ICU
MANAGEMENT & PRACTICE

ICU Volume 15 - Issue 3 - 2015 - Cover Story

Fluid Choices in Brain Injury

Prof. Nino Stocchetti
******@***policlinico.mi.it

Professor of Intensive Care Medicine - Milan University - Ospedale Policlinico IRCCS

Fluid management for acute brain damage has changed profoundly in the last decades. In the recent past brain oedema has been identified at autopsies as an overwhelming cause of raised intracranial pressure (ICP) and death after brain injury. In order to reduce the brain water content, dehydration, and even drastic dehydration, with 250 ml/day total, has been proposed for ICP treatment in severe brain trauma (Benabid et al. 1980). At the other extreme a generous fluid infusion, leading to hypervolaemia, was recommended to counteract vasospasm after subarachnoid haemorrhage (SAH) (Kassel et al. 1982). These extreme approaches were based on incomplete understanding of water dynamics in the brain and cerebral blood flow (CBF) autoregulation.

Water moves from the intravascular to the extra- and intra-cellular space along osmotic gradients, while sodium, with an intact blood brain barrier (BBB), does not.

This has two consequences: any subject with a normal plasma osmolarity will not reduce his brain water content as a consequence of dehydration. Moreover, osmolar gradients can move water from the tissue toward the plasma compartment: therefore osmotic agents have been infused to reduce brain oedema (Qureshi and Suarez 2000).

If pressure autoregulation is preserved, CBF doesn't depend on volaemia or cardiac output, but on cerebral perfusion pressure (CPP) and cerebrovascular resistances. Hypervolaemia, under these conditions, will not increase CBF nor counteract vasospasm.

Goals of Fluid Therapy in Acute Brain Injury

The choice of fluids for severe patients with acute brain injury should respect three priorities:

1. To preserve cerebral perfusion;

2. To control brain volume; and

3. To assure appropriate substrate delivery.

Maintaining Cerebral Perfusion: Haemoglobin and Volaemia

Oxygen content and delivery are essential. The appropriate level of haemoglobin (Hb) for patients at risk of cerebral ischaemia has been debated and is still not firmly established. There are arguments in favour and against liberal transfusion policies (Utter et al. 2011). A recent iterature review found insufficient evidence to confirm or refute a difference in effect between lower and higher Hb groups in eurocritically ill patients (Desjardins et al. 2012). A randomized study in 200 traumatic brain injury (TBI) patients Robertson et al. 2014) has not demonstrated an improved neurological outcome at 6 months aintaining haemoglobin concentration of greater than 10g/dL, but the design of the study and the low patient numbers reduce the external validity of the study.

The more recent trend, which suggests a threshold as low as 7g of Hb (Hébert and Carson 2014), may be risky if microcirculation doesn't guarantee adequate flow to the injured brain. Higher thresholds are currently suggested by guidelines (Diringer et al. 2011; Retter et al. 2013). Initial enthusiasm for volume expansion and hypervolaemia to prevent ischaemic neurologic deficits after SAH (Kassell et al. 1982) has been blunted by more rigorous examination. While avoidance of hypovolaemia and hypotension has a strong rationale, benefits from hypervolaemia are not proven, according to a systematic literature review (Treggiari et al. 2003). When hypervolaemia has been tested in comparison with induced arterial hypertension in the treatment of ischaemia after SAH, scarce benefits were demonstrated in restoring tissue oxygenation, at the expense of increased systemic complications (Raabe et al. 2005). A more recent study on 10 SAH patients demonstrated a modest CBF improvement following hypervolaemia, unfortunately associated with worse brain tissue oxygenation (Muench et al. 2007).

Volaemia should be normal, and there are no data supporting colloids rather than crystalloids. Hypotension in the first phase after trauma is associated with higher mortality and unfavourable outcome, so that appropriate fluid infusion, with the target of normo-volaemia and normal arterial pressure, is mandatory. Prehospital management with intravenous hypertonic saline, compared with resuscitation with conventional fluids, has been tested in patients with severe TBI, who suffered hypotension in the early phase after injury. Hypertonic fluids did not improve long-term neurological outcome (Cooper et al. 2004).

Albumin 4% has also been tested in the first 28 days after TBI. Its use, unfortunately, was associated with worse outcome compared to controls. One plausible explanation of this finding is that albumin was associated with a higher ICP level (Cooper et al. 2013). On the contrary, albumin is still often used in SAH patients, probably because volume expansion, even if of unproven benefit, remains popular (Suarez et al. 2014).

Controlling Intracellular Volume

Normal plasma osmolarity is essential for prevention of intracellular swelling. As mentioned, water moves from the extracellular space to the intracellular compartment when an osmotic gradient is created, so that careful avoidance of hypo-osmolarity is key in neurointensive care. Hyponatraemia may worsen cerebral oedema and mass effect, leading to an ICP increase, with potential deleterious effecton outcome. Unfortunately hyponatraemia is frequent during the acute phase following TBI or aneurysmal SAH (Qureshi et al. 2002).

Ideally, the BBB should be intact, making the transit of large molecules into the brain tissue tightly controlled. Under these conditions, a predictable water movement is created, simply based on the osmotic gradients from the intravascular compartment to the brain tissue.

The reflection coefficient describes the selectivity of the BBB to a given molecule. Compounds with a coefficient of 1 are totally excluded by the BBB, while lower coefficients indicate an easier BBB crossing. Sodium chloride has a coefficient close to 1, while mannitol, with a higher molecular weight, has a coefficient of 0.9 (Qureshi and Suarez 2000).

Often, however, the BBB is damaged, as in case of brain contusion, which is associated with increased permeability and oedema. Water and proteins can enter the brain through areas of disrupted BBB, causing oedema (vasogenic oedema). If the BBB is damaged, the net flow of water and molecules from the intravascular compartment to the tissue becomes very complex. Since several molecules can pass the altered BBB and accumulate in the tissue, there is a significant risk of increasing brain tissue osmolarity, if osmotic compounds are infused. In this case a worsening of brain oedema becomes likely.

Studies on the BBB behaviour in the clinical setting are difficult, while this issue has been explored in experimental conditions. In a rodent model of closed brain injury, for instance, trauma was associated with a rapid BBB opening lasting only 30 minutes (Barzó et al. 1996). More recently, in a limited sample of TBI patients, BBB dysfunction (defined as a cerebrospinal fluidplasma albumin quotient of ≥0.007) has been investigated. More than one-third of the patients showed signs of BBB alteration (Saw et al. 2014).

Water movements in response to osmotic gradients can, however, be used to withdraw water from the injured tissue, by using osmotically active molecules. If plasma osmolarity could be increased without affecting intracerebral concentration of osmoles, the brain water content will be reduced.

Historically, urea and glycerol have been used in order to control brain oedema and reduce ICP, but with relevant side effects. Mannitol has gained popularity for being more effective and associated with fewer complications. Its effects are not limited to brain dehydration, since mannitol might also have vascular effects, with an initial CBF increase and a subsequent vasoconstriction (Muizelaar et al. 1984).

Hypertonic saline solutions have been used for ICP control in the last 30 years. In animal models with focal injury and in several clinical studies hypertonic saline causes a prompt ICP reduction that is thought to be caused by a reduction in water content in areas of the brain with intact BBB (Dias et al. 2014; Torre-Healy et al. 2012; Kamel et al. 2011; Battistella and Wisner 1991). Comparisons with mannitol suggest almost equal efficacy in reducing ICP, but there are conflicting data concerning the respective duration of action (Battison et al. 2005; Qureshi and Suarez 2000).

Providing Appropriate Substrate Delivery

The brain uses preferentially glucose for its energy metabolism and has very limited glycogen storage. Continuous glucose delivery is therefore mandatory. Glucose enters the brain through a mechanism of facilitated transport, and the brain extracellular concentration depends on the plasma concentration. The deleterious effects of acute and chronic hyper- and hypoglycaemia on the brain have been demonstrated, so that maintenance of normoglycaemia is desirable (Vespa 2008; Suh et al. 2007; Tomlinson and Gardiner 2008).

The possible benefits of tight glycaemic control, however, should be weighed against the risks of hypoglycaemia. Several studies have demonstrated (Nasraway 2007) glycaemic values below 40 mg/dL in various proportions: from 4% in high quality centres up to 18-19% in other institutions. Vespa and colleagues (2006) have shown that intensive insulin therapy reduces brain extracellular glucose concentrations without modifying the lactate/pyruvate ratio. Magnoni, moreover, has demonstrated that the interstitial levels of glucose are reduced, for the same systemic glucose concentration, in the metabolically injured brain (Magnoni et al. 2012). For all these reasons, great attention should be given to the avoidance of hypoglycaemia.

Conclusion

After acute brain damage choices in fluid therapy should aim at a normal systemic haemodynamic, in order to guarantee adequate CBF, while providing adequate oxygen and substrate (mainly glucose) content in the general circulation. Special attention to osmolarity is also necessary to prevent, or mitigate, brain oedema.

Published on : Tue, 29 Sep 2015