gung Med J 2011;34:418-25.
3. An JN, Lee JP, Jeon HJ, Kim DH, Oh YK, Kim YS, et al. Severe hyperkalemia requiring hospitalization: predictors of mortality. Crit Care 2012;16:R225.
4. Kwak JR, Gwon M, Lee JH, Park MS, Kim SH. Non-oliguric hyperkalemia in extremely low birth weight infants. Yonsei Med J 2013;54:696-701.
5. Tintinalli JE. Emergency Medicine: A Comprehensive Study Guide. 6th ed. New York: McGraw-Hill; 2004. p.173.
6. Stein W, Hellmeyer L, Schmidt S, Tekesin I. Intraobserver and interobserver reliability of transvaginal cervical length measurements and quantitative ultrasound tissue characterization of the cervix in the second and third trimester of pregnancy. Ultraschall Med 2011;32 Suppl 2:E169-74.
7. McGrew JH, Stull LG, Rollins AL, Salyers MP, Hicks LJ. A comparison of phone-based and on-site assessment of fidelity for assertive community treatment in Indiana. Psychiatr Serv 2011; 62:670-4.
8. Desirable Specifications for Total Error, Imprecision, and Bias, derived from intra- and inter-individual biologic variation. [accessed on 2013 July 15]. Available at: http://www.westgard.com/biodatabase1.htm.
9. Vos G, Engel M, Ramsay G, van Waardenburg D. Point-of-care blood analyzer during the interhospital transport of critically ill children. Eur J Emerg Med 2006;13:304-7.
10. José RJ, Preller J. Near-patient testing of potassium levels using arterial blood gas analysers: can we trust these results? Emerg Med J 2008;25:510-3.
11. Chhapola V, Kanwal SK, Sharma R, Kumar V. A comparative study on reliability of point of care sodium and potassium estimation in a pediatric intensive care unit. Indian J Pediatr 2013;80:731-5.
12. Jain A, Subhan I, Joshi M. Comparison of the point-of-care blood gas analyzer versus the laboratory auto-analyzer for the measurement of electrolytes. Int J Emerg Med 2009;2:117-20.
13. Bloom BM, Connor H, Benton S, Harris T. A comparison of measurements of sodium, potassium, haemoglobin and creatinine between an Emergency Department-based point-of-care machine and the hospital laboratory. Eur J Emerg Med 2013. [Epub ahead of print]