Blood Products Advisory Committee Meeting
June 14-15, 2001
Gaithersburg, MD

Summary for Topic IV: Transfusion Related Acute Lung Injury (TRALI)

Introduction

Data submitted to the FDA over the past three years indicate that transfusion related acute lung injury (TRALI) has been implicated in 10.5 % - 14% of annually reported post-transfusion fatalities. FDA reports of non-fatal TRALI reactions for a similar period appear to be increasing (3 in FY 97,12 in FY 98, and 17 in FY99). Studies estimate the incidence to be 1 in 2500 to 1 in 5000 transfusions per year with suggestions that it may be much higher than reported due to the number of cases with less dramatic symptoms.

Background

TRALI is recognized as a life-threatening complication of blood component transfusion therapy representing the third most frequent cause of transfusion-related death after ABO incompatibility and bacterial contamination. TRALI usually manifests 1-6 hours post transfusion, as a clinical constellation of signs and symptoms characterized by dyspnea, hypotension, fever, and bilateral noncardiogenic pulmonary edema. Recognized TRALI cases are effectively treated by stopping the transfusion and providing supportive care. Blood products collected from multiparous and/or previously transfused donors are most often implicated in TRALI. Transfusion of products from anti-HLA or anti-granulocyte positive donors may represent as many as 89 % of all TRALI cases. An alternative mechanism involving biological response modifiers generated in the blood components during storage, acting on a “preprimed” recipient has also been postulated for a number of cases.

Recipient exposure to donor plasma represents the greatest risk for TRALI, however, other blood products including red blood cells, random donor platelets, apheresis platelets, cryoprecipitate, and IGIV have all caused the complication.

Discussion

Because the actual incidence of TRALI may be higher than either reports to FDA or the literature would suggest, it is important to raise awareness of this post-transfusion risk in the medical community so that affected transfusion recipients may be treated promptly and appropriately. Strategies may also be needed to identify donors whose blood components are most likely to place transfusion recipients at risk for TRALI so that preventive measures can be applied.

Possible options for reducing TRALI morbidity and mortality include:

1. Considering deferral of donors implicated in single unit TRALI or in more than one multiple unit TRALI case.

2. Introduction of donor screening procedures to identify donors who may have risk factors that are associated with TRALI followed by a) deferral, b) implementation of donor screening for anti-HLA or granulocyte antibodies, or c) diversion of plasma collections from these individuals to further manufacture of non-injectable products

3. Establishment of improved physician education about TRALI and improved surveillance mechanisms for donors implicated in non-fatal, as well as fatal TRALI cases.

Questions for the committee:

1. Should FDA consider interventions at this time to identify donors and/or donations with an increased risk for producing TRALI in a recipient?

   1a. If not, what data are needed to further define appropriate prevention measures.

2. If yes (in 1.), would it be appropriate to identify blood donors with a history of
   i. multiparity (three or more pregnancies)
   ii. history of allogeneic transfusion (two or more donor exposures)
   iii. history of implication in a single unit TRALI case, or >1 multiple unit TRALI cases.

2b. If yes (in 1.), for donors with risk factors (as in 2.), would it be appropriate to
   i. limit collections for transfusion use to plasma reduced products (e.g. washed-resuspended red cells; apheresis platelets)
   ii. divert the plasma collections to manufacture of non-injectable products
   iii. screen for anti-HLA and anti-granulocyte antibodies and permit negative donors to continue donating routinely.
   iv. defer such donors