BLOOD TRANSFUSION FOR THE CRITICALLY ILL

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ABSTRACT

The critically ill patients are often multi-systemically dysfunctional and requiring metabolic and/or blood transfusion support. Blood support for patients ranges from whole blood to components (packed cells, platelet concentrate, fresh frozen plasma and growth factor replacement) therapy. The predisposing factors for transfusion in critically ill include sepsis, overt or occult blood loss (including frequent blood sampling), decreased production of endogenous growth factors (e.g. erythropoietin), systemic inflammatory response and immune-associated functional deficiency.

There is a common occurrence of anaemia and wide usage of packed red cells in the critically ill patient. Efficient use of blood and blood components transfusion can improve clinical outcome, restore organ functions, and reduce mortality in the critically ill. There is an increasing need to explore and use growth factors more in the management of critically ill individuals.

INTRODUCTION

A critical illness is a life-threatening multisystem process that can result in significant morbidity and mortality.[1] Characteristic key features of critically ill patients are severe respiratory, cardiovascular or neurologic derangement, often in combination.[2] Hence, in most patients, the critical illness is preceded by physiological derangement and deterioration, but evidence suggests that early signs are often missed.[1]

Blood transfusion is a commonly used medical procedure that involves the transfer of screened blood or blood products obtained from one person (donor) into another person's circulation (recipient) through an intravenous route. It is primarily aimed at replacing diminished blood or blood products or targeted at enhancing functional activity. Blood transfusion in critically ill patients is an important component of their management. It can serve as life-saving resuscitative care, supportive care, and treatment of the primary critical illness and prevention of a secondary complication(s).
This review examines the use and application of blood and blood components therapy to manage critically ill individuals.

RED BLOOD CELL TRANSFUSION

Anaemia is common in critically ill patients affecting about 95% of Intensive Care Unit(ICU) patients by the third day.[3] The reasons for this include: acute blood loss, sepsis, iatrogenic blood loss for diagnostic testing, blunted red cell production from decreased production of erythropoietin, haemodilution secondary to fluid resuscitation, abnormalities in iron metabolism.[4,5] Red blood cell (RBC) transfusion rates in the ICU has been reported to be about 20%-40%, with an average of 2-5 units per individual.[6] RBCs are often transfused to increase oxygen transport and delivery and prevent tissue hypoxia by restoring tissue oxygenation. However, evidence suggests it has not been seen to improve oxygen consumption.[4,6]
The heterogeneity of critical illness and the absence of universally accepted guidelines influence RBC transfusion practice in ICUs worldwide.[7] The transfusion requirement in Critical Care (TRICC) trial recommends a transfusion trigger of 10g/dl in the liberal strategy and 7g/dl in the restrictive strategy, it demonstrated that a restrictive strategy was equivalent to a liberal transfusion strategy but was superior and associated with less mortality in less acutely ill patients.[7]

In the setting of a critically ill patient, factors affecting clinical outcomes following RBC transfusion include:

- Age of the blood: RBC storage is associated with adverse changes in erythrocytes. Standard practice worldwide involves transfusing the oldest compatible RBC unit, which increases the likelihood that RBCs older than 2 weeks will be transfused into critically ill patients as it can be stored for up to 42 days.[6]

- Type of critical illness: Patients with cardiac disease are transfused at higher haemoglobin thresholds, and evidence suggests cardiac disease to be an independent predictor of mortality.[8]

- Other factors include: patient characteristics such as the severity of the illness, dose or amount of blood transfused, development of hyperkalemia, length of stay in the ICU.[3,6,9]

Complications of RBCs transfusion could be infectious, which could be viral, parasitic or bacterial, although the frequency of this has reduced in the last decade; or non-infectious, globally referred to as Non-infectious Serious Hazards Of Transfusion(NISHOT), which is now more common and leads to greater morbidity and mortality includes febrile, allergic/ anaphylactic and hemolytic transfusion reactions, transfusion-related acute lung injury(TRALI), transfusion-associated circulatory overload(TACO), Transfusion-Related Immunomodulation(TRIM). [4,5]

An alternative to blood transfusion involves the use of blood conservation techniques which includes the use of haemostatic agents (antifibrinolytic agents, desmopressin, and recombinant activated factor VII, artificial oxygen carriers (haemoglobin substitutes) and blood recovery techniques.[4]

PLATELET TRANSFUSION

Thrombocytopenia is a very common haemostatic disorder in critically ill patients. They could have abnormalities of platelet number and function, which are the most common coagulation disorders seen among ICU patients and is an independent predictor of mortality in adults.10–12 A systematic review by Phil Hui et al. showed that thrombocytopenia was present in 8.3% to 67.6% of adult patients on admission to the ICU and acquired by 13% to 44% of patients during their ICU stay.[12] This can be caused by increased consumption, decreased production, drug interactions, dilutional or distributional causes.13 Platelet transfusions are commonly used in the ICU; 9% to 30% of critically ill patients receive a transfusion.[12]

Its indication (figure 1) could either be therapeutic in patients who are bleeding or prophylactic to reduce the risk of bleeding in patients with thrombocytopenia; although its benefit in non-bleeding critically ill patients with thrombocytopenia has been questioned.[14] However, platelet transfusions are generally contraindicated in Thrombotic Thrombocytopenic purpura (TTP) or Type II Heparin-Induced Thrombocytopenia (HIT), in these cases, it may fuel thrombosis and worsen clinical signs and symptoms.[13]

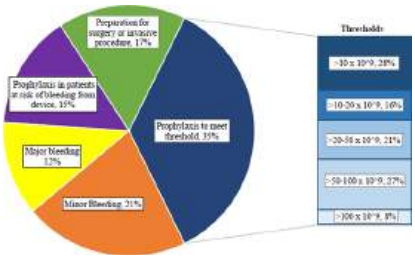

Figure 1: Indications for platelet transfusion.[15]

Local clinical guidelines and recommendations for platelet transfusion thresholds for critically ill patients vary and are based largely on expert opinion, but the decision to transfuse must always consider clinical conditions.[13,16] A threshold platelet count of 5,000 to 10,000/µl can be used in patients with no bleeding or only petechiae and ecchymoses, while a higher threshold of 15,000 to 20,000/µl is recommended in patients with concomitant fever or infection.[13] Extensive mucous membrane bleeding dictates platelet transfusion irrespective of platelet count, to avoid significant haemorrhage. In patients with active bleeding or in need of invasive procedures, the threshold platelet count should be 50,000/µl and 100,000/µl if neurological complications like intracranial bleed may have occurred.[13,16]

Studies have shown platelet transfusion to be independently associated with nosocomial infections. Other complications include severe allergic reactions, transfusion-related acute lung injury, and thrombosis;[12,14] which affects the overall outcome of patients.

TRANSFUSION OF PLASMA DERIVED PRODUCTS

The plasma is the fluid portion of the whole blood obtained via apheresis and contains plasma proteins such as albumin, immunoglobulins, acute phase proteins, and pro and anticoagulants.[17] The variety of plasma products in clinical use includes fresh frozen plasma (FFP), plasma frozen within 24hrs (FP), cryosupernatant, cryoprecipitate-reduced plasma.

Others include:

- Factor VIII,
- Factor IX,
- Factor VIIa,
- Factor VIII Inhibitor Bypassing Agent (FEIBA),
- Prothrombin complex,
- Antithrombin III,
- Protein C,
- Fibrogammin,
- C1 esterase inhibitor,
- Factor XI and
- Factor XIII.

Although plasma products' transfusion plays a crucial role when indicated, many studies have shown that a considerable percentage of perioperative plasma transfusion in the ICU is inappropriate.18-22 Relevant factors like INR, coagulation test results, amongst others, should be closely scrutinized to determine the necessity of such transfusion in the critically ill to avoid inappropriate transfusion of plasma products. FFP is frozen within 8 hours of collection, stored between −18°C and −30°C,[23] and can be used up to 1 year after donation. Once thawed, it can be kept refrigerated for up to 5 days.

Transfusion of FFP is indicated in the following conditions;

- Plasma protein deficiencies. [24]
- Case of multiple coagulation factor deficiencies with associated severe bleeding disseminated intravascular coagulation and massive transfusion.[25-26]
- As a component of plasma exchange in patients with thrombotic thrombocytopenic purpura.[26]
- Emergency reversal of warfarin toxicity when massive haemorrhage is present, and prothrombin complex concentrates are unavailable.[26]

Although FFP has its various benefits in the critically ill,[27] an undesirable effect seen with FFP is the development of antibodies capable of causing complications like hemolytic reactions and transfusion-related acute lung injury.[28] Cryoprecipitate is a blood product obtained from fresh frozen plasma. It contains fibrinogen, von-Willebrand factor, factors VIII and XIII, and fibronectin.[29] Cryoprecipitate is the cold precipitable protein fraction obtained from FFP thawed at 1–6°C. Cryoprecipitate is indicated in patients with von Willebrand's disease and haemophilia.[30]

Cryoprecipitate is re-suspended in 9–16 mL of residual plasma supernatant, refrozen, and stored at −18°C for up to 1 year. This supernatant plasma extracted from cryoprecipitate is known as Cryosupernatant. Cryosupernatant differs from cryoprecipitate in that it has lower levels of fibrinogen and Factor VIII.[30]

HAEMATOPOIETIC GROWTH FACTORS IN THE CRITICALLY ILL PATIENTS

Haemopoietic growth factors are involved in the production of the various blood cells from progenitors in the bone marrow, making them useful in a range of clinical situations. Erythropoietin (EPO) is a 165 amino acid protein belonging to the type 1 cytokine family with a molecular mass of 30kDa and was first discovered by Carnot and DeFlandre in 1906.[31]

Erythropoietin is a hematopoietic growth factor responsible for red blood cell production made by kidneys in adults and the liver in fetuses. Various researchers have reviewed the use of recombinant human erythropoietin in the management of the critically ill.[32-33] Preclinical trials indicate that not only does EPO relieve anaemia, but it also limits organ dysfunction associated with stroke, myocardial infarction, sepsis.34 Erythropoietin has also been used to manage CKD-related anaemia[35].

One of the downsides to the use of EPO is the 7-8 days period it requires to have an effect on the hematocrit level,31 which may be fatal in a critically ill patient but more suited for the treatment of chronic illnesses. Critically ill patients commonly develop anaemia during the acute recovery period; EPO plays a major role in the treatment of resulting ischemic stroke.[36]

Granulocyte Colony Stimulating Factor (G-CSF) comes in numerous formulations (e.g., filgrastim) and acts mainly on the neutrophils. It is indicated in immunodeficient conditions like Chemotherapy-induced neutropenia and congenital neutropenia.[37] On the other hand, GM-CSF stimulates the production of monocytes, eosinophils, and neutrophils and is also indicated in Chemotherapy-induced neutropenia.

Oprelvekin is a recombinant interleukin-11 that stimulates megakaryocytes 'production and maturation to produce platelets.[37] Although it is indicated in the prevention of Chemotherapy-induced thrombocytopenia, studies have shown it to produce severe side effects like oedema, cardiac arrhythmias, and dyspnea.[37] There is also evidence that suggests the possibility of antibody development against Oprelvekin.[38]

CONCLUSION

Blood transfusion is a common intervention in critically ill patients and can be life-saving but has also been associated with several adverse effects which could be severe; hence this must be considered before transfusion. The general approach should be minimization and strategies employed at reducing blood loss with an increasing need to explore the use of growth factors.

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