Measurement of Whole-Blood Potassium—Is It Clinically Safe?

To the Editor:

Potassium measurement in whole-blood specimens is fast and convenient and is increasingly offered as an adjunct to blood gas analysis. However, the presence of hemolysis in whole-blood samples cannot be determined by such analytical systems at present. There thus is a risk of reporting misleadingly increased whole-blood potassium for unrecognized hemolyzed samples, with potential for subsequent patient misdiagnosis and mistreatment. The real importance of this theoretical concern is unclear. This study describes the prevalence of hemolysis in blood-gas specimens and assesses the subsequent misreporting of whole-blood potassium as a result of hemolysis. It also assesses the importance of low sample volume, age, and gender as risk factors for sample hemolysis.

For 10 days, whole-blood potassium was measured with an AVL Omni 6 blood gas analyzer (Roche Diagnostics) in all arterial blood-gas specimens received by the laboratory. The manufacturer’s suggested reference interval for whole-blood potassium is 3.5–4.5 mmol/L. All results were classified.

Table 1. Effect of hemolysis on classification of whole-blood potassium results.

<table>
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<th>Whole-blood potassium corrected for hemolysis, mmol/L</th>
<th>Measured whole-blood potassium, mmol/L</th>
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<tr>
<td>&lt;3.5</td>
<td>&lt;3.5</td>
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<tr>
<td>3.5–4.5</td>
<td>3.5–4.5</td>
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<td>&gt;4.5</td>
<td>&gt;4.5</td>
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Data represent the number of samples in each classification.

References


(1.5 × 30 cm; Pharmacia) calibrated with the Pharmacia high-molecular-weight calibrators, and the elution profile showed that almost all of the LH eluted as a high-molecular-weight form (Mₐ >250 000; Fig. 1). Recovery after precipitation with polyethylene glycol (6) was only 7% compared with a mean recovery of 87.5% (range, 56–108%) obtained for 23 sera from female patients with LH values >40 IU/L. Serum application to a protein G-Sepharose column (Pharmacia) showed complete binding of the LH immunoreactivity, which was eluted by lowering the pH to 2.8. Gel filtration in dissociating conditions (0.1 mol/L glycine-HCl, pH 2.8) shifted the LH peak to the expected molecular size.

What called our attention to this case, and prompted additional studies, were the unexpectedly high LH values, with concomitant estradiol values within the appropriate reference intervals. The etiology and frequency of the phenomenon as well as its relationship with autoimmune diseases remains to be defined. Nevertheless, this new possibility must be considered in the event of a finding of unexpectedly high LH values.

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14%) to normokalemic and 6% (0–6%) to hypokalemic.

For all samples, median sample volume was 0.6 mL (range, 0.2–2.1 mL), with 25% having ≤0.4 mL and 17% having ≥1 mL. The percentage of hemolized (H >1 g/L) samples varied with sample volume: 27% of samples with a volume of 0.3 mL, 24% of samples with a volume of 0.4–0.5 mL, 19% of samples with a volume of 0.6–0.7 mL, 10% of samples with a volume of 0.8–0.9 mL, and 7% of samples with a volume of ≥1 mL showed hemolysis. The percentage of samples with a whole-blood potassium error ≥0.5 mmol/L similarly varied with sample volume: 14% (8–17%) of samples with a volume of 0.3 mL, 15% (9–18%) of samples with a volume of 0.4–0.5 mL, 5% (1–7%) of samples with a volume of 0.6–0.7 mL, 3% (0–3%) of samples with a volume of 0.8–0.9 mL, and 4% (0–6%) of samples with a volume of ≥1 mL had a whole-blood potassium error ≥0.5 mmol/L. Although multiple logistic regression analysis showed that low sample volume (≤0.4 mL) was independently associated with sample hemolysis (P <0.05), neither age (>60y) nor gender were significant risk factors.

Hemolysis correction is not recommended in clinical practice given the wide population range of K/Hb ratios (1). Nevertheless, this study allows some estimate of the impact of potassium misreporting attributable to hemolysis. It shows a higher rate of sample hemolysis among blood-gas samples than the serum potassium sample rate of 3.4% reported previously (2). This leads to a significant overreporting of whole-blood potassium concentrations with >33% of hypokalemic cases missed. Hemolysis is particularly associated with low sample volume, perhaps reflecting difficulties in sample collection, and such samples unfortunately make up the majority of those submitted for analysis in this laboratory. Laboratories can minimize the likelihood of hemolysis by encouraging larger blood gas sample volumes, but errors ≥0.5 mmol/L will still be encountered in some larger volume samples, raising doubts about the acceptability of whole-blood potassium measurement on blood-gas samples. Those facilities offering whole-blood potassium measurement should ensure that the degree of sample hemolysis in their samples does not lead to the reporting of misleading potassium concentrations.

References

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New Scenarios in Antidoping Research

To the Editor:
The search for improved athletic performance by use of ergogenic aids has been a common feature of competitive sports. The use of performance-enhancing substances has evolved over time, giving rise to novel and intriguing challenges for laboratory medicine, the biomedical branch of science traditionally designated to unmask cheating (1).

The tremendous progress recorded in the fields of physiology, molecular genetics, and biotechnology has promoted the development of new doping techniques. Antidoping policies have evolved for the identification of illegal administration of exogenous substances, mainly drugs, synthetic peptides, and finally, recombinant counterparts of natural glycoproteins and hormones, which are virtually identical in structure and function to the endogenous molecules. Fortunately, advances in laboratory technology have allowed the introduction of efficient antidoping strategies (2), as exemplified by the cases of doping with recombinant human growth hormone and erythropoietin (3, 4). However, there is evidence that the horizons of doping might have been enlarged further, embracing gene therapy and pharmacogenomics (5).

The possibility to either transfer genes into human cells or modulate endogenous gene expression has led to novel and revolutionary therapeutic opportunities, especially for single-gene disorders such as hemoglobinopathies (6, 7). Unfortunately, in addition to clinical applications, these futuristic techniques might also become ideal doping practices.

The diversity in athletic performance among elite athletes traditionally has been recognized to derive from two factors: congenital predisposition (physical and/or biological features) and environmental influences (quality and intensity of training). It is now well established that some genetic polymorphisms might confer substantial advantages in numerous athletic disciplines, as reflected in enhanced performance as a result of muscular strength, endurance, or both, and thus delineate the distinctive phenotypes of champions (8).

Although there is currently no evidence for gene doping, it is conceivable that the identification of such polymorphisms may further promote the use of gene therapy and pharmacogenomics among top-class athletes, as has happened for doping with drugs and synthetic or recombinant molecules. Such a development would force laboratory medicine to face a new and intricate enigma: how could these new potential forms of doping be recognized? As with other potential doping practices, gene cheating diminishes the spirit of sports and involves severe risks, some of which are known and expected, whereas others are unknown and potentially catastrophic for an athlete’s health.

We all should be aware that at