



LETTERS TO THE EDITOR

Acute respiratory distress secondary to blood transfusion[☆]



Distrés respiratorio agudo secundario a la transfusión sanguínea

Dear Sir,

We have read the recent histopathological review entitled: “acute respiratory distress” (ARD)¹ with interest. However, we found that the publication made no mention of ARD associated to blood transfusion.² A differential diagnosis must be established among transfusion-related acute respiratory distress (TRD), transfusion-related acute lung injury (TRALI), and cardiogenic lung edema or transfusion-associated circulatory overload (TACO).⁴

Transfusion-related acute lung injury is defined as “acute dyspnea with hypoxia and bilateral pulmonary infiltrates during or in the 6 hours after transfusion, unrelated to overload or other likely causes”.³ The presence of TRALI is to be suspected in “patients without evidence of acute lung injury prior to transfusion” who develop ARD.³ Table 1 describes the diagnostic criteria. Transfusion-related acute lung injury is a clinical syndrome, and the presence of antibodies is not strictly necessary to establish the diagnosis.⁴

Transfusion-associated circulatory overload lacks a consensus-based definition. According to the current definition of the International Society of Blood Transfusion (ongoing revision),³ any four of the following conditions must be met within the first 6 h after transfusion: acute respiratory failure, tachycardia, increased arterial pressure, acute lung edema or worsening of edema, or evidence of a positive fluid balance. The diagnosis is established on an exclusion basis and requires a high degree of suspicion³: “TACO is to be suspected in the presence of respiratory difficulties that improve with treatment for circulatory overload (diuretics, morphine and nitrates)”, and “it is important to report these cases”. The experts that review these cases find it difficult to classify them—often because the essential data are not available and the transfused patients are frequently elderly (over 70% of the units being administered to patients over 70 years of age) or in critical condition (over 40% in emergency care or in Intensive Care Units), and with

Table 1 Definitions and diagnosis of transfusion-related acute respiratory distress.

Transfusion-related acute lung injury (TRALI)^a

In a patient without evidence of acute lung injury prior to transfusion

Diagnosis: acute onset + hypoxemia + bilateral pulmonary infiltrates + no evidence of left atrial hypertension (i.e., circulatory overload) + no time relation to some alternative risk factor for lung injury during or in the 6 h following transfusion

Transfusion-associated circulatory overload (TACO)

Appearance of acute dyspnea, tachycardia, hypotension, hypoxia and hypercapnia, accompanied by a bilateral alveolar radiological pattern in the 24 hours following blood transfusion

Allergic reaction^b

Acute reaction manifesting in the 24 h following the transfusion of any blood component and which evolves with characteristic signs and symptoms of allergy or anaphylaxis

Clinical manifestations: *Mild forms:* fundamentally skin manifestations such as urticaria, erythema, pruritus
Severe forms: bronchospasm with dyspnea, rhonchus, wheezing, laryngeal stridor, gastrointestinal manifestations such as nausea or diarrhea, cardiac manifestations such as hypotension, tachycardia, arrhythmia, syncope or cardiac arrest

Source: Adapted from the State Hemovigilance report.⁴

^a TRALI is a clinical syndrome, and the presence of anti-HLA or anti-HNA antibodies in the donor or receptor is not strictly necessary to establish the diagnosis.

^b Laboratory: Determine whether the patient has IgA deficiency and anti-IgA antibodies. It should be remembered that recent transfusions can increase the real IgA titers.

considerable comorbidities.⁵ Furthermore, some patients may have both TRALI and TACO.³

In 2014, a total of 64 cases of TACO and 30 cases of TRALI were reported in Spain, versus 76 and 30 cases, respectively, in 2013. Any blood component can be implicated in TRALI: red cells (15 patient), platelets (5 patients), plasma (7 patients) or multiple components (3 patients).

In Spain, one-half of all transfusion-related deaths were due to ARD. Of the 30 cases associated to transfusion reported since 2007, 10 corresponded to TRALI and 5 to TACO. In the United Kingdom, of the 93 transfusion-related

[☆] Please cite this article as: García Erce JA, Quintana Díaz M. Distrés respiratorio agudo secundario a la transfusión sanguínea. Med Intensiva. 2017;41:444–445.

deaths recorded between 2010 and 2015, 55% corresponded to ARD associated to allogenic blood transfusion: 39 cases of TACO, 9 cases of TRALI and three cases of TRD.

In view of the above, and considering the clinical importance, healthcare impact and therapeutic relevance involved, we consider it essential to contemplate episodes of ARD associated to blood transfusion in this document. Likewise, we wish to underscore the obligation to report all cases to the hematological surveillance system, and the fact that "one unit may be enough".

Conflicts of interest

There are no conflicts of interest in relation to this study.

Dr. García-Erce has given talks and has acted as moderator at congresses and sessions, with grants or funding from Vifor-España, Sandoz, Amgen, Alexion, Braun, GSK, Octapharma, Novartis and Sanofi.

Acknowledgements

Thanks are due to all those transfusion centers that supply the best and freshest blood components.

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In reply to "Acute respiratory distress secondary to blood transfusion"



En respuesta a «Distrés respiratorio agudo secundario a la transfusión sanguínea»

Dear Editor,

We would like to thank the authors of the letter entitled "Acute respiratory distress secondary to blood transfusion" for their interest in our article.¹ We agree with them that blood derivatives transfusion (whole blood cells, red cells, apheresis platelets, fresh frozen plasma, cryoprecipitates, stem cell products and endovenous immunoglobulins) are well recognized, but infrequent, risk factors for Acute respiratory distress syndrome (ARDS).² In the original manuscript,¹ blood derivatives products and other ARDS risk factors are not mentioned because it is focused on what is required to define a "disease" and the relation between ARDS and diffuse alveolar damage (DAD). From our point of view, the effect of each risk factor in ARDS susceptibility or outcome should be clarified after the ARDS has been agreed upon as a disease (see below).

Currently, given that it has been demonstrated that only half of ARDS patients present DAD^{1,3} – which is considered the histological ARDS hallmark⁴ – as well as the effect of DAD in the ARDS outcome,^{3,5} we consider that including DAD as an ARDS diagnosis criteria would increase the accuracy of the definition.¹ If this proposal is accepted, the ARDS with DAD should be considered the real disease and the others (ARDS without DAD) as a misdiagnosis or mimic.⁶ This new interpretation determines that old paradigms and approaches should be changed.

In reference to the transfusion related acute lung injury (TRALI), firstly, its association with DAD is not well demonstrated, as because studies with pathological analysis are scarce and biased, due to the short time between the blood product administration and the deceased.⁷ Secondly, accepting that TRALI is risk factor for ARDS with DAD, it is unknown if the DAD induced by blood transfusion is similar to those induced by other risk factors. This fact could be of paramount importance because ARDS with DAD is a complex entity with several different physio-pathological pathways. For that reason, different subtypes of DAD would be recognized according to the processes which predominate (e.g. apoptosis, tight junction dysfunctions or alveolar clearance impairment). Finally, all of these pathological findings should be settled in a specific clinical context, in which