Advanced Fluid Therapy: From Colloids to Hypernatremia

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The purpose of this lecture is to go beyond a simplistic view of fluid therapy as salts, sugars, and their interaction with the body, and to delve deeper. This lecture assumes a working knowledge of fluid physiology and therapy and will address some specific novel and intricate approaches to fluid therapy.

Topics to be covered include

- Synthetic colloid product physiology
- Alternate fluid resuscitation plans: low-volume, hypotensive, supraphysiologic
- Select fluid therapy cases: Hypernatremia,

Colloids

Colloidal solutions used in fluid therapy are crystalloid based and contain a large synthetic or natural molecule many magnitudes larger in size than electrolytes. Colloids are impermeable to capillary and cell membranes and operate to increase vascular volume by augmenting colloid oncotic pressure and utilizing Starling's forces to draw interstitial and intracellular water into the vasculature. As colloids are essentially sugar molecules (synthetic) or proteins (albumin) they can be degraded by enzymes. The half-life of the colloid can be determined by 2 factors: molar substitution and carbon atom placement at the C2 or C6 positions. This lecture will focus on synthetic colloids.

The most common synthetic colloids are the hydroxyethyl starch compounds. There are various trade names for various concoctions depending on their compositions. The dextran products are less available and less used due to higher incidences of untoward reactions from their use.

The hydroxyethyl starch compounds are glucose-type sugars made from plant sugars (amylopectin and amylose) and are degraded by amylase in vivo. In order to prolong the oncotic effect carbon atoms can be substituted at positions on the molecule. These positions, C2, C3, C6, alter half-life and increase oncotic pull when greater substitutions are made on the C2 positions versus the C6 one. All solutions contain a variety of sizes of molecules; some are filtered by the glomerulus and are excreted into the urine, and larger ones remain in the vasculature and are subject to enzymatic degradation.

If we look at a typical hydroxyethyl starch product: (Hespan ^{TM}): it has 3 different parts to it:

- 6% HES 450/0.7
- 6%: Refers to the concentration of HES molecules. Most products are either 6% or 10%. Oncotic pull and volume expanding effects increase with greater concentrations
- 450: This refers to the weight-averaged molecular weight (Mw) and is somewhat complicated:
    1. The M_n is the mean of molecular weights of molecules in the solution
    2. The M_w is the total number of mean molecular weights divided by total number of molecules in solution.

An easy way to picture this is by using a population example. The M_n represents total weight of a solution and that is divided by the number of molecules in solution- so a true "averaging." The M_w is a weighted- average, which means small and large molecule percentages are taken into account. The true average may not account for the fact that a random sampling of the solution may yield molecules that are larger and smaller than the calculated average because molecules are not evenly distributed by weight. Let's use our population example:

Los Angeles, CA 9, 862,049 people
Springfield, IL 116250 people
Kingmon, AZ. 7719 people

The true average is: (9,862,049) + 116250 + 7719 / 3 = 3,328,671. This means that on average over 3 million people live in one of these cities. But that is incorrect! So we have to use a weighted average- which takes into account the percentage of the total that is present in each city. It is computed as such:

- Total population: 9,986,018 people
- Los Angeles: 9,862,049 / 9,986,018 = 0.987 (or 98.7 % live in LA)
- Now take 0.987 x 9,862,049 = 9,739,618. This number represents the average in LA that will be used to calculate the weighted average.
- Springfield, IL: 116,250 / 9,986,018 = .011 x 116,250 = 1353
- Kingmon, AZ: 7719 / 9,986,018 = .0007 x 7719 = 5.4
- When all of these populations are added up- that is the weighted average.
- 0.7 = Refers to the degree of substitution of carbon atoms.

Colloids have two major negative side-effects to their use. The first is their effects on the coagulation system. It appears that all synthetic colloidal solutions:

- Affect von Willebrand factor function
- Affect Factor VIII function
- Affect platelet function
- Fibrinogen deficiency

The other adverse effect of these colloids is their effect on the kidneys. They can potentiate acute renal failure potentially through osmotic affects in the kidney cells.

Daily maximums exist for colloidal solutions to affect their influence on coagulation, which remains a serious concern for patients with other reasons to have coagulopathies or may require surgical intervention for a disease process. With 6% HES 450/0.7 formulations, this is limited at 20-30 ml/kg/day. It appears that by lowering the M_w and degree of substitution, daily maximums can be exceeded with minimal affects on coagulation. Voluven™ (6% HES 130/0.4) can be delivered up to 50ml/kg/day and is labeled as such in people.

HES Trade name	Percent	M_w	Degree of substitution	COP (mmHg)
Hespan ™	6%	450	0.7	26
Hextend ™	6%	670	0.75	31
Voluven ™	6%	130	0.4	36
Tetraspan™	6%	130	0.42	36

Approaches to fluid therapy

Limited fluid-volume resuscitation (LFVR):

As the goal of administration of fluids to critical patients involves restoring vital organ perfusion and reversing the shock syndrome, it follows that only the amount of fluid needed to do this would be best for the patient and optimize outcome. LFVR refers to a fluid strategy that aims to administer a fluid volume that restores perfusion but is conservative in its volume. This is in contrast to older theories of fluid therapy where blood volumes were rapidly re-infused (90 ml/kg, dog and 60ml/kg, cat). Utilizaation of crystalloids and colloid therapy can assist in lowering fluid volume requirements in these patients. As with any "plan" there must be goals, and these goals point to a normalizing of perfusion parameters including: HR, RR, mentation, MM/CRT, Temperature, Systolic BP, MAP, CVP, Lactate, and UOP. With LFVR these end-points are achieved through titration of fluids as opposed to over-shooting the mark.

End-point	Goal
HR	Cats: <180-220BPM, Dgs: 60-160 BPM
RR	20-40 BPM
Temp	>100F
Mentation	From obtunded to alert
CVP	5-10 cmH20
Lactate	< 2 mmol/L
Systolic BP	>100 mmHg
MAP	>80 mmHg
Urine output	>1ml/kg/hr

Hammond, Limited-Volume Fluid Resuscitation. Compendium. 31 (7), 2009

The procedure followed with LFVR is

1. Assess the perfusion deficit (hyperlactatemia, tachycardia, hypotensive, oliguric, etc)
2. Administer a fluid bolus (10-20ml/kg crystalloids, 2.5-10ml/kg HES solution, 4ml/kg hypertonic saline solution)
3. Re-assess perfusion status (recheck HR, BP, MM/CRT, Lactate etc)
4. Decide whether additional boluses are required.

Fluid options for LFVR include: hypertonic saline solutions, crystalloids, and synthetic colloid solutions.

1. Hypertonic saline: Typically a 7% or greater solution. Causes a rapid shift of water from intraceullar and interstitial spaces into intravascular space utilizing an osmotic gradient. Acheives rapid volume expansion. Since it is essentially a crystalloid fluid, intravascular water will start to re-equilibrate with other fluid compartments and thus the effects are short lived. Can be combined with colloidal solutions (affectionately termed "turbostarch") to add an increase in COP which functions to retain more intravascular water. Additional benefits include increased cardiac output (direct inotropic effect), reduction of intracranial effects, and anti-inflammatory effects. It is contraindicated in hypernatremic or hyperosmolar patients and can cause hypotension/arrhythmias is administered too quickly. Recommendation is to not exceed 1ml/kg/min. Dose is 3-8ml/kg

2. Synthetic colloids: Affect intravascular volume by increasing intravascular COP and augmenting Starling's forces to drive water into the vascular space. Can have adverse renal and coagulation effects. Larger volumes required than hypertonic saline, but still greater increase for less volume compared to crystalloid solutions. Dose ranges from 2.5-5ml/kg in cats (do not exceed 10ml/kg/day) and 5-10ml/kg boluses in dogs (do not exceed 20-30ml/kg/day).
3. Crystalloid solutions require the greatest volume administered to cause changes in blood pressure and vascular volume. Typically 20-30ml/kg boluses are used in dogs and 10-15ml/kg boluses are used in cats. Frequent re-assessment of perfusion parameters is required as 75-80% of the intravascular fluid redistributes to the intracellular and interstitial spaces within one hour.

An additional benefit and indication for using LFVR is the adverse effects of massive fluid administration of circulating coagulation factors. Dilutional coagulopathies can occur when large amounts of fluids are administered rapidly; reducing the concentrations of natural coagulation factors and impairing the body from responding to a hemorrhagic insult.

Hypotensive fluid resuscitation

This is a controversial and under-studied method of resuscitation in the patient with uncontrolled hemorrhage that is being prepped for surgical intervention. BP is titrated to a systolic of 90 mmHg or a MAP of around 60 mmHg- the minimal requirements for core organ perfusion. This method is employed when additional hemorrhage or clot disruption may be detrimental to patient survival.

The hypernatremic patient

Hypernatremia is a confusing and labor intensive fluid therapy case. Patients that are volume-contracted and hypernatremic may require fluid resuscitation in addition to free-water replacement. Typically a patient that is hypernatremic requires the addition of free-water to re-establish osmotic gradients. Typically replacement of fluid in an emergent, shocky, hypernatremic patient should be resuscitated with a fluid that has a sodium concentration similar to that of the patient- allowing for volume expansion but no intracellular shifts of water. Once the patient's perfusion is restored free-water replacement can occur.

The free-water deficit formula is as follows:

$$\text{FWD (liters)} = 0.6 \times \text{body weight (kg)} \times \left[\frac{\text{Patient Na}}{\text{Normal Na}} - 1\right]$$

Example

- Patient Na is 180 meq/L- patient weights 5kg
- 0.6 x 5 x (180/150 – 1) = 0.6 liter deficit

Means that 600mL of free water need to be replaced. Typically this is done slowly to lower the Na to normal levels not exceed a 0.5-1meq/L/hr drop.

If the patient's Na is 180meq/L and you need to lower it 30 meq and can't exceed 1meq/L/hr- you want to lower the Na in 30 hours. So 600mL / 30 hours = 20ml/hr. This rate shouldn't cause the Na to drop too fast but you will want to re-check Na values quite often.

References available upon request.