Q & A Column, 6/14

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Submit a Question

Uric acid analysis for patients on rasburicase

Platelet agglutinates, platelet counts

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Q. Treatment with rasburicase seems to affect the uric acid analysis. Drawing the specimen in a pre-chilled lithium heparin tube appears to eliminate the falsely low uric acid results we see. Are there current studies regarding uric acid test analysis on patients receiving rasburicase?

A. Rasburicase (Elitek) is a recombinant uricolytic agent (uric acid oxidase) that catalyzes the conversion of urate to allantoin, which is water soluble and readily excreted by the kidney, and to hydrogen peroxide.[1] Rasburicase is indicated for the management of anticancer-therapy–induced hyperuricemia, and it is effective and well tolerated in pediatric and adult patients.1 In two multicenter trials, rasburicase rapidly prevented or corrected hyperuricemia in ≥ 99 percent of pediatric and adult leukemia and lymphoma patients at risk for hyperuricemia, and its administration resulted in a significant decrease in plasma urate levels within four hours.[1] Compared with allopurinol, rasburicase was significantly more effective in preventing hyperuricemia and in decreasing exposure to uric acid over 96 hours after administration in pediatric patients.[1]

Rasburicase causes enzymatic degradation of uric acid in blood/plasma/serum samples, potentially resulting in spuriously low plasma uric acid levels.[2] The manufacturer recommends that blood be collected in pre-chilled heparinized tubes, immersed immediately in an ice water bath, spun in a pre-cooled (4°C) centrifuge, and analyzed for uric acid within four hours of collection.[2]

A study was conducted recently in 65 pairs of blood samples from 34 patients receiving rasburicase.[3] The study found that cold handling (pre-chilled tubes, iced transportation, 4°C centrifugation) was equivalent to room temperature for immediate measurement of plasma uric acid, but that a one-hour delay at room temperature resulted in a 20 percent decrease in urate.[3] The study concluded that the cold handling measures recommended by the manufacturer are not needed for uric acid analysis of patients receiving rasburicase treatment if uric testing is done immediately, but that delay of an additional hour is associated with an approximate 20 percent decrease in uric acid. In practice, however, the authors continue to comply with the manufacturer's recommendations.[3]

1. Oldfield V, Perry CM. Rasburicase: a review of its use in the management of anticancer therapy-induced hyperuricaemia. *Drugs*. 2006;66(4):529–545.
2. litek (rasburicase) prescribing information, 2002. Sanofi-Synthelabo Inc., New York, NY.
3. Lindeman NI, Melanson SE, McDonnell A, DeAngelo DJ, Jarolim P.

Refrigeration is not necessary for the measurement of uric acid in patients treated with rasburicase. *Clin Chem Lab Med.* 2013;51(5):1053–1057.

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Q. I have been conducting a study to see if we can use blue-top tubes for platelet clumpers. I have multiplied 1.1 by the platelet count, and the platelet count is consistently 15–60 × 109/L lower than in the EDTA tube. Is there a different math ratio, or is it acceptable to run the blue-top tube to see if there are clumps and, if not, just report the EDTA answer for the platelets?

A. As you have mentioned, when platelet agglutinates (clumps) are present in EDTA, alternative approaches to obtaining an accurate platelet count are necessary. As Steven Kroft, MD, explained in a question and answer published in 2001, this can include vortexing and use of alternative anticoagulants, such as sodium citrate. A subset of patients with platelet clumping will have EDTA-dependent antibodies that result in platelet aggregation/clumping. If blood from these patients is drawn in an alternative anticoagulant, clumping will no longer occur. However, use of these different coagulants will require corrective calculations for reporting platelet numbers.

For example, in comparison to an EDTA sample, it is well known that sodium citrate results in 10 percent dilution of the blood sample due to the volume of the liquid sodium citrate anticoagulant in the blood collection tube. As such, platelet counts will be 10 percent lower in sodium citrate, and thus a conversion factor of 1.1 is used to calculate a platelet count from a sodium citrate tube. Since this 10 percent dilution is based on the volume of citrate anticoagulant, this method requires complete filling of the blood tube. If the citrate tube is underfilled, one would expect more dilution of the sample by anticoagulant, and the calculated platelet count can be artifactually lowered. Unfortunately, since some patients' platelets clump in EDTA but not in citrate, lack of clumping in the citrated sample does not allow you to report the EDTA platelet count unless you have confirmed lack of clumping in EDTA. Confirmation of platelet clumping (or lack thereof) requires morphologic review of a blood smear and estimation of the number of platelets. If the estimated number of platelets seen in the blood smear appears to correlate with the instrument result, many labs will report the instrument result for the platelet count obtained from the EDTA tube with an appropriate footnote documenting the agreement of the morphologic review of the blood smear with the instrument platelet count.

In some patients, platelet clumping will persist despite use of an alternative anticoagulant. Under these circumstances, some laboratories review the peripheral smear and classify platelets as "decreased," "adequate," or "increased" without reporting a numerical value. Other laboratories may choose to report a numerical count when the instrument result is above a defined threshold, such as >100 × 109/L. In this circumstance, it is appropriate to append a comment noting that clumping is present and the reported count may be lower than the true platelet number. Each laboratory should define its own procedures for reporting platelet results when clumping is present and appropriately communicate these results to the clinicians and to the patient's medical record.

1. Kroft SH. Can EDTA blood specimens be vortexed to obtain a platelet count when platelet aggregates are found [Q&A]? CAP TODAY. 2001;15(4):94–95.

2. Schrezenmeier H, Müller H, Gunsilius E, Heimpel H, Seifried E. Anticoagulant-induced pseudothrombocytopenia and pseudoleucocytosis. *Thromb Haemost.* 1995;73(3):506–513.
3. Lippi G, Plebani M. EDTA-dependent pseudothrombocytopenia: further insights and recommendations for prevention of a clinically threatening artifact. *Clin Chem Lab Med.* 2012;50(8):1281–1285.

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