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The Challenge Of Fluid Choices For Trauma Patients In Emergency Settings

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***Abstract*—Trauma is a leading cause of death worldwide, and almost 30% of trauma deaths are due to blood loss. A number of concerns have been raised regarding the advisability of the classic principles of aggressive crystalloid resuscitation in traumatic hemorrhagic shock. Some recent studies have shown that early volume restoration in certain types of trauma before definite hemostasis may result in accelerated blood loss, hypothermia, and dilutional coagulopathy. This review discusses the advances and changes in protocols in fluid resuscitation and blood transfusion for treatment of traumatic hemorrhage shock. The concept of low volume fluid resuscitation also known as permissive hypotension avoids the adverse effects of early aggressive resuscitation while maintaining a level of tissue perfusion that although lower than normal, is adequate for short periods. Permissive hypotension is part of the damage control resuscitation strategy, which targets the conditions that exacerbate hemorrhage. The elements of this strategy are permissive hypotension, minimization of crystalloid resuscitation, control of hypothermia, prevention of acidosis, and early use of blood products to minimize coagulopathy.**

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

Keywords—Fluids, Choices, Challenge, Emergency, Trauma, Burn-patients, Life-saving.

Introduction:

In trauma patients, fluid resuscitation aims to prevent a cardiac arrest due to severe hypovolemia and at achieving a satisfying level of mean arterial pressure to ensure adequate tissue perfusion. Fluid resuscitation is indicated in trauma patients for traumatic hemorrhage, sympatholytic, due to spinal injury or sedation and vasoplegia due to inflammation (tissue attrition and ischemia reperfusion).

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 first line therapy to correct hemodynamic instability during blood spoliation due to traumatic hemorrhage. The European guidelines recommend that crystalloids be applied initially to treat the hypotensive bleeding trauma patient (1). 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 $mmol.L^{-1}$) 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 $mmol.L^{-1}$) 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 $mmol.L^{-1}$ and the SID of Ringer's lactate is 26 $mmol.L^{-1}$. Since a solution with a SID inferior to plasma SID (40 $mmol.L^{-1}$) leads to hyperchloremic acidosis, the formulation of the lactate Ringer solution proposed by Dr Hartmann in 1930 results in less hyperchloremic acidosis than isotonic saline. Excessive chloride administration could have renal adverse effects (2), and an association was reported between intravenous chloride load and mortality in intensive care (3). 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 randomized 50 trauma patients with hemorrhagic shock to receive either isotonic saline or balanced solution (Plasmalyte with a SID of 50 $mmol.L^{-1}$) during the first 24 hours of resuscitation (4). 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 $mmol.L^{-1}$) with less severe hyperchloremic 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, (5) 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, which reported less bleeding during surgery and fewer hematology value disorders after surgery with Plasmalyte than with lactated Ringer's solution (6).

A randomized controlled trial of 2278 patients requiring crystalloid fluid therapy in the ICU compared isotonic saline to Plasmalyte (4). 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 randomized 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 (7). 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) (8). Moreover, randomized 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 (9).

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) (10). 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 polymerization of fibrinogen and the platelet function. Studies that assessed hemostasis 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 (11). This can lead to greater need for red blood cell transfusions (9,10). Because of these effects, the use of HES is considered at the initial phase of hemorrhagic 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 hemorrhagic 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 (12).

As regards the other synthetic colloids, coagulation and kidney function alterations have been described with gelatins, but high-quality studies are lacking to know if these recommendations can be extended to them (12,13). The Colloids Versus Crystalloids for the Resuscitation of the Critically Ill (CRISTAL) study compared different colloids (including gelatins) to crystalloids in hypovolemic 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) (14).

On albumin, the Saline versus Albumin Fluid Evaluation (SAFE) study has shown that albumin does not interfere with coagulation and kidney function (15). 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, this finding was attributed to the albumin-induced increase in intracranial pressure due to its hypo-osmolarity (16,17).

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 hemorrhagic shock or with severe TBI (18,19,20). Its use in hemorrhagic shock patients was even reported to be associated with an over mortality in the subgroup of patients that was not transfused during the first 24 hours (20). The authors suggest that hypertonic saline masked the clinical hemorrhage signs (hypovolemia) with subsequent misdiagnosed hemorrhage.

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 (21). Thus, the differences between these two solutions are not related to their brain effects but rather to their hemodynamic 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. hypovolemic 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 hematoma 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 favorable ICP control than mannitol in TBI patients with raised ICP (22). In a second randomized study, the same team compared an infusion of 0.5 $mL.kg^{-1}.h^{-1}$ 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 osmolarity, since it was comparable in both groups (23,24).

Sodium lactate could act by increasing chloride extrusion from the cerebral cells associated with a decrease in cerebral water content. This favorable effect needs further investigation to define the therapeutic place of sodium lactate in TBI patients.

fewer hospital days annually, and reductions in hospital expenditures of over $1.5 billion [31].

The costs related to long-term impacts of sepsis have not been quantified but are likely very

substantial, including subsequent medical care: the true fiscal burden, considering delayed

return to work, the need for families to adjust lifestyles to support, and rehabilitation cost

is likely to be huge.

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 osmolarity (close to plasmatic osmolarity) 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 hemodynamic situations (i.e. hemorrhagic shock) did not demonstrate any benefit. The attractive properties of sodium lactate remain to be investigated to better define its place in neurosurgery ICU.

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