Q&A column, 6/16

Editor: Frederick L. Kiechle, MD, PhD

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Submit a Question

Q. Can you offer feedback on the growing trend of using type A fresh frozen plasma in emergencies instead of type AB? Is this being used mainly in trauma hospitals and military sites or is the trend becoming more popular in smaller hospitals too?

A. When transfusing patients of unknown blood group, group AB "universal donor" plasma is typically used because it does not contain the naturally occurring anti-A and anti-B antibodies that are incompatible with non-group O red blood cells. However, the AB blood group in the U.S. population has a prevalence of only about four percent. Many level one trauma centers maintain thawed plasma inventories so plasma can be provided early in the resuscitation to avoid a clotting factor deficit due to product thawing time. For rural-based trauma centers with less predictable trauma volumes, maintenance of a thawed AB plasma inventory may, to avoid waste, result in much of it eventually being diverted to non-group AB hospital inpatients when these units approach expiration. The American Association of Blood Banks, in anticipation of concerns about a shortage of group AB plasma following implementation of its standard (April 1, 2014) to reduce the risk of transfusion-related acute lung injury (TRALI) caused by plasma-containing blood products, offered strategies to reduce the use of group AB plasma. These strategies included the following: "Consider keeping a supply of thawed group A plasma available for transfusion in emergent situations for patients with unknown ABO type . . . using either untitered plasma or titered plasma shown to have a low level of anti-B." This recommendation was based on published single center retrospective studies of several rural U.S. trauma hospitals in which their successful experiences using group A plasma in trauma were described.[1-3]

In light of the changing environment, a survey-based study was undertaken in January 2015 to understand current plasma transfusion strategies in American level one trauma centers.4 Virtually all level one trauma center survey respondents maintain a thawed plasma inventory—54 of 56, or 96 percent. Among those that maintain a group A thawed plasma inventory, 34 of 49 (69 percent) use group A plasma for recipients of unknown ABO group. Although the experiences of single centers that use group A plasma in trauma resuscitation are increasing, large multicenter studies are clearly needed to definitively demonstrate its safety. The Biomedical Excellence for Safer Transfusion (BEST) Collaborative is currently conducting a multicenter study examining the impact of the use of thawed A plasma on trauma patient survival.

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thawed plasma suitable as the first option for emergency release transfusion? *Transfusion.* 2014;54(7):1751–1755.
4. Dunbar NM, Yazer MH; Biomedical Excellence for Safer Transfusion (BEST) Collaborative. A possible new paradigm? A survey-based assessment of the use of thawed group A plasma for trauma resuscitation in the United States. *Transfusion.* 2016;56(1):125–129.

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Q. Our coagulation department staff is debating the usefulness of incubated mixing studies for prolonged prothrombin times that do not correct. We incubate only for APTT studies. Even though none of the prothrombin time factors are time dependent (despite rumblings concerning factor V), we still see on CAP participant summary reports a significant number of labs that perform incubated prothrombin time studies. Half of the staff want to do incubated PTs to make sure we are not missing important information, but none can explain the value of doing so. What is the value of doing incubated mixing studies on prolonged prothrombin times?

A. There are few data in the literature regarding the performance of mixing studies and even fewer that address prothrombin time (PT) mixing studies specifically. In general, PT mixing studies can be performed similarly to activated partial thromboplastin time (APTT) mixing studies and for similar indications (i.e. to determine if clotting time prolongation is more likely due to a factor deficiency versus an inhibitor). Most commonly, a 1:1 mixture of patient plasma and normal pooled plasma is assayed in the test system showing initial prolongation (PT or APTT). The results are interpreted as correction (suggestive of a factor deficiency) or non-correction (suggestive of an inhibitor), with mixing study correction defined and validated by each individual laboratory. The current CLSI guideline discussing APTT and PT (document H47-A2) states that PT mixing studies are less commonly performed since PT prolongation is rarely due to lupus anticoagulants or factor inhibitors. The guideline notes, though, that if a PT prolongation is suspected to be due to an inhibitor, then a mixing study is recommended and both immediate and incubated mixing studies "can" be performed, similar to the APTT.

In practice, there are few instances in which an incubated PT mixing study may add value to the immediate mixing study. Factor V inhibitors have rarely been reported to demonstrate time dependence; however, the majority of factor V inhibitors will demonstrate their effects in an immediate mixing study. For laboratories that handle secondary specimen aliquots, incubated PT mixing studies may provide supporting evidence that a sample represents potassium EDTA plasma rather than sodium citrate plasma. However, the presence of EDTA can be determined using other simple and widely available laboratory methods (namely, measuring calcium and potassium in the sample). Based on the limited available evidence, routine performance of incubated PT mixing studies does not appear to offer a significant incremental benefit over the performance of immediate PT mixing studies. In cases in which there is a strong clinical and/or laboratory suspicion of factor V inhibitor but correction of the immediate mixing study, incubated PT mixing studies may provide a clue to the correct diagnosis. However, laboratories would do well to remember that mixing studies are screening tests for inhibitors, and if the level of clinical or laboratory suspicion for an inhibitor is high, proceeding directly to specific factor assays and inhibitor titers (measured in Bethesda units) for the factor(s) suspected to be involved would also be a reasonable step.

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