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Review Article

Blood Component Therapy in the ICU for the Paediatric Patient

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Abstract: Blood and its components have been as important as drugs in the medical armamentarium. Whole blood on processing furnishes packed RBCs, platelets, plasma, cryoprecipitate, immunoglobulins, albumin, and specific coagulant Factors. Given that each transfusion is an invasive and immunogenic procedure, focus is now centered on possible ways of reductions in transfusions. Studies have propagated the concept of restrictive transfusion strategies for packed RBCs. The indications and triggers for plasma and platelet transfusion also have been strictly defined. The physiology and unique long-term consequences associated with transfusion related complications in children makes it important to establish different guidelines for the Pediatric ICU. The decision to transfuse however remains a clinical judgement individualized to each patient based on the known facts.
Keywords: Blood components, packed RBCs, platelets, plasma

ARTICLE

Children are not small adults. Their developing bodies make their physiologies vary at different stages of growth. This needs to be remembered especially when dealing with critically ill children in the ICU. Blood and its components have been as important as drugs in the medical armamentarium.

Whole blood on processing furnishes packed RBCs, platelets, plasma, cryoprecipitate, immunoglobulins, albumin, and specific coagulant Factors. Each of these on separation requires different storage and utility conditions. Given that blood as a whole is still not reproducible artificially, and that platelets and factors in whole blood lose their effectivenesson storage, whole blood is now rarely used other than in exchange and autologous transfusions, with emphasis being given to use of components. Whole blood can be reconstituted by combining packed RBCs with fresh frozen plasma [1]. As transfusion medicine progresses apheresis has now made it possible to obtain single components from individual donors, thus, increasing donation frequency with reduction in donor exposure and its risks. Given that each transfusion is an invasive and immunogenic procedure, focus is now centered on possible ways of reductions in transfusions.

This article aims to touch upon the unique needs of blood components in critically ill children in the ICU. Transfusion triggers in children are divided based on ages more and less than 4 months. This article deals with blood component therapy in children more than 4 months of age. Anaemia, thrombocytopenia, hypoalbuminaemia, and coagulopathies are frequent in the PICU. But how less is too less? This question has no defined answers. Guidelines for transfusion in the PICU are not all defined on good quality evidence, and all come with the prelude underscoring the importance of individualizing the need for a transfusion based on clinical assessment and physician judgement.

TRANSFUSION OF RBCs

Anaemia is rampant in the PICU, due to blood loss, chronic illness, bone marrow failure, procedural blood draws especially in infants and smaller children. The body has a huge margin for compensation in anaemia. Changes in cardiac output, blood distribution, and RBC production come into play to ensure adequate oxygen delivery (DO2) to cells inspite of reduced Hb.

Severe anaemia facilitates a greater oxygen extraction from cells [2].

Certain conditions specific to intensive care unit admissions as well as to children can impair the adaptive mechanisms. Children have greater metabolic demands for oxygen. Those at the lower age spectrum also have physiologically increased heart rates with reduced capacity for cardiac compensation. Increased foetal variant of Hb makes cellular extraction difficult. PICUs also see more cases of congenital heart diseases with normal Hb requirements as high as 20gm/dl. Conditions like MODS and sepsis decrease the body's capacity for compensation even further. This explains the higher Hb levels needed in critically ill children [3-5].

Studies in patients refusing transfusion for religious reasons and in children that could not receive transfusions due to absent resources found that an Hb of <5 results in greater mortality. Ischaemic heart disease and critical illness requires an even higher trigger [6-9].

The Hb at which a patient must be transfused is not defined. RBCs transfusions are fraught with complications. TRIM with its predisposition to MODS in patients with sepsis is a known risk of RBC transfusion [10]. Storage of RBCs decreases 2, 3-DPG, and increases free Hb which binds with NO causing microcirculatory vasoconstriction [11-13]. Changes in haematocrit with RBC transfusion may lead to microcirculatory stasis. The immunologic complications of RBC transfusion can be minimized with leucocyte reduction (less than 5×106 leukocytes per unit) [14], with pre-storage reduction being superior. Leucocyte reduction though widely practiced in the USA and European countries, is not standard of care in developing countries.

Given this background, practice patterns are advocated to be goal- directed toward attaining an Hb that is adequate for the physiology of the patient and his disease [15]. The seminal TRICC and TRIPICU trials have advocated a transfusion trigger of 7gm/dl in stable critical patients [1]. No conclusive trials are available for transfusion needs in unstable critical children like those with acute massive bleeding or uncontrolled sepsis. Some data suggests RBC transfusion to maintain SvCO2 >70% in these patients [16-18]. Data for transfusion in cardiac disorders especially cyanotic heart diseases are still awaited for conclusive determinants of RBC needs.

Certain specially processed packed RBCs including washed, irradiated, dedicated, autologous and cytomegalovirus (CMV) seronegative units are required in certain special clinical situations like sickle cell anaemia, infants, and immunocompromised children.

TRANSFUSION OF PLASMA

Plasma frozen within 6-8 hours of collection, known as fresh frozen plasma (FFP), contains about 87 % of Factor VIII present at the time of collection and, according to standards in most countries, must contain at least 0.70 UI/mL of Factor VIII. Several countries also use plasma frozen within 24 h of collection, known as frozen plasma (FP). Factor VIII levels in frozen plasma are approximately 70–75 % of the levels present at the time of collection [19].

The appropriate use of plasma is limited to the treatment or prevention of clinically significant bleeding due to deficiency of coagulation factors. Vitamin K deficiency states, DIC, massive transfusion, warfarin associated intracranial bleeding and isolated congenital coagulation factor deficiency for which a safer and/or more appropriate product does not exist are valid indications for a plasma transfusion. Plasma is also used in exchange transfusion in conditions like thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), Guillain-Barré syndrome, acute disseminated encephalomyelitis (ADEM), and sepsis, though the role of intravenous immunoglobulins is under review for the same. FFP is contraindicated for intravascular volume expansion or repletion (where crystalloids, synthetic colloids or purified human albumin solutions are preferred), correction of hypoproteinaemia, hypogammaglobulinaemia, and the treatment of hemophilia A or B and von Willebrand disease (where desmopressin, virus-inactivated plasma-derived or recombinant factor concentrates are preferred) [20].

Transfusion of plasma is associated with a greater risk of TRALI and TACO [21].

TRANSFUSION OF PLATELETS

Thrombocytopenia is defined by a platelet count <150,000/mm3. A low platelet count and/or significant platelet dysfunction places a patient at risk for bleeding because of an impaired ability to form a platelet plug. Causes of thrombocytopenia in the ICU include sepsis, DIC, massive transfusion, bone marrow histiocytic hyperplasia with hemophagocytosis (acquired hemophagocytosis syndrome), as well as drug-related and heparin-induced thrombocytopenia. Platelet dysfunction can be due to toxins, drugs (salicylates, nitric oxide etc), ECMO, renal failure; and inherited diseases.

Platelet concentrates can be prepared from separation from whole blood or via apheresis. Both

types of platelet concentrates are stored at 20–24 °C for up to 5 days. This predisposes platelets transfusions to be a major source of bacterial infection due to contamination.

A platelet transfusion is indicated if the platelet count of a patient with an active haemorrhage falls below 50,000/mm3, or if the haemorrhage is severe and there is platelet dysfunction, as occurs frequently following cardiopulmonary bypass. Consider the risk of pulmonary haemorrhage in mechanically ventilated patients with platelets <50,000/mm3. A threshold of 100,000/mm3 is generally recommended for patients with multiple trauma, central nervous system injury, or for patients on extracorporeal membrane oxygenation (ECMO) (19). In patients with thrombocytopenia due to decreased platelet production, prophylactic platelet transfusion should be considered if the platelet count is <10,000/mm3 or if there are additional risk factors for bleeding.

Platelets are associated with a sevenfold increased risk of acute transfusion reaction compared to RBC.

Platelet transfusion should not be used for the treatment of idiopathic thrombocytopenic purpura except in the presence of intra-cerebral or life-threatening bleeding. Platelets are also contra-indicated in cases of heparin-induced thrombocytopenia and of thrombotic thrombocytopenic purpura. Alternatives to platelet transfusion, such as DDAVP or antifibrinolytic agents, should be considered as first choice therapies when appropriate [22].

TRANSFUSION COMPLICATIONS

Transfusion associated reactions are many and mostly under detected and underreported. By definition early reactions occur while the transfusion is being given or within 24 hours of the transfusion. Late and delayed reactions can manifest days and even years later. A transfusion reaction in a paediatric patient can have life-long repercussions. Transfusion transmitted infection ricks though lowered after intense testing for pathogens is still a risk in developing countries where regulatory systems are often lax or non-existent.

Fever is the most frequent reaction to a blood product transfusion. A febrile non-hemolytic transfusion reaction. (FNHTR) is defined as a *de novo* rise in temperature equal to or greater than 1 °C that cannot be explained by the patient's clinical condition (i.e. other causes of fever must be ruled out).

Acute hemolytic transfusion reactions are characterized by hemoglobinuria and/or hemoglobinemia (blood level of free Hb above normal range) with at least one of the following symptoms and signs: *de novo* fever, dyspnoea, hypotension and/or tachycardia, anxiety/agitation, pain.

A TRALI is an acute lung injury (ALI) that appears during or within 6 h after the end of a transfusion.

Massive transfusion is defined as the administration of more than one blood volume of blood products within a 24 h period, or more than 50 % of the circulating blood volume in 3 h or less, or ten RBC units in adults. Serious acute complications of massive transfusion include fluid overload, hypothermia, coagulopathy and thrombocytopenia, acidosis, citrate intoxication, hyperkalemia and hypocalcemia [23, 24].

CONCLUSION

Transfusion medicine, especially transfusion in the paediatric population is currently a dynamic area of research. Regional guidelines and regulations regarding the collection, storage, requisition, monitoring, dosing, and indications are available. The evidence for and against transfusion in children is often extrapolated from adult studies. Limited resources and infrastructure along with unique presenting conditions of PICU admissions in developing countries makes it incumbent upon the treating physician to be through in his or her understanding of the pathophysiology of diseases in children before deciding to transfuse.

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