Editorial

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Hemolysis-resistant reagent: another part of the puzzle for preventing errors in laboratory testing

Keywords: errors; hemolysis; laboratory diagnostics; preanalytical variability; quality.

It is now universally acknowledged that preanalytical variability represents the leading source of problems throughout the total testing process, wherein inappropriate procedures for collection, handling and storage of blood samples jeopardize the quality of specimens and the medical decisions that may be taken when “biased” test results are obtained on otherwise unsuitable specimens [1]. It is also clear to most that spurious hemolysis, i.e., injury and breakdown of erythrocytes and other blood cells that most frequently occur during venipuncture, is by far the leading cause of unsuitable specimens in clinical laboratories worldwide [2]. The potential consequences on laboratory diagnostics of undue presence of cell-free hemoglobin in blood specimens include biological, chemical and photometrical interference, which may virtually affect all areas of testing, thus including clinical chemistry [3], immunochemistry [4], hematological [5], blood gas [6], and coagulation tests [7]. Although the biological bias is roughly unavoidable and virtually insurmountable, the chemical and photometrical interference is instead technically preventable by adjustment of sample blank, use of different wavelengths or measurement times [8], as well as by reformulation of reagents with additives so that the interference of cell-free hemoglobin and other intracellular components can be largely or completely abolished.

Several lines of evidence now attest that even major refinements of current test protocols are not effective to completely abolish the bias, so that the development of hemolysis-resistant reagent(s) represent an appealing perspective, especially for those analytes whose concentration is only influenced by chemical or photometrical (rather than biological) interference. One first example of such approach is published in this issue of Clinical Chemistry and Laboratory Medicine. Specifically, Ronda et al. developed an experimental reagent for assessment of α-amylase in hemolyzed specimens, showing that all test results could be maintained within the total allowable error for this parameter by using the experimental assay, whereas this critical threshold was exceed in the vast majority of samples (up to 85%) using a similar commercial method [9].

Besides α-amylase, other potential applications of hemolysis-resistant reagents, expectedly combined with inhibitors of leukocyte proteases (e.g., ethylenediaminetetraacetic acid, aprotinin, [4-(2-Aminoethyl)benzenesulfonyl, bestatin and leupeptin, among others] [10] that may be released after white blood cell injury, include the measurement of all those molecules that are not significantly contained in erythrocytes, white blood cells, platelets or endothelial cells, and thus would not be influenced by injury or breakdown of these cells. At the top of a virtually infinite list we obviously place stat tests, being characterized by a short turnaround time, and for which the practice of sample recollection would raise not only economic issues (e.g., raw cost of phlebotomy set, blood tubes and nurse’s occupation) and organizational concerns (e.g., disputes between emergency physicians and laboratory staff), but also clinical problems including a delay in triage, diagnosis and treatment of patients, with unavoidable overcrowding of emergency departments (EDs) [11]. One paradigmatic example is the assessment of cardiac-specific troponin(s) in the emergency room, especially when using high-sensitive immunoassays [12]. Since results of most troponin immunoassays are dramatically biased by the presence of spurious hemolysis in the sample [4] and considering that the rate of hemolyzed specimens can be as high as 8% from the EDs [13, 14], it is rather obvious that the implementation of hemolysis-resistant reagents coupled with inhibitors of leukocyte proteases may be a reasonable approach for assessing an appropriate panel of stat tests (i.e., without measurement of potassium, lactate dehydrogenase and aspartate aminotransferase), thus generating remarkable advantages for the healthcare systems and contributing to prevent diagnostic delays and unnecessary expenditures. The biochemical and immunochemical analysis of biological fluids other than blood, serum or plasma is another interesting perspective of hemolysis-resistant reagents, especially for urines,
peritoneal or pleural fluids, which can be frequently contaminated by the presence of injured erythrocytes.

It is rather clear that hemolysis-resistant reagents are not intended to be the panacea, but they may represent indeed another part of the puzzle for preventing interference in laboratory diagnostics along with several other aspects that are synthesized in Figure 1. First and foremost, however, further efforts should be placed to improve blood collection procedures and for enhancing compliance with existing guidelines, inasmuch as these practices are still considered a mainstay for improving healthcare operators’ education and training, and for assuring patient safety in laboratory testing [15].

Conflict of interest statement

Authors’ conflict of interest disclosure: The authors stated that there are no conflicts of interest regarding the publication of this article.

Research funding: None declared.

Employment or leadership: None declared.

Honorarium: None declared.

References


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