

Blood Transfusion Reactions

Introduction

Many individuals require blood components and blood products. As per the BC Transfusion Medicine Advisory Group (BCTMAG), a blood component is “at therapeutic component of blood intended for transfusion,” and includes red cell, platelets, plasma, cryoprecipitate, and granulocytes. The BCTMAG describes blood products as “any therapeutic product, derived from human blood or plasma, and produced by a manufacturing process,” including human serum albumin, immunoglobulin preparations, and recombinant or porcine coagulation factors. Receiving any of these products may result in a transfusion reaction.

Definitions

In accordance with national consensus guidelines, a transfusion reaction is defined as “an undesirable and unintended occurrence during or after the administration of any blood component/product, that could be considered to be related to the said product.”

Although blood transfusions are generally safe, adverse reactions may occur for a number of different reasons. Most of the time, the reaction is mild and non-life threatening, but serious reactions do occur and require immediate treatment.

Blood transfusion reactions can be classified based on the timing of onset (acute vs. delayed) and the pathophysiological mechanism (immune vs. non-immune related). Acute reactions occur within 24hours of the start of the transfusion, whereas delayed reactions occur more than 24hours after the start of infusion. Immune reactions typically involve antibody reactions between the donor and recipient’s cells. Non-immune reactions may be caused by the properties of the different components within the stored blood.

In addition, blood transfusion reactions may be caused by introduction of infectious organisms and secondary sepsis.

The following is a table summarizing the most common blood transfusion reactions:

Table 1. Common blood transfusion reactions

| | Acute | Delayed |
|------------|--|--|
| Immune | ABO incompatibility Allergic reaction Anaphylaxis Acute Hemolytic Transfusion Reaction Febrile Non-Hemolytic Transfusion Reaction Transfusion-Related Acute Lung Injury | Delayed Hemolytic Transfusion Delayed Serologic Transfusion Reaction Allo-Immunization Transfusion-associated Graft versus Host Disease Post-transfusion Purpura |
| Non-immune | Transfusion-Associated Circulatory Overload Hypotensive Transfusion Reaction Metabolic imbalance | Infectious (HBV, HCV, HIV, EBV, CMV, syphilis, malaria, West Nile virus, lyme disease, prion |

| | | |
|--|------------------------|---|
| | Infectious (bacterial) | diseases) Iron overload IVIg aseptic meningitis |
|--|------------------------|---|

The most common causes of transfusion-related deaths across all age groups in Canada are transfusion related acute lung injury, transfusion associated circulatory overload, acute haemolytic transfusion reaction secondary to ABO incompatibility, and transfusion associated sepsis.

Pathogenesis and Clinical Presentation

The clinical presentation of the different types of blood transfusion reactions varies depending on the pathogenic mechanism. Although the same reactions can occur in both pediatric and adult populations, the frequency of occurrence varies for some conditions. Note that different transfusion reactions may present with similar signs and symptoms, and therefore be difficult to differentiate.

The following is a table summarizing the pathogenesis and clinical presentation of the most common transfusion reactions:

Table 2: Pathogenesis and Clinical presentation of common blood transfusion reactions

| Transfusion reaction | Pathogenesis | Clinical presentation |
|--|---|--|
| Transfusion related Acute lung injury | <ul style="list-style-type: none"> - Leukocyte antibodies in the donor blood attack host - Associated with higher concentrations of plasma, e.g.: fresh frozen plasma | <ul style="list-style-type: none"> - Within 2 to 6hrs of start of transfusion - Shortness of breath, work of breathing - Coughing - Tacchypnea, hypoxemia - Tachycardia - Hypotension - Fever - Bilateral pulmonary infiltrates |
| Transfusion associated circulatory overload | <ul style="list-style-type: none"> - Rapid or excess volume delivery in a susceptible patient (e.g.: neonate, cardiac abnormality, delicate hemodynamic status, renal failure) | <ul style="list-style-type: none"> - Within 6hours of end of transfusion - Shortness of breath, chest tightness - Cough - Headache - Tacchypnea - Tachycardia - Hypotension - Signs of volume overload: jugular venous distension, cardiac S₃, - Pulmonary edema |
| Acute haemolytic transfusion reaction | <ul style="list-style-type: none"> - ABO incompatibility - Other RBC antigen | <ul style="list-style-type: none"> - Fever - Chills, rigors |

| | | |
|--|---|--|
| | incompatibilities (eg. Rh, Duffy, Kell) | <ul style="list-style-type: none"> - Apprehensiveness - Pain in lower back, flanks, chest, along infusion vein - Hypotension - Bleeding - Hemoglobinuria - Renal failure |
| Sepsis | <ul style="list-style-type: none"> - Bacterial contamination in blood product enter recipient - Result in bacteremia and immune reaction. | <ul style="list-style-type: none"> - Fever, chills, sweats - Warm or clammy skin - Vomiting - Rash - Tachycardia, tachypnea - Hypothermia |
| Delayed haemolytic transfusion reaction | <ul style="list-style-type: none"> - Allo-immunization to other antigens. | <ul style="list-style-type: none"> - Fever, chills - Jaundice - Malaise - Back pain - Unexpected anemia, usually within first two weeks after transfusion |
| Febrile non-hemolytic transfusion reaction | <ul style="list-style-type: none"> - Humoral and cellular-mediated inflammatory reaction - Second most common type of blood transfusion reaction in pediatric population | <ul style="list-style-type: none"> - Onset 1-2 hours after transfusion - Fever - Chills, rigors, malaise - Headache - Nausea/ vomiting - Increase in diastolic BP |
| Allergic transfusion reaction | <ul style="list-style-type: none"> - Inflammatory reaction resulting in release of histamine by mast cells - Most common type of blood transfusion reaction in pediatric population | <ul style="list-style-type: none"> - Urticarial rash - Pruritus - Nausea, vomiting - Diarrhea, abdominal cramps - Anxiety - Hypotension (less common) - Dyspnea (less common) |
| Anaphylactic transfusion reaction | <ul style="list-style-type: none"> - Severe allergic reaction against transfused blood | <ul style="list-style-type: none"> - Immediate respiratory distress (seconds to minutes) - Upper airway edema→obstruction - Lower airway signs and symptoms (bronchospasm, wheezing, retractions, SOB) - Loss of consciousness - Vomiting - Hypotension, weak pulses, with ultimately circulatory collapse |

Assessment

The cornerstone to the approach of most problems in medicine includes a thorough history and physical exam. This is then followed by ancillary investigations as required.

Important aspects to include in the history of a patient suspected of developing a transfusion reaction include:

- Confirm that the patient had recently received a blood transfusion
- Constitutional symptoms, including fever, chills, sweats, decreased appetite
- Elicit symptoms of difficulty breathing, such as dyspnea or wheezing
- Gastrointestinal symptoms, including abdominal cramps, diarrhea, nausea, vomiting
- Headache, dizziness
- Past medical history: previous transfusions and whether there were any reactions

Perform a comprehensive physical exam, with particular attention to:

- Vital signs: presence of hypotension, hypertension, tachycardia, tachypnea, fever $>38^{\circ}\text{C}$ and a rise of $>1^{\circ}\text{C}$ since the onset of transfusion, sudden onset hypoxemia $<90\%$
- Patient affect: anxiety, apprehension
- Erythema or tenderness at IV site
- Cutaneous changes: erythema, urticaria, pallor, jaundice
- Appearance of urine: red or brown urine may indicate hemolysis and hemoglobinuria

Investigations

- ABO blood typing and cross matching: to assess donor-recipient ABO and Rh compatibility
- Direct antiglobulin test (direct Coombs test): to identify immune-mediated hemolysis
- Complete blood count (CBC): to assess extent of anemia, rule out DIC
- Serum haptoglobin: low values suggest intravascular hemolysis
- Urinalysis: look for hemoglobinuria
- Serum creatinine and blood urea nitrogen (BUN): monitor renal function
- Serum LDH: elevated values can be due to hemolysis

Management

Whenever a transfusion reaction is suspected, it is crucial to stop the transfusion and send the blood product with its tubing to the blood bank for further testing. As with all potentially fatal reactions, initial management is aimed at establishing and maintaining a patient's ABCs. Next, reconfirm that the patient is receiving the correct product, unit/lot, and that it is destined for this specific patient. Notify the blood bank of any suspicions or errors. Finally, investigation as appropriate, including blood cultures, chest radiographs. Ensure that a member of the health care team informs the patient of what is going on.

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Writer: Donald Yung

Resident Editor: Katryn Paquette