Plasma—The Preferred Sample Type for Clinical Chemistry Testing?

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Advances in medicine in the 17th century provided the foundation for diagnostic laboratory testing. The discovery of the circulation of blood by William Harvey and subsequent development of procedures to withdraw blood from a patient's vein for therapeutic purposes have enabled physicians to utilize blood to detect and monitor disease.[1] Today, laboratory medicine remains as an integral component of patient care. An estimated 60-70% of medical decisions are based on the results from laboratory testing.[2] Therefore, timely receipt of test results may enable more rapid diagnosis and treatment, which can impact patient outcomes. Yet, laboratory test turnaround time (TAT) has been cited as a primary source of dissatisfaction among physicians and nurses. In surveys conducted by the College of American Pathologists involving physicians and nurses from 138 and 182 institutions, respectively, satisfaction with TAT received below average ratings. [3-4] Many physicians believed that laboratory TAT caused delays in treatment in the Emergency Department (ED) (42.9%) as well as increased the length of stay in the ED more than 50% of the time (61.4%).[5]

As such, improving turnaround time has become a key barometer of laboratory performance and an addition to quality improvement initiatives in hospitals and institutions. To meet these objectives, laboratories may consider utilizing plasma instead of serum for clinical chemistry testing.

Why Plasma?

While serum has typically been used for clinical chemistry testing due to the ability to test a wide range of assays, it may compromise the time to test receipt due to the required clotting (generally ranging from 30-60 minutes). The clotting time for patients on anticoagulant therapy may be longer. Serum is also subject to latent fibrin formation when clotting is inadequate or may be present in samples from patients receiving anticoagulant or thrombolytic therapy. Fibrin, which may range from thin strands to large cloud-like masses, may be caused by inadequate tube mixing or incomplete or delayed clotting. It may also contribute to obstruction of the sample probe in automated instruments and subsequent instrument downtime.

Plasma offers distinct advantages over serum. Plasma—the liquid component of blood—contains blood cells and anticoagulant following centrifugation of whole blood. Heparin is the most commonly used anticoagulant in plasma, which acts primarily through a complex that it forms with anti-thrombin III, a protein that helps to control blood clotting. It also prevents the formation of fibrin from fibrinogen.

Conversely, clotting is not required for plasma; enabling plasma to be centrifuged upon receipt of the specimen in the laboratory. Specimens can be processed more quickly, shortening the turnaround time for test results. There is a potentially higher sample volume yield with plasma, with approximately 15-20% more plasma obtainable from whole blood than with serum.[6] This helps laboratories to adhere to ISO standard 15189, in which laboratories should periodically review sample volume requirements to ensure that excessive amounts of blood samples are not collected.[7]

In addition, interference due to coagulation is eliminated, as coagulation post centrifugation does not occur in plasma.[6] There is also a lower risk of hemolysis and thrombocytolysis. In a healthy population, free hemoglobin is about 10 times less concentrated in plasma than in serum.[6] In anticoagulated blood, there is no obstruction to upward gel movement; therefore, the time required for gel to complete its

upward course is generally shorter with plasma tubes. This may result in more reproducible gel barrier formation.

Most significantly, it is imperative that the *in vivo* state of a constituent remains unchanged after withdrawal from the body fluid of a patient. Constituents in plasma are more accurately representative of the *in vivo* status of the patient than those in serum.[8]

Assay Compatibility – the "True" *In Vivo* State

Generally, most assays in clinical chemistry are compatible with both serum and heparin plasma, enabling the same reference ranges to be used. However, for certain assays or test methods, both serum or plasma may not be acceptable or differences in results obtained in plasma specimens may warrant a change in reference range.[9] For instance, glucose concentrations were noted to be 5% higher in serum than plasma as a result of fluid shift from erythrocytes to plasma due to anticoagulants.[10] In addition, potassium and phosphorus levels may be increased in serum due to release from cells/platelets during the clotting process.[10-11] Pseudohyperkalemia has been found over the level of 5.5 mmol/L in patients with essential thrombocythemia and serious thrombocytosis. This appears to have been corrected when measured in plasma.[12] Insufficient clotting of serum specimens and fibrin formation within the analyzer reaction vessel may lead to erroneous follicle stimulating hormone results,[13] with the presence of microclots shown to impact lactate dehydrogenase.[14]

The faster processing time with heparinized plasma samples is preferable when urgent critical decisions are based on STAT test results (e.g. for patients suspected to have an acute myocardial infarction). In clinical studies, cardiac markers Troponin T and Troponin I have shown clinically equivalent or clinically acceptable values in both serum and plasma, although one study showed falsely elevated Troponin I due to fibrin in serum samples.[15-16] Both Creatine Kinase-MB and Myoglobin have demonstrated clinically equivalent results using both specimen types.[15]

While the benefits of plasma have been discussed, it is important for laboratories to consider the limitations. The presence of anticoagulants may interference with some analytical methods. A slight increase in total protein may be seen in plasma as a result of fibrinogen. Differences in some enzymes (lactate dehydrogenase, alkaline phosphatase, asparate aminotransferase) may be present in plasma. In addition, high levels of lithium and sodium may be observed due to contamination with cations from the anticoagulants.[6] For samples collected in plasma gel tubes, rapid gel barrier movement may trap cellular debris and platelets in the plasma compartment prior to complete separation, which may compromise sample purity. It is important to note that variations may depend on specimen handling and processing as well as the assay platform and manufacturer.

CONCLUSION

Plasma specimens offer the best opportunity for achieving desired turnaround time, which may help laboratories in their performance improvement goals. Faster turnaround of results is particularly vital for STAT testing, in which rapid decisions are necessary for critically ill patients. Additionally, plasma more accurately reflects the patient's *in-vivo* state and provides a higher volume yield from the sample.

While standardizing the laboratory for one sample type may be desirable, it may not always be practical. Therefore, laboratory professionals should assess each specimen type to determine the most suitable for a particular clinical setting or patient population. It also important to follow established protocols in the laboratory and the appropriate reference ranges for each assay.

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