

Hemolysis Threshold for Potassium Specimens: How Low Should We Go?

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In a customer bulletin (TP-00995) released in June 2020, Roche Diagnostics details an update to their potassium hemolysis criteria for the cobas clinical chemistry and ion-selective electrode (ISE) analyzers. The semiquantitative hemolysis index (H index; approximately mg/dL) acceptable limit for potassium was lowered from 90 (or 100, dependent on the instrument) to 20. Further, the language was updated from “Avoid hemolyzed specimens” to “Do not use hemolyzed samples.” The customer bulletin was updated in October 2020 (TP-00995 V2) with “Avoid hemolyzed specimens” for the cobas pro ISE analyzer only. Herein examines the impact of the stricter criteria on cancellation rate at our facility and an internal investigation of hemolysis interference on 2 popular chemistry analyzers (cobas 8000 ISE module and c501) from Roche Diagnostics.

The clinical laboratory is responsible for the accuracy of their results to help ensure high-quality patient care. One common preanalytical error is in vitro hemolysis, which is the rupture of red blood cells. These suboptimal specimens may lead to inaccurate results due to spectral interferences, nonspecific binding to immunoassays, reduction-oxidation reaction interference, and intracellular material contamination. Potassium results are subject to the latter, where intracellular

potassium is approximately 20-fold higher compared to plasma (1); ultimately, leading to spuriously increased results. To identify the presence of hemolysis, most chemistry analyzers employ an automated index, which estimates the hemoglobin concentration in a serum/plasma specimen. The legacy potassium H index thresholds on the cobas c311, cobas c501, and cobas 8000 analyzers were 90, and on the cobas pro ISE analyzer was 100. However, in a recent Roche customer bulletin, the H index was drastically reduced to 20. The reduction of the H index acceptable limit was due to a concern regarding falsely elevating mildly hypokalemic samples into normokalemic ranges.

At our facility, a large academic hospital that services the emergency department, inpatients, outpatients, and an outreach program, we receive approximately 3400 serum/plasma potassium orders every day. Among those specimens, 1.0% have an H index above 90 (legacy threshold from Roche Diagnostics). If the H index threshold of 20 was implemented, the cancellation rate would surge to 7.7%, which is an addition of approximately 225 cancellations per day. The increased cancellation rate would potentially translate to increased blood redraws, longer waiting times, less patient satisfaction, and delayed diagnosis and treatment. Moreover, the additional cancellations

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and sample redraws would have a potential financial burden. Using the model developed by Maul et al., the additional 6.7% cancellation rate would add an extra cost of \$120 000 annually in phlebotomy supplies and labor alone for emergency department samples (2).

To investigate the impact of hemolysis, potassium was measured in samples spiked with increasing hemolysate concentrations and compared with nonspiked baseline values, where diluent was added in place of hemolysate (CLSI C56-A) (3). Three potassium lithium heparin sample pools [low (3.0 mmol/L), mid (4.3 mmol/L), and high (6.1 mmol/L)] were made in singlecate. Hemolysate was prepared by collecting red blood cells, washing 3 times with saline, adding water, freezing, and centrifuging to remove the cellular

material. After the addition of the hemolysate, the samples were subsequently diluted with the non-hemolyzed sample pools. Measurement of the hemolyzed potassium samples and H index were performed on the cobas 8000 ISE module and c501. The potassium concentrations were compared to the baseline, and the percentage difference from neat was calculated. The percentage difference was then plotted against the H index. Passing–Bablok regression was performed for the samples with the lowest potassium concentration, which are most susceptible to higher percentage increases due to low baseline potassium concentration (Fig. 1). Based on the regression equations and a desirable total allowable error of 5.8%, which was calculated based on the potassium’s intra- and intersubject biological variations (4),

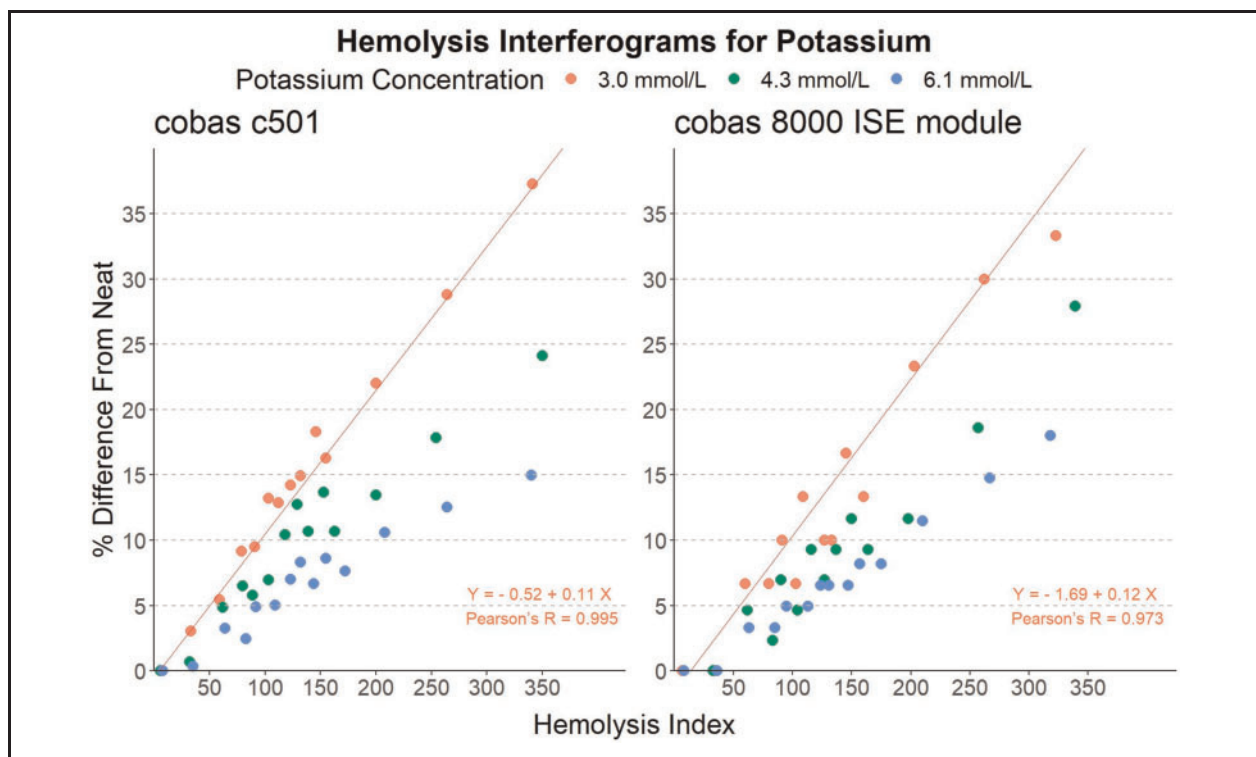


Fig. 1. Hemolysis interferograms. Hemolytic effect on plasma potassium concentration across various hemolysate-supplemented plasma samples on cobas c501 and cobas 8000 ISE modules. Passing–Bablok regression was performed for the low potassium samples.

H indices of 62 and 57 were acceptable for the cobas 8000 ISE module and c501, respectively.

In conclusion, we demonstrated that reducing the H index cutoff from 90 to 20 might not be practical at our facility or clinically relevant. The stricter criteria would significantly increase our order rejection rate and blood redraw volumes. By performing hemolysis studies, we were able to

expand this threshold while maintaining a 5.8% total allowable error. Outside expanding the acceptable hemolysis threshold, formulas have also been published in the literature to correct potassium values from hemolyzed samples (5). Establishing and validating H index thresholds that are feasible and suitable for each institution's clinical need might be a sanguine approach.

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