Transfusion Medicine

Ari Jutkowitz, VMD, DACVECC
Michigan State University
East Lansing, MI

Anemia is a common problem in the emergent patient and may result from blood loss, hemolysis, or decreased erythrocyte production. Anemia may be detrimental to the critically ill patient when it causes a decrease in oxygen delivery to the tissues. In the following session, we'll review indications for blood transfusion in veterinary patients as well as guidelines for ensuring safe collection, storage, and delivery of blood products. This document is meant to serve as a reference for practitioners who wish to provide blood product support, but lack blood banking capabilities.

The transfusion trigger

For many years there has been an ongoing search for a universal "transfusion trigger", a set of conditions under which transfusion is considered to be indicated and for which no further justification is required. One of the earliest examples of a transfusion trigger was the "10/30 rule", first published by Adams and Lundy in 1942, which stated that presurgical patients should be transfused if their hemoglobin concentration was less than 10 g/dl or their hematocrit was less than 30%.[1]

More recently, concerns in human medicine about transmission of infectious diseases and a growing awareness of other risks associated with blood transfusion lead to a reassessment of transfusion practices. It was recognized during this time that healthy animals[2] and people[3] could tolerate very low hematocrits as long as intravascular volume was maintained. Furthermore, human patients who declined blood transfusion for religious reasons were also able to survive surgical procedures despite suboptimal hematocrits.[4] In recognition of these observations, the practice of transfusing to a target hematocrit has begun to give way in favor of risk to benefit analysis for the individual patient.

Risks of transfusion

Some of the more commonly cited risks of blood transfusion include fever (febrile non-hemolytic transfusion reactions), hypersensitivity reactions, and acute or delayed hemolytic reactions. These types of transfusion reactions are thought to occur in approximately 3% of veterinary patients receiving blood products. Disease transmission is another potential complication of blood transfusion, though the prevalence has not been reported in veterinary patients. Acute lung injury, microembolic disease, electrolyte and acid-base disturbances, and coagulopathy are other known risks. In addition to these well-recognized risks, there is also increasing evidence that blood transfusions may have significant immunosuppressive effects. In a landmark study of 1717 human patients admitted to an ICU trauma unit, patients receiving transfusions were 6 times more likely to develop nosocomial infections than those who did not receive blood products. Mortality in the transfused group was also twice that of the non-transfused group.[5] Similar findings of increased infection rates and mortality following transfusion have been documented in human patients undergoing surgery for penetrating abdominal trauma, fracture repair, gastrointestinal cancer, cardiac bypass, spinal surgery, and hip replacement. Although the association between blood transfusion and harmful effects such as immunosuppression, acute lung injury, and proinflammatory responses are still poorly understood, there is enough evidence at this time to warrant caution in their use.

Benefits of transfusion

The main goal of red blood cell transfusion is to reduce the morbidity and mortality associated with inadequate delivery of oxygen to the tissues. In order for this goal to be valid, it is important to establish (a) that anemia in fact contributes to morbidity, (b) at what level adverse effects are likely to occur, and (c) that transfusion in these patients is associated with improved outcome. In experimental models, healthy animals subjected to acute hemodilution were able to tolerate hematocrits as low as 10-15% as long as intravascular volume was maintained. Below hematocrits of 15% electrocardiographic changes consistent with ischemia began to appear, and at hematocrits of less than 10%, increased lactate production, myocardial depression, and death occurred.[2] Healthy human volunteers subjected to hemodilution were similarly able to tolerate hematocrits as low as 15% with no evidence of inadequate oxygen delivery. At the lowest hematocrits, many subjects complained of fatigue, but no other symptoms were reported.[3]

However, there is some evidence that even mild to moderate anemia may contribute to mortality in clinical patients. In a study of nearly two thousand human patients undergoing surgery who refused transfusions for religious reasons, risk of death was shown to increase as hematocrits decreased below 30%.[4] In this study, even mild anemia was associated with some increase in the risk of death, and patients with concurrent cardiovascular disease were much less tolerant of anemia than those without concurrent disease. Because no patient in this study received transfusions, the study was not able to show, however, that administration of transfusion would have resulted in an improved survival rate. In a follow-up study of transfused versus non-transfused patients undergoing hip surgery, at hematocrits of 24% or higher, the administration of blood transfusions was not shown to decrease mortality.[6] In another recent study, human ICU patients were randomized to restrictive (hematocrits maintained at > 21%) or liberal (hematocrits maintained at >30%)

transfusion strategies. Hospital mortality rates, multiorgan dysfunction scores, and cardiac complication rates all favored the restrictive transfusion strategy.[7] Benefits to liberal transfusion were only seen in patients with underlying cardiovascular disease.

From studies such as these, it seems clear that anemia is associated with poor outcome. However, it is less clear that transfusion in certain populations of patients will provide benefits in terms of improved tissue oxygen delivery and survival. We may be able to extrapolate that critically ill patients with hematocrits below 15% may benefit from transfusion, while those with stable blood volume and hematocrits greater than 24% are unlikely to benefit from transfusion. In between these values is a gray zone where some patients may benefit from transfusion and others will not.

When to transfuse?

Students frequently ask how low the hematocrit must fall before we decide to transfuse. Hopefully the point has been made by now that hematocrit levels alone should not serve as a transfusion trigger. However, they may still be used as a rough guideline for when to consider transfusion as a possible treatment. In *otherwise healthy patients*, current guidelines supports the safety of hematocrit levels as low as 18% as long as normovolemia is maintained.[8] Other factors to consider when deciding on the need for blood transfusion should include clinical signs of anemia, the rate of ongoing losses, the chronicity of the anemia, and the presence of co-morbidity that may limit the ability of the patient to compensate for their anemia.

Blood donor screening

Canine blood donors should be at least 25 kg (to donate ½ unit of blood or 225 ml), in good health and temperament, current on vaccinations, and not receiving any medications. At Michigan State University, donors are tested for all blood group antigens for which a commercial test is available, but at a minimum testing for 1.1 and 1.2 should be performed as these antigens are associated with acute hemolytic transfusion reactions in sensitized individuals. Infectious disease screening should include: Heartworm antigen, Babesia spp, Ehrlichia spp, Anaplasma, Mycoplasma, Brucella, and Leishmania. Trypanosoma and Bartonella should be considered in places where endemic.[9]

Feline blood donors should be at least 5 kg, strictly indoors, in good health, and current on vaccinations. Echocardiogram is strongly recommended for donor safety to rule out occult cardiomyopathy. Feline donors should be blood typed and screened for infectious disease as follows: FeLV, FIV, Mycoplasma, heartworm antibody, and Bartonella. Cytauxzoon and Ehrlichia should be considered in places where endemic.[9]

Blood collection and storage

Blood is collected from the jugular vein into a closed collection system following aseptic preparation of the skin. If the blood is to be administered immediately, it may be anticoagulated with heparin (625 u per 50 ml blood) or 3.5% sodium citrate (1 ml anticoagulant/9 ml blood). Because these anticoagulants lack preservatives, the blood collected in this fashion may not be stored for any length of time. CPDA-1 (14 ml anticoagulant/100 ml blood) is an anticoagulant with a preservative that increases red cell survival by serving as a substrate for synthesis of ATP. Packed red blood cells in CPDA-1 may be stored for 4 weeks 4^{o} C. The use of Adsol (an electrolyte solution containing adenine, saline, glucose, and mannitol) may further improve length of storage and post transfusion viability.

Typing and crossmatching

Blood typing should ideally be performed in all dogs to optimize allocation of resources (administering 1.1 positive blood to 1.1 positive recipients and reserving universal blood for 1.1 negative recipients) and to avoid sensitizing recipients to blood alloantigens. In an emergency, a dog that has never been transfused previously may safely receive transfusion without blood typing, because dogs lack naturally occurring alloantibodies. Dogs that have previously been transfused (5 or more days prior), that have had litters of puppies, or that have an unknown transfusion history should have a major crossmatch performed prior to transfusion to rule out incompatibility.

All cats have naturally occurring alloantibodies to foreign blood types.[10] Transfusion of type A blood to B cats results in a potentially fatal transfusion reaction. Transfusion of type B blood to type A cats may result in hemolysis and less severe transfusion reactions. Consequently, all cats must be blood typed prior to transfusion.

Recently, a new blood type (Mik), distinct from the AB blood group system, has been reported in cats. Most cats are positive for the Mik antigen. However, Mik-negative cats do exist, and possess naturally occurring Mik-alloantibodies. These cats may experience acute hemolytic transfusion reactions after receiving AB compatible blood. Given the clinical relevance of naturally occurring Mik alloantibodies, all cats should be crossmatched prior to transfusion, even if they have not previously received blood products.[11]

Administration

The optimal route of blood administration is intravenously, through the largest catheter diameter possible for the size of the patient. When large quantities of blood and fluids must be given rapidly in the face of exsanguination, 14 or 16 gauge over the needle catheters (Angiocath®, Becton Dickinson Infusion Therapy Systems Inc) can be used in the jugular veins.

Refrigerated blood products should ideally be warmed to room temperature prior to administration to avoid inducing hypothermia in the recipient. Cold blood also has a much higher viscosity than that of warmed blood and as a result cannot be given as quickly. Packed cells may be warmed by immersing the unit in a warm water bath at 37° C or by passing the coils of the transfusion tubing through a fluid heater or basin of warm water. Plasma may also be warmed in a warm water bath at 37° C. Care should be taken when handling plasma prior to warming as the plastic blood bag is fragile when frozen and susceptible to cracking.

Blood products should always be administered using a commercial blood administration set with an in-line filter (Baxter Healthcare Corp, Deerfield, IL) to remove blood clots and particulate debris. For small blood volumes administered to cats and small dogs by syringe, a pediatric 18 µm blood filter (Hemo-Nate Filter, Gesco International, San Antonio, Tx) may be placed between syringe and extension set.

Blood should not be administered with any fluid other than 0.9% sodium chloride. Calcium containing solutions such as lactated Ringer's (B. Braun Medical Inc, Irvine, CA), Normosol (Abbott Laboratories, Abbott Park, IL), or Plasmalyte (Baxter Laboratories, Deerfield, IL) may bind citrate and thus initiate coagulation. Hypotonic fluids like D5W or half-strength saline may result in red cell lysis as a result of osmotic fluid shifts. Concurrent administration of other drugs through the same catheter should also be avoided.

Volume and rate

The volume of blood to be transfused can be calculated as follows:

Transfusing 10 ml/kg of packed cells or 20 ml/kg of whole blood typically raises the PCV by approximately 10%.[12] In the setting of acute blood loss, PCV may not provide a reliable indicator of blood loss. In these cases, blood should be given to effect or in proportion to estimated losses.

Rates for blood transfusion are variable, depending on the degree of blood loss and the rate of ongoing losses. Ideally, the transfusion time for a unit of blood should not exceed 4 hours due to concerns about bacterial proliferation once the product has been warmed. An initial rate of 0.25 ml/kg for the first 30 minutes has been recommended while the patient is monitored for transfusion reactions. If no adverse effects are noted, the rate may then be increased to as much as 10-20 ml/kg/hr. However, in the setting of exsanguinating injury and imminent death, blood may be given as rapidly as possible.

Autotransfusion

Direct aspiration and reinfusion is easily accomplished using a 60 cc syringe and three-way stopcock. Using this method, blood may be aspirated from the thoracic or abdominal cavity into a blood collection bag or container and then reinfused through a micropore filter (Hemo-Nate Filter, Gesco International). Anticoagulants are generally not needed because blood has been sitting in contact with pleural or peritoneal surfaces for over one hour undergoes defibrination. However, with rapid hemorrhage there is insufficient time for defibrination, and CPD-A should be added at a dose of 7 ml per 50 ml blood. Direct aspiration and reinfusion can be very useful in cases like hemothorax secondary to rodenticide or trauma where evacuation of the chest cavity is needed and preservation of viable cells is desired.

Autotransfusion has a number of advantages and disadvantages that need to be taken into consideration prior to administration. The biggest advantage is a ready source of compatible blood that can be given quickly and inexpensively, without the need for warming, typing, crossmatching, or infectious disease screening. Disadvantages include the potential for hemolysis, coagulopathy, blood contamination, and acute lung injury. Autotransfused blood is subject to hemolysis as a result of prolonged contact with injured serosal surfaces and from mechanical trauma when suction systems are used. Coagulopathies may also be a concern because pleural or peritoneal contact activates the coagulation system, resulting in reduced platelet and clotting factor levels in autotransfused blood that may lead to dilutional coagulopathy when large volumes are reinfused. Additionally, because autotransfused blood may contain large amounts of FDPs, red blood cell fragments, activated leukocytes, platelets, and inflammatory mediators that may initiate coagulation, autotransfusion may exacerbate consumptive coagulopathies. Acute lung injury is another potential complication following autotransfusion, and is believed to result from microembolization of cellular aggregates, fat, and protein to the pulmonary vasculature. For this reason, the use of micropore filters (18 µm) has been recommended when autotransfused blood is administered. Because there is the potential for spread of neoplasia if the shed blood contains tumor cells, and for contamination with bacteria if GI perforation may have occurred, autotransfusion should not be used in these situations.

Monitoring of blood administration

Prior to administration of blood products, baseline values for PCV, total solids, and vital signs should be obtained and blood components should be checked carefully for signs of discoloration. During administration, vital signs should be rechecked initially every 15 minutes for the first half hour, then every 30 minutes thereafter to monitor for signs of transfusion reaction. A rise in body temperature of 1° C, the development of tachycardia, bradycardia, tachypnea, vomiting, urticaria, erythema, angioedema, or pigmenturia should prompt investigation into the possibility of transfusion reaction.

Conclusion

Blood transfusion is a valuable and potentially life-saving technique that should not be withheld in patients at risk. However, there is a growing body of evidence that transfusions may contribute to increased morbidity and mortality, and this perception has lead to a change in the way that transfusion requirements are assessed. By weighing the risks of transfusion against the potential benefits, by carefully screening blood donors, and by using appropriate precautions in the collection, storage, and administration of blood products, clinicians may be better able to optimize blood transfusion management in the emergent patient.

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