Fluids: what's new?

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Ⓟ **Peer reviewed © Medpharm** **S Afr Fam Pract 2013;55(3)(Suppl 1):S28-S31**

Introduction

An adequate intravascular volume replacement is an essential part of managing a critically ill surgical or intensive care patient. Failure to treat or prevent hypovolaemia may progress to organ dysfunction, or even death.

Although the importance of adequate volume replacement is widely accepted, there are still no universally accepted recommendations. Different crystalloid solutions, the naturally occurring human albumin (HA), and different non-protein or synthetic colloids, have been promoted to treat volume deficits.

Over the years, some misconceptions about volume replacement have been established and these need to be reconsidered and corrected.

Approaches to fluid management

The "classic" and now outdated approach to the management of fluids in the perioperative setting was to try to predict the amount of fluids needed, based on the duration and severity of a particular operation, and empirically replace fluids based on these estimates. It involved calculating preoperative losses, ongoing maintenance requirements and anticipated surgical losses.

The problem with giving arbitrary amounts of fluid, without advanced monitoring, was recently highlighted by the Fluid Expansion as Supportive Therapy (FEAST) trial. While many problems were identified with this trial, it served to illustrate that fluid management needs to be goal-directed.

The "modern approach" to fluid management is based on the concept of goal-directed therapy, based on which it is believed that interventions should be performed specifically to affect a meaningful clinical variable. The reality is that fluids can be harmful, and should only be given when they are expected to produce some benefit. Management of fluids so that stroke volume is optimised is an extremely well validated approach and has been shown to reduce morbidity repeatedly. Numerous strategies and devices have now been optimised to specifically target stroke volume.

Types of fluids

Crystalloids

Conventional crystalloids are fluids that contain a combination of water and electrolytes. They are divided into "balanced" salt solutions, hypotonic and hypertonic solutions. Either their electrolyte composition approximates that of plasma, or they have a total calculated osmolality, that is similar to that of plasma.

Normal saline is an isotonic crystalloid. It has been termed physiological or "normal", but when compared with the composition of plasma itself, this hardly seems to be physiologically sound. It is known to be associated with hyperchloraemic metabolic acidosis. As a low-base excess may serve as a surrogate marker with which to identify patients with underperfused tissues, the administration of normal saline may well mask the diagnosis of a perfusion deficit and result in inappropriate clinical interventions because of the inaccurate assumption that ongoing tissue hypoxia is secondary to hypovolaemia.

When an electrolyte-free solution, such as D5W (5% dextrose in water), is administered, less than 10% remains intravascular. Approximately two thirds is distributed to the intracellular space. Intravascular resuscitation is minimal and cellular swelling occurs. The administered free water causes a decrease in the serum and interstitial electrolyte concentrations (a dilutional effect) and may lead to symptomatic hyponatraemia.

When solutions such as 0.2% or 0.45% saline are administered, similar, although slightly less pronounced, redistribution occurs. Therefore, a balanced salt solution with a sodium concentration of 130 mmol/l or more is normally chosen when major operative procedures are performed, and when excessive blood loss is anticipated.

Normal saline (0.9% saline solution)

- 9 g of NaCl/l water.
- 154 mmol/l sodium.
- 154 mmol/l chloride.
- Osmolality = 308 mOsm/l.
- pH = 5.

Hartmann's solution

- Na+ 131 mmol/l.
- Cl = 111 mmol/l.
- Lactate = 29 mmol/l.
- K^+ = 5 mmol/l.
- Ca^{++} = 2 mmol/l.
- pH = 6.5.
- Osmolarity = 279 mOsm/l.

Colloids

Colloids also contain water and electrolytes. Some are isotonic and others hypertonic, but they also contain a colloid, a large molecule that does not diffuse across semipermeable membranes. Therefore, the colloid exerts an osmotic pressure in the blood, causing fluid to remain within the intravascular system. Colloids are not the same. They have significant physiochemical differences, together with differences in their pharmacokinetic and safety profiles.

Two big categories can be defined:

- Natural, e.g. HA.
- Artificial, e.g. gelatins, dextran and hydroxyethyl starches (HES).

The behaviour of colloids is determined by several factors, namely:

- Molecular weight.
- Molecular number.
- Osmolarity.
- Oncotic pressure.
- Plasma half-life.
- Plasma volume expansion.
- The acid base.

Human albumin

HA may be used to correct hypovolaemia or hypoalbuminaemia. HA is dissolved in a saline solution that may result in acidosis, secondary to its high chloride content. The superiority of HA for volume replacement, compared with other plasma substitutes, has never been shown to increase mortality or major side-effects, such as bleeding.

The beneficial effects of HA have also been reported, especially in patients with liver cirrhosis and spontaneous bacterial ascites, where the use of HA, in conjunction with antibiotics and diuretics, compared to the use of antibiotics and diuretics alone, showed a significantly improved outcome. However, in both these studies, the control group (no HA) did not receive any volume replacement by other means. It is likely that hypovolaemia was present and correction by other non-protein colloids may have avoided acute kidney injury.

Albumin is also assumed to serve as a free radical scavenger and to bind toxic substances. Theoretical benefit may be seen in patients with sepsis, where toxic oxygen radicals may play a role in the pathogenesis. To date, data have not confirmed the benefits of HA with regard to morbidity or mortality in humans, secondary to its scavenging properties.

Evidence from the Saline versus Albumin Fluid Evaluation (SAFE) trial, which randomly assigned patients who were admitted to the intensive care unit (ICU) to either 0.9% normal saline, or 4% albumin, over a 28-day period, concluded similar outcomes. Of the 6 997 patients who underwent randomisation, 3 497 were assigned to receive albumin and 3 500 to receive normal saline. There were a reported 726 deaths in the albumin group versus 729 deaths in the saline group.

Other colloids include dextran, gelatins and starches.

Gelatins

Gelatins are formed by hydrolysing collagen, thereby creating a large, soluble molecular-weight protein.

Three main groups of gelatins exist:

- Succinylated or modified fluid gelatins (Isoplex® and Volplex®).
- Urea-cross-linked gelatins (Haemaccel®).
- Oxypolygelatins (Gelifundol®).

The electrolytes vary with each gelatin. In Volplex® and Gelofusine®, the electrolytes consist of sodium (154 mmol/l) and chloride (125 mmol/l). Isoplex® contains sodium (145 mmol/l) and chloride (10 5mmol/l). The lower the chloride content, the lower the risk of causing hyperchloraemic metabolic acidosis. The half-life of succinylated gelatins is approximately four hours, making it greater than a crystalloid, but shorter than a starch.

The advantages of using gelatins are the fact that there is no upper limit to the amount that can be infused, whereas starches and dextrans have an upper-infusion limit; and compared with starches, gelatins are small-sized molecules and are easily renally excreted, with no effect on renal impairment.

Disadvantages of using gelatins are an increase in anaphylactoid reactions, when comparing them with those of natural colloids. However, the frequency of these reactions is rare, with an incidence level of between 1:6 000 to 1:13 000.

Starches

In the UK, HES are more commonly used in the ICU. They are a derivative of amylopectin, which if left unmodified, break down too rapidly. Therefore, some of the HES groups, mainly at C2 and C6, are substituted with anhydroxyethyl glucose groups. HES are identified by three numbers. The

first indicates the concentration, the second represents the molecular weight, and the third and most significant, the molar substitution.

Advantages of using starches are a longer duration of action, a lower cost compared to albumin, and the potentially encouraged restoration of cell-mediated function and macrophage function after haemorrhagic shock.

The disadvantages of the first- and second-generation starches were potential coagulation risks, from a reduction in factor VIII and vWF, and thus an increase in bleeding complications; accumulation within the interstitial spaces and reticuloendothelial system; and the risk of renal impairment being caused.

With the introduction of third-generation starches and newer tetrastarches, fewer side-effects were noted, while they have still maintained their volume-expanding efficacy.

The Crystalloid Versus Hydroxyethyl Starch (CHEST) trial randomly assigned 7 000 patients who had been admitted to the ICU to either receive 6% HES (6/130/0.4/) or 0.9% normal saline for all fluid resuscitation until ICU discharge, death, or 90 days after randomisation. The primary outcome was death within 90 days. Secondary outcomes included acute kidney injury and failure and treatment with renal-replacement therapy. It was concluded that in patients in the ICU, there was no significant difference in 90-day mortality. However, more patients who received resuscitation with HES were treated with renal-replacement therapy. This further questions whether or not we should continue to use colloids in this particular environment.

Few topics in anaesthesia and surgery have generated as much controversy as the relative merits of colloids and crystalloids with regard to intraoperative fluid replacement and resuscitation. Numerous animal and human studies have been undertaken to prove that one or the other is superior. In most cases, choice is based more on personal opinion and dogma, rather than scientific merit.

In 1989, a meta-analysis by Velanovich examined mortality in eight published human trials in patients receiving either crystalloid or colloid for resuscitation. It showed an overall 5.7% decrease in mortality rate in patients who were resuscitated with crystalloid, rather than colloid, solutions. Subgroup analysis showed that trauma and sepsis patients had a 12.3% decrease in mortality when crystalloids were used. However, when crystalloids were administered to patients undergoing elective surgery, there was a 7.8% increase in mortality.

The proposed explanation was that patients with trauma and sepsis have an increase in capillary permeability that allows the administered colloid to leak out of the vasculature, to be less effective as an intravascular volume expander, and to slow resolution of oedema from the affected tissues. In patients undergoing elective procedures, the amount of capillary leak, in contrast to that in major trauma, is more discretely limited to the surgical site. Thus, the use of colloids may be more efficacious in increasing intravascular volume. This study does not resolve the controversy, but it does provide some insight into specific situations in which one or the other may be preferable. Most colloid advocates do not recommend these substances as the sole resuscitative fluid. The usual protocol is initial infusion of crystalloids, followed by the administration of colloids when large volumes are necessary to reduce the amount of crystalloids. In general, crystalloids need to be administered in volumes that are approximately 2-3 times that of iso-oncotic colloid to obtain the same haemodynamic effect.

The latest surviving sepsis guidelines make three recommendations:

- Crystalloids should be used as the initial fluid of choice in resuscitation cases in which there is severe sepsis and septic shock.
- The use of HES for fluid resuscitation in severe sepsis and shock should be avoided. The recommendation is based on the results of the Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis (VISEP), Effects of Voluven on Hemodynamics and Tolerability of Enteral Nutrition in Patients With Severe Sepsis (CRYSTMAS) and the CHEST trials.
- Albumin should be given for fluid resuscitation in severe sepsis and shock when patients require substantial amounts of crystalloids.

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