

References

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Transfusion-related Acute Lung Injury: More Questions Than Answers?

To the Editor:

We congratulate Clifford *et al.*¹ on their important contribution to the transfusion-related acute lung injury (TRALI) literature. There were a number of important findings in their article. First, the incidence of postoperative TRALI (1.3 to 1.4%) was higher than anticipated. Interestingly, in a previous study including the same center, the incidence of TRALI was estimated to be between 1 in 4,000 and 1 in 12,000 transfused units.² Also, the mitigation strategies of leukoreduction and elimination of female donor plasma had no effect on TRALI incidence in Clifford *et al.*'s study. This is also contradictory to the findings by Toy *et al.* who suggested that transition to all male donor plasma decreased the incidence of TRALI substantially.

The data presented by Clifford *et al.* also suggest that there is substantial TRALI risk in patients who receive only red cell transfusion, and there were zero cases of TRALI in patients who received only plasma transfusion in their study. This is similar to the data presented in the Serious Hazards of Transfusion (SHOT) 2012 and 2013 annual reports (table 1).^{3,4} These data bring into question whether there is an alternative mechanism for TRALI. According to the Food and Drug Administration

Center for Biologics Evaluation and Research, the putative cause of TRALI is anti-human leukocyte antigen or granulocyte antibodies in the donor blood product with 89% of TRALI cases having these antibodies.⁵ Clifford *et al.* did not present data on these antibodies, but the 2013 SHOT annual report suggested that antibodies were present in 40% of TRALI cases. Assuming the anti-human leukocyte antigen/granulocyte antibody mechanism is correct, it is important to explain why patients who receive only red cell transfusion appear to have a higher incidence of TRALI than those who receive only plasma. One possibility is that because red cell units are still collected from female donors and there is a small amount of plasma present in these units, they may presently carry a higher risk for TRALI. Alternatively, stored erythrocyte units may cause TRALI through a different mechanism that has not yet been elucidated.

The study by Clifford *et al.* also suggested that increased volumes of transfused blood products were associated with TRALI, which demonstrates the blurred lines that exist between TRALI and transfusion-associated circulatory overload. In their study, Clifford *et al.* classified patients as having both diagnoses when neither diagnosis alone could fully explain the clinical picture. We believe there is considerable overlap between these two diagnoses, and this may account for the underreporting that occurs with TRALI to some degree.

Recent alternatives to standard allogeneic plasma transfusion (e.g., prothrombin complex and solvent detergent plasma) potentially eliminate the risk for TRALI from plasma transfusion altogether, but to date, there are questions about their safety and high costs. These products are prepared through large-scale pooling, and thus, the causative antibodies for TRALI may be diluted to insignificant levels. Thus far, there have been no cases of TRALI reported with solvent detergent plasma or prothrombin complex, but there has been limited surveillance.⁶ In addition, the data from Clifford *et al.* and the SHOT annual reports suggest that

This letter was sent to the author of the original article referenced above, who declined to respond.

Table 1. Recent TRALI Studies

	Toy	Clifford*	Clifford*	SHOT	SHOT
	2006–2009	2004	2011	2012	2013
Whole blood only	1 (1.1)	—	—	—	—
Erythrocyte only	20 (22.5)	7 (30.4)	8 (36.4)	7 (63.6)	4 (40.0)
Plasma only	13 (14.6)	0	2 (9.1)	0	0
Platelets only	5 (5.6)	0	1 (4.5)	2	1 (10.0)
Mixed	50 (56.2)	16 (69.6)	11 (50.0)	0	5 (50.0)
Others†	—	—	—	2 (36.4)	0
Total TRALI cases	89	23	22	11	10

Numbers in rows represent total number (and %) of TRALI events stratified by individual blood products.

* Included both definite and possible TRALI cases. † Included intravenous immunoglobulin and granulocyte transfusion.

SHOT = Serious Hazards of Transfusion; TRALI = transfusion-related acute lung injury.

eliminating harmful antibodies from the plasma pool may not fully eradicate TRALI. Residual plasma in red cell units and platelet units may cause TRALI or these products may cause TRALI through alternative mechanisms. Considering these factors, there may be additional opportunities for anesthesiologists to prevent TRALI through preoperative optimization of anemia, careful management of antiplatelet agents during the perioperative period, and proper hemostatic interventions.

Competing Interests

The authors declare no competing interests.

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