Transfusion and Apheresis Science xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Perioperative transfusion-related acute lung injury: The Canadian Blood Services experience

Asim Alam [a,b,*], Mary Huang [c], Qi-Long Yi [c,d], Yulia Lin [b,e], Barbara Hannach [c]

[a] Department of Anesthesia, Sunnybrook Health Sciences Centre, Canada
[b] Department of Laboratory Medicine & Pathobiology, University of Toronto, Canada
[c] Canadian Blood Services, Central Ontario, Canada
[d] Dalla Lana School of Public Health, University of Toronto, Canada
[e] Department of Clinical Pathology, Sunnybrook Health Sciences Centre, Canada

ARTICLE INFO

Article history:
Received 16 January 2014
Received in revised form 24 March 2014
Accepted 9 April 2014
Available online xxxx

Keywords:
Transfusion reactions
TRALI
Lung injury
Perioperative
Surgery

ABSTRACT

Purpose: Transfusion-related acute lung injury (TRALI) is a devastating transfusion-associated adverse event. There is a paucity of data on the incidence and characteristics of TRALI cases that occur perioperatively. We classified suspected perioperative TRALI cases reported to Canadian Blood Services between 2001 and 2012, and compared them to non-perioperative cases to elucidate factors that may be associated with an increased risk of developing TRALI in the perioperative setting.

Methods: All suspected TRALI cases reported to Canadian Blood Services (CBS) since 2001 were reviewed by two experts or, from 2006 to 2012, the CBS TRALI Medical Review Group (TMRG). These cases were classified based on the Canadian Consensus Conference (CCC) definitions and detailed in a database. Two additional reviewers further categorized them as occurring within 72 h from the onset of surgery (perioperative) or not in that period (non-perioperative). Various demographic and characteristic variables of each case were collected and compared between groups.

Results: Between 2001 and 2012, a total of 469 suspected TRALI cases were reported to Canadian Blood Services; 303 were determined to be within the TRALI diagnosis spectrum. Of those, 112 (38%) were identified as occurring during the perioperative period. Patients who underwent cardiac surgery requiring cardiopulmonary bypass (25.0%), general surgery (18.0%) and orthopedics patients (12.5%) represented the three largest surgical groups. Perioperative TRALI cases comprised more men (53.6% vs. 41.4%, $p = 0.04$) than non-perioperative patients. Perioperative TRALI patients more often required supplemental O_2 (14.3% vs. 3.1%, $p = 0.0003$), mechanical ventilation (18.8% vs. 3.1%), or were in the ICU (14.3% vs. 3.7%, $p = 0.0043$) prior to the onset of TRALI compared to non-perioperative TRALI patients. The surgical patients were transfused on average more components than non-perioperative patients (6.0 [SD = 8.3] vs. 3.6 [5.2] products per patient, $p = 0.0002$). Perioperative TRALI patients were transfused more plasma (152 vs. 105, $p = 0.013$) and cryoprecipitate (51 vs. 23, $p < 0.01$) than non-perioperative TRALI patients. There was no difference between donor antibody test results between the groups.

Conclusion: CBS data has provided insight into the nature of TRALI cases that occur perioperatively; this group represents a large proportion of TRALI cases.

* Corresponding author. Address: Staff Anesthesiologist and Transfusion Medicine Specialist, Department of Anesthesia, Sunnybrook Health Sciences Centre, Canada. Tel.: +1 4164804864.
E-mail address: asim.alam@sunnybrook.ca (A. Alam).

http://dx.doi.org/10.1016/j.transci.2014.04.008
1473-0502/

1. Introduction

1.1. Background on TRALI

Transfusion-related acute lung injury (TRALI) is a leading cause of transfusion-related morbidity and mortality [1–5]. Although this clinical entity was first described in 1983 [6], the lack of a widespread definition prevented large scale studies on the subject until 2004 [7]. TRALI is a clinical syndrome, based on clinical and radiographic findings, defined as new acute non-cardiogenic pulmonary edema associated with hypoxia that occurs within 6 h of completion of a transfusion [7]. Although laboratory tests are not necessary for diagnosis [7,8], they can be helpful in identifying a plausible biological mechanism [7,8].

The pathogenesis of TRALI has not been fully elucidated [1]. This clinical syndrome is thought to be related to neutrophil-mediated damage to the pulmonary microvasculature [1]. One specific hypothesis deems that antibodies directed against either human leukocyte antigens (HLA) Class I, Class II or human neutrophil antigens (HNA) are the causal agents of this damage [1]. However, antibodies are not detected in a number of TRALI reactions. Alternative hypotheses suggest that in patients in whom the pulmonary endothelium or neutrophils have already been preactivated by underlying disease, the addition of transfusion containing biologically active mediators accumulated during the storage of blood components may be sufficient to trigger TRALI [1,9,10].

TRALI patient risk factors have been elucidated based on the plausible biological mechanism. However, because the immunological mechanism cannot account for all TRALI reactions, it is important to elucidate other risk factors for developing TRALI. Yet, very few studies have reported patient specific risk factors in detail. This is especially important as the pre-transfusion clinical condition of the recipient population may be a major factor in developing TRALI [1,11,12]. As more than 40% of blood components are transfused in a perioperative setting [13], it makes sense that 34–48% of TRALI cases have been reported to occur in this setting as well [1,14]. However, little is known regarding this specific cohort of perioperative patients who develop TRALI and whether there are any associations with surgical characteristics and TRALI development. Utilizing a retrospective cohort design, we aimed to determine the patient, component and surgical characteristics of perioperative TRALI cases. We also hoped to determine whether any significant differences exist between perioperative and non-perioperative TRALI patients in Canada.

2. Materials and methods

2.1. Canadian Blood Services and TRALI Database Creation

Canadian Blood Services (CBS) provides blood components to all provinces in Canada, except Québec [4]. It issues greater than 800,000 red blood cell (RBC) units, 100,000 platelet doses (apheresis concentrates or buffy coat pools), and 70,000 plasma doses annually [15]. In 2001, CBS established a formal investigation protocol for reporting cases of suspected TRALI across Canada (excluding Québec) using a standardized data form. The idea behind this investigation process was to enable CBS to identify donor components with possible antibodies implicated in TRALI cases and potentially exclude those donors (and donated components) from the donor pool.

Information collected on the data form included recipient demographics, event details, and components transfused within 6 h of the transfusion reaction. Cases were classified as definite TRALI, possible TRALI or TRALI inconclusive or not related to TRALI using the table definitions based on the Canadian Consensus Conference (CCC) definitions (Table 1). Inconclusive TRALI cases were defined as cases that did not fully meet all the CCC criteria for a probable TRALI, but could not be ruled out as a TRALI case by consensus. Before June 2006, cases were retrospectively reviewed by two independent investigators (YL, BH) and classified. Disagreements were resolved by consensus. In July 2006, CBS formed the TRALI Medical Review Group (TMRG). This group comprised of six to eight physicians with diverse transfusion expertise background: hematology, anesthesiology, and laboratory medicine. The goal of this group was to review and classify all potential TRALI cases reported to CBS, as above. Initially, each member of the TMRG classified cases independently based on a summarized case review. These cases were then discussed by TMRG members and agreement on final classification was reached by consensus. All donors associated with cases of definite, possible TRALI and TRALI inconclusive were contacted to submit a sample for investigation regardless of donor sex or component type. The exception was cases of massive transfusion where more than 20 high-plasma-volume (defined as containing more than

Table 1
Canadian consensus criteria for TRALI and possible TRALI.

1. TRALI criteria
   a. ALI
      i. Acute onset
      ii. Hypoxemia
         Research setting:
         $PaO_2/FiO_2 \leqslant 300$
         or $SpO_2 < 90\%$ on room air
         Nonresearch setting:
         $PaO_2/FiO_2 \leqslant 300$
         or $SpO_2 < 90\%$ on room air
         or other clinical evidence of hypoxemia
      iii. Bilateral infiltrates on frontal chest radiograph
      iv. No evidence of left atrial hypertension (i.e., circulatory overload)
   b. No preexisting ALI before transfusion
   c. During or within 6 h of transfusion
   d. No temporal relationship to an alternative risk factor for ALI
2. Possible TRALI
   a. ALI
   b. No preexisting ALI before transfusion
   c. During or within 6 h of transfusion
   d. A clear temporal relationship to an alternative risk factor for ALI

Taken from Kleinman, S., Caulfield, T., Chan, P., Davenport, R., McFarland, J., McPhedran, S., et al. (2004). Toward an understanding of transfusion-related acute lung injury: statement of a consensus panel. Transfusion, 44(12), 1774–1789. with permission.

Please cite this article in press as: Alam A et al. Perioperative transfusion-related acute lung injury: The Canadian Blood Services experience. Transf Apheres Sci (2014), http://dx.doi.org/10.1016/j.transci.2014.04.008