Journal of Pharmacy and Pharmacology 5 (2017) 902-906
doi: 10.17265/2328-2150/2017.12.009

Correction of Factitious Hyperkalemia in Hemolysed Specimens from Adult Emergency Department Using the Beckman Coulter Unicell DxC 880i® Analyzer Derived Factor

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Abstract: Hemolysis in ED (emergency department) patients is common due to difficult blood draws. Values of serum potassium (K^+) become falsely elevated secondary to release of intracellular contents. Objective: The aim of the study was to establish a correction factor for factitious elevated K^+ in samples for de adult ED. Methods: We used samples from 125 adult ED patients, in which the 2nd sample was drawn due to hemolysis of the first tube. Results: Firstly, we derived a correction factor expressing an increase in potassium concentration in 0.21 mmol/L (95% confidence interval, 0.17-0.24 mmol/L with $p < 0.01$) for each hemolysis index increment. Conclusions: A reliable correction factor for factitious hyperkalemia in a clinical relevant range exists.

Key words: Potassium; Hemolysis; correction factor.

1. Introduction

Hemolysis in emergency department patients is common due to difficult blood draws. Hemolysis is a major pre-analytical issue in current clinical pathology, prevalence can be as high as 3.3% of all routine samples, accounting for up to 40%-70% of all unsuitable specimens identified [1]. It may interfere in many lab tests, such as potassium, bilirubin, haptoglobin, liver enzymes, amylase, folic acid and iron [1-5]. Hemolysis is the main reason for the re-collection of blood samples, and so increasing TAT (turnaround time), costs on blood collection materials and other clinical products.

CHTS-CPL (Centro Hospitalar do Tâmega e Sousa Clinical Pathology Laboratory) is equipped with two Beckman Coulter Unicell DxC 880i analyzers where potassium is measured using indirect potentiometry.

The H-index (hemolysis index) is determined following the content on hemoglobin, as shown in Table 1.

At CHTS-CPL, samples with an H-index of 1 or 2 (free hemoglobin < 100 mg/dL) have the K^+ released with a commentary warning of a possible positive interference. For H-index of 3 or higher, K^+ value is blocked and the 2nd blood collection is requested.

Concentration values of serum K^+ become falsely elevated secondary to release of intracellular contents.

Correction factors have been proposed for estimating true potassium in blood samples with evidence of *in vitro* hemolysis. The variability in the correction factor is great. A variety of issues may account for this difference: mechanism used to stimulate *in vitro* hemolysis, interindividual variability and the effect of erythrocyte age on intracellular potassium concentrations [2].

If a reliable correction factor existed for this factitious elevation, sample re-collections and K^+ measurements could be avoided. However, the mathematical correction of K^+ results in hemolytic

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Table 1 Hemolysis index.

Hemolysis (index level)	Approximate hemoglobin range (mg/dL)
0	Not detected
1	0 to 50
2	50 to 100
3	100 to 150
4	150 to 200
5	200 to 250
6	250 to 300
7	300 to 350
8	350 to 400
9	400 to 450
10	450 to 500

samples can only be carried out once intravascular hemolysis is ruled out [4]. The aim of the study was to establish a correction factor for factitious elevated K^+ in hemolysed serum samples.

2. Study Design

In order to perform our study, we evaluated all samples that required a second sample for a fifty-day period, following a total of 219 samples. These samples correspond to the K^+ requests from all the patients, the sample must have had a hemolysis index of 3 or more to be considered for the study. A second sample from the same patient was requested by the laboratory. All samples were analyzed, in the Beckman Coulter Unicell DxC 880i® analyzer, as soon as they reached the laboratory. When treating the data, samples from the wards and from pediatric emergency department were excluded, resulting in a total of 125 samples from the ED-considered for the study.

Most of our ED patients have respiratory complains, therefore, we also evaluate the K^+ value registered in the blood gasometry, performed at admission in the POCT (point-of-care testing) equipment GEM Premier 4000 ® (direct potenciometry), in 36 of the patients. Other confusing factor could be the medication administered to the patient between the first and second blood collection for K^+ evaluation. We found that 83 of 125 patients were treated with fluids or diuretics between the blood drawns.

3. Method

Both hemolysis index and K^+ value were measured with Beckman Coulter Unicell DxC 880i® analyzer. The change in serum measured K^+ concentration was plotted versus the change in serum hemolysis index for each pair of samples [5]. The database was treated for outliers, only 2 SDs (standard deviations) where allowed in relation to the medium time (2 h) between drawn, medium ΔK^+ and medium hemolysis index, with a total N of 114.

The K^+ value measured in the POCT blood gas analyzer was plotted against the K^+ value of the nonhemolyzed sample and against the corrected K^+ value after using the correction factor calculated before. All data were treated using Microsoft Excel®.

4. Results

Firstly, we derived a correction factor using a linear regression and obtained an increase in potassium concentration of 0.21 mmol/L (95% confidence interval, 0.17-0.24 mmol/L with $p < 0.01$) for each hemolysis index increment. (Fig. 1-3)

When comparing the K^+ value of the POCT with the nonhemolyzed samples we obtained a 90% correlation.

The correlation of the same POCT values with those obtained after applying the correction factor to the hemolysed sample value was of 79%.

Sixty-six percent of the patients were administered with fluids or had diuretic treatment between the 1st and 2nd blood draw, hence, as the arterial gasometry was performed early at admission, the K^+ value is presumably less affected by any therapeutic.

In conclusion, the authors plotted the interval of corrected K^+ value (0.17-0.24 mmol/L) from the 147 initial samples with the K^+ value from the second blood collection. Only 0.03% of second drawn results had a K^+ value out of the range of the correction made by the laboratory.

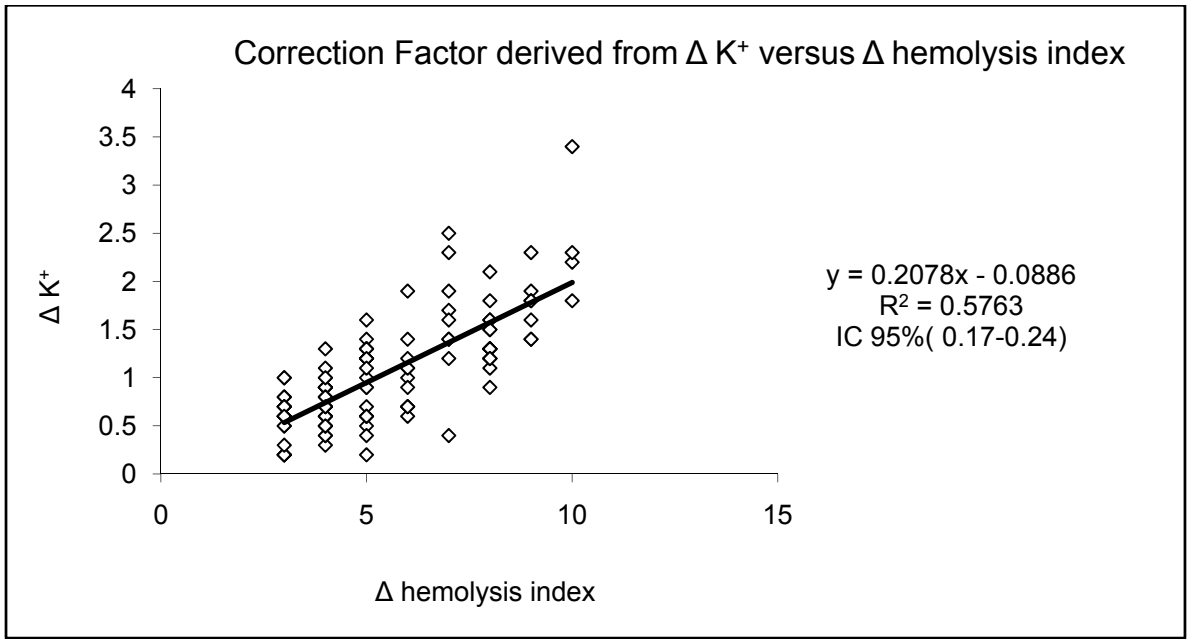

Fig. 1 Correction Factor derived from Δ K^+ versus Δ hemolysis index.

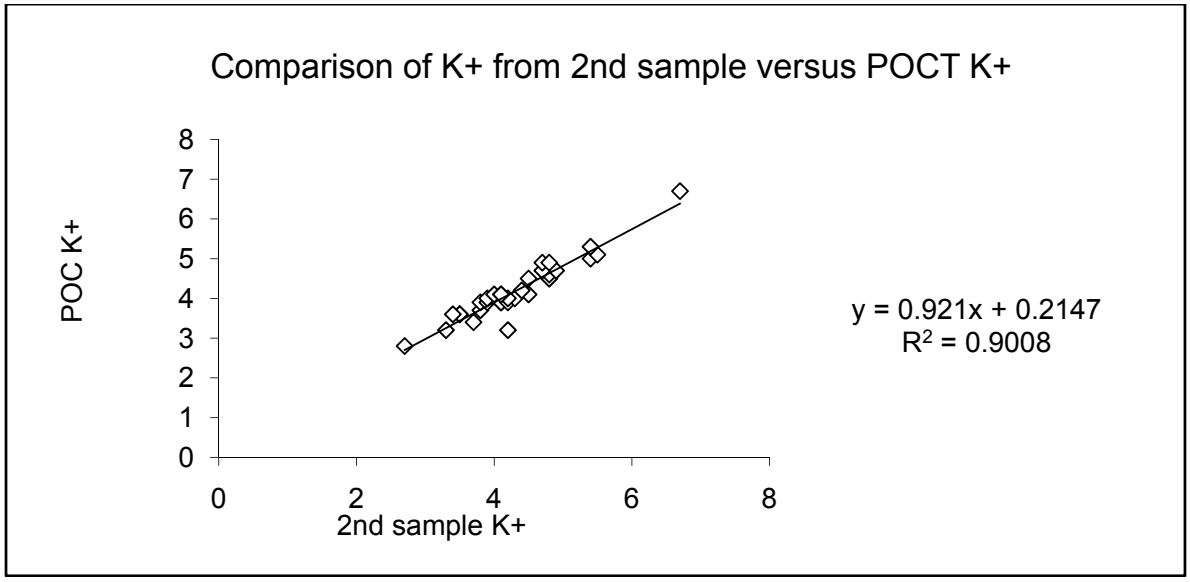

Fig. 2 Comparison of K^+ from 2nd sample versus POCT K^+.

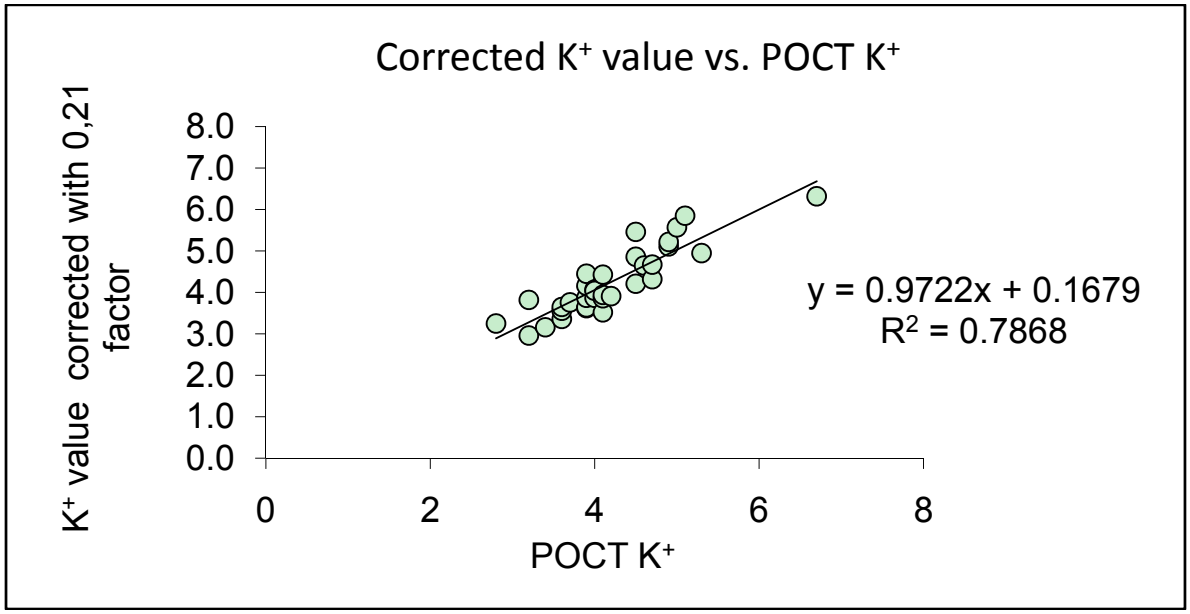

Fig. 3 Corrected K^+ value vs. POCT K^+.

5. Discussion

There are many studies about the correction factors and its applicability, many different conclusions with some conflicting results. Therefore, any simple solution for a complicated process is inappropriate. Moreover, the K^+ release by the erythrocyte is affected by a number of circumstances, reflecting different mechanisms, different populations and ultimately different results [1-5].

Other studies advocate that the H-index is useful for screening inadequate samples, justifying a new request for blood collection or even, providing an alert message for the clinicians.

When facing a hemolysed sample the laboratory may take distinct paths: reporting the test result with a warning alert for clinician; adjusting test results by correcting the value; rejecting the sample and asking for a new sample, then informing the clinician about the specific interference.

Unfortunately, there is no consensus on this point and the policies adopted by the laboratories are heterogeneous [6].

Liberating a corrected or non-corrected result with an advert notice does not protect the laboratory from any legal process generating an important topic of discussion. There are no recommendations upon the release of the K^+ result in a hemolysed sample. However, if the laboratory uses a correcting formula, the results should be reported as an interval with the uncertainty degree.

By May 2011, CHTS-CPL started the automatic semi-quantitative measurement of serum indexes (hemoglobin, bilirubin and lipids). The samples are checked for serum indexes using a spectrophotometric semi-quantitative measurement. Before, the sample quality evaluation was made by the lab technician, and hemolysis was manually classified into 3 groups (light, medium, intense).

In 2011 CHTS-CPL accounted for a total of 6.7% hemolysed samples and 5.3% in 2016. It is important to notice that hemolysed samples are not constant in frequency nor location with 60% of the hemolysed samples in 2016 being accounted in the ED (data retrieved from the LIS—Clinidata XXI).

Our study started by the need to optimize the results released to the clinicians, as well as, improved all the procedures in order to reduce our hemolysis rate to the reference values of less than 2% [7].

In our study we compared the potassium

concentration between the first and second sample, and assumed that mechanical factors were responsible for the hemolysis in the process of blood drawn. No other tests were taken in account for the exclusion of *in vivo* hemolysis.

The coefficient of variation for the methodology applied was 3%.

The authors obtained a 0.21 mmol/L correction factor (95% confidence interval, 0.17-0.24 mmol/L with $p < 0.01$) for each hemolysis index increment. This value is in concordance with the present literature including studies conducted in Beckman LX analyser (Beckman Instruments) [4]. A vast variety of correction factors has been reported independently of the method used to obtain the hemolysed sample and from the equipment used.

6.Conclusions

A reliable correction factor for factitious hyperkalemia in a clinical relevant range exists, however corrected results should not be reported without specific guidelines.

The authors believe that in cases of low hemolysis, and H-index of 1 or 2, the result may be reported with a warning comment to alert the clinician about the positive interference of hemoglobin and other recommendations.

If the H-index is equal or greater than 3, the result should be suppressed and a second sample should be drawn. The CHTS-CLP has decided not to correct the K^+ value. The H-index is transmitted through the middleware (LIS) where validation rules and complementary actions are associated for posterior evaluation and storage.

In case of patients with difficult venous accesses, in which the samples have H-index of 3 or 4, if the corrected value is within reference range, the laboratory might release the raw result in the information field. This result should be completed with a specific note implying the positive interference of hemolysis. The clinicians should be alerted for the necessity of correlating the result with clinical findings and the gasometry result, eventually a second blood collection could be necessary for confirmation.

This measure was implemented after disclosure of the results of our study to the clinical staff of the hospital.

The authors agree that guidelines should be created in order to standardize the laboratory actions when facing a hemolysed sample. These should include recommendations for the best approach in hemolysis detection and harmonization of H-index results across analyzers. Moreover, the establishment of H-index thresholds for sample rejection and H-index cut-off should be defined. Last, there should be guidance on how to report results. We believe this is the sole stone condition for improvement and standardized practice.

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