Use of Potassium Concentrations as a Quality-of-Service Metric for Phlebotomists Detects Systematic Preanalytical Biases and Facilitates Their Correction

To the Editor:

The detection and monitoring of preanalytical bias in the clinical laboratory can be challenging, as bias can be introduced at any point from specimen collection to sample processing, and those biases stemming from sample collection or handling before delivery to the laboratory can be difficult to measure and eliminate. In particular, variations in potassium concentrations due to preanalytical sources of error are a pervasive and clinically significant problem (1–3).

Initial concern regarding spuriously increased potassium concentrations (>5.2 mmol/L) occurring in the laboratory of the Dana Farber Cancer Institute was raised by clinicians reporting patients displaying increased potassium without any apparent clinical justification. Review of the medical records of the patients involved demonstrated that the majority had potassium values within the reference interval on the draw before the in-

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Fig. 1. LC-MS/MS method comparison with Beckman Coulter Access Immunoassay for analysis of Tg in FNA samples (n = 73); inset corresponds to a subset of FNA samples with Tg concentrations <70 ng/mL (n = 37). Solid lines are Deming regression lines; dotted lines are lines of identity.

Letters to the Editor

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creased value, with a mean increase in potassium of 1.2 (0.7) mmol/L vs the prior value. Retesting on an alternative platform confirmed hyperkalemia. To assess for a preanalytical cause of these values, samples were redrawn on the same day from a series of patients with potassium values >5.2 mmol/L. This assessment demonstrated that in 27 of 28 patients tested, potassium was in the reference interval upon retesting with an independent sample. The mean degree of decrease in potassium upon redraw was 0.9 (0.7) mmol/L. The maximum decrease observed was 2.2 mmol/L.

Altogether, these findings strongly suggested that a preanalytical source of error was responsible for the increases in potassium. After excluding hemolysis, potassium release from leukocytes, or cell lysis during centrifugation as contributing factors, we considered whether the phenomenon of spuriously increased potassium values might relate to the draw technique used by specific phlebotomists. Analysis of mean potassium values by specific phlebotomists demonstrated a significant effect ($P < 0.0001$ by 1-way ANOVA) of the phlebotomist performing the draw (data not shown). As an example, a histogram of the potassium values from each draw from 2 phlebotomists displaying higher average potassium values was plotted relative to the potassium values across the institution (Figure 1).

Demonstration that specific phlebotomists were strongly associated with increased rates of hyperkalemia prompted a systematic evaluation of phlebotomy practices at the institution. In particular, it was noted that several phlebotomists were either using squeeze balls or encouraging fist clenching during draws, despite these maneuvers being prohibited by institutional policy. Additionally, occasionally excessive vein tapping before draw and variations from the policy of using 20-gauge needles to minimize hemolysis were observed. In response to this, a period of direct observation and phlebotomist retraining was instituted in November through December 2013, emphasizing correction of the deviations from institutional protocol noted above.

The observation that selected phlebotomists consistently displayed increased potassium values in their draws suggested that the degree of deviation in average potassium values could function as a quality-of-service metric reported back to each phlebotomist. After the period of retraining, phlebotomy staff had monthly meetings with supervisors where data regarding the mean potassium values and number of potassium values >5.2 mmol/L from their draws during the prior month were reviewed.

Continued monitoring demonstrated that this program was successful in substantially lowering the incidence of pseudohyperkalemia across the institution. Without any alterations to the potassium assay itself, the percentage of potassium values >5.2 mmol/L reported each month fell by approximately 39% relative to the start of the study. For a subset of 5 phlebotomists displaying initially increased mean potassium values, the collective mean percentage of potassium values >5.2 mmol/L fell by 70% over the same period. Similarly, the increased mean potassium values noted in Figure 1 largely normalized over the study period. Thus, the deviations in phlebotomy technique observed were correctable and were successfully addressed by a combination of observation, retraining, and the use of potassium as a quality-of-service metric for phlebotomists.

Plasma potassium concentrations are particularly sensitive to variances in phlebotomy technique and thereby provide an opportunity to detect those deviations in technique without direct observation. Increases in potassium concentrations would be expected to capture a wide range of errors such as incorrect needle choice resulting in hemolysis, excessive periods of tourniquet application or manipulation of the draw site, exercise of the affected arm, or fist-pumping (1, 4, 5). Thus, monitoring of potassium concentrations can detect all of the common errors in phlebotomy technique, suggesting that this approach could provide an effective means for periodic surveillance and continuous quality improvement of phlebotomy services.
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Proposed Regulatory Framework for Direct-to-Consumer Genetic Testing: Diagnostics vs Genetic Screening

To the Editor:

On December 6, 2013, 23andMe stopped marketing direct-to-consumer (DTC)1 disease-predictive genetic testing to comply with the FDA’s directive (1). Although the FDA’s action was intended to protect the American public from questionable disease risk predictions, we believe the agency failed to assess all the benefits of DTC testing. Despite assurances asserting support for consumer genetic testing (2), the FDA’s action strongly discourages DTC providers from offering the tests to consumers, undermining the investments the US government has made in the genome project. We list examples where, in our opinion, the FDA’s regulatory requirements for the DTC industry are excessive.

Is there too much emphasis on the analytical specificity rather than the diagnostic sensitivity of a test? The performance of a genetic test depends on both sensitivity and specificity. Yet the FDA’s focus on reproducibility overemphasizes analytical specificity while diminishing the role of diagnostic sensitivity, resulting in a bias toward simplified single-nucleotide polymorphism (SNP) panels. Luminex and Autogenomics have received FDA approval for smaller genotyping panels for cytochrome P450 genes with 4 alleles, and extended panels with 19 alleles have secured European Union In Vitro Diagnostic Directive certification and are marketed in Europe. Reducing the number of markers improves technical replication but reduces the tests’ sensitivity and clinical relevance for the ethnically diverse US population.

Is the FDA excessively protective? The FDA expressed concern at 23andMe disclosing genotype data on the 3 SNPs mentioned on Warfarin drug labels directly to consumers. Is it really dangerous, and can this knowledge cause more harm than an accidental skipping of a pill or accidental drug overdose? Also, the FDA’s concern of “risk of prophylactic mastectomy as a result of [breast cancer gene] BRCA-related risk” is overstated; this form of intervention is unlikely to be done without an expert medical professional who should be able to consult with the patient.

The FDA recently allowed the marketing of one manufacturer’s next generation sequencing (NGS) device as a clinical diagnostic tool for a gene-specific panel [CFTR,2 cystic fibrosis transmembrane conductance regulator (ATP binding cassette subfamily C, member 7)] and granted de novo petitions for its use with the manufacturer’s universal kit reagents as an FDA-