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Review Article

FLUID THERAPY IN HAEMORRHAGIC SHOCK

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Summary: Haemorrhagic shock is a clinical syndrome manifested by inadequate tissue oxygenation due to poor perfusion because of decreased effective circulating blood volume. Isotonic and hypertonic salt solutions and various colloids have proven efficacy in resuscitation. Isotonic crystalloids freely cross capillary membrane and large quantities must be infused to restore plasma volume. The poor intravascular retention of isotonic crystalloids supports intravascular volume transiently but later can cause tissue oedema formation with impaired oxygen perfusion. The addition of colloids considerably reduces total fluid requirements, prolongs volume expansion, and obtains haemodilution with increased microvascular perfusion. Hypertonic salt solutions with or without colloids have been shown to expand plasma volume three to four times the volume infused through an endogenous fluid redistribution. They also have positive inotropic effects and the increasing cardiac output is apparently mediated by a reflex arc involving the vagus nerve with receptors in the lung. Microvascular blood flow is not only enhanced by haemodilution but also by hyperosmolar shrinkage of blood and endothelial cells. Regardless of the fluid therapy used, the treatment of haemorrhagic shock reqiures rapid restoration of circulating volume to limit potential complications of long-standing hypoxia. It is important to recall that the endpoint of fluid therapy for an animal in haemorrhagic shock is the normalization of the vital signs rather than administration of a specific volume of fluids.

Key words: haemorrhagic shock; fluid therapy; crystalloids; colloids

Introduction

Haemorrhagic shock is a clinical syndrome manifested by reduced perfusion of vital organs leading to inadequate delivery of oxygen and nutrients necessary for normal tissue and cellular function (1). Haemorrhagic shock occurs when circulating blood volume decreases due to haemorrhage, which leads to decreased venous return to the heart. This in turn causes decreased cardiac output and activation of a variety of homeostatic mechanisms including hormonal modulation and cardiovascular neurologic reflexes. The compensatory mechanisms help to improve blood volume, sustain the blood pressure, and maintain perfusion to the vital organs such as heart and brain. The perfusion can be maintained for a short period of time following mild to moderate volume loss, however without the intervention the compensatory mechanisms eventually fail and the complications of shock ensue. Oxygen delivery decreases and the tissues switch to anaerobic metabolism and accumulate the oxygen debt. The goal of treatment is the improvement of tissue perfusion and oxygenation, and the mainstay of the treatment for the haemorrhagic shock is the expansion of the intravascular volume by intravenous fluid therapy (2).

The average estimated adult dog blood volume represents 8% to 9% of body weight (77 to 78 ml/kg) and in cat 6% to 7% of body weight (62 to 66 ml/kg). Estimating blood loss is complicated and to help guide volume replacement, haemorrhage can be divided into four classes. Class I is a non-shock state, such as occurs when donating a blood (up to 15% of estimated blood volume). Class II haemorrhage occurs at estimated blood volume loss of 15 to 30% and class III at 30 to 40%, respectively. Class IV is a pre-terminal event requiring immediate therapy (3). Massive haemorrhage may be determined as loss of total estimated blood volume within a 24-hour period, or loss of half of the estimated blood volume in a 3-hour period (4).

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Controlled and uncontrolled haemorrhagic shock

Haemorrhagic shock occurs when a patient loses 30% or more its estimated blood volume (5). The source of the haemorrhage should be determined and controlled as soon as it is possible during the initial stabilization. Although the basic approach to fluid therapy of dogs and cats in haemorrhagic shock remains the same for the most situations, special consideration is given to the circumstances in which the fluid therapy itself may cause the problems (e.g. head trauma) (2).

Studies from 1960s and 1970s using Wiggers animal model of graded controlled haemorrhagic shock demonstrated that a large extracellular fluid deficit occurred in prolonged severe haemorrhagic shock (6). Only the infusion of both shed blood and lactated Ringer's solution was effective in terms of replacing the red cell mass, plasma volume, and extracellular fluid. The advocates of early fluid resuscitation with large volumes of fluids, i.e., isotonic crystalloids in volumes 2 to 3 times the estimated blood loss, argued that the need for increasing cardiac output and oxygen delivery to maintain microvascular perfusion and oxygenation exceeds any risk of accentuating haemorrhage. Aggressive fluid resuscitation during the Vietnam War with crystalloid solutions and blood products allowed patients who previously would have succumbed to haemorrhagic shock to survive. Likewise, renal failure became less frequent clinical problem, but acute respiratory distress syndrome appeared as an early cause of death after severe haemorrhage (1).

Large volume fluid resuscitation has been challenged in clinical trials (7, 8) and experimental models (9, 10, 11, 12) of uncontrolled haemorrhagic shock. Any attempts to increase blood pressure to normal by aggressive fluid resuscitation resulted in increased bleeding from injured vessels, haemodynamic decompensation, and increased mortality, when compared to no fluid resuscitation (8,13, 14) or hypotensive resuscitation (15, 16). Aggressive fluid infusion to achieve normal haemodynamic parameters is therefore contraindicated in uncontrolled haemorrhagic shock because it may renew internal bleeding; it is withheld until the time of surgical intervention.

The route of fluid administration

The main goals of resuscitation are to stop the source of haemorrhage and to restore circulating blood volume. Vascular access must be obtained to begin adequate volume resuscitation, because fluids administered subcutaneously or into peritoneal cavity are not considered adequate for shock therapy. The neurohormonal response to low cardiac output results in peripheral vasoconstriction and poor absorption of fluids administered subcutaneously or intraperitoneally. Central veins (v. jugularis) allow larger volumes of crystalloids to be administered faster, but usually the catheterization of a peripheral vein is completed before placing a catheter in the jugular vein. The intraosseous route (trochanteric fossa, tibial crest, iliac wing or proximal humerus) of administration may come into consideration in animals weighing less than 2 kg, for instance puppies and kittens (17).

Isotonic crystalloids

Isotonic crystalloids have been the most common type of fluid recommended initially for the shock patient. Examples of isotonic crystalloids include lactated Ringer's solution and physiologic saline or 0.9% NaCl. Lactated Ringer's solution is probably the most widely and frequently used balanced salt solution for fluid resuscitation in haemorrhagic shock. It provides a source of bicarbonate as a result of metabolism of lactate to CO_2 and H_2O, which is particularly beneficial in shock patients with clinically relevant metabolic acidosis. Hyperchloraemic metabolic acidosis has been reported after administration of large doses of physiologic saline, therefore it is less suitable for the acute volume resuscitation (17).

Isotonic crystalloids freely cross capillary membranes and large quantities must be infused to restore plasma volume. The poor intravascular retention of isotonic crystalloids supports intravascular volume transiently but later can cause tissue oedema with impaired oxygen perfusion. Approximately 75% to 80% of isotonic crystalloids move to the interstitial space within the first hour after intravenous administration, therefore four times the amount of crystalloids (compared with blood loss) should be administered to support the circulation (17, 18). Large volumes of isotonic crystalloids decrease intravascular oncotic pressure due to dilution of impermeant protein anions. Decreased oncotic pressure impairs maintenance of intravascular volume and promotes extravasation of fluids into the interstitial space (17).

Several studies have raised questions regarding the effects of resuscitation regimens on aspects of

the immune response to haemorrhagic shock. It was observed, that lactated Ringer's solution exacerbated neutrophil superoxide burst activity and increased neutrophil adherence (19). Also, it has been shown that aggressive crystalloid resuscitation was followed by increased cytokine activation including IL-1, IL-6 and TNF (20).

Colloids

Colloid solutions are divided into biologic (e.g., whole blood, albumin, plasma) and synthetic (hydoxyethyl starch derivatives, dextrans, gelatins, haemoglobin-based oxygen carriers). They have been advocated for the treatment of haemorrhagic shock as they tend to remain in the intravascular compartment. The addition of colloids to crystalloids considerably reduces total fluid requirements, prolongs volume expansion, and obtains haemodilution with increased microvascular perfusion. Ideally, a shock bolus of crystalloids and synthetic colloids is an excellent starting point to increase intravascular volume, venous return, cardiac output, and tissue perfusion. As these fluids are given, fresh whole blood or blood constituents can be obtained to be used for transfusion (2).

Whole-blood transfusion may be warranted as a first choice biologic colloid during haemorrhagic shock. Packed red cells together with fresh frozen plasma may be used as well. Adequate haemoglobin levels are required to maintain oxygen-carrying capacity and to deliver oxygen to the tissues. In addition, plasma is an excellent source of coagulation factors and proteins such as albumin, which are required for drug binding and buffering. The colloid oncotic pressure of albumin is nearly identical to that of plasma (20 to 25 mmHg). However, albumin distributes throughout the extracellular space, and the amount of time it spends in the intravascular space is longer than that of crystalloid but shorter than that of hetastarch. The plasma half-life of albumin is 16 hours, and more than 90% of infused albumin remains in the intravascular space (21).

In animals with acute blood loss of more than 30% estimated blood volume and haematocrit values below 25%, packed red blood cells are administered at doses of 15 to 20 ml/kg, fresh frozen plasma at doses of 10 to 15 ml/kg, and whole blood at doses of 20 to 25 ml/kg (2). Under most of circumstances, the recommended rate of whole-blood transfusion has been reported not to exceed 22 ml/kg/h, but a clinical situation such as haemorrhagic shock may require quicker administration (22).

Synthetic colloids are high molecular weight substances that remain in the vascular space. They fall into following major groups: the hydoxyethyl starch derivatives, the dextrans, the gelatins, and haemoglobin-based oxygen carriers (to be discussed later). The hydroxyethyl starches are synthesized by partial hydrolysis of amylopectin (the branched form of plant starch), the dextrans from a macromolecular polysaccharide produced from bacterial fermentation of sucrose, and the gelatins from hydrolysis of bovine collagen followed either by succinylation or linkage to urea (23).

Among the synthetic colloids, hydoxyethyl starches (HES) have the fewest anaphylactoid reactions and are the most commonly used colloids in Europe. The extent of hydoxyethylation (degree of substitution), and its pattern, determine the degradation of HES by serum α-amylase, and therefore account for the pharmacological differences between various HES specifications (24). The average molecular weight plays only a minor role in determining the pharmacological profile of HES solution (25, 26). HES may interfere with coagulation and accumulate in plasma and tissues (23).

The most pronounced side effects were found with large and highly substituted HES molecules, like hetastarch HES 450/0.7 which has an average molecular weight of 450,000 dalton and high degree of molar substitution (i.e., ratio of hydroxyethyl groups to glucose residues) of 0.7 (27). HES 450/0.7 prolongs partial thromboplastin time, but clinical episodes of bleeding have not been reported in human or veterinary patients when daily administration does not exceed currently recommended guidelines (10 to 20 ml/kg in the dog and 10 to 15 ml/kg in the cat). The dosage may be administered as a rapid bolus in dogs and over 10 to 15 minutes in cats because rapid administration has been reported to cause nausea in cats. HES 450/0.7 at a dosage of 20 ml/kg results in 70% to 200% (average 141%) increase in plasma volume, and the duration of plasma volume expansion is 12 to 48 hours, with longer retention time with higher doses (17).

In Europe, several hydroxyethyl starch products are available with smaller average molecular weights and smaller degree of molar substitution, including pentastarch or HES 200/0.5 with average molecular weight of 200,000 dalton and degree of molar substitution of 0.5 (HAES-steril 6%, Fresenius Kabi, Bad Homburg, Germany) and a novel HES type 130/0.4 with an average molecular weight of

130,000 dalton and a degree of substitution of 0.4 (Voluven, Fresenius Kabi, Bad Homburg, Germany). The molecular weight of the latter is the narrowest of all available HES types, i.e., the proportion of very large and very small molecules is reduced. Voluven® has a volume effect of approximately 100% (of the infused volume) and a 4- to 6-hour duration, which is comparable with the current European standard HES, i.e., HAES-steril 6%®. These products have been developed to maximize volume expansion effects while minimizing the risk of adverse effects on the haemostatic system by reducing the number of large molecules (22, 26).

Hypertonic saline

Hypertonic salt solution, i.e., 7.5% NaCl in a dose of 4 ml/kg has been shown to expand plasma volume three to four times the volume infused through an endogenous fluid redistribution (28, 29). It also has positive inotropic effects and the increase in cardiac output is apparently mediated by a reflex arc involving the vagus nerve with receptor in the lung. Microvascular blood flow is not only enhanced by haemodilution but also by hyperosmolar shrinkage of blood and endothelial cells (30). Small-volume hypertonic resuscitation is effective in achieving haemodynamic stability, restoring splanchnic organ perfusion (31, 32), attenuating neutrophil margination (33) and reducing the increases in postresuctitation intracranial pressure (34, 35). The use of hypertonic saline requires preexisting normal hydration and serum sodium concentration as it causes considerable increases in serum sodium concentration leading to salt poisoning (17).

The duration of effects is similar to that of isotonic crystalloids, and additional intravascular support with colloids is required to maintain effective volume expansion. Complications of hypertonic saline administration may occur when solutions are infused too rapidly (not faster than 1 ml/kg/minute) and include bradycardia, hypotension, bronchoconstriction, and rapid, shallow breathing. Cellular dehydration is another potential complication of administering hypertonic solutions, an effect that is more likely when multiple doses are used or when hypertonic saline is used in dehydrated patients (17).

Oxygen-carrying blood substitutes

Oxygen-carrying blood substitutes hold a promise as effective resuscitation fluids that may improve oxygen carrying capacity without problems of storage, compatibility, and disease transmission that are associated with standard blood transfusion.

The haemoglobin-based oxygen carrier Oxyglobin (Biopure Corporation, Cambridge, Massachusetts, USA), which is a polymerized haemoglobin of bovine origin, has been released to the veterinary market. Oxyglobin® exerts a colloid effect in blood, potentially making it the ideal fluid for resuscitation. Supplemental oxygen is not required for the positive effects on oxygen-carrying capacity, and it has prolonged shelf life (approximately 2 years at room temperature) (17). Disadvantages include short plasma-half life, potential renal toxicity, hypertensive effects, and the potential of immunogenic effects (1).

Conclusion

Shock is defined as inadequate tissue oxygenation due to poor perfusion. Haemorrhagic shock ensues when circulating blood volume decreases secondary to haemorrhage and a patient loses 30% of its blood volume. The main goal of therapy in haemorrhagic shock is obtaining adequate tissue oxygenation. Intravenous fluids, crystalloids, and/or colloids should augment cardiac output, thus increasing tissue perfusion and potential oxygen delivery to the tissues. Blood products may be necessary to improve haemoglobin content and oxygen-carrying capacity.

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TEKOČINSKA TERAPIJA HEMORAGIČNEGA ŠOKA

A. Seliškar

Povzetek: Hemoragični šok je klinični sindrom, ki se kaže z nezadostno oskrbo tkiv s kisikom zaradi slabe prekrvitve kot posledice zmanjšanega efektivnega volumna krvi. Pri zdravljenju hemoragičnega šoka so se kot učinkovite izkazale izotonične in hipertonične raztopine soli in različni koloidi. Izotonični kristaloidi neovirano prehajajo skozi kapilarno membrano, zato jih moramo injicirati v veliki količini, da nadomestimo izgubljeno količino plazme. V znotrajžilnem prostoru ostanejo le kratek čas, kasneje pa zaradi prehajanja v zunajžilni prostor lahko povzročijo edem tkiv in njihovo okrnjeno oskrbo s kisikom. Dodajanje koloidov znatno zmanjša potrebe po skupni količini tekočin, podaljša volumensko ekspanzijo, zaradi razredčitve krvi pa se zveča mikrovaskularna prekrvitev. Hipertonične raztopine soli z dodanimi koloidi ali brez njih z endogeno preraz-poreditvijo tekočin zvečajo količino plazme tri do štirikratno glede na injicirano količino raztopine soli. Učinkujejo pozitivno inotropno, k zvečanju minutnega volumna srca pa naj bi prispevala tudi aktivacija refleksnega loka, ki vključuje n. vagus in receptorje v pljučih. Mikrovaskularni pretok se po dajanju hipertoničnih kristaloidov ne zveča samo zaradi razredčitve krvi, temveč tudi zaradi hiperosmotskega skrčenja krvnih in endotelijskih celic. Ne glede na vrsto tekočine, ki jo uporabimo pri zdravljenju hemoragičnega šoka, je nujno čimprej vzpostaviti učinkovito cirkulacijo, s čimer omejimo morebitne zaplete zaradi dalj časa trajajoče hipoksije. Poudariti je tudi treba, da je cilj tekočinske terapije normaliziranje življenjskih funkcij živali in ne zgolj dajanje vnaprej določenega odmerka tekočin.

Ključne besede: hemoragični šok; tekočinska terapija; kristaloidi; koloidi