



Fluid Management in Neurosurgical Patients

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Wojciech Dabrowski, Robert Wise,
and Manu L. N. G. Malbrain

26.1 Introduction

Fluid administration in the perioperative management of neurosurgical patients is challenging. Inappropriate intravenous (IV) fluid administration is associated with postoperative complications and increased mortality [1–3]. However, there is little data on how fluid therapy affects neurosurgical patients treated for tumors, cerebral aneurysms, or angiomas. Intravenous fluid therapy is frequently used to correct and maintain adequate cerebral blood flow (CBF) and cerebral perfusion pressure (CPP). Perioperative problems are created by the administration of hypo- or hyperosmotic fluids or by administering too much or too little. Added to this complexity is the

risk of causing hypotension on induction of anesthesia in hypovolemic patients, hence creating a situation where intravenous fluids are often administered rapidly. Thus, maintaining euvolemia, without the morbidity associated with hypovolemia or hypervolemia, becomes a challenging exercise.

Available intravenous fluids are generally classified into two main groups: crystalloids and colloids. Fluid constitution differs with respect to ion content, buffer, strong ion difference (SID), tonicity, and oncotic pressure. Intravenous fluids should be considered as drugs, as their administration strongly affects intravenous homeostasis and intra-/extravascular water balance. As with other drugs, as their administration can either correct or disturb end-organ function.

W. Dabrowski (✉)

Department of Anaesthesiology and Intensive Therapy, Medical University of Lublin, Lublin, Poland

R. Wise

Department of Anaesthetics, Critical Care and Pain Management, Pietermaritzburg Metropolitan, Pietermaritzburg, South Africa

Discipline of Anaesthesiology and Critical Care, Clinical School of Medicine, University of KwaZulu-Natal, Durban, South Africa

M. L. N. G. Malbrain

Intensive Care Unit, University Hospital Brussels (UZB), Jette, Belgium

Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel (VUB), Brussels, Belgium

26.2 Crystalloid Fluids

26.2.1 General Principles

Crystalloids are the most popular fluids administered for correction of intravascular volume. Crystalloids are solutions of inorganic ions and organic molecules dissolved in water. An ideal crystalloid solution is described as one similar to interstitial fluid, but not inducing electrolyte or acid-base disturbances [4–6]. Use of crystalloids in neurosurgical patients has been the subject of several studies [7–9]. All isotonic

balanced solutions consist of water with different Na^+ , K^+ , Ca^{++} , Mg^{++} , and Cl^- ions which are buffered by anions such as acetate, malate, lactate, or citrate. This differs from plasma containing proteins, organic acids, phosphate, sulfate, and acidic carbonates. Hence, the theoretical osmolality (as indicated on the fluids information package) is calculated by using a multiplication factor of 0.926 to estimate the fluid's "in vivo" osmolality [10]. Based on this principle, many isotonic fluids are actually hypotonic.

Hypotonic solutions should be avoided in neurosurgical patients and patients with traumatic brain injury (TBI) (Grade 1C) [11]. A slight reduction in plasma osmolality by 1 mOsm/L increases the pressure of fluid shifts across the blood-brain barrier (BBB) to 19 mmHg. Furthermore, a decline in plasma osmolality by 3% leads to overt cerebral edema with a 30% reduction in intracranial blood cerebrospinal fluid volume [7, 12, 13].

Some crystalloids are buffered and termed balanced solutions. A buffer is a partially neutralized acid that resists changes in pH. Citrate, a crystalloid buffer, binds intravascular ionized calcium, thus stimulating coagulation disorders. Use of large volumes of such fluids may cause serious problems, particularly when rapidly infused during sudden perioperative bleeding.

Strong ion difference (SID), calculated as the sum of all ions, should be taken into consideration in patients undergoing neurosurgical procedures due to the effect on pH. Administration of fluids with a SID of zero, such as 0.9% sodium chloride (NaCl), induces metabolic acidosis, whereas administration of fluids with SID >40 induces metabolic alkalosis [14].

Also, chloride-rich solutions may induce hyperchloremic acidosis, associated with impaired renal blood flow [15–17]. Again, maintaining euolemia becomes important as any disorders in renal blood flow may lead to acute kidney injury (AKI), one of the most important postoperative complications following major surgery [16, 18]. A large meta-analysis of 22,851 patients with preoperatively low chloride concentration and normal renal function confirmed

the strong correlation between acute postoperative hyperchloremia and the incidence of renal dysfunction. Hyperchloremia was also associated with increased 30-day mortality and length of hospital stay in non-cardiac surgical patients [18]. An association between hyperchloremia and administration of 0.9% NaCl has been widely analyzed in experimental and clinical studies [16, 17, 19–21]. A normal plasma chloride concentration ranges between 95 and 110 mEq/L, in contrast to 0.9% NaCl containing 154 mEq/L of chloride. Both animal and clinical studies documented a dose-dependent 0.9% NaCl-induced hyperchloremia [19, 20]. Evidence also suggests that chloride-rich fluids contribute to delayed recovery of gut function and reduced gastric blood flow [21, 22], which may stimulate postoperative vomiting and subsequent increases in intracranial pressure (ICP). Therefore, treatment with balanced isotonic crystalloids is preferred over administration of 0.9% NaCl in patients undergoing neurosurgical procedures.

26.2.2 Saline Solutions

There are two kinds of saline solutions in clinical practice: 0.9% normal saline (NS) and hypertonic saline (HS). Importantly, all saline solutions have a SID of zero. Normal saline has been the mainstay therapy for patients undergoing cerebral surgery, but its effect on the progression of brain injury has not been well documented [23, 24]. Experimental animal studies comparing resuscitation with NS and fresh frozen plasma have documented pronounced cerebral edema and a larger lesion size when using NS. When comparing NS and synthetic colloid solutions in resuscitation, NS was noted to increase cerebral edema but resulted in a lesion size equal to that caused by the synthetic colloid resuscitation [23]. Administration of NS also affects coagulation parameters, increasing activation of natural anticoagulation in the brain that results in activated fibrinolysis in serum and upregulation of vascular adhesion molecule expression in the injured brain [24]. Also, administration of large volumes of NS

may result in extravasation of intravascular fluid, with increased extravascular water accumulation causing tissue edema and gastrointestinal dysfunction [25, 26].

Adverse effects, similar to those seen in patients given NS, have been documented in patients treated with HS [27, 28]. The increased risk of hyperchloremic metabolic acidosis and AKI should prompt physicians to limit the liberal use of NS and HS. Nevertheless, HS is frequently used with good effect to treat elevated ICP. It may be safer to use repeated boluses of HS as opposed to continuous infusions, as infusions are associated with higher rates of hyperchloremia and AKI [28]. It has been suggested to use an infusion of NS or HS in hypovolemic TBI patients with metabolic alkalosis due to massive alcohol-related vomiting [29]. The administration of saline solutions in these situations corrects volume deficit and acid-balance disorders via induction of metabolic acidosis, while HS has the added advantage of potentially reducing ICP.

26.2.3 Balanced Solutions

In recent years buffered (balanced) salt solutions have been the most common choice of resuscitation fluid in clinical practice [30]. Their composition more closely resembles the extracellular (intravascular) fluid and thus is considered a better choice, for many of the reasons already outlined. Balanced crystalloids do not affect acid-base balance to the same degree and have a lower incidence of hyperchloremic acidosis, perioperative AKI, need for blood transfusion, and systemic inflammation [31–36]. Recent large retrospective trials documented beneficial effects in patients treated with balanced crystalloids compared to NS. They demonstrated significantly lower postoperative complications, such as electrolyte disturbances, postoperative occurrence of AKI requiring renal replacement therapy, postoperative infections, and need for blood product transfusions [36].

In traumatic brain injury patients, the administration of balanced solutions did not affect ICP, SID, phosphate, sodium, or chloride levels,

whereas saline solutions lowered blood pH, SID, and phosphate and also significantly increased chloride and sodium [37]. Balanced crystalloids have also been presented as a more effective treatment of hypovolemia-induced acidosis [38]. Therefore, the use of balanced isotonic crystalloids appears to be a more attractive choice than saline solutions in perioperative fluid resuscitation of TBI and other neurosurgical patients.

26.2.4 Synthetic Colloid Fluids

Synthetic colloids are frequently used in patients undergoing intracranial surgery. These solutions have large insoluble molecules that increase the intravascular oncotic pressure, thus potentially drawing water from the extravascular space. Their high oncotic pressure decreases cerebral edema and improves mean arterial blood pressure via increased intravascular volume [39]. Gelatin and hydroxyethyl starch (HES) solutions are the most popular colloids used in neurosurgical patients. Gelatins consist of polydispersed polypeptides from degraded bovine collagen with molecular weights between 30 and 35 kDa, while HES is an artificial polymer of amylopectin obtained from potatoes, waxy maize, or sorghum. Unfortunately, both types of fluids can diffuse into the interstitium via an injured glycocalyx following surgery-induced general inflammation, and their administration affects the transendothelial filtration rate (Jv) [40, 41]. Evidence regarding the effects of HES on coagulation are conflicting. Several authors have shown HES to increase coagulation disorders by decreasing the concentration of blood coagulation factors VII, VIII, and von Willebrand and impairing platelet aggregation [42, 43]. Others did not confirm these disorders in patients undergoing neurosurgical procedures; however, they did note increases in thrombin-antithrombin levels postoperatively without plasmin-antiplasmin activation. This may have resulted from the administration of HES [44]. Several studies also documented an increased incidence of AKI following HES

administration in critically ill [16, 45, 46]. Administration of HES potentially corrects intravascular volume deficit but does not necessarily remain intravascularly. According to the revised Starling Principle, unsolved molecules can deposit in the skin, liver, muscle, spleen, endothelial cells, and kidneys leading to organ dysfunction [7, 40, 41, 47]. However, some researchers have suggested that the adverse effects of HES are dependent on dose and molecular weight [48]. Several retrospective studies in patients with subarachnoid hemorrhage (SAH) have not yet confirmed a correlation between high volumes of HES and the incidence of AKI [48, 49]. Therefore, the effect of HES on renal function has remained controversial, and the precise understanding of kidney injury following HES administration requires further investigation in neurosurgical patients.

The effect of gelatin solutions on renal function is not yet well understood. A case report documented AKI following Gelofusine administration in a patient undergoing aortobifemoral grafting [50]. This patient received 2 liters of Gelofusine together with mannitol, which may have impaired renal function per se [51]. Experimental studies seem to confirm an unfavorable effect of infusions of gelatin solutions on renal function [52]. An infusion of 4% Gelafundin, at the dose 1 mL/100 g body weight, resulted in serum creatinine and neutrophil gelatinase-associated lipocalin (NGAL) elevation in septic rats, and histological examination showed significantly increased interstitial edema, loss of brush border in the proximal tubules, and higher defragmentation of cell nuclei in kidneys [52]. Clinical studies also confirmed that only higher cumulative doses (>33 mL/kg body weight) of gelatin were associated with an increased risk of AKI in septic patients [53]. Thus, it seems reasonable to avoid large volumes of gelatin infusions, particularly in patients with impaired renal blood flow, history of renal disease, or combination with other osmotically active fluids such as mannitol.

Recently the Coordination Group for Mutual Recognition and Decentralised Procedures—Human (CMDh) endorsed the recommendation

of European Medicine's Agency PRAC (Pharmacovigilance Risk Assessment Committee) to suspend the marketing authorizations of HES solutions for infusion across the European Union. HES solutions are used as plasma volume replacement following acute (sudden) blood loss, where treatment with alternative products known as "crystalloids" alone is not considered sufficient. The suspension was due to the fact that HES solutions have continued to be used in critically ill patients and patients with sepsis, despite the introduction of restrictions on use in these patient populations to reduce the risk of kidney injury and death in 2013.

26.2.5 Mannitol

Current guidelines recommend mannitol at the dose of 0.25–1 g/kg body weight as basic hyperosmotic therapy in patients with intracranial hypertension (ICH) [54]. Mannitol is a six-carbon alcohol of mannose sugar and is frequently used as hyperosmotic therapy to reduce ICH, as well as intraocular hypertension and tissue edema. The mechanism is thought to be via an increase in water drawn from the extravascular space. It should preferably be used in patients with low plasma osmolality, whereas it needs to be avoided when plasma osmolality is above 320 mOsm/kg H₂O. Mannitol is not reabsorbed in the renal tubules, and as such it increases the osmolality of the glomerular filtrate, resulting in a diuresis through inhibition of sodium and chloride reabsorption [55, 56]. Many studies document a close association between mannitol and postoperative AKI in TBI patients [57, 58]. Deng and colleagues demonstrated that the use of mannitol intraoperatively (as compared to preoperatively) was an independent risk factor for postoperative AKI with a 1.97-fold increase in the risk-adjusted odds ratio [57]. Hence, more than 50% of clinicians prefer HS for treatment of ICH [59]. Mannitol-related AKI develops within 1 week of administration, with a more rapid cessation of mannitol resulting in a better AKI prognosis [57].

26.3 Hemodynamic Goals

The main goal of perioperative fluid management is to optimize the circulatory system with adequate CBF during neurosurgery. However, elevated net fluid balance may worsen postoperative outcome [60]. It is difficult to improve CBF without appropriate monitoring. Various authors have suggested continuous blood pressure monitoring via an arterial line in patients undergoing surgery for cerebral aneurysm, brain tumor, angioma, or endovascular mechanical thrombectomy [61–68]. Unfortunately, analysis of continuous blood pressure has been frequently criticized when used as the only method for evaluating volume status in neurosurgical patients [64–66]. Rapid and uncontrolled infusion of fluids immediately after induction of anesthesia may negatively affect local, tumor-related brain edema in fluid-unresponsive patients. Hence, many clinicians recommend the use of dynamic variables, such as pulse pressure variation (PPV), stroke volume variation (SVV), or pleth variability index (PVi[®]), to identify fluid responsiveness and to guide intraoperative fluid management [66–71]. Stroke volume variation is a sensitive predictor of fluid responsiveness in previously healthy patients before brain surgery [68, 69], especially in patients receiving hyperosmotic therapy in the perioperative period. Goal-directed therapy has been recommended for patients undergoing neurosurgical procedures [65, 68, 72]. Pleth variability index (PVi[®]) is a noninvasive parameter that may be superior to other dynamic parameters, especially when used in combination with continuous hemoglobin measurements [73]. It has been proposed as a sensitive, noninvasive measurement to optimize fluid treatment in major non-cardiac surgery under general anesthesia [70, 71]. Rapid infusion of crystalloids immediately after anesthesia induction may result in iatrogenic hemodilution in patients receiving hyperosmolar therapy in the preoperative period. Iatrogenic hemodilution may further induce dilutional coagulopathy leading to increased surgical bleeding and increased use of intraoperative blood transfusion. Continuous noninvasive measurement of

hemoglobin concentration together with PVi[®], in accordance with intravascular volume status, allows real-time detection of iatrogenic hemodilution in non-bleeding patients [73].

26.4 Fluid Management in Specific Neurosurgical Procedures

The multiplicity of neurosurgical procedures calls for fluid diversification. Traumatic brain injury is frequently associated with hypovolemia and hemodynamic instability. Patients undergoing surgery for cerebral aneurysms are frequently hypertensive, while patients undergoing surgery for brain tumors sometimes require preoperative hyperosmotic treatment and forced diuresis which is in contrast to patients undergoing elective spinal surgery who are generally normovolemic. Therefore, fluid treatment should be individualized and tailored in accordance with the patient's clinical condition and needs.

26.4.1 Traumatic Brain Injury

The main goal of fluid therapy related to neurosurgery is to restore and maintain adequate CPP. Fluid management in TBI will be discussed elsewhere (see chapter “Fluid Management in Neurointensive Care”). The perioperative administration of fluids in TBI should be guided by hemodynamic monitoring using dynamic variables such as SVV, PVV, and PVi[®] [65, 74, 75]. Primary cerebral injury is the main factor determining final outcome, but secondary brain injury following pre- and perioperative cerebral hypoperfusion can contribute to unfavorable outcomes [76]. Perioperative hypotension has been observed in 36–65% of patients undergoing emergency craniotomy following TBI [77–79]. Balanced crystalloids should be the first line choice of fluid to correct hemodynamic instability (in patients who remain fluid responsive), and hypotonic solutions should be avoided. Also, synthetic colloids can be used together with crystalloids, but their administration should be guided

by plasma AKI biomarkers. Inotropic support should be added in all cases with fluid-unresponsive hypotension.

26.4.2 Brain Tumor Surgery

The primary goal of perioperative fluid therapy is to maintain preoperative mean arterial pressure during the intraoperative and early postoperative period. Rapid changes in mean and diastolic blood pressure, fluid balance, and length of surgery are all independently associated with perioperative cerebral infarct size and overall survival after elective brain tumor surgery [80]. Therefore, appropriate fluid therapy is essential to reduce perioperative brain injury and subsequent morbidity and mortality. Treatment options to restore intravascular volume deficiencies include crystalloids and colloids, but an elevated plasma osmolality following preoperative hyperosmotic therapy significantly limits the use of hypertonic crystalloids during the perioperative period. Hypotonic solutions should be avoided. The use of balanced crystalloids seems to be the best option for initial fluid resuscitation, since colloids impair coagulation during and after surgery [44]. The occurrence of colloid-related coagulation disorders is a controversial issue in brain tumor surgery. Some pediatric studies did not confirm a relation between colloid administration and coagulopathy suggesting that colloids may be safely used during intracranial tumor resection [81]. However, large amounts of colloids may impair kidney function, especially in patients receiving hyperosmotic therapy with mannitol in the preoperative period.

26.4.3 Cerebral Aneurysm Surgery

Delayed cerebral ischemia (DCI) following intra- or postoperative cerebral vasospasms is the main cause of poor outcome and raised mortality in patients undergoing cerebral vascular surgery [82, 83]. The incidence of vasospasm can be as high as 70% between day 5 and 14 after the onset of subarachnoid hemorrhage (SAH); however, clinical

symptoms are only noted in 30% of patients [83, 84]. Both hyper- and hypovolemia increase the risk of vasospasm and DCI [82–86]. A randomized pilot trial showed a fourfold increase in hypervolemia-related adverse effects in patients with SAH [86]. Appropriate management of fluid therapy is crucial for patients with cerebral aneurysm, and balanced crystalloids seem again to be the best choice. The use of colloids in patients with SAH is associated with increased inflammatory responses, more requirements for blood transfusion, and altered cerebral autoregulation when compared to those treated with balanced crystalloids [87]. Interestingly, a study using transpulmonary thermodilution in SAH showed that the magnitude of DCI was related to the global end-diastolic volume index (GEDVI) and cardiac index (CI) [88]. Achieving a mean 822 mL/m² (680–800 mL/m²) was deemed appropriate to prevent DCI. The use of invasive hemodynamic monitoring in combination with goal-directed fluid therapy significantly decreased DCI incidence and improved outcome [74]. Thus, dynamic hemodynamic variables seem to be superior to static, but fluid administration has to be closely monitored in patients undergoing cerebral vascular surgery.

26.5 Conclusions

In summary, the choice of fluid during neurosurgical procedures depends largely on the patient's clinical condition, particularly renal function. Balanced, isotonic crystalloids are a good first choice to restore and/or maintain intravascular volume and hemodynamic stability and are superior to normal saline. Generally, normal saline should be avoided; however (hypertonic) saline solutions can be administered in selected patients, but their infusion has to be guided by plasma electrolyte concentrations and acid-base balance. Hypotonic solutions and colloids (HES) should be avoided. Fluids should be treated as drugs, and the clinician should always consider the dose and duration of fluid administration, moving toward de-escalation when fluids are no longer needed. Fluid administration should be guided by dynamic variables assessing fluid responsiveness.

Key Points

- Inappropriate intravenous (IV) fluid administration is associated with post-operative complications and increased mortality.
- Hypotonic solutions and colloids should be avoided in neurosurgical patients.
- Treatment with balanced isotonic crystalloids is preferred over administration of 0.9% NaCl in patients undergoing neurosurgical procedures.
- The choice of fluid during neurosurgical procedures depends largely on the patient's clinical condition, particularly renal function.
- Fluid administration should be guided by dynamic variables assessing fluid responsiveness.

Competing Interests Wojciech Dabrowski, Manu Malbrain, and Robert Wise declare that they have no competing interests.

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