CRITICAL CARE

COMMENTARY

The conundrum of persistent inappropriate use of frozen plasma

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See related research by Stanworth *et al.*, http://ccforum.com/content/15/2/R108

Abstract

Frozen plasma (FP) is commonly used for the treatment of bleeding or the prevention of bleeding in critically ill patients, but clinical evidence to help aid the critical care clinician make decisions on whether to transfuse or not is at present limited. Despite the limited evidence, it appears FP is administered not infrequently in the absence of bleeding or with no required procedure when the international normalized ratio (INR) is essentially normal (<1.5) or only mildly deranged (<2.5). The study by Stanworth and colleagues in a recent issue of *Critical Care* raises awareness of FP transfusion use in the critically ill, should prompt a consideration of curbing its use when it is not clearly appropriate, and illustrates the need for future high quality evidence to guide FP use in the critically ill when the risk:benefit ratio is less clear.

Frozen plasma (FP) is commonly used for the treatment of bleeding or the prevention of bleeding in critically ill patients. In the acutely bleeding patient, there is no question that FP transfusions can be life saving, but the benefit of FP transfusions in the prophylactic setting is much less clear, with a lack of high quality evidence to guide use. In a recent issue of *Critical Care*, Stanworth and colleagues [1] describe the clinical settings associated with FP transfusions in a rigorous prospective observational study in 29 UK general ICUs. Of 1,923 ICU admissions, 13% of patients received FP transfusions for 404 FP treatment episodes; 24% of them were given in the absence of bleeding or requirement for an invasive procedure, and with pre-transfusion international normalized ratios (INRs) that were essentially normal (INR <1.5, n = 32) or mildly deranged (INR 1.6 to 2.5, n = 65), which prompts the question of why these transfusions were given in the first place. Although not all factors that contribute to a clinician's decision to give an FP transfusion may have been captured in this study (for example, the presence of severe thrombocytopenia that may have further increased the perceived risk of bleeding), it would appear that some of these transfusions were clearly inappropriate.

High rates of FP transfusions that are considered inappropriate are a consistent finding in audits of FP transfusions [2,3]. This may seem surprising, especially given the concerns and public awareness regarding the harms associated with transfusion (particularly HIV and hepatitis C transmission, and more recently transfusion-associated acute lung injury and transfusion-associated circulatory overload have been recognized). While the risk of transmitting HIV or hepatitis C is now rare (estimated at 1 in 3 to 4 million transfusions), there is mounting evidence of adverse events associated with FP transfusions in particular (increased new onset lung injury) [4] and excess fluid administration in general in the critically ill [5,6]. For all these reasons, one might expect lower rates of inappropriate FP use.

A major difficulty in making decisions about whether to transfuse FP or not is that the clinical evidence to guide use of FP transfusions in the critically ill is currently sparse. The few randomized clinical trials evaluating FP have not shown any benefit for FP for prophylaxis and no other randomized controlled trials have evaluated the effectiveness of FP in reducing bleeding [7]. Clearly, more randomized controlled trials are needed so that we can base the decision to transfuse FP on good evidence.

In the absence of strong clinical evidence, critical care clinicians base their decisions to transfuse FP on their clinical rationale, balancing perceived potential risks with benefits, as well as with use of published FP transfusion guidelines that are not critical care specific. The common rationale for the transfusion of FP may be flawed. First, abnormal coagulation tests do not necessarily represent an increased risk for blood loss. The INR is a poor measure of the hemostatic level of individual coagulation

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proteins. With a single coagulation factor deficiency, an INR of 1.5 represents a clinically important (<30%) reduction in that factor [8], but in situations where multiple coagulation factors are affected, such as in critically ill patients, the levels of the individual coagulation factors are sufficient for hemostasis (>30%) when the INR is 1.5 and perhaps even higher [8]. Second, as was demonstrated in the study of Stanworth and colleagues and others, FP transfusions do not result in significant correction of the INR when the levels are mild to moderately increased [9,10]. Thus, the question remains, at what INR level do we need to transfuse FP and what factors should modify our threshold? FP transfusion guidelines are general and they universally recommend FP use to be limited to instances when the INR is greater than 1.5 times normal and there is bleeding or risk of bleeding (that is, surgery or an invasive procedure) [11-13]. This definition may qualify up to one-third of critically ill patients for an FP transfusion [14]. In the cohort of patients included in the study of Stanworth and colleagues, the rate of coagulopathic patients (30%) [14] is nearly twice the rate of patients transfused with FP (18%), which suggests variation in the decision to transfuse. This variability may be explained by differences in patient-specific factors and/or variation in perceived risks of bleeding, factors that should be minimized by the generation of evidence that is specific and applicable to the critically ill.

In summary, the study by Stanworth and colleagues should aid to raise awareness of FP transfusion use in the critically ill and prompt a consideration of curbing FP use when it is not clearly appropriate. It also illustrates the need for further high quality evidence to guide FP use when the risk:benefit ratio is less clear.

Abbreviations

FP, frozen plasma; INR, international normalized ratio.

Competing interests

The authors declare that they have no competing interests.

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