CLINICAL USE OF COMPONENT THERAPY VS. WHOLE BLOOD

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INTRODUCTION

Blood transfusions play a critical role in the management of animals with anemia, bleeding disorders and hypoalbuminemia. The transfusable components of blood are erythrocytes, leukocytes, platelets, coagulation factors and albumin. Historically, veterinarians have relied on in-house donor dogs and cats as a source of blood for transfusion purposes. Whole blood was collected for immediate use and sophisticated collection and storage techniques were not well developed. The growing need for transfusions has led to advances in the processing of donated blood as well as to the development of large blood donor programs in veterinary institutions. More recently, commercial animal blood banks have been successful in the marketing of blood products to veterinary practitioners and there has been a move away from the use of whole blood towards the use of selected components of whole blood.

Separation of blood into its cellular and plasma components allows for more efficient replacement of the patient’s needs. Component therapy also reduces the likelihood of transfusion reactions resulting from unnecessary cellular or plasma protein administration. Selection of appropriate components also reduces the likelihood of volume overload following transfusion therapy in an anemic, euvolesmic patient. It also provides a way to maximize the benefit from one whole blood donation – multiple patients may be treated with one donation.

BLOOD COMPONENTS

Fresh whole blood (FWB) provides red blood cells, plasma proteins, viable platelets and all clotting factors. Indications for the use of FWB include excessive hemorrhage and bleeding disorders (related to platelet or clotting factor deficiencies). Stored whole blood (SWB) provides red blood cells, plasma proteins, stable clotting factors and fibrinogen. SWB has the same indications for use as fresh whole blood, but is less useful in the treatment of coagulation abnormalities as platelets and certain clotting factors (Factors V and VIII) are no longer viable. A unit of canine whole blood consists of 450 mls; a unit of feline whole blood consists of 300 mls.

Whole blood can be separated into the following components: packed red blood cells (PRBC) and whole plasma. Plasma may be further classified as fresh, stored, frozen, or fresh-frozen plasma (FFP). Further plasma derivatives include cryoprecipitate, cryo-poor plasma (or cryosupernatant), platelet-rich plasma and platelet concentrate. A canine PRBC unit consists of 250-300 mls; a feline PRBC unit consists of 25-30 mls. Packed red blood cells are prepared by removing plasma from a unit of whole blood. They are suspended in anticoagulant and preservative additive solutions and stored at 1-6°C. The shelf life varies from 21 to 35 days. Packed red cells are used in anemic patients, to increase oxygen carrying capacity, where there is no need for platelets or clotting factors. After separation of red cells from the unit of blood, the remaining plasma is frozen within 4 to 6 hours of collection. This fresh frozen plasma (FFP) contains coagulation factors, antithrombin, vWF, albumin and globulins, and may be used to treat patients with hemophilia, von Willebrands disease, and anticoagulant rodenticide toxicity. Storage at or below -20°C maintains activity of hemostatic factors for up to 1 year. It may also be used in severely hypoproteinemic patients although large volumes are required to raise recipient serum albumin concentrations. Plasma stored frozen for more than one year (FP) is still useful for supplying albumin and globulins. A canine FFP unit consists of 250-260 mls; a feline FFP unit consists of 25 mls.

Cryoprecipitate is a concentrated solution of Factor VIII, von Willebrand factor, fibrinogen and fibronectin. It is obtained by slowly thawing FFP at 4°C and separating and collecting the resulting cold-precipitated material. The resultant volume is approximately 1/10 the volume of the starting plasma. The cryoprecipitate is used for the treatment of hemophilia A and von Willebrands disease (vWD) as well as fibrinogen deficient patients. Cryoprecipitate therapy should be guided by the Buccal Mucosal Bleeding time; incremental doses of cryoprecipitate are given until the buccal mucosal bleeding time is within normal limits.

Cryosupernatant (cryo-poor plasma) is plasma remaining from cryoprecipitate preparation. It contains active clotting factors (except FVIII and fibrinogen) and albumin and globulin. Cryosupernatant is used to treat hemophilia B, hereditary factor deficiencies, vitamin K deficiency, hypoalbuminemia and hypoglobulinemia.

Platelet concentrate is frozen and available from certain commercial blood banks. It contains 1.0x10^11 platelets, frozen plasma, and 5 mls of DMSO. This product is used for the treatment of bleeding due to thrombocytopenia or thrombocytopenia. It is stored at least -20°C and expires 6 months from the time of processing. Once thawed, it must be used within 4 hours. Platelets should be allowed to come to room temperature by taking them out of their protective envelope and placed on a counter, or can be warmed in a warm water bath set at body. The platelet bag should be gently swirled every 5 minutes during the thaw process. Once the platelet concentrate is fully thawed, allow it to sit on the counter for 15 minutes before using.

INDICATIONS FOR BLOOD TRANSFUSION

Red Cell Replacement: Use FWB, SWB or PRBC

In anemic patients, red cell transfusions are given to increase blood oxygen carrying capacity. While the hematocrit can guide the transfusion decision, clinical status is the most important determinant for transfusion. Clinical indications for red blood cell (RBC) transfusion include pallor, prolonged capillary refill, exercise intolerance, weakness, and tachycardia and tachypnea at rest. Clinical signs will be seen at higher hematocrit value when the drop in hematocrit is sudden; patients having chronic anemia are more stable at lower hematocrit values. In acute blood loss, the ‘rule of thumb’ for RBC transfusion is a hematocrit of 20 to 25% in dogs and 15-20% in cats. Other guidelines for acute blood loss include when >30% of blood volume is lost (30 ml/kg in dogs, 20 ml/kg in cats), when there is ongoing hemorrhage or poor response to conventional therapy for shock. In chronic anemia the ‘rule of thumb’ for RBC transfusion is a hematocrit of <20% in dogs and 12 to 15% in cats. Use clinical judgment based on patient’s status, underlying disease process, and owner commitment when deciding whether or not to transfuse.
Hemostatic Protein Replacement: Use FFP, Cryoprecipitate or Cryo-poor plasma.

Both acquired and inherited bleeding disorders are responsive to transfusion with plasma products. These products can be given prophylactically and repeatedly without risking red cell sensitization. With the small volumes of cryoprecipitate, volume overload is also usually a non-issue. Common indications for plasma components include acute rodenticide toxicity with deficiencies of Factors II, VII, IX and X (use FFP, FP or cryo-poor plasma), liver biopsy/shunt correction (use FFP), DIC (use FFP), vWD (use Cryoprecipitate or FFP), hemophilia A (use Cryoprecipitate or FFP), hemophilia B (use Cryo-poor plasma or FFP) and other hereditary factor deficiencies (use FFP, Cryoprecipitate or Cryo-poor plasma).

Replacement of Non-Hemostatic Proteins: Use FFP, FP or cryo-poor plasma

Hypoproteinemia caused by increased protein loss from the gastrointestinal tract (inflammatory or infiltrative disease), urinary tract (protein losing nephropathy), skin (burns) or peritoneum (peritonitis with effusion), or by hepatic synthetic failure (acute or chronic hepatic failure) can be temporarily improved by Plasma transfusion. There is also some thought that acute pancreatitis can be treated with FFP, through the provision of acute phase proteins to inactivate pancreatic enzymes.

Platelet Replacement: Use FWB, Platelet rich plasma (PRP) or Platelet Concentrate

Severe thrombocytopenias, due to immune mediated disease, blood loss, or thrombopathic or aplastic disorders can result in inadequate hemostasis. If platelet counts are higher than 30,000 to 50,000/µL, spontaneous hemorrhage is unlikely if the platelets have normal function. If the counts drop below 30,000 or spontaneous hemorrhage is seen, then platelet transfusion can be used to raise functional platelet count above the minimum level for adequate hemostasis. Platelet transfusions are rarely of benefit for primary or secondary Immune Mediated Thrombocytopenia (ITP) as the transfused platelets are removed from circulation within hours. In contrast, transfusion to supply platelets is often effective in temporarily preventing or controlling hemorrhage caused by acquired or inherited thrombopathy or aplastic disorders.

DOSAGE AND ADMINISTRATION

1) Whole blood: 20 ml/kg, over 1-4 hours; may give more rapidly when treating hemorrhagic shock. Monitor hematocrit.

2) Packed Red Blood Cells: 10 ml/kg, over 1-4 hours; may give more rapidly when treating hemorrhagic shock. Monitor hematocrit.

3) Plasma:
   a) For coagulation factor replacement – 10-20 ml/kg, over 1-4 hours. Monitor coagulation profile. Long transfusion times will compromise the viability of coagulation factors and result in potentially ineffective transfusion.

   b) For albumin supplementation – 45 ml/kg, to increase serum albumin concentration by 1 g/dl. Monitor serum albumin levels. If plasma is being administered for replacement of albumin (in hypoalbuminemic patients), it may be delivered over a longer period of time.

4) Cryoprecipitate: 6-20 ml/kg over ½ - 1 hour. Monitor buccal mucosal bleeding time. Cryoprecipitate should be administered as rapidly as possible, (maximum rate of 3-6 ml/minute for a mid size dog) in order to achieve therapeutic levels of hemostatic proteins. Long infusion times (>1 hour) for a single unit are not appropriate for this product. The plasma half-life of Von Willebrand’s factor is 12 hours. For post surgical cases, the aim is to reach a plasma concentration of at least 15% for 24-48 hours after surgery. This may necessitate multiple transfusions within this time period.

5) Platelet Concentrate: One platelet concentrate unit/10 kg; give over 1-2 hours. Rapid infusion may lead to bradycardia due to the presence of DMSO. At this dosage, the platelet count should elevate 20,000/µL when counted 1-2 hours post transfusion, provided there is no ongoing platelet loss or consumption. An in-line blood filter should be used for administration.

Except for urgent restoration of blood volume, blood products should be given slowly for the first 15 minutes. If the initial dose is well-tolerated, the infusion rate is then increased. In emergency situations (hemorrhagic shock; life-threatening coagulopathy), a more rapid initial rate is used, however, there is increased risk of transfusion reaction. Whole blood, packed red blood cells and frozen plasma should be administered after slow warming to 37°C. Blood administration sets containing filters are commonly used; these filters remove blood clots and other particles.

TRANSFUSION REACTIONS

Blood transfusions can produce various adverse reactions, ranging from allergic urticaria to life-threatening hemolytic reactions. The severity of most transfusion reactions is dose dependent; early recognition of a problem can avert disaster. Patients should be carefully observed, particularly during the first 30 minutes of the transfusion. Monitoring parameters include measurements of temperature, heart rate, pulse strength and synchronicity, and respiratory rate. These parameters should be monitored 15, 30 and 60 minutes into the transfusion. If a reaction is suspected, the transfusion must be stopped immediately. Clinical signs associated with transfusion reactions include fever, vomiting, facial edema, hemolysis, tachycardia, agitation, tachypnea, urinary and fecal incontinence, tremors and hypotension/shock. Severe reactions are rare when patients have been correctly typed and cross-matched. Blood typing is absolutely essential prior to transfusion; cross matching is essential for second and subsequent transfusions (if >4-5 days have elapsed since the first transfusion). Cats must be transfused with type compatible blood. Dogs may be transfused with DEA 1.1 positive (if type compatible) or DEA 1.1 negative (universal donor) blood.
The benefit of the prophylactic use of antihistamines and glucocorticoids has been debated. Pre-treatment with 0.5 mg/kg of diphenhydramine administered intramuscularly or subcutaneously, may reduce the risk of acute hypersensitivity reactions and may be of value at second and subsequent transfusions. Glucocorticoids do not acutely suppress the production of IgG or IgM antibodies and therefore are not considered to be useful in prevention of transfusion reactions.

**STEPWISE TREATMENT OF TRANSFUSION REACTIONS:**
1) Stop the transfusion
2) Infuse Intravenous crystalloids at ‘shock’ dose
3) Dexamethasone sodium phosphate, at 2-4 mg/kg slow IV
4) Diphenhydramine, at 2 mg/kg IM
5) Epinephrine, at 0.01 mg/kg IM (if life threatening/severe)
6) If reaction is mild, restart the transfusion at a slower administration rate
7) If reaction is severe, abandon the transfusion. Cross match the patient to other units and transfuse appropriately cross-matched units.

**References** available from author upon request.