

Chapter 11

Transfusion and Acute Respiratory Distress Syndrome: Clinical Epidemiology, Diagnosis, Management, and Outcomes

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Overview

From an infectious disease standpoint, the overall safety of blood transfusion has improved over the past decade. Transmission of viral infections, including human immunodeficiency virus (HIV) and hepatitis C are as low as one per two million blood products transfused [1]. However, other transfusion related complications persist, which can be life threatening. Transfusion related acute lung injury (TRALI) is the most serious respiratory complication in transfusion medicine. Since 2003, it has been the leading cause of transfusion associated death in the USA. The Food and Drug Administration reports 43 % of transfusion related deaths due to TRALI from 2007 to 2011 [2, 3]. Due to the high morbidity and mortality, TRALI has moved to the forefront of transfusion medicine. As a consequence, a better understanding of the pathophysiology, risk factors, and mitigation strategies in TRALI prevention has developed.

Epidemiology

Definition

TRALI is defined as acute hypoxemia and respiratory distress within 6 h of a blood transfusion in the absence of hydrostatic pulmonary edema. The clinical correlation between blood transfusions and acute lung injury was first described in the 1950s [4].

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The association was made into a distinct clinical entity with specific clinical criteria in 1983 by Popovsky and colleagues and redefined by the National Heart, Lung, and Blood Institute (NHLBI), as well as the Canadian Consensus Conference (CCC) in 2004 [5–7]. Two key points were highlighted in the revision of the definition. The first was emphasizing an *acute* and *new* presentation of respiratory distress. The second focus was to eliminate other temporally associated, alternative risk factors to explain the new lung injury (Table 11.1). Two other terms were also defined—*Possible TRALI* and *Delayed TRALI*. Possible TRALI occurs when the acute respiratory distress takes place in the setting of a blood transfusion, as well as other co-existing risk factors for development of Acute Respiratory Distress Syndrome (ARDS), including: trauma, sepsis, pancreatitis, aspiration, inhalation, drug overdose, or burns. *Delayed TRALI* is defined as TRALI which occurs after 6 h but within 72 h of a blood transfusion (Table 11.1). These distinctions between TRALI, possible TRALI, and delayed TRALI help to further elucidate incidence, pathophysiology, and treatment of this condition by clarifying the disease for future research investigations.

Mechanisms of TRALI

Two pathophysiologic mechanisms of TRALI have been recognized, *immune-mediated TRALI* and *non-antibody mediated TRALI*. Anywhere from 65 to 90 % of reported cases are found to be immune-mediated TRALI, which occurs when leukoagglutinating antibodies from the donor blood bind to conjugate recipient antigens [8]. By definition, evidence of antibodies from the blood donor are present; most commonly anti-HLA and anti-HNA antibodies, with anti-HNA3a associated with worse clinical outcomes [9, 10]. The second mechanism for development of TRALI

Table 11.1 NHLBI/CCC definition of TRALI

TRALI	Possible TRALI*	Delayed TRALI**
<ul style="list-style-type: none"> •NEW, ACUTE onset of dyspnea and hypoxemia (PaO₂/FiO₂ < 300, SpO₂ < 90% on RA, or other clinical evidence of hypoxemia) •Bilateral pulmonary infiltrates on chest x-ray •No evidence of hydrostatic pulmonary edema •No temporal relationship to an alternate risk factor for new development of ARDS* •Symptoms occurring within 6 hrs of a blood product transfusion** 	<ul style="list-style-type: none"> •TRALI •WITH a temporal relationship to an alternate risk factor for new development of ARDS (ie-sepsis, aspiration, pneumonia, burns, inhalation, drug overdose, drowning, trauma, cardiac bypass, acute pancreatitis) 	<ul style="list-style-type: none"> •TRALI •Symptoms occurring > 6 hours but within 72 hours after transfusion of a blood product

is classified as non-antibody mediated TRALI and stems from an antibody independent mechanism. Approximately 15 % of TRALI falls into this category, in which no antibodies are found in the donor blood product. Silliman and colleagues have described the non-antibody mediated mechanism as a two-hit model. The first hit involves neutrophil priming and sequestration secondary to a preexisting condition in the recipient. In the second hit, biologic modifiers such as lipids in the blood product activate neutrophils and lead to capillary leak in the lung endothelium [11, 12] (see Chap. 10).

Risk Factors

Risk factors for the development of TRALI can be broken into two categories, recipient and donor related risks. The recipient of the blood product may have underlying disease states and clinical conditions, which put them at increased risk (Table 11.2). Also the donor profile and blood components being transfused may also put the recipient at higher risk for development of TRALI.

Recipient Risk Factors

Multiple recipient related risk factors are noted in the literature. Most of these studies are retrospective and small. However, it is evident from clinical data that the critically ill population is at the highest risk for the development of TRALI

Table 11.2 Recipient related risk factors for development of TRALI

Recipient related risk factors
Sepsis
Shock
Positive fluid balance
Liver disease/history of liver transplant
Chronic alcohol use
Active tobacco use
Mechanical ventilation/increased peak airway pressures
Increased IL-8 serum levels
Major surgery (i.e., cardiac, orthopedic surgery)
Hematologic malignancy
Massive transfusion
High APACHE II scores

[13]. In one multicenter, prospective trial, history of liver transplant, chronic alcohol use, active tobacco use, shock, increased IL-8 levels in serum, increased peak airway pressures of >30 cm H₂O on the ventilator, and an overall positive fluid balance were all significant risk factors for TRALI [14]. Multiple studies reveal sepsis and shock as major risk factors. Not only being critically ill, but also being on mechanical ventilation at the time of transfusion may increase risk independently. A prospective cohort study showed 33 % of patients on mechanical ventilation at the time of transfusion developed acute lung injury [15]. Multiple other studies have also shown recipient risk factors such as: major surgery within 72 h of blood transfusion, hematologic malignancy, higher APACHE II scores, and active liver disease [16]. The risk for development of TRALI also increases with the number of transfusions, as seen commonly in the trauma population where patients are receiving massive transfusions [13]. Not only critically ill patients, but cardiac and orthopedic surgery patients are also at higher risk for TRALI development [17]. The time on cardiac bypass appears to be correlated as well, with longer bypass times leading to higher risk of TRALI development [18]. Despite the multitude of recipient risk factors reported, most of which are seen in the critically ill population, TRALI is also reported in otherwise healthy individuals at the time of transfusion [19]. The development of TRALI in this healthy patient population supports the realization that the risk of TRALI is not dependent on the recipient alone.

Donor and Blood Component Risk Factors

All forms of blood products have been reported to cause TRALI, including: whole blood, packed red blood cells, apheresis platelets, fresh frozen plasma, cryoglobulin, intravenous immunoglobulin, granulocytes, and allogeneic stem cells [12]. However, blood products with higher plasma volume are at the greatest risk, specifically fresh frozen plasma, apheresis platelets, and whole blood. In the FDA reported cases of death due to TRALI, fresh frozen plasma was the most implicated [7]. In one retrospective cohort study from 2007, fresh frozen plasma and platelet transfusions led to a higher incidence of TRALI versus red blood cell transfusion in the ICU population [20]. It remains unknown the exact amount of plasma which must be transfused in order for TRALI to develop. Reports of as little as 10–20 ml of plasma transfused before TRALI development are in the literature; however, plasma volumes greater than 50–60 ml are thought to be the threshold which puts patients at a higher risk [12].

Another important risk factor is the gender of the donor, and preventive strategies in the past 15 years have focused on gender related donor deferral. Female, multiparous donors have allo-immunization from pregnancy. Blood from this particular group of donors has a much higher risk of TRALI development in the recipient secondary to the anti-HLA and anti-HNA antibodies, which bind to recipient antigens and lead to immune-mediated TRALI. The prevalence of antibodies in this

population increases with parity. A 26% approximate frequency of anti-HLA antibodies exist if a female has had more than three pregnancies [21]. Another potential risk factor where studies have shown controversial data is blood product storage time. Experts in the field hypothesize that longer storage times of red blood cells may lead to a higher incidence of TRALI. Experimental models in preclinical trials show a positive correlation between longer blood storage times and TRALI; however, there remains no overt clinical evidence to support the finding [22]. Studies done in the preemie population showed no difference in the incidence of TRALI based on blood storage time. An ongoing study in the adult intensive care unit population is underway that hopefully will help to clarify the importance of blood storage time as a potential risk factor [23].

Incidence

The true incidence of TRALI is unknown secondary to prior lack of a concise definition, the inconspicuousness of the diagnosis, and lack of a structured reporting system. It occurs in all age groups, including children and the geriatric population. It occurs at the same frequency in women and men. Reported TRALI incidence varies between 0.08 and 15% of patients transfused and 0.01–1.12% per product transfused, with the higher incidence in the critically ill patient population [24]. Up to 50–70% of patients in an intensive care unit receive some form of blood product transfusion, and more independent patient risk factors exist in the critically ill population, which may account for this increase in incidence (see section “Risk Factors”). Even though the overall reported incidence of TRALI remains low, it is almost certainly an under-recognized and underdiagnosed condition. In the setting of no gold standard for diagnostic testing, a passive reporting system, and an array of mild cases which do not meet the consensus definition of the disease, TRALI remains under-reported [25]. Despite the underestimated incidence of TRALI, the overall frequency has decreased since the mid-2000s secondary to preventative strategies for plasma and platelet transfusions (see section “Prevention”).

Blood Product Variation

As stated before, all blood products have been implicated in TRALI development, and the incidence of TRALI varies based on blood product components. Products with higher plasma volume have higher incidence of TRALI. Reports reveal incidences at approximately 1/432 whole blood products vs. 1/7900 fresh frozen plasma vs. 1/557,000 red blood cells [12, 22]. However, the incidence of TRALI in plasma products has decreased in the past decade secondary to risk mitigation strategies, leaving the incidence of red blood cell transfusions at a higher rate in the more recent years [26].

Diagnosis

Clinical Presentation

TRALI can present with a large variation in disease severity. By NHLBI and CCC definition 100% of patients with TRALI have hypoxemic respiratory failure and bilateral pulmonary infiltrates on chest X-ray. Clinically, the most common complaint of patients is dyspnea. However, a large number of patients are critically ill and on mechanical ventilation at the time of blood transfusions leading symptoms to be unhelpful. Despite patients being unable to report symptoms, clinical signs of respiratory distress and failure are present, typically within one to 2 h of a blood transfusion in the majority of patients. Predominately, patients are tachypneic, and in approximately one-third of patients, fever and/or hypotension may develop. Rarely patients may develop new onset hypertension. Most notably in the vital signs, SpO₂ should be decreased compared to before the transfusion. Patients on mechanical ventilation may experience a change in pulmonary compliance with an increase in peak and plateau pressures. Pink, frothy secretions from the mouth or endotracheal tube occur in roughly half of patients who develop TRALI. Physical exam should help rule out other etiologies of respiratory distress and should be thorough including a complete lung, heart, and skin exam. Lung auscultation reveals bilateral crackles. Exam findings suggestive of cardiac failure should not be present, such as jugular venous distention and an S3 on cardiac auscultation. It is important to keep in mind that very mild cases of TRALI do exist, which may not fall into the NHLBI and CCC definitions. Mild cases may go unrecognized or present with a similar presentation to the underlying disease process, albeit in a less severe form.

Diagnostic Workup

Practitioners should have a high index of suspicion for TRALI when administering blood products, especially in the critically ill population. Diagnosis can be difficult as there is no gold standard diagnostic test for TRALI. Any person who develops even the least amount of dyspnea or respiratory distress in temporal association with a blood product transfusion should have further clinical and diagnostic evaluation for TRALI. Patients who meet the 2004 NHLBI and CCC definition (Table 11.1) including, new hypoxemic respiratory failure with a PaO₂/FiO₂ ratio <300 and bilateral pulmonary infiltrates within a 6 h time frame from blood product transfusion, deserve further workup to confirm the diagnosis. One of the goals of the diagnostic workup should be to rule out other possible etiologies for the new development of ARDS, which would then classify the patient as possible TRALI. No diagnostic lab tests are available that confirm the diagnosis of TRALI. An arterial blood gas can be helpful to quantify the degree of hypoxemia. The most common laboratory finding is acute and transient leukopenia, which is thought to be secondary to neutrophil

sequestration into the pulmonary vasculature and can be seen in 5–35% of patients [27]. Thrombocytopenia has also been reported in TRALI. Other laboratory tests, although not diagnostic may also be helpful. In other etiologies of ARDS such as sepsis, a leukocytosis may be present. An elevated brain natriuretic peptide can be seen in transfusion associated circulatory overload (TACO) and should not be elevated in TRALI alone. As stated before, a chest X-ray revealing bilateral pulmonary infiltrates is a ubiquitous finding in TRALI, and should be performed for any patient with suspicion of the diagnosis. Historically the pulmonary infiltrates in TRALI were described as “white out lungs.” This may be the scenario in extreme cases; however, both alveolar and interstitial infiltrates have been described in a spectrum from bilateral and patchy to diffuse territories of the lung fields. Despite the findings being nonspecific, the presence of bilateral infiltrates should reach 100% in this patient population. The chest X-ray is also helpful to eliminate other etiologies of acute respiratory failure, such as pneumothorax.

Blood Bank Reporting

For any suspected TRALI reaction, it is of vital importance the associated blood bank be contacted. Typically a transfusion reaction lab panel is sent, which is directed by the blood bank or transfusion medicine director. The panel includes a complete blood count, haptoglobin, bilirubin, direct Coombs test, and most importantly HLA and HNA antibody testing in the donor blood sample. Anti-HLA and anti-HNA antibodies strongly support the diagnosis of TRALI but are not essential for diagnosis. 15–25% of TRALI reactions are found to be non-antibody mediated [21]. However, positive antibody results can guide future TRALI prevention if found in the donor blood product (see Section “Prevention”). Antibody testing may take days to weeks for results, and therefore no acute treatment decisions should be made based on antibody testing alone.

Differential Diagnosis

In distinguishing TRALI from other disease states it is important to consider other causes of ALI/ARDS, as well as other transfusion reactions.

Possible TRALI

In 2004, new terminology was instituted as part of the TRALI definition, termed, *possible TRALI*. This definition takes into account other etiologies of ALI/ARDS, which the patient may be at risk for at the time of blood transfusion (Table 11.1). Since no gold standard diagnostic test exist for TRALI, and it occurs most commonly in the critically ill population with multiple other comorbidities, possible

TRALI remains a very relevant diagnosis. If any of these other conditions exist or are suspected, a definitive diagnosis of TRALI cannot be made. Further diagnostic workup should be done in order to eliminate the additional etiologies. Fever can occur as part of TRALI; however, pneumonia, pancreatitis, and sepsis should be suspected as well as an etiology of the acute lung injury. CBC, blood cultures, and chest X-ray can all help to further delineate other disease states. Other conditions such as inhalation, drowning, cardiac bypass, drug overdose, and trauma may be more obvious from history alone.

Other Transfusion Reactions

Various other blood transfusion reactions exist, all of which can overlap with aspects of the clinical presentation of TRALI. Each blood transfusion reaction is managed differently, therefore it is vital to establish the correct diagnosis. The transfusion reaction that mimics TRALI the most is TACO (see Chap. 12). TACO may coexist with TRALI and distinguishing between these two diagnoses may be difficult (Table 11.3). Both conditions present acutely during or after blood product transfusion. Also, both lead to acute respiratory distress and hypoxemia with bilateral infiltrates on chest X-ray. While TRALI's clinical presentation stems from non-hydrostatic pulmonary edema with capillary leak, TACO is secondary to hydrostatic pulmonary edema. The two conditions are both transient but managed differently. Diuretics are the mainstay of treatment for TACO, but may be detrimental in the treatment of TRALI (see section "Medications"). A positive fluid balance is a risk factor for development of TRALI, and if the positive fluid balance is secondary to compromised cardiac function a higher awareness for TACO should exist. While no definitive test exists to distinguish between the two, diagnostic tools such as elevated jugular venous pressure, an S3 on cardiac auscultation, a transthoracic echo showing depressed cardiac function, and/or an elevated BNP may suggest TACO vs. TRALI. If the patient has a pulmonary artery catheter in place, an elevated pulmonary capillary wedge pressure and/or central venous pressure also

Table 11.3 Differentiating TRALI from TACO

Clinical characteristics	TRALI	TACO
SpO ₂	Hypoxia	Hypoxia
Blood pressure	Usually hypotensive	Usually hypertensive
Lung exam	Diffuse crackles	Diffuse crackles
Cardiac exam	+/- Tachycardia	JVD, +S3, +/- displaced PMI
CXR findings	Bilateral infiltrates	Bilateral infiltrates
PCWP/ CVP	Normal	Elevated
Arterial blood gas	Hypoxemia	Hypoxemia
CBC	Leukopenia, thrombocytopenia	Normal
BNP	Low/Normal	Elevated
Echo	Normal Cardiac function	Depressed cardiac function

favors the diagnosis of TACO. As stated before, chest X-ray is unhelpful in distinguishing between the two diagnoses.

Other transfusion reactions may also overlap in clinical presentation with TRALI; however, they are usually more obvious to diagnose. Like TRALI, an anaphylactic reaction from a blood product transfusion may also lead to hypoxia and hypotension. Conversely, the clinical presentation of patients undergoing an anaphylactic reaction may demonstrate signs of airway compromise, such as stridor, bronchospasm, laryngeal edema, and/or wheezing, as well as an associated rash, urticaria, and/or diarrhea, all of which are not seen in TRALI alone. In septicemia from blood product transfusion, which can occur in the setting of contaminated blood products, microbiology is usually positive. Patients may also have a leukocytosis, which is very uncommon in TRALI. Platelets are most commonly associated with septicemia from a transfusion. Lastly, hemolytic transfusion reactions develop acutely with blood product transfusion, but hypoxia and acute respiratory distress are not the mainstay. Fever and hypotension occur in almost all patients with hemolytic reactions and less often in TRALI. Laboratory tests will also reveal a hemolytic pattern, such as a low haptoglobin, elevated unconjugated bilirubin and an elevated lactate dehydrogenase.

Management

Similar to the diagnosis, the management of TRALI is also nonspecific. No exact therapy for TRALI exists, and supportive therapy is the mainstay for treatment. If TRALI is suspected while a blood product is actively being transfused, it should be stopped immediately. All subsequent blood product transfusions should also be held in the acute setting until the diagnosis is made and treatment ensued. As mentioned before, the blood bank or transfusion medicine physician should be notified with any suspicion of TRALI in order to potentially identify and exclude involved donors if relevant antibodies are present.

Supportive Therapy

Oxygen

Oxygen supplementation is the primary management in TRALI. Although mild cases are reported where little to no oxygen is necessary, almost all patients require some form of oxygen. Studies show up to 70–80% of patients develop severe enough hypoxemia to require mechanical ventilation [28, 29]. There are no specific studies looking at mechanical ventilation strategies in TRALI specifically; however, it is reasonable to adopt the ventilation strategies from the ARDS Network trial [30]. The restrictive tidal volume approach with tidal volumes set at 6 ml/kg of

predictive body weight vs. 12 ml/kg has been shown to improve mortality in ARDS, and therefore should be the mainstay ventilation approach in the TRALI patient population. Maintaining plateau pressures <30 cm H₂O has also been shown to improve mortality and the incidence of barotrauma in the ARDS population [30]. In severe cases where mechanical ventilation fails to support the patient's physiologic demands, the use of extracorporeal membrane oxygenation (ECMO) has been described in case reports [31, 32]. However, no randomized control studies exist to support the use of ECMO for TRALI specifically.

Hemodynamic Support

The volume status of patients who develop suspected TRALI should be examined carefully, as management decisions are dependent on this judgement. As mentioned above, in the patient who appears to be volume overloaded with depressed cardiac function the diagnosis of TACO should be strongly considered, and diuretics should be administered. Commonly patients who develop TRALI are found to be hypovolemic [33]. TRALI in the hypovolemic patient may lead to hypotension and shock. Intravenous fluids should be given in this setting, as well as pressors if needed, to support end organ perfusion during the acute episode.

Medications

Steroids

While steroids have been studied extensively in ARDS, no randomized control trials looking at the use of steroids in patients with TRALI have been completed. The use of steroids in the ARDS population remains controversial, but data suggest use after 14 days may be harmful [34]. In patients with TRALI, case reports with intravenous corticosteroids do exist [27]. However, in the setting of no true prospective clinical trials, the negative side effects, and the transient clinical course of TRALI, the use of corticosteroids is not routinely recommended in the treatment of TRALI.

Diuretics

Evidence from the FACTT trial supports the use of a conservative fluid strategy in the ARDS population [35]. However, as stated before patients who develop TRALI are at risk for hypotension and shock, especially in the setting of hypovolemia. Intravenous fluids are the mainstay of therapy for hemodynamic support early on in TRALI, especially without evidence of coexisting TACO. Diuretic therapy should be used judiciously in this patient population, as it may worsen outcomes early on. Based on evidence from the ARDS population, if patients are still requiring high levels of oxygen supplementation once they are hemodynamically stable and volume resuscitated, a role for diuretic use in TRALI may still exist [8, 36].

Prevention

With no specific management strategies for TRALI exist, prevention measures are of the utmost importance. Over the past 10 years policies have been put into place at blood product donation centers in order to guide risk mitigation. The largest risk mitigation strategies so far have focused on plasma donation. No practical risk reduction measures are established for red blood cell transfusion prevention from a donation perspective. Some experimental models suggest washing of stored red blood cell products to prevent TRALI, but it is yet to be determined if this strategy makes a difference and can be feasible in a clinical setting. However, strategies exist to assist in the prevention of all adverse transfusion reactions, most importantly being the use of conservative transfusion practices.

Restrictive Transfusion Strategy

An overall judicious approach to blood product transfusion is the simplest and most effective strategy for TRALI prevention. Evidence from a randomized, double-blinded control trial shows the incidence of ARDS is decreased with a conservative red blood cell transfusion strategy vs. a liberal one [37]. Other studies suggest FFP is still over utilized at times by physicians with no clear indications for its use [24]. With electronic medical records in the forefront of today's health care, data suggest that electronic decision support to further guide the ordering of blood product transfusions not only decreased the amount of blood transfusions given but also decreased the incidence of acute lung injury [38]. Blood utilization guidelines and blood conservation programs should be established in health care centers to help minimize unnecessary transfusions. A patient tailored approach should be taken for patients who do need non-emergent blood product transfusions. Patient related risk factors for TRALI should be considered, and an attempt to minimize these risk factors prior to transfusion is an important component of primary TRALI prevention.

Implicated Donor Deferral

As mentioned above, the reporting of any suspected or confirmed TRALI episode is vital to secondary prevention. The American Association of Blood Banks (AABB) advocates that implicated donors abstain from any type of blood product donation until leukocyte antibody testing has been complete. In the donors who are found to have leukocyte antibodies which match or are likely to match recipient leukocyte antigens, deferral from at least plasma and platelet apheresis donation is mandatory. If the donor is found to have anti-HNA3a antibodies, which have been shown to lead to an increase severity of TRALI, they are deferred from all types of blood donation [39].

Multiparous Female Donor Deferral

In the mid-2000s, risk mitigation strategies for TRALI were instilled in order to exclude “at risk” donors from certain types of blood product donation. An observational study, Leukocyte Antibody Prevalence Study (LAPS) looked at antibody levels in 8000 volunteers for blood donation using flow cytometry. Only 1–2 % of anti-HLA and anti-HNA antibodies were present in the male, never-pregnant female, and prior blood product recipient populations compared to multiparous female donors with approximately 24 % of antibodies present [40]. Other studies report higher frequency of antibodies in the multiparous, female population as well, putting patients who receive blood products from this population at an increased risk for immune-mediated TRALI [10, 41]. In 2007 the AABB published the recommendation, “...blood collecting facilities should implement interventions to minimize the preparation of high plasma-volume components from donors known to be leukocyte-allo-immunized or who are at increased risk of leukocyte allo-immunization.” Based on this recommendation, the deferral of multiparous, female donors from plasma donations was implicated. The policy to use solely male donors for plasma donation led to a two-thirds decreased incidence in TRALI [24]. Data also shows since the deferral of multiparous females from plasma donation, the reported cases of deaths to the FDA from plasma associated TRALI decreased from 48 % before 2007 to 27 % from 2008 to 2011 [42]. The multiparous, female donor deferral strategy also has been used in platelet apheresis donation; however, with the shortage of donors available to meet the demanding needs of platelets, it is not completely feasible to implement complete deferral of high risk donors.

Leukocyte Reduced Blood

Another option for primary prevention of TRALI is the concept of leukocyte reduced blood. Reduction of leukocyte antibodies in high volume plasma products has been shown to reduce TRALI incidence [21]. However, patients still may be at risk for the non-immune mediated form of TRALI.

Solvent Detergent Plasma

Pooled solvent detergent plasma was approved by the FDA in 2013 as an alternative to FFP. In observational data, there was no reports of TRALI in ten million units of solvent detergent plasma [43]. Multiple studies from other countries as well have confirmed the lack of TRALI in transfusions with solvent detergent products [8, 24, 44]. The pooling and dilution of anti-HLA antibodies is thought to play a large role in this decreased incidence. Potential risks of pooling high volume plasma products also exist including, exposure to multiple donors and increased transmission of viruses.

Outcomes

The majority of patients who develop TRALI require close monitoring in an intensive care setting. The degree of hypoxemia and lung injury is variable but commonly can be very severe. However, a subset of patients who develop TRALI will only require minimal supportive care and may even go undiagnosed. No studies have shown clinical severity correlating to the type of blood product or the amount of plasma transfused. Worse clinical outcomes have been shown in patients who are positive for HNA-3a and HLA-A2 antigens [9]. Despite the potential severity of TRALI, the timeframe is short-lived. Studies show that even when patients require mechanical ventilation, the respiratory distress from TRALI resolves on average within 48 h. In the patient population who is already critically ill, the time course may extend up to 3–10 days [14, 29]. One report found that 80 % of TRALI cases resolved within 48–96 h [8, 45].

Mortality Rates

Unlike ARDS from other etiologies where mortality rates can range from 29 to 70 %, TRALI has significantly lower rates of death. Studies show that mortality rates from TRALI alone range from 5 to 10 %, with higher percentages quoted from the ICU population [24, 46]. Reports as high as 67 % mortality have been shown in TRALI patients who were critically ill at the time of TRALI diagnosis; however, the cohorts utilized in these studies included some “possible TRALI” cases as well [14, 16, 32].

Sequelae of TRALI

Despite a very similar clinical presentation as ARDS, TRALI also differs in the fact that it has minimal to no physical or pulmonary sequelae. In ARDS, patients are known to have decreased exercise capacity and decreased lung function on pulmonary function tests for up to 5 years after initial pulmonary insult [47]. In patients who recover from TRALI there are no residual pulmonary complications. This population of patients returns back to baseline pulmonary function and does not have complications of pulmonary fibrosis. Permanent lung damage is rare [48, 49]. Based on limited evidence, it also appears patients who develop TRALI are not at increased risk for recurrent episodes of blood transfusion reactions from other donors. Caution should be taken with blood transfusions from previously implicated donors; however, overall patients should not be restricted from receiving blood products in the future [27, 50, 51].

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