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Incidence, risk factors, and outcome of transfusion-related acute lung injury in critically ill children: A retrospective study☆

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ABSTRACT

Purpose: Acute lung injury (ALI) that develops within 6 hours after transfusion (TRALI) is the leading cause of transfusion-related morbidity and mortality. Both incidence and patient and transfusion-related risk factors are well studied in the adult critically ill patient population. Clinical data on TRALI in the pediatric population are sparse and are mainly limited to case reports and hemovigilance reporting systems. The objective of this study was to determine incidence, risk factors, and outcome of TRALI in critically ill children.
Materials and Methods: In a retrospective cohort study, all first-time admissions to the pediatric intensive care unit from January 1, 2009, until December 31, 2012, were screened for onset of TRALI using the consensus criteria.
Results: Of 2294 admitted patients, 304 were transfused, of whom 21 (6.9%) developed TRALI. Compared with transfused control subjects, risk factors for TRALI were mechanical ventilation (odds ratio, 18.94 [2.38-2452.56]), sepsis (odds ratio, 7.20 [2.69-19.69]), and high Pediatric Risk of Mortality III score (odds ratio, 1.05 [1.01-1.10]). Patients with TRALI had a higher mortality and a longer duration of mechanical ventilation when compared with transfused control subjects.
Conclusions: Transfusion-related ALI is relatively common in critically ill children. The incidence in the pediatric intensive care unit population is similar to that in adult intensive care unit patients. High PRISM score on admission, mechanical ventilation and sepsis were identified as independent risk factors, which may help to assess the risks and benefits of transfusion in critically ill patients.

1. Introduction

Transfusion-related acute lung injury (TRALI) is a serious complication associated with increased morbidity and mortality after the transfusion of blood products [1–4]. The estimated incidence of TRALI amongst adults varies between 0.08% and 15% per transfused patient [5]. This wide variation can be explained by the fact that TRALI is often underrecognized and underreported, due to a previous lack of a uniform definition of TRALI and by differences in study design. According to the international definition, acknowledged by the American-European Consensus Conference in 2004, TRALI is defined as acute lung injury (ALI) developing during or within 6 hours of transfusion, with a Pao_2/Fio_2 ratio of 300 mm Hg or less or worsening of Pao_2/Fio_2 ratio, bilateral chest infiltrates in the absence of cardiogenic pulmonary edema, and no other risk factor for ALI present [1,6,7]. This distinct clinical syndrome is characterized as classical or suspected TRALI. Possible TRALI is defined as ALI developing during or within 6 hours of transfusion, and there is a clear temporal relationship to an alternative risk factor for ALI (eg, sepsis, pneumonia, and lung contusion) [1,6,7]. As with ALI/acute respiratory distress syndrome (ARDS), there is no specific treatment of TRALI besides supportive care measures and a restrictive transfusion policy.

Studies on TRALI in the pediatric population are mostly limited to case reports. A recent survey of the Canadian Blood Services showed an incident rate of *reported* TRALI cases of 5.58 in children and 3.75 in adults per 100 000 red blood cell (RBC) transfusions, suggesting a similar incidence of TRALI in children and adults [8]. However, data on the incidence of TRALI in critically ill children are still lacking.

The main objective of this study was to determine the incidence, risk factors, and outcome of TRALI in critically ill children. We performed a retrospective cohort study on our pediatric intensive care unit (PICU) using the consensus TRALI definition.

2. Materials and methods

2.1. Setting

The study was performed on a 16-bed, tertiary, mixed medical-surgical PICU within a university hospital in the Netherlands. The PICU

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is a closed unit in which patients are under the direct specialist care of the PICU team consisting of intensivists, subspecialty fellows, and residents.

2.2. Study design

The study was approved by the Ethics Committee of our hospital, and the criteria for informed consent were waived as a result of its retrospective nature. Using an electronic patient data monitoring system, all patients admitted to our PICU from January 1, 2009, until December 31, 2012 who received 1 or multiple blood products were screened for TRALI in accordance with the consensus TRALI definition (Figure). Patients who were readmitted and cases with insufficient data were excluded. No other exclusion criteria were applied. Control subjects were transfused patients not developing TRALI.

Suspected TRALI was defined as new-onset of hypoxia or deterioration defined as Pao_2/Fio_2 ratio less than 300 mm Hg (or Spo_2/Fio_2 ratio < 250 when Spo_2 < 97% if no arterial catheter was present), within 6 hours of transfusion with bilateral pulmonary infiltrates on the chest radiographs in the absence of cardiogenic pulmonary edema [1,6,7]. Cardiogenic pulmonary edema was assessed either clinically or by echocardiogram. An echocardiogram was performed at the discretion of the intensive care team. All echocardiograms were interpreted by attending cardiologists on staff. Patients judged to have moderate to severe left ventricular dysfunction and/or left atrial hypertension were excluded from this study. Possible TRALI was defined as the occurrence of TRALI in patients with other risk factors for ALI. Chest radiographs were scored for the presence of new-onset bilateral interstitial abnormalities by 2 independent physicians who were blinded to patient data. When interpretation differed, chest radiograph and screening for onset of TRALI were reviewed by a third independent physician to reach consensus.

2.3. Patient data collection

The Pediatric Risk of Mortality (PRISM) III score was calculated for each patient according to the published algorithms [9]. Clinical and laboratory data for the PRISM III score were collected within the first 24 hours after PICU admission. The following data were retrospectively collected in a Microsoft Access database, Redmond, WA, USA from patient clinical files or from our patient data management system: standard demographic data, comorbidities, laboratory test results, medication, mechanical ventilator settings, duration of mechanical ventilation, and length of PICU stay.

Potential risk factors were scored as positive when present 48 hours before onset of TRALI. Factors included were based on TRALI risk factors in the adult population as well as risk factors for ALI in the pediatric population [10–12]. These factors included liver failure, diabetes, elective and emergency (cardiac) surgery, hematologic malignancy, mechanical ventilation, sepsis, aspiration, pneumonia, trauma, disseminated intravascular coagulation, immune compromised condition, and near drowning.

Prior to the onset of TRALI, the following data were collected: body temperature, platelet count, and leukocyte count. Tidal volume was retrieved from the electronic patient data monitoring system. Mean tidal volume per kilogram body weight was calculated using data from the 6-hour period preceding transfusion. Fluid balance was determined 24 hours prior to onset of TRALI. All previously mentioned data were also collected for the control group, with the first transfusion used as a reference time point.

2.4. Transfusion data collection

Transfusion was defined as infusion of filtered RBCs, fresh-frozen plasma (FFP), or platelets. A restrictive transfusion policy was pursued

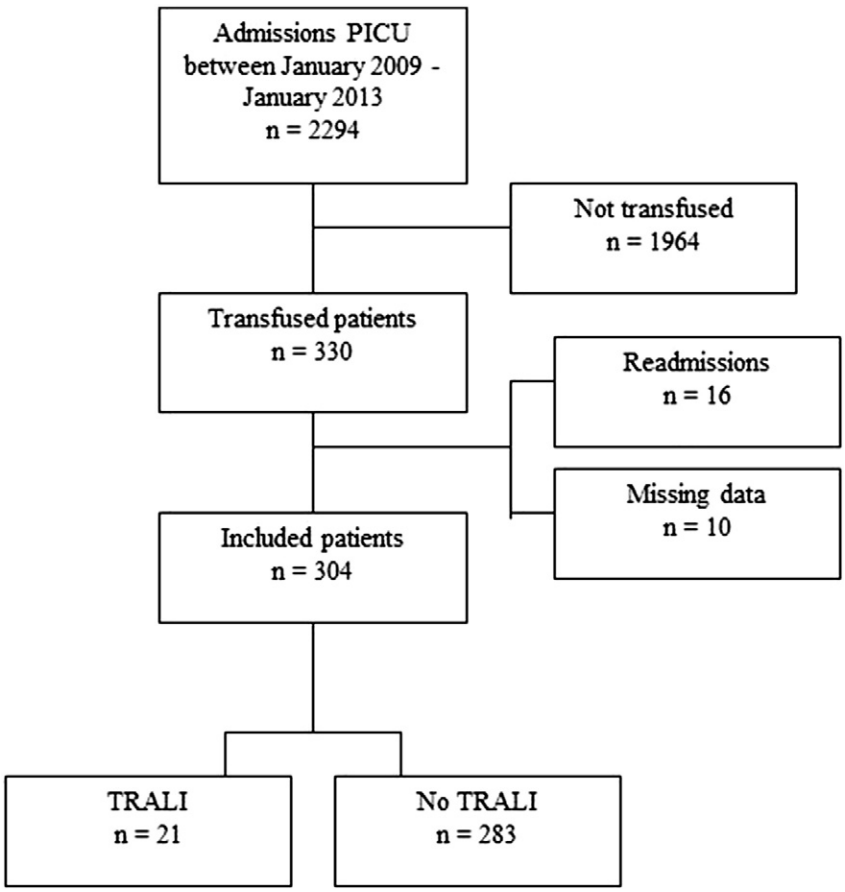

Figure. Flowchart outlining the inclusion of patients in this cohort study.