

Colloid versus crystalloids in shock

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Abstract

This is a review of the use of colloid and crystalloid in shock. The article discusses the pathophysiological consequences of ischaemia and shock; reviews the underlying physiology of fluid compartments and how they may be affected by disease; examines the physiological determinants of intravenous (IV) fluid use; and finally reviews the literature on colloid and crystalloid use for the management of shock.

Key Words: Shock, Fluid resuscitation, Colloids, Crystalloids

The debate about whether to use crystalloids or colloids for the resuscitation of hypovolaemia is not as important as the challenge of continually maintaining a normal intravascular volume. In this article we will discuss hypovolaemia and its consequences, the physiology of body fluids and finally the choice of the most appropriate fluid, touching on the colloid-crystalloid controversy.

Hypovolaemia is one of the most common and potentially reversible crises in acute medicine. It occurs as the result of fluid loss (e.g. bleeding, burns, vomiting and diarrhoea) or vasodilatation of the circulating volume (e.g. septic shock). In either case, rapid correction is mandatory. In the setting of Intensive Care, there is the initial challenge of shock and resuscitation but there is also the often overlooked challenge of maintaining euvolaemia over the ensuing days.

In the daily routine of Intensive Care we continually monitor hypovolaemia with vital signs such as blood pressure (BP) and pulse rate (PR) as well as by monitoring end organ function such as urine output and peripheral perfusion. Even minor degrees of hypovolaemia can cause ischaemia and organ dysfunction.¹ It is therefore, not surprising, that we are constantly on the alert for the

first signs of hypovolaemia, and then having detected it, rapidly correcting any deficit. The usual strategy in the Intensive Care Unit (ICU) is to either increase the rate of IV fluid infusion or deliver a bolus of 300-400 ml – a fluid challenge – assess the effect and adjust the fluid rate accordingly.

The importance of maintaining the intravascular space (IVS) is related to the deleterious effects of ischaemia. There is no conclusive data on exactly how much ischaemia can be safely tolerated. Particularly important are cells with high metabolic rates such as the brain, heart and kidney. These organs initially have their blood supply protected by autoregulation at the expense of decreased blood supply to non-vital organs such as the skin and muscle. Ischaemia can be better tolerated in organs such as the skin or muscle as they have a low metabolic rate. However, there comes a point when even these cells begin to malfunction. Even minor degrees of hypovolaemia predisposes to splanchnic hypoperfusion,² predisposing to translocation of bacteria and bacterial breakdown products.³ This can in turn predispose to multiorgan dysfunction syndrome (MODS) and even death.³⁻⁶ Cytokines are also released as a result of the ischaemia itself, adding to the MODS.^{7,8}

The concept of early detection and correction of ischaemia, as well as rapid establishment of an airway and delivery of adequate oxygen delivery is the basis of the 'Golden Hour', emphasising the importance of rapid resuscitation in order to prevent cellular damage. The

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so-called 'Golden Hour' applies not only to initial resuscitation but also to continually maintaining the IVS, while the patient is in the ICU.

There is no proven place for deliberately tolerating even the smallest degree of ischaemia. While deliberate hypoventilation or permissive hypercarbia is a proven strategy to protect overventilation of lungs and damage to alveoli; permissive hypercarbia does not mean permissive hypoxia. And permissive hypercarbia and its benefits do not equate to permissive hypotension, which in fact is "permissive shock and ischaemia". In special circumstances such as penetrating injury to the torso, it may be better to perform definitive surgery rapidly rather than attempt to restore circulating volume.⁹ This does not mean that ischaemia is an acceptable state. It simply means that early definitive surgery is probably a better option in that relatively unique clinical circumstance. Unfortunately, because surgery may be a higher priority than IV resuscitation in this particular and relatively rare circumstance, there has been an extrapolation to other situations, inferring that ischaemia is acceptable in other circumstances. This is not the case.

The Body's Fluid Spaces

There are approximately 40 l of water in a 70 kg adult male - 60% of the body's weight.¹⁰

In the newborn it is closer to 80% and in the very old, approximately 40%. In other words, the young require higher maintenance fluid and as you age, you contain less water.

The water is distributed between three spaces, each with a distinct function and set of physiological principles governing its volume - the IVS; the interstitial space (ISS); and the intracellular space (ICS).

Intravascular Space

The IVS contains about 5 l of blood - red cells and plasma. The circulation delivers nutrients and oxygen to cells and removes carbon dioxide and products of metabolism. The IVS is contained within the circulation by the endothelial cells which, while allowing some leakage of large molecules such as proteins, largely encourages their retention within the IVS, generating a colloid oncotic pressure (COP), which encourages fluid movement from the interstitial space (ISS), counteracting the

effect of the hydrostatic pressure within the capillaries.

Interstitial Space

The ISS contains about 12 l of water and represents the fluid between the IVS and cells, facilitating transport between the two and, because of its connective tissue, contributing to the general structure and shape of the body. Apart from water, the ISS contains electrolytes, with the predominate cation being sodium (Na) in the same concentration as the IVS. Sometimes the ISS and IVS are together labelled as the extracellular fluid (ECF). This is an artificial construct as the IVS and ISS have very different functions and constituents.

Intracellular Space

The ICS is the largest space (approximately 23 l) and has potassium (K⁺) as its major cation. Therefore, sodium containing fluids will therefore not be distributed to the ICS.

Assessing the Fluid Space

Intravascular Space

The IVS is the most amenable to measurement. There are two major ways we can achieve that. Firstly, the global capacity of the IVS is estimated by measurements such as systemic BP; PR; central venous pressure (CVP) and jugular venous pressure (JVP); pulmonary artery wedge pressure (PAWP); Pulse Contour Cardiac Output (PCCO); and cardiac output (CO).

All of these measurements have limitations. The major one is that they are estimations of global blood flow and not the more important measures of organ perfusion. Bearing this shortcoming in mind, global measurements nevertheless give an indication of the adequacy of the circulating volume when looked at together with measures of organ perfusion and in the light of the clinical setting.

Systemic BP tracks the IVS more accurately in the elderly as they tend to have less of a sympathetico-adrenal response which allows younger patients to maintain BP until almost total circulatory collapse has occurred.

Similarly with PR - younger patients will mount a more vigorous tachycardia in response to hypovolaemia. The CVP may increase with heart failure or decrease with hypovolaemia. However, younger patients generate a

more active vasoconstriction as a result of hypovolaemia, resulting in an increase in CVP or JVP, compared to the elderly. There are similar shortcomings related to pathophysiological assumptions with the use of PAWP and CO, resulting in widespread reduction in the use of pulmonary artery catheters in the ICU.

The PCCO System has been developed, where continuous estimation of cardiac output is made by using an arterial pulse contour algorithm via a peripheral arterial line and trace.¹¹ The system is initially calibrated using a transpulmonary thermodilution measurement. A bolus of intravascular fluid is injected through a central venous catheter and the curve recorded by an arterial thermodilution catheter, which also serves as a pressure monitoring source.¹² The system also estimates intrathoracic blood volume; global end-diastolic volume; extravascular lung water; pulmonary vascular permeability index; and global ejection fraction.¹³⁻¹⁵

Another way of estimating adequacy of circulatory volume is by determining peripheral organ perfusion. Vital organs such as the heart and brain have their blood supply preserved even at very low levels of IVS and so are late indicators of indicators of the IVS, often immediately preceding death, especially in the young.

The kidney, also a vital organ, is, however, a very useful organ to determine adequacy of the circulating volume. Hourly urine output measurement is one of the simplest and most accurate ways of determining adequacy of the IVS. Moreover, renal failure as a result of hypovolaemia has such disastrous and expensive consequences that it should be avoided, where possible, by the simple administration of IV fluid. Obviously renal perfusion and urine output can also be affected by cardiac failure and, as such, needs to be interpreted in the light of other clinical findings. However, even with a failing heart, decreased urine output may result from inadequate volume as the filling pressure of the heart in these circumstances needs to be high. Decreased urine output can also be caused by other factors in the setting of an ICU, such as underlying renal disease or drugs such as diuretics.

Another organ which can reflect hypovolaemia is the skin. Hypovolaemia is detected by pressure receptors in the circulation resulting in increased sympathetico-ad-

renal activity, which in turn results in vasoconstriction of many of the less vital organs, including the skin. Early hypovolaemia is reflected in cooling of the most peripheral parts of the limbs - i.e. fingers and toes. Obviously pump failure can have the same effect as hypovolaemia and so the clinical setting needs to be taken into account.

The circulation is a dynamic organ controlled by many complex interactions. Rather than estimate the IVS with one measurement at one point in time, it is better to use as many of the measurements as possible and consider them as trends and to dynamically determine the adequacy of filling by a fluid challenge - i.e. administering 200-300 ml fluid rapidly, and measuring the response of the observations both before and after the challenge.¹⁶ If the measurements improve, then repeat the challenge and continue the fluid challenges until improvement in measurements is minimal. This point is an indication of an ideal IVS. Obviously the state of the circulation will be continually changing, necessitating close observation, repeated challenges and appropriate action.

Maintaining an appropriate IVS at all times is so important that perhaps the clinician who continually cares for the patient (usually a nurse) should be instructed on how to deliver fluid challenges and adequate fluid volumes as soon as any signs of hypovolaemia are noted. Obviously they would need to refer to their medical colleagues when there is any doubt.

Interstitial and Intracellular Space

Although these spaces are much larger than the IVS, they are less amenable to measurement. 'Softer' and less accurate measures such as thirst and mucosal dryness have to be used. The most accurate indicator of the ISS is probably peripheral oedema. This is easily assessed at the bedside. In clinical practise, the most accurate indicator of total body water is the serum sodium.¹⁷ The total body water is, in turn, the best guide to the ICS as the majority of body fluid is contained within cells. The reasons for serum sodium being an accurate indicator of body water is related to the balance between water and sodium in determining the concentration levels of sodium. The serum sodium concentration is, almost always, determined by total levels of body water, rather than the total levels of body sodium.

History of Fluid Administration

The first IV fluid was administered in 1832 for a cholera victim.¹⁸ Shock was a term first used to describe war casualties to describe their appearance as they seemed to die as a result of hypovolaemia, rather than as a direct result of their injuries. Cournand¹⁹ first described physiological abnormalities of shock. Shires²⁰ advocated the use of large amounts of crystalloids in the postoperative period in the 1950s. This was probably a reasonable approach as renal failure as a result of hypovolaemia was at that time, invariably fatal. As a result most postoperative patients were overtransfused with large amounts of crystalloids, usually charted in an inflexible way, in order to avoid renal failure in the small number of patients who had abnormal perioperative fluid losses.

Today's postoperative fluid prescribing is a legacy of that period - large amounts of crystalloid are administered in the postoperative period in a wide variety of inflexible recipes with little regard to the nature of fluid needs of the patient. Fortunately most operations are without complication and the body's finely tuned mechanisms for responding to fluid overload usually prevents serious complications.

The use of crystalloids in the postoperative period was then taken up for resuscitation of the seriously ill in ICUs.¹ Moreover, there were very few colloid solutions available at that time. Another factor for the failure to seriously question the approach to fluid therapy first developed in the 1960's is that with increasing specialisation in medicine, fluid and electrolyte therapy has not had the critical attention applied to its scientific foundations as, for example, if the field was confined to a single free standing organ such as the heart, gastrointestinal tract, lungs, brain, etc. In other words, important several body functions such as fluids and electrolytes and the lymphatics are not owned by any single specialty and therefore have tended to be neglected in terms of research and a critical appraisal of their role in acute medicine.

Crystalloids or Colloids

Colloids are mainly distributed to the IVS.¹⁰ Even with increased capillary leakage, a greater proportion of a colloid solution will remain in the IVS compared to a crystalloid solution.

On the other hand crystalloid solutions are mainly dis-

tributed to the ISS. Approximately two-thirds of all infused crystalloid must be distributed to the ISS, according to basic physiology, ie there are 17 l of fluid in the ECF and a crystalloid solution, without any inherent COP, must distribute equally across the whole 17 litres, with little or no fluid going to the ICS.²¹

In other words if the IVS is underfilled according to all the measurements we have, then a fluid that is distributed to that space such as blood or colloid is the ideal fluid. To use a crystalloid (which is mainly distributed to the ISS), according to measurements of a different space (the IVS), does not make physiological sense.

Moreover, the ISS is rarely underfilled in the seriously ill. In fact, most patients in the ICU have peripheral oedema. Giving crystalloids in these circumstances would add to peripheral oedema.

Disadvantages of an Expanded Interstitial Space and Crystalloid use

As little as 1 litre of normal or isotonic saline adversely affects pulmonary function by increasing closing volume and decreasing static and dynamic compliance.²² Increasing volumes of crystalloid result in overt hypoxia and increasing degrees of pulmonary oedema.²³⁻²⁶ This is not due to heart failure but simply due to the natural compartmentalising of saline into the ISS.

As well as expansion of the ISS in the lungs, peripheral oedema also occurs.^{24,25,27} Peripheral oedema can markedly decrease oxygen consumption.²⁸ This may be related to increased distance between the cells and capillary or be as a result of occlusion of the thin walled capillaries by an increase in the surrounding ISS pressure. This may explain why colloids have been demonstrated to improve tissue oxygenation compared to crystalloids.²⁹

Peripheral oedema also results in delayed wound healing.³⁰ Doubling the volume of the ISS decreases oxygen delivery to such an extent that capillary blood flow needs to be increased by 20-fold in order to maintain the same oxygen tension.³¹

Crystalloids result in a hypercoagulable state which can result in increased incidence of intravascular thrombosis.^{32,33}

A significant hyperchloraemic acidosis can occur when large amounts of isotonic saline are used.³⁴ The use of Ringer's Lactate is not associated with this phenomenon.³⁵

Clinical differences between Colloids and Crystalloids

There is compelling physiological evidence to use colloids for resuscitation of hypovolaemia. But what of clinical evidence?

In most cases the clinical differences between the two fluids may be marginal. The patients own adaptive neuroendocrine systems senses fluid overload and, with intact kidneys, will correct it. Moreover the lymphatic system also becomes a hero of fluid abuse. They drain excessive fluid from the ISS, thus limiting fluid expansion which would otherwise result in peripheral and pulmonary oedema.³⁶

As expected, clinical differences in the amount of peripheral oedema are accentuated with crystalloids compared to colloids.³⁷⁻⁴⁰

Similarly, with pulmonary oedema, crystalloids cause greater oedema and hypoxia.^{24,41-43} There is also a good evidence that increased leaky capillaries in the lungs does not occur with sepsis^{24,26} and that it is more likely related to simple overexpansion of the ISS by excessive crystalloid solution.

However, using extreme end-points such as mortality, some larger comparative studies favour crystalloids⁴⁴⁻⁴⁷ and other studies favour colloids.^{26,48-51} A meta-analysis of colloid versus crystalloid studies in 1989⁵² demonstrated that pooled data from eight studies showed no difference. However, in the eight studies which did not use mortality as an end-point, six showed colloids to be more efficacious, one showed more benefit from crystalloids and one showed no difference.

More recent meta-analysis studies have been similarly inconclusive. Some have clearly favoured crystalloid therapy.⁵³ In a Cochrane Review, there was no evidence that resuscitation with colloids reduced the risk of death in patients with trauma, burns and following surgery.⁵⁴ When albumin was used as the colloid solutions, there was no overall benefit of that particular colloid.⁵⁵ The use

of meta-analysis can be questioned as most studies do not use mortality as the end-point.⁵⁶

It seems obvious that we need more original research in this area rather than attempting to match all trials with new statistics⁵⁷ + 52 – see B attached.

Conclusion

No matter what the cause of hypovolaemia, e.g. trauma, sepsis, excessive GIT losses, diabetic ketoacidosis, the first priority is to rapidly restore the circulation.

There are many patients in acute hospitals who remain hypovolaemic either in general wards or in Emergency Departments for long periods before they are transferred to ICUs.⁵⁹⁻⁶³

For these patients, expensive drugs or magic bullets aimed at counteracting the deleterious effects of cytokines after they are released, have little or no effect.⁶⁴⁻⁶⁷

Early detection and rapid reversal of ischaemia and hypoxia is a cheaper and more logical approach.⁶⁸ To this end a hospital-wide approach has been developed, where abnormalities in vital signs such as hypotension and tachycardia cause activation of a Medical Emergency Team (MET).⁶⁹⁻⁷³ The MET is organised by the ICU and replaces the hospital's cardiac arrest team. It is called to easily measured signs measured at most patient's bedside (e.g. system BP <90 mmHg; PR <40 >140 rate/min; respiratory rate <4 >36 rate/min; or sudden loss of consciousness). The aim is early resuscitation and restoration of a normal circulatory volume rather than admission to the ICU at a later stage when the patient may have MODS with a poorer outcome.

For high risk patients, the rapidity of replacement of fluid is more important than the actual type of fluid administered. The colloid/crystalloid controversy is largely an artificial construct. If the ISS is dry use a crystalloid and if the IVS is dry, use a colloid.

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Abbreviations

BP	Blood pressure
CO	Cardiac output
COP	Colloid oncotic pressure
CVP	Central venous pressure
ECF	Extracellular fluid
ICU	Intensive Care Unit
ICS	Intracellular space
ISS	Interstitial space
IV	Intravascular
IVS	Intravascular space
JVP	Jugular venous pressure
K ⁺	Potassium
MODS	Multiorgan dysfunction syndrome
Na	Sodium
PAWP	Pulmonary artery wedge pressure
PCCO	Pulse contour cardiac output
PR	Pulse rate