DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
U.S. Food and Drug Administration – Center for Biologics Evaluation and Research
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville MD 20852-1448

Transfusion Related Acute Lung Injury

(You are encouraged to copy and distribute this letter)

Dear Colleague:

This is to alert you to the possibility that patients who receive blood products, particularly plasma-containing products, may be at risk for Transfusion Related Acute Lung Injury (TRALI), a serious pulmonary syndrome that can lead to death if not recognized and treated appropriately. Even small amounts of plasma in packed red blood cells may induce TRALI. Recognition of symptoms and immediate treatment are imperative.

Reports

The first TRALI fatality was reported to the Center for Biologics Evaluation and Research (CBER) in 1992. Since then, CBER has received more than 45 fatality reports of TRALI. As of FY2000 this represented 13 percent of all transfusion fatalities. TRALI is thought to be the third leading cause of transfusion related death. The majority of deaths were associated with fresh frozen plasma transfusions; fewer were caused by packed red blood cell transfusions and platelet transfusions. In most cases, follow-up donor antibody screens implicated donors who were multiparous females and were positive for anti-HLA or anti-granulocyte antibodies. Non-fatal TRALI events reported by licensed blood establishments through Med Watch or as Biological Product Deviation reports are also on the increase. There have been 26 such reports since 1999. This finding may be attributable to better recognition and reporting of events. Because of misdiagnosis and/or underreporting, the full scope of TRALI is not known.

Description and Cause of Problem

TRALI is a well-characterized clinical constellation of symptoms including dyspnea, hypotension, and fever. The radiological picture is of bilateral pulmonary infiltrates without evidence of cardiac compromise or fluid overload. Symptoms typically begin 1-2 hours after transfusion and are fully manifest within 1-6 hours. Products typically implicated in TRALI are whole blood, packed red blood cells, fresh frozen plasma, cryoprecipitate, platelet concentrates, apheresis platelets, and rarely IGIV[1]. The etiology of TRALI may be attributable to the presence of anti-HLA and/ or anti-granulocyte antibodies in the plasma of multiparous females or donors who have received previous transfusions. TRALI recipients have no specific demographics such as age, gender, or previous transfusion history. Although TRALI does not always occur through transfusions from donors with anti-HLA or anti-granulocyte antibodies, one or both of these antibody types have been found in 89% of TRALI cases[2].

Diagnosis and Treatment

It appears that unlike allergic or anaphylactic immune-mediated transfusion reactions, antibodies implicated in TRALI are usually of donor origin. Once transferred to the recipient, these antibodies may cause complement activation resulting in neutrophilic influx into the lungs and damage to the

---

[1] Rizk A, Gorson K, Kenny L, and Weinstein R: Transfusion-related acute lung injury after the infusion of IVIG. *Transfusion 2001; 41:264-268.*

[2] Popovsky, MA, Chaplin, HC, and Moore, SB. Transfusion-related acute lung injury: a neglected serious complicaton of hemotherapy. *Transfusion 1992; 32:589-592.*

pulmonary microvasculature. The clinical result may be subtle or significant. In either case, there is typically a marked hypoxemia, hypotension, fever, and severe bilateral pulmonary edema. Respiratory support should be as intensive as dictated by the clinical picture. Diuretics play no role in TRALI as the underlying pathology involves microvascular injury, rather than fluid overload.

Recommendations

1. Be alert that any respiratory distress occurring during or following blood or blood component(s) transfusion could potentially be TRALI. Discontinue the transfusion immediately. Begin oxygen and supportive therapy.

2. Notify the Blood Center that supplied the blood component and return remaining product to be tested for anti-HLA and/or anti-granulocyte antibodies in the donor.

3. Fatalities from TRALI should be reported to CBER in accordance with 21CFR 606.170(b). FDA encourages voluntary reporting of TRALI as a serious adverse reaction to transfusions. Reports can be filed via MedWatch by phone at 1-800-FDA-1088, by fax at 1-800-FDA-0178, by US mail at MedWatch, HF-2, 5600 Fishers Lane, Rockville, MD 20852, or by email at http://www.fda.gov/medwatch.

For More Information

If you have questions regarding this alert, please contact Dr. Leslie Holness, Center for Biologics Evaluation and Research, FDA, 1401 Rockville Pike, Mail Stop HFM-375, Rockville, MD 20852-1448, by fax at 301-827-3534, or by e-mail at HOLNESS@cber.fda.gov.

Sincerely yours,

Kathryn C Zoon, Ph.D.
Director
Center for Biologics
Evaluation and Research