End of Colloid Era

Essay

Submitted for partial fulfillment of Master degree in

Intensive Care

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2014

Acknowledgement

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List of Abbreviations

AKI : Acute kidney injury

ALI/ARDS : Acute lung injury/acute respiratory distress syndrome

BP : Blood pressure

CBF : Cerebral blood flow

CHEST : Crystalloid versus hydroxy ethyl starch trial

COP : colloid oncotic pressure

CRYTMAS : Cristalloids morbidity associated with severe sepsis

CI : Confidence interval

ESRD : End stage renal disease

GFR : Glomerular filtration rate

HES : Hydroxy ethyl starch

ICU : Intensive care unit

IV : Intra venous

KIDGO : Kidney disease improving global out comes criteria

LMD : Low molecular dextran

LR : Lactated ringer

NO : Nitric oxide

NS : Normal saline

RIFLE : Risk, injury, failure, loss, end stage renal disease

RRT : Renal replacement therapy

6S : Scandinavian starch for severe sepsis/septic shock

S cr : Serum creatinine

SAFE : Saline versus albumin fluid evaluation

VISEP : Efficacy of volume substitution and Insulin therapy in severe sepsis

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Introduction

The colloid-crystalloid debate has lingered for decades, resulting in the overall conclusion that composition of fluids for resuscitation does not influence morbidity or mortality in the general intensive care unit population and that the only difference involves cost *(Finfer, et al., 2004)*.

Even with the advent of 'safer' hydroxyethyl starches (HESs) *(Zarychanski et al., 2009)*, a mortality benefit remains elusive. However, human studies *(Barron et al., 2009)* suggest that fluid therapies may not be as innocuous as once thought and they may cause renal injury and perhaps affect mortality in specific subgroups.

The first adequately powered, randomized, blinded study drawing attention to these potential differential effects was the SAFE trial. This study found no differences in mortality in the general ICU population, but did find trends towards increased survival in patients with sepsis and increased mortality in patients with traumatic brain injury *(SAFE et al.,2007)*, suggesting that these differential effects do exist and that they may be determined by the population studied. More recently, the VISEP (Volume Substitution and Insulin Therapy in Severe Sepsis)

trial *(Brunkhorst   et al., 2008)* addressed the safety and efficacy of HES versus lactated ringer's solution in patients with severe sepsis and septic shock.

These investigators demonstrated that HES increases risk of acute kidney injury (AKI) and renal replacement therapy. Similarly, a meta-analysis that included the VISEP trial showed an increased risk of AKI in the general population and an increased risk of AKI and use of renal replacement therapy in patients with sepsis. However, the VISEP trial used high doses of hyperoncotic HES and may not be relevant to usual practice. Finally, a meta-analysis by Perel and colleagues *(Perel   and Roberts, 2012)*, which included both SAFE and VISEP trials, failed to show differences in mortality in hospitalized patients but recommended that future trials focus on specific subgroups. Taken together, these data suggested that fluid composition may be important, at least in certain subgroups of critically ill patients, especially in patients with sepsis. The Scandinavian 6S trial attempted to answer this question by randomly assigning patients with severe sepsis to receive HES in a ringer's acetate solution compared with carrier solution alone. The 6S trial found a higher risk of 90-day mortality (relative risk = 1.17, $P = 0.03$) and greater use of renal replacement therapy with HES as compared with those receiving ringer's acetate *(Perner et al., 2013)*.

However, whether the increased mortality and morbidity risk were present in a more heterogeneous ICU population was still unknown.

CHEST was a well-conducted, blinded, randomized trial, that used a patient-centered outcome such as 90 day mortality as primary aim, and that was adequately powered to find differences between groups using the intention-to-treat principle. *Post hoc* analysis suggested that increases in creatinine were more pronounced in the HES group, perhaps prompting the small but significant increased use of renal replacement therapy *(Shaw and Kellum, 2013)*.

Aim of the Work

- Reviewing the advantages and disadvantages of crystalloid and colloid.

- Highlighting the benefits from using crystalloid instead of colloid.

- Demonstrate the effect of using crystalloids in critically ill patients.

Advantages and Disadvantage of crystalloid and Colloid

Objectives of fluid replacement are cardiovascular compensation in severe hypovolemia, increase cellular perfusion and oxygen delivery and eliminate the profound lactic acidosis*(Dunham et al., 1991)*.

If oxygen delivery is not restored quickly, cell membrane pumps fail and cellular function will not recover even if adequate oxygen delivery is restored*(Chiara et al., 2002).*

To review the different between the hydrostatic and colloid oncotic pressure here the starling equation.

The principles behind the equation are considered useful for explaining physiological phenomena happening at the capillary*(Woodcock et al.,2012) .*
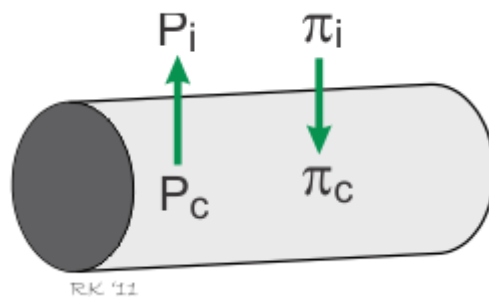
Fig. (1): Demonstrate the physiological phenomena happening at the capillary

The Starling equation reads as follows:

$$J_v = K_f([P_c - P_i] - \sigma[\pi_c - \pi_i])$$

where:

- J_v is the net fluid movement between compartments.
- $[P_c - P_i] - \sigma[\pi_c - \pi_i]$ is the net driving force,
    1. Pc is the capillary hydrostatic pressure.
    2. Pi is the interstitial hydrostatic pressure.
    3. πc is the capillary oncotic pressure.
    4. πi is the interstitial oncotic pressure.
    5. Kf is the filtration coefficient – a proportionality constant.
    6. σ is the reflection coefficient.

By convention, outward force is defined as positive, and inward force is defined as negative. The solution to the equation is known as the net filtration or net fluid movement (Jv). If positive, fluid will tend to leave the capillary (filtration). If negative, fluid will tend to enter the capillary (absorption Pressures are often measured in millimetres of mercury (mmHg), and the filtration coefficient in millilitres per minute per millimetre of mercury (ml·min−1·mmHg−1).

In essence the equation says that the net filtration (Jv) is proportional to the net driving force. The first four variables in the list above are the forces that contribute to the net driving force *(West et al.,2012).*

The filtration coefficient is the constant of proportionality. A high value indicates a highly water permeable capillary. A low value indicates a low capillary permeability.

The filtration coefficient is the product of two components:

- Capillary surface area.

- Capillary hydraulic conductance

(Levick et al.,2003).

The reflection coefficient is often thought of as a correction factor. The idea is that the difference in oncotic pressures contributes to the net driving force because most capillaries in the body are fairly impermeable to the large molecular weight proteins. (The term ultrafiltration is usually used to refer to this situation where the large molecules are retained by a semipermeable membrane but water and low molecular weight solutes can pass through the membrane) *(Woodcock et al.,2012).*

Table (1): Composition of crystalloid and colloid solutions used for fluid resuscitation

Component	Normal saline 0.9%	Lactated ringer's	p-lyte	Hypertonic saline 3%	Albumin 5%	Heta starch 6%	Dextran 70 (6%)	Gelatins	Human serum (m-mol/L)
Sodium (meq/l)	154	130	140	513	-145	154	154	145	135-145
Potassium (meq/l)	0	4	4	0	0	0	0	5.1	3.6-5.1
Chloride (meq/l)	154	109	98	513	-145	154	154	145	95-105
Lactate (meq/l)	0	28	0	0	0	0	0	0	
Calcium (meq/l)	0	2.7	0	0	0	0	0	0	2.1-2.8
Acetate (meq/l)	0	0	27	0	0	0	0	6.25	
Gluconate (meq/l)	0	0	23	0	0	0	0	0	
Magnesium (meq/l)	0	0	3	0	0	0	0	0	
Osmolarity (mosm/l)	310	275	294	1025	310	310	310	Isotonic	285-295
Oncotic pressure (mmhg)	0	0	0	0	20	30	60	35 - 39	
Ph	5	6.5	7.4	5	6.9	5.5	3 - 7	7.3	

(Lepaniemi et al.,1996)

Normal range of human plasma osmolarity is about 285-295 milli-osmoles per kilo gram

To calculate plasma osmolarity use the following equation :

$$= 2[Na+] + [Glucose]/18 + [BUN]/2.8$$

Where [Glucose] and [BUN] are measured in mg/dL.

If the patient has ingested ethanol, the ethanol level should be included in the calculated osmolality:

$$= 2[Na+]+[Glucose]/18+[BUN]/2.8 +[Ethanol]/3.7$$

(Purssell et al.,2001).

Crystalloid fluids

The more commonly used crystalloid solutions are:

- Normal saline;

- Hartman's solution;

- Ringer's solution.

Crystalloid fluids are balanced salt solutions that freely cross capillary walls *(O'Neill and Perrin 2002)*. They stay in the intravascular space for a shorter time than colloids, the half-life of crystalloids being 30 to 60 minutes *(O'Neill 2001).*

Crystalloid fluids will demonstrate an early marked plasma expansion, which is short lived but can be maintained by using a colloid as well *(Webb, 1999)*. Therefore crystalloids

are shown to be useful for fluid replacement or maintaining fluid balance in the short term only.

The volume of fluid replacement to be given is a major consideration when replacing lost volume with a crystalloid solution. Three times the volume lost has to be administered *(O'Neill, 2001)*.

This is because only approximately one-third of the fluid administered will stay in the intravascular space, with two-thirds passing directly into the tissues *(Bradley, 2001).*

Advantages and disadvantages:

The advantage of crystalloid fluid resuscitation is that volume has not only been lost from the intravascular space, but also extracellular water has been drawn to the intravascular space by oncotic pressure.

Solutions with lower sodium concentrations distribute more evenly throughout the total body water. This means that crystalloid solutions with higher sodium concentrations are more effective as plasma expanders *(Platt and Wade, 2002).* Crystalloid therapy may, however, adversely affect microcirculatory blood flow and oxygenation when used in cases of shock, resulting in hypoxia even after resuscitation *(Krau, 1998).*