We Need Blood STAT! Emergency Transfusions

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The ability for a practice to perform emergency transfusions is crucial to have better chances in treating patients like the one described. While the patient was unable to be saved, time for diagnosis and the owner's decision making process was gained. In many less extreme cases of hemorrhaging and anemia, red blood cell (RBC) transfusion is a life-saving therapy. Present day, transfusions are not uncommon. Many practices bank blood products in-house with most relying on commercial banks for supply, while some develop their own donor program and even process blood components in-house.

Step 1: Know when a transfusion is required

When an animal loses a significant amount of blood, replacing the blood may seem like common sense. In actuality, not all patients who have lost blood require blood to be transfused in order to prevent shock.

Blood circulating within the vasculature serves to deliver oxygen to various tissues. Oxygen is required for efficient production of cellular energy in the form of adenosine triphosphate (ATP), utilized for maintenance of life at molecular levels. Cell signaling, DNA and RNA synthesis, cytoskeletal maintenance, active transport, and muscle contraction are just some of the critical processes utilizing ATP. Oxygen delivery is determined by arterial oxygen content and cardiac output (how fast the blood can be pushed around the body).

As long as there is adequate blood volume, even an anemic patient can deliver sufficient oxygen to meet metabolic oxygen demands. This required blood volume can be provided for the short term with crystalloid infusion. There is a point, however, where the anemia is severe enough that restoring blood volume is not sufficient to provide adequate oxygen delivery. As hemorrhaging progresses, blood volume replacement with crystalloids will continue to dilute the blood, decreasing the packed cell volume (PCV) to the point that the compensatory increase in cardiac output (through increasing heart rate and stroke volume) is insufficient to keep up with oxygen demand. When the patient reaches, or is expected to imminently reach this critical oxygen extraction level, a transfusion of RBCs is required.

Determining when a patient has reached this "critical oxygen extraction" level is important because transfusions are not benign; they may cause immunosuppression, immunologic reactions, or inflammatory consequences. If a transfusion is not truly necessary, these effects are only harmful to the patient.

Clinical signs of anemia will be seen in patients reaching critical oxygen extraction levels, such as weakness and impaired mentation even though they may be considered to be at a good fluid balance. Patients would also exhibit compensatory signs of shock including tachycardia, increased respiratory effort, pale mucous membranes and prolonged capillary refill time. Laboratory values evaluating acid-base status would point towards metabolic acidosis with an increased plasma lactate level if the anemia is significant and prolonged. The decision to perform a RBC transfusion cannot be based on any laboratory value such as PCV or hematocrit alone, but on the presence of these signs of hypoxia in the patient.

Step 2: Use the proper type of blood product

With severe hemorrhaging, whole blood is lost, i.e. RBCs, platelets, leukocytes, and plasma. Replacing this loss with a whole blood transfusion is reasonable, and sometimes even beneficial, preventing dilutional coagulopathy. However, each of these components possesses the potential to cause negative effects when transfused. Each component has antigenic elements which stimulate the immune system to react. Because of this, component therapy, or the act of replacing only the components required by the patient in a purposeful manner, is advocated. Whole blood is separated into components and stored separately to be used at a later time.

In the case of reduced oxygen carrying capacity due to anemia (low RBC level in blood), only red blood cells (RBCs) are required. Whole blood is centrifuged and the plasma removed. The remaining RBCs, packed RBCs (PRBC), are a concentrated solution that can be used for RBC transfusions. Leukocytes can also be removed through a process called leukoreduction, further reducing the immunologic potential. The cost of filters required for the process makes regular application of leukoreduction difficult in veterinary settings, though many blood banks will provide leukoreduced PRBC on request.

Plasma contains hemostatic proteins, albumin, and other plasma proteins. Due to the concentration levels of each of these plasma components, therapeutic use of plasma transfusions are appropriate only to replace hemostatic proteins for coagulation factor deficiencies and the resultant hemorrhaging. Plasma is no longer preferred in hypoalbuminemic patients because in order to increase serum albumin by 1 g/dL, a dosage of 40-50 mL/kg is required. The risks of immunologic complication and fluid volume overload, as well as the drain on both financial and biological resources, would be reasons against using plasma for albumin supplementation.

In a similar manner, platelet supplementation may be desired in cases of thrombocytopenia or thrombopathia. It is difficult to maintain a healthy stock of platelet products as its shelf-life at room temperature is short (approximately 5 days). The viability of frozen platelets are significantly reduced using the current methods of cryopreservation. In most practices, platelets are provided in the form of whole blood, where the quantity available to the patient will be limited by a typical concentration of platelets in whole blood. Repeated whole blood transfusions for the sake of replacing platelets is not a good option due to the potentially unnecessary components and volume of RBCs and plasma.

The majority of emergency transfusions will be performed to supplement oxygen carrying capacity for anemic patients via PRBC. Transfusion of cellular components, such as RBCs, are accompanied by a strong antigenic (foreign substance triggering the immune system) load. RBCs are accompanied by a set of erythrocyte antigens which are used to characterize the blood type of an individual and affect the compatibility of RBC transfusions from a donor to a recipient.

In canines, the dog erythrocyte antigen (DEA) system is the standard nomenclature used to describe blood types. DEA 1, 3, 4, 5, 6, 7, and 8 have been described. Each dog can be positive or negative (null) for the expression of each DEA. For example, a dog can be DEA 1 and 4 positive, while negative for 3, 5, 6, 7, and 8. DEA 1 is considered the most antigenic of the various DEA types, because a mismatch can lead to severe, acute hemolytic anemia (AHTR). The key word here is "can," because the first time DEA 1 positive blood is transfused to a DEA 1 negative recipient, AHTR does not result. Sensitization, or the triggering of acquired immunity against the DEA through antibody production, occurs 4-6 days after exposure. Subsequent mismatched transfusions *will* result in AHTR, however. In addition, transfusion of DEA 1 positive blood to DEA 1 negative recipients will lead to delayed hemolytic transfusion reaction the first time around, only allowing the transfused RBCs to survive in circulation 4-6 days. Because of this, blood type matching for each canine transfusion is important. DEA 1 positive blood should only be given to DEA 1 positive recipients, while DEA 1 positive patients can receive DEA 1 positive or negative blood without negative consequences. Additional antigens such as *Dal* and Kai are known to exist, though there currently are no practical methods in determining this blood type.

In felines, the AB system and the *Mik* antigen have been identified as existing blood types. A cat can express either A, B, or AB as their phenotype. Type A blood will be most compatible with type A cats, and type B blood will be most compatible with type B cats. Type A cats have a mild level of anti-B antibodies circulating in the plasma, causing significant, but often non-life threatening transfusion reactions when transfused with type B blood. Type B cats have a high titer level of anti-A antibodies, causing severe, acute hemolytic transfusion reaction and anaphylaxis when transfused type A blood. The *Mik* antigen is also observed to cause AHTR on first mismatch. Commercial testing kits are not available.

Because of the lack of commercial kits for many RBC antigens, crossmatching is an important form of compatibility testing, especially if the patient has been exposed to previous transfusions (and potentially sensitized). Crossmatching tests for the potential for immunologic complications by mixing recipient and donor plasma and observing for agglutination or hemolysis. A positive result in agglutination or hemolysis indicates the likelihood of immunologic complications occurring if the transfusion goes forward. The major cross-match tests for the likelihood of donor RBCs being hemolysed by the recipient, and is performed by mixing donor RBCs with recipient plasma. The minor cross-match tests for the likelihood of donor plasma proteins affecting the recipient RBCs, performed by mixing recipient RBCs with donor plasma. Any positive result makes the match non-ideal for transfusion. Blood type matching AND cross-matching is recommended for both dog and cat transfusions.

Even in the case of an emergency, there often will be time for blood typing of the patient (approximately 5 minutes) with an in-house kit for blood types that can be typed (DEA 1 for dogs, A/B for cats). The time required for a cross-match (approximately 30 to 45 minutes) may be longer than optimal and are more frequently omitted. In the case a judgment is made that a proper cross-match cannot be made in a timely manner, transfusing with RBCs with the least immunogenic potential would be ideal. In dogs, "DEA 4 positive only", or blood negative in DEA 1, 3, 5, 6, 7, and 8 would be considered "universal", since 98% of the canine population is known to be positive for DEA 4.

In cats, keeping both type A and type B blood on hand is the most ideal scenario in the case of emergency need for transfusions because there is no universal blood type with cats. Storing of type B PRBC is both a financial and biological resource commitment, however, since the majority of the population is type A. However, without stored type B RBCs available, your type B patients will be left to wait for donors to come in and have whole blood collected, or in worse cases be left without the option of RBC transfusions. Especially for type B blood products, though not exclusive, creating a regional network with neighboring veterinary practices to help each other in the case of dire need is beneficial.

Step 3: Keep other sources of blood in mind

Traditionally, blood transfusions are performed in an allogenic manner, or performed between one member to another within the same species. There are, however, some other forms of transfusions that can be used in specific situations which reduce the demand for blood products from donors and may prove its usefulness in emergency situations; autotransfusion and xenotransfusion.

Autotransfusion

The first of which is autotransfusion, or the act of salvaging blood lost by the patient and reinfusing the blood into the same patient. In veterinary medicine, autotransfusion is most commonly performed as unwashed red cells transfused through a filter. This is accomplished through transfer of suctioned blood into an intravenous fluid bag and administered with a blood administration set. An alternative method involves the use of a 3-way stopcock attached to a syringe and extension sets. The stopcock is first opened to the extension leading to a blood filled cavity (e.g. abdomen) and the syringe, and blood pulled into the syringe. The stopcock is then turned to be open to the syringe and another extension leading to an intravenous catheter, and the blood pushed through an in-line blood filter into the patient. The syringe method can also be employed prior to surgical intervention, through percutaneous insertion of a catheter into a body cavity the hemorrhaging is occurring in. Autotransfusion is observed to be effective in alleviating compensatory signs from anemia and improvement in consciousness

in a study involving severely anemic subjects, whereas replacement of the volume with lactated ringers did not result in the same effect.

Autotransfusion has advantages in addition to alleviating RBC product demand. By administering autologous blood, the concerns of immunologic complications are eliminated. Blood typing and cross-matching can also be omitted, since there should be no better match to a recipient than their own blood. The effects of storage lesions can be avoided through autotransfusion, since storage time is not involved. Storage lesions, which include accumulation of hazardous levels of electrolytes, metabolites, and inflammatory mediators, as well as RBC changes (which reduces their efficacy as oxygen carriers), occur in blood stored longer than 14 days causing it to be less effective in the treatment of anemia, have shorter cell survival time, and incite negative effects in the recipient.

Xenotransfusion

Can dog blood be used to help cats? This question was studied during the 1960's to evaluate the effect of dog to cat transfusions, a form of transfusion termed xenotransfusion. Xenotransfusion is simply the act of taking blood from a member of one species, and transfusing it into a member of a different species. The results of the studies have been summarized in a systematic review recently published (Bovens C, Gruffydd-Jones T. *Xenotransfusion with canine blood in the feline species: review of the literature*. J Fel Med Surg 2012;15(2):62-67.)

The systematic review summarized that dog to cat transfusions result in a delayed hemolytic transfusion reaction 4-7 days post-transfusion and sensitization of the patient to dog blood. The transfusion looked to be effective in reducing clinical signs of hypoxia upon transfusion. Subsequent transfusions after 4-7 day mark resulted in severe AHTR and anaphylaxis in 100% of cats, with 66% of these reactions being fatal. There are now many emerging examples in the news, of dog to cat transfusions performed with an overall positive outcome for the patient.

On the surface, dog to cat transfusions may seem like a viable way to increase the supply of blood to our feline patients. However, for the same reason we now discourage canine transfusions without at least type matching (alloimmunization or sensitization), we should discourage dog to cat transfusions as well. However, this can be considered a final therapeutic option for situations where the patient meets all of the following criteria:

1. Has no source of compatible cat blood (Type B cat with no stocked blood, donor, or nearby hospital with stock, for example) or hemoglobin based oxygen carrier solutions (not available in the US).
2. Is imminently going to pass away without a transfusion or compatible blood will not be obtained soon enough. A truly dying animal.
3. Is expected to benefit from a short term oxygen carrying capacity supplement
4. The owner understands risks and consequences.

Veterinary professionals are urged to display discipline and be responsible in the use of this method. Whether the patient really needs the blood, is up to the clinical judgment of each veterinary team, and each team should be absolutely sure the patient requires the blood prior to xenotransfusions because there are real and certain consequences associated with dog to cat transfusions.

Conclusion

Preparing ourselves to be equipped for emergency transfusions requires a working knowledge in the assessment of an anemic patient, when a patient truly needs transfusions, blood types, preparation in creating multiple sources of blood products and components, and utilize some situation specific options that will further expand the ability to provide transfusions. Is your practice prepared for emergency transfusions?

References

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