Type of article : *Review Article*

Blood Transfusion and Its Effects

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Abstract

Sometimes blood transfusion causes adverse reactions. Better prognosisis obtained by understanding the clinical features of acute and delayed transfusion reactions.Current clinical practise involves better and newer blood screening methods to reduce the complications. Selecting leukoreduction of red blood cells (RBCs) and male donors for plasma and restriction of RBC storage avoids infectious complications.

Key words: *Adverse reactions, blood transfusion, complications.*

Introduction

An adverse reaction of blood transfusion is an inadmissible response or effect in a patient to whom blood or blood component administered temporarily.[1]Currently even in developed countries, the risk to the patient lies in non-infectious complications of transfusions is higher where they account for significant morbidity and mortality.[2] The American Association of Blood Banks technical manual issues guidelines for the identification , diagnosis, analysis and classification of non-infectious transfusion reactions, which acts as a ready reference for clinicians and other health care providers dealing with blood transfusion.[3] The acute and delayed NIATRs are classified based on time of occurrence and it is further divided by presumed aetiology into immune-mediated and non-immune mediated subtypes. NIATRs classification, pathophysiology, clinical presentations, and management is bestowed in table 1.

Acute Non-Infectious Blood Transfusion

Adverse reactions which are occurring within 24 h after transfusion are classified as Acute immune mediated blood transfusion reactions and Acute Non-immune mediated – blood transfusion reactions. Acute immune mediated – blood transfusion reactions are sub-classified into

Acute haemolytic transfusion reactions:

A haemolytic transfusion reaction is one where transfusion produces symptoms and clinical or laboratory signs of increased red cell destruction. In acute haemolytic transfusion reactions (AHTRs) symptoms can be observed within minutes after initiating the transfusion. There are certain common laboratory features present . They are haemoglobinemia, haemoglobinuria, decreased serum haptoglobin, unconjugated hyperbilirubinaemia, increased Lactate dehydrogenase and serum glutamic-oxaloacetic transaminase levels and decreased haemoglobin.

TABLE 1: NONINFECTIOUS ADVERSE TRANSFUSION REACTIONS (MODIFIED FROM AABB TECHNICAL MANUAL) [3]

Febrile nonhaemolytic transfusion reactions :

Febrile nonhaemolytic transfusion reactions (FNHTRs) exhibits unexplained rise in temperature of at least 1°C during or shortly after transfusion. Antipyretic premedications may prevent fever but they do not usually mask chills and rigors, which are caused by cytokine mediated systemic inflammatory response. Other causative agent of fever should be ruled out before deriving a diagnosis of FNHTR. FNHTRs are observed most commonly after platelet transfusion (up to 30% of platelet transfusions) than red blood cells (RBCs) because platelets are stored at room temperature and thus it induce leucocyte activation and cytokine accumulation.[4] Treatment of FNHTRs is symptomatic.

ALLERGIC REACTIONS

Urticaria

Urticaria is the mild form of an allergic reaction that appear suddenly causing itching and it lasts for hours or up to several days before fading. More extensive cases is escorted by angioedema. The percentage of urticaria is 1-3%.[3,5] Severe reactions are treated with methylprednisolone (125 mg intravenously) or prednisone (50 mg orally).

Anaphylaxis

Anaphylaxis is a severe form of an allergic reaction with a prevalence of 1:20,000-1:50,000 transfusions,[6]where severe hypotension, shock, and loss of consciousness may develop .[7] Anaphylaxis is usually observed in IgA deficient recipients because it is caused by antibodies against donor IgA. [8] The term 'anaphylactoid' refers reactions with symptoms similar to anaphylaxis but they are not mediated by IgE. Supposing that the patient is unconscious or in shock, adrenaline is given intravenously with cardiac monitoring.[9]

Transfusion Related Acute Lung Injury

Transfusion related acute lung injury (TRALI) is a variant of acute lung injury (ALI) and it plays a vital role in transfusion-associated morbidity and mortality. TRALI is defined as:[1]

- Acute lung injury with hypoxemia and PaO2 / FiO2 ≤300 or SpO2< 90 % on room air
- Bilateral pulmonary oedema on frontal chest radiograph
- No indication of left atrial hypertension
- No pre-existing ALI before transfusion
- Onset of symptoms within 6 h of transfusion
- No temporal relationship to an alternative risk factor for ALI.

The prevalence of TRALI has been estimated nearly 1 in every 5000 blood component transfusions. Antibodies can be developed against leucocytes (polymorphous neutrophil [PMN]), both for neutrophils and human leucocyte antigen after contacting foreign antigens through pregnancy, transfusion, or transplantation. Two different aetiologies have been explained.[10] It can be a single antibody-mediated event including the transfusion of anti-human leukocyte antigen (HLA) or antigranulocyte antibodies into patients whose leukocytes produce the cognate antigens. In several cases with antibodies, the source of the antibody is the donor. A two-event model of the mechanism of TRALI has also been proposed where neutrophil activation results in pulmonary endothelial damage, capillary leakage, and pulmonary oedema. Immediate respiratory support produces marked clinical improvement within 48-96 h.[11]In order to protect the blood supply, the United Kingdom (UK) has disqualified all multiparous females from plasma donation because plasma from females might be a major factor in TRALI.[12]

Management of TRALI

Treatment is supportive. Productive measures for decreasing the prevalenceof TRALI involving the use of male plasma and apheresis platelets. Understanding of blood component and patient risk factors for TRALI will optimistically lead to novel treatment and preventive strategies for decreasing the risk of life-threatening syndrome. TRALI management comprises of preventing future adverse reactions.[13]By cross-matching donor plasma against recipient's leucocytesincompatibility and HLA and HNA antibodies are tested. A donor with antibodies which are incompatible with the patient is expelled from further blood donation for transfusion.

ACUTE NON-IMMUNE MEDIATED ADVERSE REACTIONS

Sepsis

Transfusion-related sepsis is fatal. The diagnosis depends on the basis of any one of the clinical features:

- v Fever ≥39°C (102°F) or rise of ≥2°C (3.5°F);
- v Tachycardia (heart rate >120/min, or rise of >40/min);
- v Shaking chills and
- v Alteration in systolic blood pressure (BP) (i.e. >30 mmHg rise or drop in systolic BP) within 90 min of transfusion.[14]

Patient may develop shock ,renal failure and disseminated intravascular coagulation (DIC) in severe

cases . In order to diagnose the transfusion-related sepsis and differentiating it from AHTRs and FNHTRs organism from both the patient and the remainder of the bag are isolated .[15] Since platelets are stored at room temperature, they are more sensitive than RBCs to bacterial contamination with a higher risk. Management of transfusion related sepsisinvolve broad spectrum antibiotics and other standard care for sepsis. Choosing "diversion technique" during blood collection and screening the blood for bacterial contamination decreases the risk.[16]

NonImmune Haemolytic Reactions

Due to transfusion Red cell haemolysismay happen in several nonimmune-mediated causes (also known as pseudohaemolysis) such as temperature-related or mechanical, erroneous use of blood warmer, use of hot water bath and microwave oven, using a needle with a small bore size or using a rapid pressure infuser, RBCs are infused through same tube with hypotonic solution or with pharmacologic agent. Treatment is similar to AHTRs.

Transfusion Associated Circulatory Overload

Morbidity and mortality rateis associated with transfusion-associated circulatory overload majorly.[17] Patients who are at greatest risk aregeriatric patients, infants, patients with renal failure, hypoalbuminaemia, anaemia, congestive heart failure or fluid overload or history of plasma transfusion. signs Signs and symptoms include dyspnoea, orthopnoea, cyanosis, tachycardia, jugular venous distension, and pedal oedema.[18] Increased BP with widening of the pulse pressure is seen in < 1% of transfused patients. TACO may expedite acute pulmonary oedema within 6 h after blood transfusion. Management is providing mechanical ventilation, fluid restriction, diuretics.[19]

Transfusion Associated Dyspnoea

It is characterised by respiratory distress within 24 h of transfusion and it is not similar to other allergic reaction.[1]

Acute Hypotensive Transfusion Reaction

Sudden drop in BP with absence of other causes of hypotension. Still it responds quickly to transfusion inhibition and supportive treatment.[20] Patients with unusual hypotensive transfusion reactions must be given a trial of washed blood products. Bedside leucoreduction filters have been involved often in acute hypotensive transfusion reaction even though it has also occurred with prestorage leucofilters.[21]

Citrate Toxicity

Transfusion of largeblood volumes containing citrate causes increased plasma citrate chelates calcium ions resulting in hypocalcaemia. It is caused by citrate overload andcan be treated by decreasing infusion rate. Calcium replacement is signified in massively transfused patients, especially those with severe liver disease or severe symptoms of hypocalcaemia.[22]

Hyperkalemia

After an hour of transfusion , total extracellular potassium load, which is 5 mmol/l or ≥1.5 moml/l net is increased. This is referred to as transfusion-related hyperkalemia.[1]

Hypokalemia

Hypokalemia is more prevalentthan hyperkalemia after transfusion since donor red cells re- accumulate the ion intracellularly, and citrate metabolism leads to further movement of potassium inside the cells. No treatment is needed.

Coagulopathy

Coagulopathy is seen in massive transfusion especially if the blood volume is initially replaced by red cells and fluids during absence of two blood volume. This causes dilution of platelets and clotting factors.

Hypothermia

Caused by transfusion of cold blood products in larger volume .This leads to cardiac arrhythmia and also interrupts with platelet function, clotting factor interaction and bleeding time.[23] Blood warmers are used to prevent hypothermia.

Air Embolism

Use of plastic blood bags reduces air embolism. Howeverair enters a central catheter during blood administration sets or blood bags are being changed

or if blood in an open system is transfused under pressure.[24]After transfusion delayed reactions occurs after 24 h or up to month/ years .

DELAYED IMMUNE MEDIATED REACTIONS

Delayed Haemolytic Transfusion Reactions (DHTRS)

DHTRs are observedbased on reactivation of pre-existing antibodies against antigens on transfused red cells. Symptoms may extend from days to weeks after transfusion. No clinical or laboratory features of haemolysis can be observed , however, alloimmune red cell antibody is detected . This is known as delayed serologic transfusion reaction (DSTR). Blood group antibodies associated with DHTRs/DSTRs are Kidd, Duffy, Kell, and MNS systems, in order of decreasing frequency.[18]DHTRs need no treatment because as antibody synthesis increases, red cell destruction occurs.

Transfusion Associated Immunomodulation

Transfusion associated immunomodulation (TRIM) is defined as the down-regulation of recipient's cellular immune response caused due to transfusion of allogeneic blood.[25] TRIM is likely to be mediated by allogeneic leucocytes or their soluble products. One of the reasonable mechanisms is immune deviation towards T-helper lymphocytes type 2 cytokine characterised by secretion of interleukin (IL-4), IL-5, IL-10 cytokines with low T-helper lymphocytes type 1 cytokines namely IL-2, IL-12, and interferon-γ. Using autologous blood or prestorageleucofiltered blood reduces the adverse reactions.[26]

Transfusion-Associated Graft Versus Host Disease (TA-GVHD)

(TA-GVHD) is a clinical syndrome characterized by fever, maculopapular rash advancing to haemorrhagic bullae, enterocolitis with watery diarrhoea, elevated liver function tests, pancytopenia and characteristic findings of histological appearances on biopsy which significantly starts 8-10 days after transfusion.[27] TA-GVHD also occur after transfusion from a blood related donor who is homozygous for an HLA haplotype to a heterozygous recipient (one-way haplotype match).[28]Mortality is 90%eventhough it is rare . Hence TA-GVHD is prevented by irradiation of all cellular blood components (RBCs, platelets, and granulocytes), particularly in patients who are under risk of TA-GVHD.[29]

Post Transfusion Purpura (PTP)

It is a rare complication of transfusion with female predominance occurring between 1 and 24 days after transfusion with a mean of 9 days. Patients significantly exhibits purpuric rash and thrombocytopenia (platelet counts often < 10,000/μL) resulting in bleeding from mucous membranes ,gastrointestinal and urinary tracts. Intracranial haemorrhage is the primary cause of mortality. Antibodies against HPA-1a is the causative agent in several cases although, antibodies to HPA-1b, other platelet antigens, and HLA antigens are also involved. High dose ofintravenous immune globulin is given as treatment .[30]

DELAYED NON-IMMUNE MEDIATED REACTIONS

Iron Overload

Patients who receive frequent blood transfusion for diseases such as thalassemia, sickle cell disease, and other chronic anaemia are at the higher risk for iron overload. RBC unit contain nearly 250 mg of iron. Due to RBC destruction, the majority of the released iron cannot be excreted and is stored in the body as haemosiderin and ferritin. Transferrin becomes saturated after infusion of 10-15 units of RBCs to a non-bleeding patient and iron is stored in the reticuloendothelial system, liver, heart, spleen, and endocrine organs resulting in tissue damage leading to heart failure, liver failure, diabetes and hypothyroidism.[3]

Conclusion

Acute transfusion reactions are at greater risk for developing serious adverse reactions or events. For a better prognosis, awareness about various clinical features of acute transfusion reactions with a capability to predict the serious reactions on time is necessary. Observation and monitoring are needed throughout transfusion. Standard operating procedure comprising the details for documentation, reporting, evaluation, and follow-up of all adverse reactions is mandatory . In current clinical practice , evidence based approach of Restrictive strategy" or "Conservative approach"

of blood transfusion for decreasing the number of unwanted transfusions has made a gross change.

Ethical Clearance – Not required since it is a review article

Source of Funding – nil

Conflict of Interest – nil

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