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Blood Component Therapy

Primer of Blood Products

WHOLE BLOOD
Description-The product of one unit of donated blood plus ACD anticoagulant/preservative (520ml). By definition contains one unit of plasma and cells. Can be stored for 5 weeks. .
Indications- Increasingly used in trauma as it provides both red cells, plasma, and some platelets.

PACKED RED CELLS (RBC)
Description-The remaining red cell mass after most of the plasma is removed is called the "packed" red cell unit (Hct = 70-80%), and so red cells are often called "packed" red cells or PRBC". To improve the flow a blood and to provide "nutrients" for the red cells a preservative is added. For example, in the Pacific Northwest region, the Red Cross supplies AS-1 red which reduces the hematocrit to about 60%. The volume is about 340ml. In the average adult one unit of RBC raises the hematocrit by 3%.
Indications-RBC are used for increasing red cell mass and thus oxygen delivery in patients who are severely compromised by their anemia

NOT indicated for anemic patients who have reversible anemias (iron deficiency for example) unless they are severely symptomatic. Young otherwise healthy patients can tolerate hematocrits in the high teens by increasing cardiac output to maintain normal oxygen delivery to the tissues. There is no evidence that "topping off" the hematocrit to above 30% before surgery improves survival or wound healing and leads to increase infections and thrombosis. Randomized clinical trials have shown for any patients - include those with GI bleeding - there seems little advantage to hematocrits higher than 21% unless coronary artery disease is present where 24% may be a better goal.

PLATELETS
Description-One platelet concentrate (one unit of random donor platelets) is derived from one unit of donor blood. Single donor plateletpheresis can be used to harvest platelets. One unit of single donor (pheresis) platelets is equivalent to 5-6 platelet concentrates. One platelet concentrate can raise the platelet count by 5-7,000/uL. Platelets are mildly "stunned" while in storage and it takes 4 hours for transfused platelets to be fully functional in the circulation. A pool of five platelet concentrates contains enough plasma to be the equivalent of a unit of FFP (all coagulation factors except the labile V and VIII). HLA-matched platelets are single donor pheresis units

that are from a HLA-matched donor. This product should only be ordered if there is evidence of HLA antibodies (see below). Remember always to check platelet counts 15 minute after platelet infusion. A poor 15 minute count may be indicative of HLA antibodies. A good 15 minute count but poor 24 hour count is more suggestive of consumption-fever, sepsis, drugs. etc., and not an indication for HLA matched platelets.

Indications – For chemotherapy patients a transfusion trigger of 10,000/uL is appropriate. For patients who are bleeding or needing surgery 50,000/ul. One should order "single-donor plateletpheresis product" when giving patients platelets. Although not always available, use of this product will expose the patient to one donor instead of 6 – 8 and have the benefit of being leukodepleted.

NOT indicated for stable thrombocytopenic patients with platelets counts over 10,000/uL. Also if platelets are given to patients with thrombotic thrombocytopenic purpura it may worsen the disease. Even with low counts, patients with immune thrombocytopenia should not be transfused unless they have life-threatening bleeding.

Platelet alloimmunization Patients exposed to cells with different HLA types will develop antibodies to HLA antigens. This is most common in patients who have received previous transfusions of blood that is not leukodepleted, or patients who have been pregnant. Since platelets carry class I HLA antigens they will be rapidly destroyed by HLA antibodies. In the past, patients who were transfused for aplastic anemia or myelodysplasia as many as 90% became HLA immunized. Nowadays the incidence is less but can be seen in patients previously pregnant or transfused. Patients who have developed HLA antibodies usually respond better to platelets matched for HLA antigens. Unfortunately some patients will either be a rare HLA type or so heavily immunized that they will not respond to any platelet transfusion. The importance of alloimmunization centers on two concepts - recognition and avoidance. Patients with HLA antibodies will often fail to have an increment of their platelet counts with transfusions. Thus patients who do not increase their count 15 minutes after the transfusion may have HLA antibodies. One can test for anti-HLA antibodies, since some patients instead have specific antiplatelet antibodies that will not respond to HLA matched platelets. In patients who are planned to undergo transplant or aggressive chemotherapy that have been pregnant or previously transfused it is wise to check anti-HLA antibodies so one can plan their transfusion needs. The evidence suggests that it is transfused white cells that are responsible for initiating the anti-HLA response. Trials have shown that giving leukodepleted blood products may reduce the incidence of alloimmunization, so patients who are not HLA alloimmunized should receive only leukodepleted products.

Bleeding in the Platelet Refractory Patient

Bleeding in patients who are refractory to platelet transfusion presents a difficult clinical problem. If patients are demonstrated to have HLA antibodies, one can transfuse HLA-matched platelets. Unfortunately, platelet transfusions are ineffective in 20 - 70% of these patients. Platelets are distributed as HLA-matched if they match even on one HLA locus but only the 3-4 loci match are effective. Since some loci are difficult to match effective products may be unavailable. As many as 25% of patients have anti-platelet antibodies in

which HLA-matched products will be ineffective. In the patient who is totally refractory to platelet transfusion, consider drugs as an etiology of antiplatelet antibodies (especially vancomycin). Use of antifibrinolytic agents such as epsilon aminocaproic acid or tranexamic acid may decrease the incidence of bleeding. "Platelet drips" consisting of infusing either a platelet concentrate per hour or one plateletpheresis unit every 6 hours may be given as a continuous infusion.

GRANULOCYTES

Description-Granulocytes are harvested by leukopheresis. 10^{10} granulocytes are the aimed for yield for each donor. The harvesting procedure can take three hours and is associated with some minor risks to the donor (e.g., citrate toxicity).

Indications-Very limited. Can be useful in the neutropenic patient with a documented bacterial infection in whom the leukocyte count is not expected to recover in the near future. Mainly used with small children.

NOT indicated for most neutropenic patients especially in the era of hemopoietic growth factors.

FRESH FROZEN PLASMA (FFP)

Description-Derived from one unit of donated whole blood. Average volume is 225ml. One unit of FFP can raise coagulation factor levels by 5-8% and fibrinogen by 13mg/dl in the average patient. Remember it can take about 20-30 minutes to thaw FFP.

Indications-Limited. Should only be used when there is a documented coagulation defect that can be corrected by a reasonable amount of FFP:

1) Factors V, XI deficiency
2) Disseminated intravascular coagulation
3) Reversal of warfarin
4) Massive transfusions

NOT indicated for most of the purposes it is used for. FFP is often used as a "Super Glue" for any type of bleeding or any type of abnormality in coagulation testing (e.g. slightly prolonged PT). This is both a waste of product and needlessly exposes the patient to viral diseases. Also transfusion of FFP is not effective at reversing minor elevations of the INR (1.3-1.8) Studies have shown use of FFP is associated with multi-organ system failure and lung injury.

CRYOPRECIPITATE

Description-Cryoprecipitate is derived from one unit of fresh frozen plasma that is thawed at 4 degrees C. The precipitate is resuspended with 10ml of saline or FFP, and re-frozen for storage. One unit contains at least 150mg of fibrinogen and 80 units of factor VIII, along with von Willebrand factor. Cryoprecipitate takes about 20 minutes to thaw.

Indications-Cryoprecipitate is useful to quickly raise the fibrinogen level in patients with DIC or massive transfusion with hemodilution. It is third line therapy in the treatment of Type 1 von Willebrand disease and is second line therapy of therapy in patients with other types of von Willebrand disease. Currently Humate-P is the preferred replacement product for von Willebrand disease. Cryo can be used as a source for factor VIII for hemophiliacs but the preferred product for these patients is the super-

pure factor VIII concentrates.

Summary

Blood Component	Contents	Volume	Shelf Life
Whole blood (autologous or directed donations)	RBC and plasma. WBC and platelets not viable after 24 hr. Factors V and VIII significantly decreased after 2 days. Hct 35%. 450mL blood and 63 Ml CPDA-1 anticoagulant	520 Ml	35 days 4^o C
Red cells (AS-1) Note: these are not "packed" red cells. Packed red cells have a Hct of 70-80%	RBC with about 25 mL of plasma and 100 mL of saline and additive solution (adenine, mannitol). Hct 60%	340 mL	42 days 4^o C
Platelet concentrate	Platelets (5.5×10^{10}); some WBC; 50 mL of plasma, a few RBC (Hct < .005)	50 mL	5 days 20^o C
Platelet pheresis	Platelets (3.5×10^{11}); some WBC; 300 mL of plasma, a few RBC	300 mL	5 days 20^0 C
Fresh frozen plasma	Plasma proteins, all coagulation factors, complement.	225 mL	1 year-18^o C
Cryoprecipitate	150 mg of fibrinogen , at least 80 units of factor VIII, von Willebrand factor, factor XIII, fibronectin, ADAMTS-13	15 mL	1 year-18^o C

(Table created by Dr Lynn Boshkov)

MANAGEMENT OF THE PATIENT WHO DECLINES BLOOD PRODUCTS

The initial step is to find out why the patient is declining blood products. Many patients have an exaggerated fear of HIV and other infectious agents, so simple consoling can often resolve the situation. The most common is religious belief. Jehovah's Witness patients will refuse blood products due to their interpretation of the Bible. All members will refuse red cells, plasma, and platelets. Decisions about use of "derived" blood products—products made by manipulation of the original donated units—are a matter of conscience. These include cryoprecipitate, intravenous gammaglobulin, and albumin.

In an elective situation, the first step is to discuss with the patient those products that are matter of conscience and clearly document this. The patient's blood count and iron stores should be assessed to identify any correctible causes of anemia or low iron stores before surgery. The use of erythropoietin to correct blood counts before surgery is controversial, as this may increase thrombosis risk and is contraindicated in curable tumors.

For patients with acute blood loss, use of intravenous iron combined with high-dose erythropoietin is the most common approach to raise the blood count. One recommended erythropoietin dose is 300 units/kg 3 times a week, dropping to 100 units/kg 3 times weekly until the goal hematocrit is reached. Another often overlooked step is to consolidate and minimize laboratory testing. The most important step is to be respectful of the patient and their beliefs. Many larger cities have liaisons that can help with interactions between Jehovah's Witness patients and the health care system.

Complications of Transfusions

HEMOLYTIC REACTION

Hemolytic reactions had two varieties-immediate and delayed. The immediate reaction is heralded by fevers, hypotension, back pain and oliguria. In severe cases DIC may occur. Most often this is due to transfusion of ABO incompatible blood. This is the most common cause of death related to transfusion and almost always a result of errors in correct identification of the patient. The delayed reaction is marked by lack of expected rise of hematocrit, fevers, Coombs-positive hemolytic anemia, and jaundice. Reactions are due to recipient antibodies attacking donated RBC's resulting in release of hemoglobin and red cell membrane-antigen complexes. These complexes are believed to lead to the hypotension, etc. Treatment is by immediately stopping the transfusion, notifying the blood bank, vigorous IV hydration to keep the urine output over 100cc/hr, and supportive therapy.

FEBRILE REACTIONS

Many patients will get a febrile reaction after the transfusion starts. This is most often due to the presence of leukocyte debris and cytokines in the donated blood. Patients who have had febrile reaction should get future transfusion either with blood delivered through leucopoor filters or blood leukodepleted at blood center. Since transfusion reactions present with a similar clinical picture, all patients with fever during transfusion need a transfusion reaction work-up.

TRANSFUSION RELATED ACUTE LUNG INJURY (TRALI)

One rare complication of transfusion is noncardiac pulmonary edema. The typical picture is hypoxemia, fever, bilateral infiltrates and hypotension developing 2-6 hours after blood is given. Ventilatory support is often required. Recovery is usually rapid (24-48 hours) and complete. It is felt to be a form of ARDS caused by the presence of HLA antibodies in the donor serum leading to destruction of host granulocyte and activation of the complement system leading to lung injury. Another etiology is transfusion of preformed cytokines that lead to endothelial damage. Treatment is supportive. Major differential diagnosis is simple volume overload from aggressive transfusion.

TRANSFUSION ASSOCIATED CIRCULATORY OVERLOAD

Increasingly it has being recognized that volume overload resulting from transfusions can lead to significant morbidity. Patients at risk for TACO are those with heart or renal disease or patients with already compromised fluid status. Also a risk factor is transfusion of multiple blood products. Symptoms are development of dyspnea within 6 hours of transfusions. Patients do not have fever or rash with the dyspnea. Diagnosis is by demonstrating circulatory overload – high venous pressure, BNP, etc. Treatment is aggressive diuresis. Prevention is several fold. One is judicious use of blood products – especially in patients at risk for TACO. Second is the use of prophylactic diuretics especially with red cell or plasma transfusions

TRANSFUSION RELATED GRAFT VS HOST DISEASE (TGVH)

Rare but deadly. Occurs when donor lymphocytes attack the blood recipient. Very rare in the normal blood recipient unless the donor and recipient share a HLA haplotype. TGVH is reported in blood recipients who are immunosuppressed- mainly patients with Hodgkin's disease and leukemia. Strangely enough TGVH does not occur in AIDS patients. Symptoms are an erythematous rash that may progress to epidermal toxic necrolysis, liver dysfunction and pancytopenia. TGVH is prevented by radiating blood products to at risk patients with 2500-3500 rads. Directed blood donation from all blood relatives should also be radiated. TGVH **cannot** be prevented by leucopoor blood!

IRRADIATED BLOOD PRODUCTS, LEUKODEPLETED BLOOD AND CMV NEGATIVE BLOOD

Irradiation of blood is performed for only one reason: to prevent transfusion-associated graft-versus-host-disease (TA-GVHD). Patients with HIV infection do not get TA-GVHD and should not receive irradiated blood.

PATIENTS WHO SHOULD RECEIVE IRRADIATED BLOOD PRODUCTS

ABSOLUTELY	PROBABLE
Stem Cell Transplant Patients	Hematological malignancies other than hodgkin's disease
Congenital immune deficiencies	Patients receiving aggressive chemotherapy
Intrauterine transfusion	
Transfusion from relatives	
Hodgkin's disease (even in remission!)	

Infectious Complications

Blood is screened for many infections by both antigen testing and PCR testing for viral genome. However, there is still a window period where patients can be infective accounting for the residual risk of infections. This is ~ 11 days for HIV, ~12 for hepatis B and ~56 for hepatitis B. Disease screen for: hepatis B, hepatitis C, HIV, HTLV, syphilis, and west Nile virus.

Risk of Viral Infections per unit

Hepatitis B: 1:100,000,000
Hepatitis C: 1:2,000,000
HIV: 1:2,000,000,000
HTLV: 1:650,000

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