Colloids - Why Bother?
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What are they?

Colloid solutions are large molecule/particle containing substances of a homogenous noncrystalline nature; these molecules do not settle out and are dispersed evenly in the solution.

Which colloids are available?

There are 2 main groups; naturally occurring and semisynthetic. Naturally occurring colloids are generally plasma derived ie: human albumin solution (HAS), plasma protein fraction, fresh frozen plasma and immunoglobulin solutions.

Semisynthetic are generally derived of geletins, dextrans and startches. The most commonly used and only semisynthetic colloid available for veterinary medicine use in Ireland is Voluven®. The most commonly used HES solution in the USA is 6% Hetastarch® (suspended in 0.9% NaCl) and is slowly degradable. Hextend®, which is suspended in a solution similar to Hartmann’s Solution, has similar properties. Also used in the US and Australia is Dextran 70, which is a glucose polymer often suspended in hypertonic saline.

For the purpose of this lecture we will mainly focus on Voluven, but the rest will be mentioned.

What do they do?

A note on osmotic pressure and Colloid osmotic pressure (COP):
Osmosis is the passage of water from a region of high water concentration to a region of low water concentration through a semipermeable membrane ie; osmosis attempts to create an equilibrium between the concentrations of 2 substances on each side of a semipermeable membrane. However, this may not occur in certain circumstances due to the presence of other forces like pressure occurring as the result of one or both compartments being of restricted or different sizes (eg interstitium versus blood vessels) in these
situations osmotic pressure is the pressure required to prevent movement of water from dilute solution to concentrated solution. In the case of membranes permeable to salts and small ions but impermeable to colloid particles (macromolecules such as plasma proteins), the pressure required to prevent movement of solvent and small ions is known as the colloid osmotic pressure (COP), or the oncotic pressure. The measurement of interest here is kilodaltons (kDa) which is the molecular weight (MW) of the molecules and this along with the pore size reflects the relative proportion of molecules retained by the semipermeable membrane and thus the effective COP. Colloids with a low MW are small molecules will be lost more rapidly from the circulation than those with a higher MW.

In normal healthy animals, albumin is the body’s most abundant natural colloid and provides most of the body’s intravascular COP it accounts for 70 – 80% of plasma oncotic pressure as there is a higher concentration of albumin in the vascular space, than in the interstitium (though one third is intravascular and two thirds extravascular the difference in sizes of these spaces accounts for the effect Albumin has on COP). Normally there is a 5% per hour leak from circulation, so a balance of creating and utilization of albumin is very important for COP and hence for circulatory volume.

Hydroxyethyl starch (HES) solutions are artificial colloid solutions used in veterinary medicine for plasma volume expansion and to increase colloid osmotic pressure. These are large starch polymers suspended in an isotonic crystalloid solution and as such are isotonic, but because most of the HES molecules are too large to cross the endothelium, they cause an increase in COP as described above. The degree of blood volume expansion and the solution’s rate of degradation depend mainly on the molecular weight (MW), but other factors are involved also. The manufactured mean MW of a HES solution can be divided into high MW (>400 kD)(Hetastarch), medium MW (200-400 kD) or low MW (<200 kD)(Voluven). DS may also be mentioned at this point and this is the mean number of hydroxyethyl groups per glucose unit within the glucose polymer, and HES solutions can be divided into high DS (>0.5) or low DS (0.4-0.5). The higher the DS generally the slower the rate of degradation and HES can be described by MW/DS (Voluven 130/04). In regards to blood volume expansion, the ability of the solution to affect fluid movement ultimately depends on the number of molecules
present within the intravascular space (that are unable to transverse the endothelium), rather than absolute size therefore lower molecular weight solutions can cause a greater fluid movement into the vascular space, with the downside being that they are rapidly degradable.

**There use:**

Colloid solutions are usually used for dogs and cats requiring intravascular volume expansion to increase oncotic pressure and oxygen delivery on an emergent basis. Examples where colloid solutions may be of benefit are:

- Hypovolemic and hypoproteinemic.
- Traumatized and hypovolemic
- Hypovolemic with head trauma
- Hypotensive and in shock
- Severe sepsis
- Ascites and peripheral edema
- Hypotension during anesthesia

In cases of shock, the disease process is generally acute in nature. (See notes on Shock). Shock may result from inadequate blood volume (hypovolemic shock), inadequate cardiac function (cardiogenic shock), or inadequate vasomotor tone (septic shock). Crystalloids have been the primary fluid choice in veterinary medicine for restoring vascular volume and organ perfusion in patients in shock. However, a combination of colloids and crystalloid is more frequently been used in situations of shock as standard resuscitation. Due to the properties of crystalloids only 25% to 30% of the administered volume remains in the vascular space, an administration rate of up to 90 ml/kg/hr may be needed for resuscitation from shock and therefore excessive amounts of crystalloid fluids can cause interstitial oedema. Resuscitation with colloids can be achieved at much lower volume (20 to 30 ml/kg) it means colloids are especially useful in patients with head trauma or pulmonary contusions. In septic shock extreme vasodilatation and increased vascular permeability contribute to severe hypotension and colloids may help prevent “vascular leak syndrome” associated with sepsis as they don’t readily cross into the interstitial space.

Patients with hypoproteinemia (specifically, hypoalbuminemia) will also have a decreased vascular volume due to the decrease in plasma oncotic pressure
caused by the low albumin. Colloids can be very useful in increasing COP and hence increasing vascular volume in these cases. However, in chronic cases, compartments tend to adapt and equilibrate with the interstitium having a lower albumin level in than normal. It is important to tailor fluid therapy in chronic cases to prevent over hydration and fluid overload and to ensure adequate vascular volume and hydration as well.

Initial Treatment
Acute Drop in Vascular Volume
- A combination of a colloid and a crystalloid can be used:
  Dogs: 1-2ml/kg/hr or 20-40ml/kg/day Voluven with 15 to 30 ml/kg of an isotonic replacement crystalloid
  Cats: 5 to 15 ml/kg of Voluven with 10 to 20 ml/kg of an isotonic replacement crystalloid.

To avoid volume overload in trauma cases, colloids can be combined with 7% hypertonic saline at 4 ml/kg IV over 5 to 20 minutes, with colloid bolus of 5 ml/kg IV every 10–15 min up to four times, this protocol is also helpful in decreasing cerebral oedema in head trauma cases. Crystalloid fluids at a rate of 5 to 15 ml/kg/hr can be added to maintain perfusion. Monitoring blood pressure is a helpful tool to monitor progress and systolic blood pressure should be between 80 to 140 mm Hg.

Chronic hypoproteinaemia/reduced plasma oncotic pressure
A combination of a colloid and a crystalloid can be used (or a colloid alone if the animal is well hydrated):
  Dogs: 1-2ml/kg/hr or 20-40ml/kg/day Voluven.
  Cats: 10 to 15 ml/kg/day of Voluven.
Hypoproteinemic patients with third spacing of fluids should be considered for colloid therapy, as should hypoproteinemic patients that require anesthesia for diagnostic testing. However, many patients with a chronic decrease in COP have compensated with fluid compartment shifts and do not require colloid therapy. Additionally, many of these diseases will require medical therapy to correct the cause of the hypoproteinemia, and it is generally not feasible to continue colloid therapy during chronic medical management.
** The manufacturer of Voluven® (HES 130/0.4) states the maximum daily dose to be 50ml/kg/day,

Supportive Treatment
In all cases it is important to maintain fluid and electrolyte balance using crystalloid solutions and should be tailored to each individual situation.

Patient Monitoring
Hydration status, electrolytes and protein levels, and COP (if possible) should be monitored to determine fluid type and amount needed to maintain patient. Urine output, systolic and/or mean blood pressure, and central venous pressure should be monitored to determine adequacy of vascular volume. Due to the large volumes of fluid therapy it is essential that patient be monitored for signs of over hydration: serous nasal discharge, signs of pulmonary oedema, pleural effusion (especially cats), jugular venous distension, weight gain, etc.

Treatment Goals

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<tr>
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<th>Optimal</th>
<th>Min/Max</th>
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<tr>
<td>HR (bpm)</td>
<td>Dogs: 80–100</td>
<td>80/140</td>
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<tr>
<td></td>
<td>Cats: 180</td>
<td>160/220</td>
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<tr>
<td>PCV (%)</td>
<td>30–40</td>
<td>20/60</td>
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<tr>
<td>TP (g/dl)</td>
<td>6–7</td>
<td>3.5/9</td>
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<tr>
<td>Alb (g/dl)</td>
<td>2.5–3.5</td>
<td>1.5/4.5</td>
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<tr>
<td>Urine output(ml/kg/hr)</td>
<td>1–2</td>
<td>0.5/6</td>
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<tr>
<td>Blood lactate (mmol/L)</td>
<td>&lt;2.5</td>
<td>3/&gt;10</td>
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Alternative colloids:
Plasma transfusions
Plasma transfusions can be used in hypoalbuminaemic patients especially if serum albumin levels drop below 2.0 g/dl and the animal is not responding to semisynthetic colloid therapy. An estimated 22.5 ml/kg plasma is required to raise the serum albumin level from 2 to 5 g/dl.
Its use as a first colloid solution is inappropriate in animals in shock as time is an issue and frozen plasma needs to be thawed.
Potential side effects:
Hypocalcemia with large volume transfusions,
Inflammatory reactions to plasma proteins and
Infection from contaminated products.

Human serum albumin
Human serum albumin solution has been used in human medicine and is an alternative to species-specific plasma. Human serum is now being used with increased frequency in the US because of its high oncotic load, intravascular volume can be increased up to five times the volume administered within 30-60 minutes and potential volume overload and pulmonary oedema is a possibility so requires careful monitoring.
Its use in veterinary medicine is still in its infancy and results from scientific studies vary from it been excellent to dangerous.

Possible problems with colloids

Platelet dysfunction:
Most of the research in regards to HES-induced platelet dysfunction has been in humans and has been attributed to decreased platelet adhesion by several mechanisms.
Decreases circulating levels of von Willebrand factor (vWF); this effect is similar to Type 1 von Willebrand’s disease.
Decreases circulating levels Factor VIII (FVIII)
Decreases agonist-induced expression and activation of platelet integrin $\alpha_{\text{IIb}}\beta_3$ (reducing platelet aggregation and formation of a platelet plug).
Coats the surface of the platelet, limiting binding of ligands to cell surface receptors.

In veterinary medicine, it has been shown that HES 670/0.75 can cause platelet dysfunction in dogs. Slowly degradable HES solutions have a greater adverse effect on human platelet function compared to rapidly degradable solutions, which makes Voluven an ideal colloid choice in veterinary medicine.

Renal dysfunction
Renal dysfunction has been associated with HES solutions of all types, in humans, and there seems to be a dose dependant effect. Evidence is lacking in veterinary medicine, however, it is practical to limit colloid therapy in patients at high risk of renal tubular injury, or renal failure. Urine output and renal function should be monitored closely.
Immunologic reactions
Immediate and delayed allergic reactions to hetastarch solutions are rare in human medicine, with a reaction rate of less than 1% reported for Voluven®. Again evidence is lacking in veterinary medicine but is likely that immune reactions are extremely rare in our patients as well, however immunologic reactions to plasma and albumin transfusions have been reported.

Refractometry
Increased urine specific gravities (USG) reading
Total protein (TP) readings are also affected however it is unlikely to be enough to influence clinical decision making and TP should still be monitored closely as part of the regimen.