



Transfusion-Associated Adverse Events

A Case Report of Nurse Hemovigilance and Recognition of Respiratory Distress

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ABSTRACT

Although blood transfusions are considered a potentially life-saving therapy, noninfectious and infectious adverse events can lead to significant morbidities and even mortality. Vital signs and visual observation of patients during blood transfusions are thoroughly taught in nursing school. Updated terms of *hemovigilance* and *transfusion-associated adverse events* (TAAEs) are presented through this case study. A patient with factor V deficiency, which requires chronic plasma transfusions, experienced 2 types of TAAEs, anaphylaxis and transfusion-associated circulatory overload. The patient's history and TAAEs are presented and discussed to provide evidence for the importance of vigilant bedside surveillance. Early identification of TAAEs may prevent unnecessary morbidity and/or mortality. The primary nursing functions and responsibilities are presented with algorithmic supplementation to facilitate better understanding of best practice. Ongoing assessment of hemovigilance practices is indicated to ascertain which monitoring tools can lead to optimal patient care.

Key words: coagulation, factor deficiency, plasma therapy, transfusion, transfusion-associated adverse event, transfusion reaction

INTRODUCTION

Blood transfusions are among the top 5 most frequent patient procedures in the United States, with more than 17 million blood products transfused per year.¹⁻³ *Hemotherapy*,

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another term for *blood transfusion*, includes the transfusion of whole blood, red blood cells (RBCs), platelets, plasma, and/or cryoprecipitate.^{4,5} Most commonly, hemotherapy is provided to patients for a multitude of reasons, including surgery, trauma, hemorrhage, or genetic or iatrogenic causes of cytopenias.⁶ Although blood transfusions are considered a potentially life-saving therapy, noninfectious and infectious adverse events can lead to fatalities.⁷ Hemovigilance, a surveillance system adopted in the United States in 2010, facilitates quality improvement and risk mitigation endeavors.^{6,8} Transfusion-associated adverse event (TAAE) data reported to the National Health and Safety Network (NHSN) is leveraged to advance transfusion science and to prevent morbidity and mortality resulting from transfusion.⁸ The term *transfusion reaction* is widely used and known among health care professionals.^{4,5} However, this terminology does not encompass all the potential safety events that can occur and may result in an adverse event.⁴ Therefore, the term *TAAE* was created and is being adopted internationally.^{3,4} Vigilant bedside surveillance of a patient receiving blood components is a core nursing function, foundational for safe transfusions, and a fundamental procedure in hemovigilance.^{4,8}

Perioperative hemotherapy accounts for 25% of the total blood products transfused annually in the United States.⁹

Given the frequency of need for transfusion and potential for bleeding during surgery, a patient's current hemoglobin, hematocrit, platelet count, and coagulation factors must be considered.⁹ Inborn coagulation errors, such as coagulation factor deficiency, can increase the risk of hemorrhage and potentiate negative patient outcomes¹⁰; adding to the complexity is the risk of TAAE.^{9,11}

The main objective of this case report was to demonstrate the importance of vigilant nursing surveillance before, during, and after blood transfusions to maximize early recognition of clinical deterioration and minimize adverse patient outcomes. The authors were involved in the patient's care delivery and/or in the development of a systemwide TAAE process. The patient's case was selected because 1 patient experienced 2 TAAEs. Institutional review board approval for retrospective case review was obtained prior to inquiry of the patient's electronic medical record. This is a case report of a teenage patient with deficiency of coagulation factor V requiring surgical repair of ventriculoperitoneal shunt (VPS). Exceptional bedside nursing surveillance identified early signs of a potentially life-threatening TAAE, facilitated timely intervention, and prevented escalation of care.

CASE PRESENTATION

Initial Diagnosis

The patient was a teenager with history of perinatal stroke (intraventricular hemorrhage) at 6 weeks of life. This resulted in right hemiparesis and hydrocephalus, a condition that causes extra cerebrospinal fluid (CSF) to accumulate in the brain. The patient underwent successful VPS placement, which is placement of a thin tunneled tube that drains extra CSF from the brain into the abdomen for absorption. Upon initial presentation for stroke, the patient was discovered to have factor V deficiency. Factor V is an essential protein for clot formation and is treatable only with plasma therapy. The deficiency most likely contributed to the patient's hemorrhagic stroke.¹² As the patient grew from childhood into adolescence, VPS revisions were required. Due to factor V deficiency, retroperitoneal and pelvic hematomas (unrelated to the procedures) required chronic plasma transfusions to provide factor V replacement. RBC transfusions were also required due to anemia from hematomas and after surgery. No other complications were reported.

First TAAE

The patient experienced a TAAE diagnosed as an anaphylactic reaction during a plasma transfusion. The department of allergy and immunology at the facility where the patient was being treated was consulted and provided recommendations for premedications prior to future transfusions and emergency medications at the bedside. Recommendations were to give diphenhydramine and hydrocortisone as premedications 15 minutes before plasma therapy began. Furthermore, orders were provided for epinephrine using

different routes (subcutaneous or intramuscular) dependent on the severity of reaction. During severe anaphylaxis, intramuscular is the preferred route for good absorption, but this requires the clinician to hold local pressure or ice application for 15 to 20 minutes.

Surgical Admission

The patient presented to the emergency center (EC) with complaints of severe headache, nausea, and upward gaze. A STAT computed tomography scan of the head was performed and revealed VPS malfunction. On admission from the EC, laboratory tests to assess coagulation were performed and factor V level was decreased at 27% (normal reference range is 59% to 150%). Given the need for urgent surgical intervention for VPS malfunction, the goal factor V level was set at 25% or higher. To maintain the level at or above the goal, the provider ordered 25 mL/kg of plasma to be transfused. Subsequently, approximately 2000 mL of fresh frozen plasma (FFP) was ordered, which required 4 separate bags that were to be transfused for 2 to 3 hours each. The FFP was thawed in the blood bank and dispensed sequentially to preserve the coagulation factor function. Both premedications were given as ordered. The bedside patient identification and blood product verification process were completed per institutional policy and procedure. The plasma hemotherapy continued intraoperatively and postoperatively.

On admission/postoperative day 2, the patient's factor V level was less than 20%; therefore, more plasma hemotherapy was indicated. The patient received premedications of diphenhydramine and hydrocortisone, and the first transfusion was administered without any adverse events. At shift change, the registered nurse (RN) started the second unit of plasma. Per the transfusion order, the rate of transfusion was started at 100 mL/h, with a goal to increase to 200 mL/h per the physician's order. The day-shift RN remained with the patient for the first 15 minutes of the transfusion to assess vital signs and to visually observe the patient for any signs of distress. The transfusion rate was allowed to be increased if vitals remained stable and there were no symptoms of a transfusion reaction.

Prior to increasing the transfusion rate to 200 mL/h, the RN noted that the patient's room air oxygen saturations decreased to <90% and the patient's respiratory rate increased to 34 breaths per minute. When asked, the patient stated, "I feel fine." However, the RN noted a cough, difficulty breathing, and tachypnea (Table 1). The RN immediately contacted the hematology physician on call. On arrival of the physician, the patient's room air oxygen saturation had decreased to 80%. The transfusion was stopped. Diphenhydramine, furosemide, and hydrocortisone were all given intravenously. A single nebulized albuterol treatment was given due to a change in respiratory assessment and a patient history of anaphylaxis. Additional support of 100% oxygen via nasal cannula was also initiated. On further assessment, the patient's signs and symptoms were not fully consistent with an anaphylactic reaction and the clinical team was unsure of the type of TAAE

TABLE 1**Patient Vital Signs Before, During, and After Case Study TAAE**

Time	Pretransfusion Start Time	15 Min After Start Time	1 h After Start Time	2 h After Start Time	4 h After Start Time
Heart rate	65	72	102	112	101
Blood pressure	130/72	135/75	138/79	133/98	137/76
Temperature (oral, °F)	97.7	98.7	Not obtained	98.3	98.1
Respiratory rate	25	28	32	29	35
Oxygen saturation (SpO ₂)	99%	Not obtained	80%	94%	97%
Oxygen device	Room air	Room air	Room air	2L oxygen nasal cannula	3L oxygen nasal cannula
Action taken	Assessment performed and proceeded with starting transfusion	Assessment performed	Stopped transfusion and notified provider team	Continued close monitoring, respiratory support, and diuresis	Continued close monitoring and respiratory support
Symptoms	None reported	None reported	Difficulty breathing Cough Increased respiratory rate Decreased SpO ₂	Difficulty breathing with mild improvement with oxygen support	Difficulty breathing and cough resolved after diuresis

Abbreviations: TAAE, transfusion-associated adverse event.

the patient was experiencing. The blood bank and transfusion medicine service were contacted, and diagnostic evaluations were ordered and quickly obtained. The tests included a STAT chest x-ray (CXR) and blood and urine laboratory tests to work up the TAAE. The CXR findings were consistent with bilateral pulmonary edema.

The laboratory evaluation did not suggest any signs of an acute hemolytic transfusion reaction. Therefore, the transfusion medicine service was able to clear the patient to receive more blood products if needed. However, given the CXR results, a pulmonary complication of transfusion was likely, and further assessment was needed to evaluate for transfusion-associated circulatory overload (TACO) versus transfusion-related acute lung injury (TRALI). The patient received additional furosemide for diuresis, and transfusions were put on hold given that the patient was not experiencing any active bleeding. Subsequent factor V levels were not obtained because the patient was now >24 hours postoperative and not showing any signs of bleeding. After diuresis, the oxygen requirement improved to 2 L via nasal cannula, and by postoperative day 4, the patient no longer required oxygen and was able to be discharged from the hospital on postoperative day 5.

BACKGROUND

Plasma therapy began in World War I and World War II to treat hemorrhage among wounded soldiers. Up to 55% of the total blood volume is made up of plasma. Coagulation factors, such as factor V, are present in plasma. Therefore, plasma is provided as hemotherapy to treat hemorrhage or

to prevent bleeding due to underlying genetic or iatrogenic causes of coagulation factor deficiency when specific concentrates are not available.¹²

Hemorrhagic stroke, or spontaneous intracerebral hemorrhage (ICH), is bleeding into the brain parenchyma, not caused by trauma, and is the second most frequent stroke subtype.¹³ The occurrence of ICH in the perinatal period is infrequent and often associated with underlying genetic conditions.¹⁴ Factor V deficiency is also a rare disorder that predisposes the patient to bleeding.¹⁰ The prevalence of factor V deficiency, an autosomal recessive trait, is approximately 1 per million people in the general population.¹⁰ Factor V is essential for the generation of thrombin, which is essential to the formation of a blood clot.¹⁰ Plasma products contain factor V; therefore, plasma hemotherapy is administered to this patient population, especially perioperatively. Doses of 15 to 20 mL/kg are required initially, and then subsequent doses of 5 mL/kg can be provided.¹⁰ In general, a level of 15% is considered safe if the patient does not have other current bleeding risk factors.¹⁰

Transfusion reactions occur in 1% to 3% of all transfusions.^{5,6,12} However, this is suspected to be an underestimation because of the passive surveillance and reporting of most hospitals and blood banks. In a study that included active surveillance of all transfusions by specially trained research nurses, researchers found that hospital systems underreported cardiopulmonary TAAEs by 30% to 50%.¹⁵ This transfusion reaction rate does not include additional safety-related incidents, which is reported to occur at a rate of 0.3% of all transfusions.¹⁶

Plasma products account for approximately 15% of reactions, with the most frequent being allergic in nature.¹⁷

Anaphylaxis is the most severe form of allergic reactions and is defined by the World Allergy Organization as “a serious life-threatening generalized or systemic hypersensitivity reaction.”¹⁸ Pulmonary TAAEs can also occur and include TRALI, TACO, and transfusion-associated dyspnea (TAD).^{3,6,8} TRALI is an immunologic and potentially fatal complication of transfusion that includes difficulty breathing and severe hypoxemia requiring respiratory support.¹⁹ In contrast, TACO occurs due to volume overload, leading to cardiogenic pulmonary edema.⁷ TAD is more ambiguous and is defined by the NHSN as “acute respiratory distress occurring within 24 hours of cessation of transfusion.”⁸ In addition, an allergic reaction, TACO, and TRALI definition criteria cannot be met for TAD to be diagnosed.⁸ Given the large volume required for plasma hemotherapy (25–30 mL/kg) to improve patient coagulation factors, there is an increased risk for TACO.¹² The typical volume of each unit of plasma is 200 to 250 mL. A jumbo plasma unit can have between 200 and 350 mL and is commonly pooled from multiple donors.¹² In addition, plasma contains antibody proteins, which can lead to a severe immunologic reaction known as TRALI.³ For patients with pulmonary edema associated with a transfusion, differentiating TRALI, TACO, and TAD is challenging, and the transfusion medicine service guides clinicians in evaluation and diagnosis.²⁰

Pediatric patients experience transfusion reactions twice as often as adults.²¹ Acknowledgement of the developmental and physiologic differences between adults and children is essential when providing blood transfusion therapy.²² Pediatric patients have unique differences of the cardiorespiratory system, such as greater airway resistance due to airway radius, different use of accessory muscles for breathing, and higher metabolic requirements.²¹ Recent studies demonstrating unique biochemical profiles among laboratory testing support the theory that pediatric patients will potentially experience a different response to blood transfusion therapy.¹¹ Definitions of TRALI, TACO, or TAD do not incorporate special considerations of pediatric patients, further contributing to the unknown prevalence of these pulmonary TAAEs among pediatric patients.^{21,22} A need for more research among pediatric hemotherapy recipients is recognized, and studies are in progress.²³

IMPLICATIONS FOR NURSES AND PROVIDERS

Nurses are essential to the recognition, management, and reporting of TAAEs.⁴ Integral to bedside surveillance is a thorough patient assessment that includes core vital signs of heart rate, blood pressure, temperature, and respiratory rate.^{4,24–26} Throughout medical and nursing literature, the vital sign frequency of within 30 minutes before start of the transfusion, within 15 minutes after start time, and at completion of the transfusion is consistently recommended.^{26–29}

However, the frequency to assess vital signs during the transfusion, whether it be hourly or less frequent, or how long after the transfusion is complete, is inconsistent in the literature, and the evidence to mandate frequency is insufficient.²⁶ Historically, the leading cause of death in the United States due to hemotherapy was acute hemolytic transfusion reaction, in which vital sign changes and patient symptoms occur rapidly, typically within the first 15 minutes.^{7,27} However, TACO is now the leading cause of transfusion-associated fatality.⁷ Signs and symptoms of TACO and TRALI typically are noted in patients well after the 15-minute time point and can occur up to 12 hours after cessation of the transfusion.^{18,30} In addition, a single center, retrospective review of adult patients who experienced a transfusion reaction on an oncology ward revealed that the mean time to reaction was 92 minutes.²⁶ Therefore, transfusion safety experts advocate for transfusion bedside surveillance to continue past transfusion completion time.²⁶

A TAAE process was proposed and approved by the medical staff and nursing Quality Practice Council and physician and nursing executive partners (Figure 1). Education was provided at multiple nursing forums, including the Education Council and Quality Practice Council. The annual training required by regulatory bodies was updated to reflect the newest practice guidelines. Hemotherapy information was updated to include extensive review of the institutional blood administration policy and procedure, transfusion reactions, and safety incidents, and an introduction to hemovigilance was begun. The education was provided via electronic training. Additionally, a nursing transfusion safety committee was formed, and more than 20 nursing members from various disciplines gather monthly to review transfusion-related safety events, including TAAEs and good catches, with the goal of learning from the past and advancing transfusion safety for patients. The inaugural nursing transfusion safety committee served as reviewers and codevelopers of the nursing education.

The hospital went live with an electronic medical record blood product administration module that requires electronic verification of positive patient identification to augment the 2 licensed health care professional verification processes. The new process requires electronic scanning of the patient's identification band (located on the patient) and the blood product. This provides verification that the transfusionist is giving the intended product to the correctly matched patient. The electronic identification step, however, does not assess or verify for a safe volume or safe transfusion rate.

A fatal TAAE that occurred at a neighboring hospital initiated a system-wide campaign to engage all health care providers in improving hemovigilance awareness.³¹ An interprofessional team of more than 60 individuals collaborated to reassess the entire transfusion process. The TAAE process was updated to incorporate key learnings. The department of nursing professional development was engaged in updating the nursing education to include just-in-time training huddles. The iterative process of optimizing

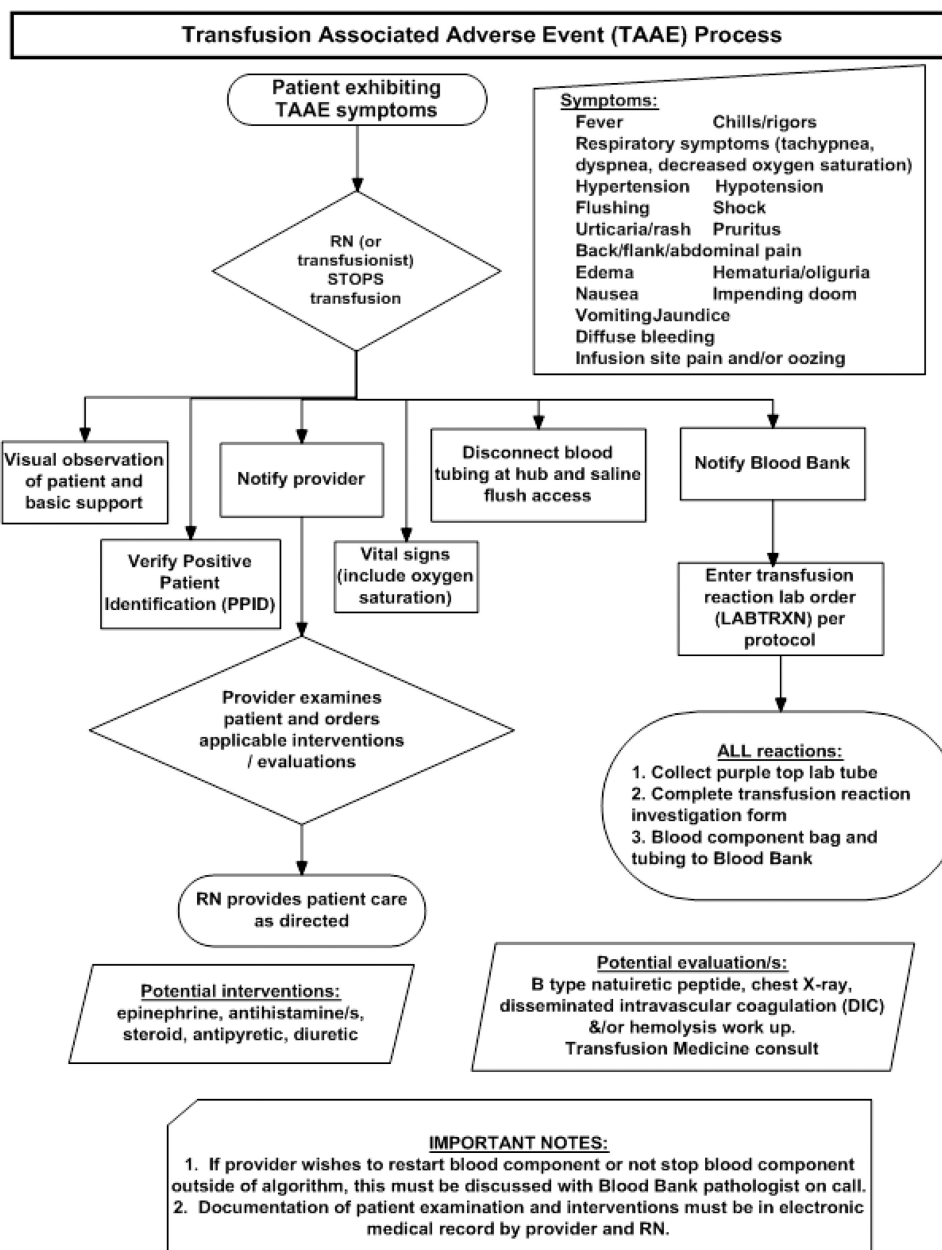


Figure 1 Transfusion-associated adverse event (TAAE) process. (Credit: Texas Children's Hospital)

hemovigilance was crucial to ensure that new learnings and evidence were incorporated into processes and practice.

The exceptional care provided by the day- and night-shift nurses of the presented case undoubtedly prevented escalation of care to the pediatric intensive care unit (PICU) and mitigated further morbidity and mortality. The patient's lung changes on CXR were quickly resolved with diuresis, and within 48 hours the patient no longer required oxygen therapy. The physician team was convinced that if the transfusion continued and responsiveness was delayed, the patient would have required transfer to the PICU and intubation with mechanical ventilation. The importance of bedside vigilance, nursing surveillance, close monitoring, and critical thinking skills of nurses and other health care providers while providing hemotherapy to patients cannot be overstated.⁴

Nurses have a unique opportunity to lead awareness and education of hemovigilance. All nurses are leaders and can provide unique insight to patients and colleagues in their specific area of responsibility. Education of hemovigilance begins in nursing school and must be incorporated into teaching about the blood transfusion process. Hemovigilance can also be incorporated with graduate nurse orientation, as it is with medication safety training. Nurse supervisors and educators play pivotal roles in advocating for ongoing hemovigilance awareness. Involvement with annual required training is an example of enhancing the learning process. Finally, active participation in ongoing writing and updating of transfusion-related policies and procedures is critical to advancing hemovigilance and advocating for transfusion safety for patients and nurses.

CONCLUSIONS

Given the frequent use of hemotherapy for patients of all ages and in both inpatient and ambulatory settings, nurses and providers must equip themselves with knowledge of hemovigilance procedures. Vigilant bedside surveillance of hemotherapy recipients can result in early identification of TAAEs and prevent morbidity and mortality. The nurse's primary function is to recognize when a patient is experiencing unexpected symptoms, stop the transfusion, and immediately notify a provider and the blood bank. Support of patients' clinical symptoms, timely reporting of concerning symptoms, and clear documentation can facilitate an optimal and safe transfusion experience.

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