

Fluid therapy in sepsis

Sepsis is characterized as a systemic inflammatory response to uncontrolled infection. Generalized vasodilatation and vascular leakage together with depressed cardiac contractility are key physiologic alterations. Hypotension is considered as distributive event and resuscitation thus consists of fluid therapy and vasopressors. Fluid is given in order to restore intravascular volume and vasopressors is prescribed when blood pressure target is not achieved after adequate intravascular volume.

Several issues regarding fluid therapy in sepsis will be addressed here, namely fluid type, algorithms and guidelines. First, type of initial fluid has long been debated. Normal saline or 0.9% NaCl solution has been recommended for decades despite the fact that hyperchloremia poses certain complication. Early studies demonstrated increase incidences of renal injury from NSS effect to vascular glycocalyx and renal tubules. However, mortality disadvantage has not been proved. Recent multicenter study revealed that worse “composite outcomes” including death, new dialysis event and persistent renal dysfunction, were noted in those who receive NSS when compared with those who received balanced salt solution. Hence, trends toward more uses of the latter is expected. As for colloidal solution, albumin has been proved beneficial in certain indications and HES is almost completely abandoned.

Regarding algorithms for fluid resuscitation, a 4-stage protocol has been proposed. Conceptually, it consists of rapid initial volume repletion or “rescue phase”, followed by careful fluid challenge toward optimal intravascular volume or “optimization phase”. After perfusion goal achievement, fluid rate is adjusted to maintain optimal volume (stabilizing phase). Finally, when systemic inflammation subsides, fluid balance need to keep zero or negative to avoid volume excess from intravascular redistribution (de-escalation phase). This concept is well noted in the 2016 Survival Sepsis Campaign and the late 2018 “first hour bundle”. Since positive volume balance is often observed. Careful fluid administration is needed and monitoring of volume excess is necessary.

The early use of vasopressors may be beneficial in this respect. Retrospective studies revealed less fluid given and improved survival in those who received norepinephrine (NE) in the early course of resuscitation. Increase in venous return and cardiac output were evident. A mice endotoxic shock model demonstrated that the group resuscitated with fluid together with early NE had better aortic blood flow, higher splanchnic perfusion and lower lactate level. In our double blind RCT, patients were allocated to receive low dose NE or placebo at the beginning of resuscitation, while other treatment followed resuscitation guidelines. Higher proportion of early NE patients achieved therapeutic goal at 6 hour with lower cardiac complications. Mortality was insignificantly lower but fluid amount was similar. Careful adjustment of norepinephrine dose may be needed in order to improve outcomes.

At present, many important questions are still unanswered, for example: appropriate fluid for leaky endothelium, safe fluid bolus technic, practical parameters for intravascular volume assessment and etc. More studies are needed in order to find appropriate solution to improve outcomes of these patients.

