OCTOBER 2021

HOW CAN WE AVOID THE UNDER-TRANSFUSION OF PLASMA AND ENCOURAGE PHARMACOLOGIC AGENTS?

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Transfusion of plasma, along with red blood cells and platelets, increased in the United States between 1993 and 2011.[1] But since 2011, the use of plasma has declined, partly because of the increased attention paid to patient blood management (PBM) strategies aimed at reducing unnecessary transfusions.[1,2] The increased use of alternative agents that enhance coagulation, including vitamin K, prothrombin complex concentrates (PCCs), recombinant factor concentrates (i.e., recombinant activated factor VII), and antifibrinolytic agents (e.g., tranexamic acid [TXA] and epsilon-aminocaproic acid [EACA]), has also contributed to reductions of plasma transfusions. Nevertheless, plasma transfusions are frequently prescribed, although the indications for their use often are empirical and not evidence-based.[3,4] For example, preprocedural plasma transfusions to reduce the international normalized ratio (INR) as a surrogate marker for hemostasis remains a common practice despite a lack of evidence about its benefits.[4]

Inappropriate dosing of plasma also remains a concern. As a rule, transfusion of 10-15 mL/kg of plasma is the recommended standard dose to correct the INR. Yet, this dosing guideline is often not followed by clinicians, frequently leading to underdosing (i.e., single-unit transfusions), as well as the occasional overdosing of plasma. In fact, an epidemiological study including more than 72,000 units of plasma transfused in 10 hospitals in the United States during a one-year period demonstrated that only 29% of doses met the minimum recommended dose of 10 mL/kg; this rate decreased to 15.5% for those that were at least 15 mL/kg.[5] The study further found that 25% of plasma transfusions resulted in no change, or even an increase in the INR value, while only 42% resulted in a post-transfusion INR of less than 1.6, correlating with significant underdosing of and/or unnecessary plasma transfusions. In support of appropriate dosing, the study results showed that the magnitude of the correction of INR increased as the plasma dose increased from 1 to 4 units. Several older studies have also correlated the correction of coagulation factor levels with higher plasma doses (i.e., 17-30 mL/kg).[6,7] To address the issue of dosing, Pham et al. validated a mathematical model to estimate the posttransfusion INR after transfusion of a given volume of plasma with good predictive ability.[4] Their formula supported the standard dosing of 10-15 mL/kg as having the most significant effect on INR reduction. This research further confirmed that transfusion of only 1 or 2 units of plasma is likely to have limited effect on the INR, exposing patients to the risks of plasma transfusion without gaining any benefit.

OPTIMIZATION OF HEMOSTASIS

One of the principal strategies of PBM, along with anemia management, interdisciplinary blood conservation strategies, and patient-centered decision making, is optimization of hemostasis.[8] Thus, implementation of a robust PBM program is one key strategy aimed at improving plasma utilization. Emphasis on strategies that assess the perioperative coagulation status of patients, including the detection of coagulation abnormalities, withdrawal of medications and supplements that increase the risk of bleeding (e.g., anticoagulants, anti-platelet agents), and use of non-blood pharmacologic agents (e.g., vitamin K, antifibrinolytics and desmopressin [DDAVP]) that may enhance coagulation is of utmost importance.

Encouraging clinicians to use pharmacologic agents in place of plasma transfusion may be challenging, particularly when time-sensitive patient care matters are at hand or when there is unfamiliarity or excessive concerns with a given agent. For example, although oral or intravenous vitamin K (phytonadione) can efficiently reverse nutritional- or warfarin-induced coagulopathy, clinicians may be more apt to give plasma or PCC along with vitamin K given the slow onset of action (ranging from 6-24 hours) of vitamin K relative to plasma/PCC and the need to reverse coagulopathy in short time prior to a procedure.[7,9] Meanwhile, some agents like TXA and EACA (antifibrinolytics) are associated with benefits in reducing excessive bleeding in various patients, including those undergoing maxillo-facial and oral surgery, orthopedic surgery, obstetrical and gynecological bleeding (i.e., menorrhagia and postpartum hemorrhage), cardiac surgery and trauma.[10] Yet, clinicians may avoid these agents given their lack of clinical experience with the products and/or their concerns about adverse events related to the products—such as thromboembolic complications associated with TXA—even though evidence may not be strong or confined to a specific situation (e.g., seizures related to high-dose TXA in patients undergoing open cardiac surgery).[10] Providing educational sessions in the form of grand rounds, through the facility's PBM program or other forums is perhaps a pathway of overcoming these barriers.

In summary, ensuring adherence to evidence-based plasma transfusion for appropriate indications and dosing remains challenging. Development of a robust PBM program with an emphasis on education is a key strategy for minimizing inappropriate plasma transfusions and underdosing. Encouraging use of pharmacologic hemostatic agents, when appropriate, can help to reduce or avoid use of plasma in select coagulopathic patients.

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