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### Fluid Choices in Trauma



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**This article focuses on the type of fluid available and respective indications in the course of trauma resuscitation according to the situation: haemorrhagic shock, trauma brain injury.**

In trauma patients, fluid resuscitation aims at preventing a cardiac arrest due to severe hypovolaemia and at achieving a satisfying level of mean arterial pressure to ensure adequate tissue perfusion. Fluid resuscitation is indicated in trauma patients for traumatic haemorrhage, sympatholysis due to spinal injury or sedation and vasoplegia due to inflammation (tissue attrition and ischaemiareperfusion).

The perfect fluid for trauma resuscitation should ideally have no interactions with clot formation, have a composition close to that of the extracellular space and be isotonic to avoid cerebral volume variations. It should have a high volume expansion property to avoid excessive fluid volume replacement that could contribute to the development of coagulopathy and complications such as abdominal compartment syndrome. However, no fluid gathers all these properties at one time and fluid choice in trauma resuscitation remains a subject of debate.

#### **Crystalloids**

Fluid resuscitation with crystalloid is the firstline therapy to correct haemodynamic instability during blood spoliation due to traumatic haemorrhage. The European guidelines recommend that crystalloids be applied initially to treat the hypotensive bleeding trauma patient (Spahn et al. 2013). Isotonic saline is the reference solution that is mostly used during trauma resuscitation. Its osmolarity is close to the osmolarity of plasma (slightly higher with  $308 \text{ mmol.L}^{-1}$ ) and its believed harmlessness made it a universal fluid for trauma resuscitation. Ringer's lactate, an alternative to isotonic saline, is frequently used in the United States. However, its hypo-osmolarity ( $273 \text{ mmol.L}^{-1}$ ) could increase intracellular space volume leading to an increase in intracranial pressure in brain-injured trauma patients. Thus, Ringer's lactate should be reserved for patients devoid of traumatic brain injury. The strong ion difference (SID) of isotonic saline is zero  $\text{mmol.L}^{-1}$  and the SID of Ringer's lactate is  $26 \text{ mmol.L}^{-1}$ . Since a solution with a SID inferior to plasma SID ( $40 \text{ mmol.L}^{-1}$ ) leads to hyperchloraemic acidosis, the formulation of the lactate Ringer solution proposed by Dr Hartmann in 1930 results in less hyperchloraemic acidosis than isotonic saline. Excessive chloride administration could have

renal adverse effects (Yunos et al. 2012), and an association was reported between intravenous chloride load and mortality in intensive care (Shaw et al. 2014). The precise mechanisms explaining these reported side effects of chloride are not well understood at the moment. However, there is growing interest in balanced solutions that were recently proposed to associate a composition and an osmolarity close to that of plasma. One study randomised 50 trauma patients with haemorrhagic shock to receive either isotonic saline or balanced solution (Plasmalyte with a SID of 50 mmol.L<sup>-1</sup>) during the first 24 hours of resuscitation (Young et al. 2014). The authors reported a significant increase in base excess in the Plasmalyte group compared to the NaCl 0.9% group (7.5 ± 4.7 vs 4.4 ± 3.9 mmol.L<sup>-1</sup>) with less severe hyperchloraemic acidosis in the Plasmalyte group. In a recent meta-analysis comparing the administration of low vs high chloride content solution in perioperative and critical care, Krajewski et al. (2015) reported less need for transfusion when using balanced crystalloids instead of isotonic saline. This was confirmed in a study conducted on 60 liver surgery patients by Weinberg et al. (2014), who reported less bleeding during surgery and fewer haematology value disorders after surgery with Plasmalyte than with lactated Ringer's solution. A randomised controlled trial of 2278 patients requiring crystalloid fluid therapy in the ICU compared isotonic saline to Plasmalyte (Young et al. 2015). No difference in severe acute kidney injury (AKI) occurrence (primary outcome) was reported. However, the overall severe AKI (according to Risk, Injury, Failure, Loss and End-stage kidney disease (RIFLE) classification I or F) incidence was only 9.4% and few trauma patients (n=125) were included. It appears that the interest in balanced solutions needs to be investigated in larger randomised controlled trials in trauma patients to explore their effects on coagulation and renal function.

### **Colloids**

The main potential benefit of colloids is that they are able to induce a more rapid and persistent plasma expansion because of a larger increase in oncotic pressure. A ratio of 1:2 to 1:3 between colloids and normal saline has regularly been proposed to obtain the same volume expansion (McIlroy et al. 2003). However, a recent meta-analysis, including studies in perioperative and critical care settings, reported an exact mean ratio of 1:1.5 (it was even 1:1.3 in the most recent studies between 2010-2013) (Orbegozo Cortés et al. 2015). Moreover, randomised comparisons of fluid resuscitation with hydroxyethyl starch (HES) 130/0.4 versus NaCl 0.9% in trauma patients have not always shown a superiority of HES on the recovery of tissue perfusion (i.e. lactate clearance) and showed no difference in fluid requirements and maximum Sequential Organ Failure Assessment (SOFA) scores (James et al. 2011).

It should be borne in mind that in this latter study patients of the HES group were more severely injured than those in the saline group. As regards to a potential effect on mortality, the Crystalloid Versus Hydroxyethyl Starch Trials (CHEST) study failed to show that a fluid strategy using HES 130/0.4 (vs. NaCl 0.9%) decreased mortality in ICU patients, in particular in the subgroup of trauma patients (n=532) (Myburgh et al. 2012). In addition, there is continuing concern about the effects of HES on coagulation. HES have the potential to decrease the Von Willebrand factor level and to interfere with the polymerisation of fibrinogen and the platelet function. Studies that assessed haemostasis by thromboelastography reported that HES infusion resulted in a weaker clot with a less stable fibrin network and less firm aggregation of platelets than did crystalloid or human albumin (Hartog et al. 2011). This can lead to greater need for red blood cell transfusions (James et al. 2011; Myburgh et al. 2012). Because of these effects, the use of HES is considered at the initial phase of haemorrhagic shock. Alteration of coagulation and potential deleterious kidney effects observed with the last generation of HES prompted the European Medicines Agency (EMA) to drastically limit usage of HES. EMA recommended not to use HES in sepsis patients and to limit their use to haemorrhagic shock patients only when crystalloids alone are not considered sufficient (European Medicines Agency (EMA) 2013). In addition, HES are contraindicated in the case of coagulopathy (EMA 2013).

As regards the other synthetic colloids, coagulation (Niemi et al. 2010) and kidney function alterations (Bayer et al. 2011) have been described with gelatins, but high-quality studies are lacking to know if these recommendations can be extended to them. The Colloids Versus Crystalloids for the Resuscitation of the Critically Ill (CRISTAL) study compared different colloids (including gelatins) to crystalloids in hypovolaemic shock. There were no differences in 28-day mortality (primary outcome) in the whole study population as well as in the subgroup of trauma patients (n=177) (Annane et al. 2013).

On albumin, the Saline versus Albumin Fluid Evaluation (SAFE) study has shown that albumin does not interfere with coagulation and kidney function (Finfer et al. 2004). However, in the subgroup of patients with traumatic brain injury (SAFE TBI patients), the mortality rate was superior with the use of albumin 4% at the initial phase vs normal saline (SAFE Study Investigators et al. 2007). This finding was attributed to the albumin-induced increase in intracranial pressure due to its hypo-osmolarity (Cooper et al. 2013).

### **Hypertonic Solutions**

Hypertonic saline (HTS, 7.5% saline with or without colloids) has long been considered a fluid of interest in trauma patients. Potential benefits of HTS include restoration of intravascular volume with the administration of a small volume, due to its osmotic effect that shifts fluid from the intracellular space to the extracellular space, reduction of intracranial pressure in TBI and modulation of the inflammatory response. However, HTS failed to improve outcomes in patients with haemorrhagic shock or with severe TBI (Bulger et al. 2008; 2010; 2011). Its

use in haemorrhagic shock patients was even reported to be associated with an overmortality in the subgroup of patients that was not transfused during the first 24 hours (Bulger et al. 2011). The authors suggest that hypertonic saline masked the clinical haemorrhage signs (hypovolaemia) with subsequent misdiagnosed haemorrhage.

In the setting of life-threatening raised intracranial pressure (ICP), mannitol and HTS are the most frequently used solution to lower ICP. At equimolar doses, HTS and Mannitol led to equivalent decrease in ICP (Francony et al. 2008). Thus, the differences between these two solutions are not related to their brain effects but rather to their haemodynamic properties. Indeed, HTS raises cardiac preload that may have some interest in patients with hypotension and compromised cerebral perfusion (mydriasis) to act on both arterial pressure and ICP at the same time. HTS will not lead to an osmotic diuresis in comparison with mannitol, which implies that mannitol administration should be followed by a fluid bolus (i.e. NaCl 0.9% 500 mL). This property can be an advantage of HTS when a prolonged vascular filling is expected (i.e. hypovolaemic patient), but on the other hand mannitol will be eliminated in the next hours following its administration, inducing a smaller positive fluid balance than HTS for the same brain effect. This can be appropriate for patients needing a transient osmotherapy while waiting for a surgical haematoma evacuation for example.

Lactate solutions have recently been proposed as an alternative to mannitol in trauma brain injury patients. Lactate is an energy substrate for the brain. In one study, equimolar doses of half molar sodium lactate led to more favourable ICP control than mannitol in TBI patients with raised ICP (Ichai et al. 2009). In a second randomised study, the same team compared an infusion of  $0.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$  of half molar sodium lactate to an equivalent infusion of isotonic saline. They reported less intracranial hypertension episodes (36% vs 66% in the half molar sodium lactate and the isotonic saline group respectively) that was not explained by the plasmatic osmolality, since it was comparable in both groups (Ichai et al. 2013). Sodium lactate could act by increasing chloride extrusion from the cerebral cells associated with a decrease in cerebral water content. This favourable effect needs further investigation to define the therapeutic place of sodium lactate in TBI patients.

### **Conclusion**

Although fluid resuscitation remains the cornerstone of trauma resuscitation, no consensus can be found for a single and ideal fluid. Crystalloid fluid should be administered as a first-line therapy to reverse hypotension. NaCl 0.9% associates an appropriate osmolality (close to plasmatic osmolality) with adequate filling properties. Solutions containing less chloride than NaCl 0.9% (i.e. balanced solutions) deserve further investigations to establish a potential benefit on coagulation and renal function. Synthetic colloids, in particular HEA, should be considered as second-line therapy only, since the lack of benefit and their potential nephrotoxicity do not support their use over crystalloids. Hypertonic solutions are indispensable in life-threatening ICP rises to buy time for a life-saving procedure preparation. Mannitol and HTS have the same efficacy. Their use in compromised haemodynamic situations (i.e. haemorrhagic shock) did not demonstrate any benefit. The attractive properties of sodium lactate remains to be investigated to better define its place in neuroICU.

See Also: [Fluid Resuscitation in Burns](#)

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