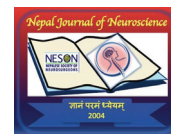


Peri-operative fluid management during neurosurgical procedures



Carlos Darcy Alves Bersot MD¹, Rafael Mercante Linhares MD²,
Carolina Araujo Barbosa MD³, José Eduardo Guimarães Pereira MD, PhD⁴

¹Department of Anaesthesiology, Hospital Federal Lagoa, Rio de Janeiro, Brazil

²Department of Anaesthesiology, Hospital Municipal Miguel Couto. Rio de Janeiro, Brazil

³Department of Anaesthesiology, Hospital Universitário Gaffrêe e Guinle RJ, Brazil

⁴Department of Anaesthesiology, Valença Medical School, Valença, Rio de Janeiro, RJ, Brazil

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Abstract

The management of fluids and electrolytes in neurosurgical patients aims to reduce the risk of cerebral oedema, reduce intracranial pressure (ICP) and at the same time maintain haemodynamic stability and cerebral perfusion. Neurosurgical patients commonly receive diuretics (mannitol and furosemide), developing complications such as bleeding and diabetes insipidus. These patients may require large volumes of intravenous fluids and even blood transfusions for volume resuscitation, treatment of cerebral vasospasm, correction of preoperative dehydration or maintenance of haemodynamic stability. Goal-oriented therapy is recommended in neurological patients, with the aim of maintaining circulating volume and tolerating the changes induced by anaesthesia (vasodilation and myocardial depression).

Key words: Brain ischemia, Neuroanaesthesia, Neurosurgery, Peri-operative fluid, Pulse pressure variation.

Introduction

The management of fluids and electrolytes in neurosurgical patients aims to decrease the risk of cerebral oedema, control of intracranial pressure (ICP), maintaining haemodynamic stability and cerebral perfusion. Treatments with diuretic agents (mannitol and furosemide), as well as complications, such as bleeding and diabetes insipidus, culminate in the physiological imbalance, which demand individualized management. These patients may require large volumes of intravenous fluids and even blood transfusions to perform volume

resuscitation, treat cerebral vasospasm, correct preoperative dehydration or maintain haemodynamic stability.¹

Initially, as brain volume increases, no changes in ICP occur. But, as it approaches the compensation mechanism's limits, further increments in volume, even in small amounts, may cause large increases in ICP.

Cerebral perfusion pressure (CPP) is a product of the relation amongst different factors, including mean arterial pressure (MAP), central venous pressure (CVP) and cerebral spinal fluid (CSF). As ICP increases it replaces CVP in the calculation. Thus, CPP is expressed by the following equation: $CPP = MAP - ICP$.

According to the formula, increases in ICP lead to a drop in CPP, thus leading to inadequate oxygen supply, ischaemia and a drop in cerebral blood flow (FSC). Therefore, it is essential to avoid hypovolemia and the depressant effects of anaesthetics in order to prevent neurological damage.²

Weed and McKibben in 1919 observed that low serum osmolarity could lead to cerebral oedema; conversely, the increase in osmolarity reduces the water content in the brain.³ Water restriction, once recommended in the management of patients with neurological pathologies, arose from the concern that the administration of fluids could result in cerebral oedema with a consequent exacerbation of intracranial hypertension. However, its effectiveness has never been proven and its consequences, such as the occurrence of hypovolemia, proved to be harmful.

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Address for correspondence:

Carlos Darcy Alves Bersot

Department of Anaesthesia, Hospital Federal Lagoa

Rio de Janeiro, Brazil

E-mail: carlosbersot@gmail.com

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Neurosurgical patient management is based on maintaining homeostasis, focusing on haemodynamic stability and cerebral perfusion. Normovolemia is crucial, the expansion of intravascular volume will not have much effect on cerebral oedema, as long as serum osmolarity is maintained. Whether this is achieved with crystalloid solutions or colloids seems to be of little relevance, although other factors must be considered in this choice, the osmolarity of the selected fluid, however, is crucial.

Physical and Physiological Aspects

Factors that influence brain water content

Knowledge of the forces involved and the characteristics of fluid movement through brain capillaries of the blood-brain barrier (BBB). Forces and characteristics are essential to avoid an increase in intracranial pressure. BBB is impervious to small ions and proteins, but not water. Therefore, for a rational choice of the type and volume of the various hydration solutions available to be used in the neurosurgical patient, an understanding of the physical-chemical colligative properties involved in the movement of brain water and the definition of certain terms is essential.

Osmotic pressure

Osmotic pressure is the force with which water moves through the semipermeable membrane from a solution containing a low concentration of dissolved substances (solutes) to another with a high concentration of solutes. The water will pass, depending on the concentration gradient (from a lower osmolarity solution to a higher osmolarity). The driving force is proportional to the water gradient across the membrane; if two solutions with the same concentration are placed on either side of a membrane, there will be no driving force. Likewise, if the membrane is permeable to solutes, this will reduce the gradient and therefore the osmotic forces.

Osmolarity

Osmolarity is determined by the number of osmotically active particles per litre of solution, the units in which the osmolarity of a solution is expressed is milliosmoles per litre of solution (mOsm /L), and is calculated by adding the concentrations in milliequivalents of various ions present in the solution. The osmotic activity of the solution requires that the particles are independent, that is, they dissociate and, thus, osmotically active particles are created. Osmolarity is a determining factor for the movement of fluids between compartments when different osmolar solutions are separated by a membrane permeable to water, but not to solutes.

Oncotic pressure

Oncotic pressure is the osmotic pressure generated by proteins in blood plasma, especially albumin and globulins. Since plasma proteins are generally unable to pass through healthy blood capillary walls, they exert significant osmotic pressure on the ions and water that pass through the capillary walls into the blood, and thus partially balance the amount of liquid leaving the capillaries by hydrostatic pressure with which it returns. It is represented by the Greek letter π (pi) in the Starling Equation

Starling equation

The Starling equation illustrates the role of hydrostatic and oncotic forces (also called Starling forces) in the flow movement through capillary membranes.

$$MF = K_f S [(P_c - P_i) - \sigma (\pi_c - \pi_i)]$$

MF is fluid movement; K_f is the capillary wall filtration coefficient (its permeability); S is the surface area of the capillary membrane; P_c is the hydrostatic pressure in the capillary; P_i hydrostatic pressure in the interstitial space; σ is the reflection coefficient, which varies from 0 (without movement of solutes through the membrane) to up to 1 (the free diffusion of solutes through the membrane) and will be different in the brain and in the periphery; and π_i and π_c is the plasma colloid and interstitial pressure respectively.⁴

Blood-brain barrier

The Starling equation describes the relationship between the factors that determine the movement of fluids between the intravascular and the peripheral space, however unlike what happens in capillaries located in any other area of the body, the endothelial cells in the brain are connected by a structure continuous semi-permeable unique in our organism; the blood-brain barrier (BBB). BBB is formed by the presence of endothelial junctions that control the coordinated opening and closing of cell-cell junctions.⁵ These junctions are composed of different multi-protein complexes, and are known as "tight junctions", the main regulators of cellular permeability.⁶ This high selectivity of the BBB that separates blood circulation and extracellular fluid from the central nervous system (CNS), is also due to the presence of non-fenestrated membranes that have trans-endothelial passageways with the effective pore size of only 7-9 Å. Thus, the brain becomes the only structure that is normally impervious to large molecules (plasma proteins, synthetic colloids), but also relatively impervious to many solutes (Na^+ , K^+ , Cl^-). The major implication in neuro-anaesthesia is related to the passage of water freely between the interstitial space of the brain and the intravascular space. According to Tommasino, the brain functions as a very sensitive "osmometer", as the water content can be altered by small changes in osmolarity.⁷

Fluid management during neurosurgical procedures

Crystalloid solutions

Crystalloids have traditionally been categorized as hypertonic, isotonic, and hypotonic solutions to contrast their composition with that of plasma. Crystalloid solutions contain small molecules (<30000 Daltons) that pass freely through cell membranes and the walls of the vascular system (65 Å). They have zero oncotic pressure and can be hypotonic, isotonic or hypertonic solutions in relation to plasma osmolality (290 mOsm / L), with or without dextrose.

Normal saline solution (NS 0.9%) and lactated Ringer's solution (RL) are the fluids most commonly used intraoperatively. Only 25% of the infused isotonic solution remains in the intravascular space. NS 0.9% is slightly hypertonic compared to plasma (308 vs 290 mOsm / L), mainly due to the increased content of Cl⁻ ions (154 mEq/L vs. 105 mEq/L). The administration of large amounts of these solutions, can produce hypernatremia and hyperchloremic metabolic acidosis (table 1).⁸

The RL is slightly hypo-osmolar (osmolality 252-277 mOsmol/L), especially when administered to patients under fluid restriction or use of hyperosmolar fluids (mannitol). Small volumes of RL (1 to 2 L) are usually not harmful and can be used safely, for example, to compensate for changes in venous capacitance that normally accompany anaesthesia induction. However, when large volumes are required (for example, multiple trauma patients), the choice of an isotonic fluid is advisable.⁹

Balanced crystalloid solutions are slightly hyperosmolar in relation to blood plasma, which raises questions about their safety in relation to the potential to provide cerebral oedema with a consequent increase in ICP. Plasmalyte® has osmolality closer to serum, compared to RL, and has been investigated as a safer option.¹⁰ The physiological implications of some components of this solution, such as gluconate, which is excreted unchanged, which can function as an osmotic diuretic, and acetate with potential vasodilating and pro-inflammatory effects,

need to be studied, while lactate, present in RL, security is well established.¹¹

The randomized clinical trial analyzed mortality and renal outcomes in critically ill patients undergoing therapy with saline and balanced crystalloids, with a statistically significant superiority. However, in the same study, patients with traumatic brain injury had worse results with balanced solutions, which were not statistically significant. Unfortunately, the outcomes were not individualized, which could contribute to clarifying the finding. It is a fact that studies that specifically evaluated neurocritical and neurosurgical patients failed to associate the development of hyperchloremic acidosis, secondary to the use of NS, with worse outcomes in this population.¹²

Hypo-osmolar Crystalloids, Glycoside Solution and Hyperosmolar Crystalloids

0.45% saline (154 mOsmol/L) and 5% glycated serum are hypo-osmolar solutions that can reduce plasma osmolality. This osmotic gradient causes water to move through the pores of brain tissue. This increases the amount of water in the brain, resulting in cerebral oedema and increased ICP.

Hypertonic saline solution (HS) and mannitol can displace water from the nervous tissue (intracellular and interstitial to the intravascular space), which is the main mechanism by which these solutions act in the reduction of ICP. In the past, HS were used mainly for fluid resuscitation in patients with trauma and haemorrhagic shock. It was observed that patients with TBI resuscitated from haemorrhagic shock with HS (NaCl 7.5% = 2,400 mOsm/L), had lower ICP values and higher CPP values. The main disadvantage of hypertonic solution is the risk of hypernatremia. In a recent study in neurosurgical patients undergoing elective procedures for supratentorial tumours, it was shown that volumes equal to 20% of mannitol and HS 7.5% reduced the volume of CSF and ICP, however it would lead to an increase in serum sodium during administration, which reached a peak of up to 150 mEq/L.

| | Isotonic saline | Lactated Ringer's | Acetated Ringer's | Plasmalyte® |
|------------------|-----------------|-------------------|-------------------|-------------|
| Osmolarity | 308 | 277 | 302 | 295 |
| Base excess | -27 | - | - | - |
| Na+ | 154 | 131 | 140 | 140 |
| Cl- | 154 | 112 | 108 | 97 |
| K+ | - | 5.4 | 5 | 4.96 |
| Ca ⁺⁺ | - | 1.8 | 2.5 | - |
| Mg ⁺⁺ | - | - | 1.5 | 1.48 |
| Lactate | - | 28 | - | - |
| Acetate | - | - | 45 | 27 |

Table 1: Composition of the most commonly used infusion solutions (all values in mmol/l)⁸

Postoperatively, the patient no longer needs large volumes of fluids, so many authors believe that Shenkin's recommendation about offering approximately 1000 mL/day is probably reasonable. In addition, periodic measurement of serum osmolarity is also recommended, especially if the patient's neurological status is deteriorated.¹³

Colloids

Solutions that have oncotic pressure similar to plasma and large molecules that give it relative impermeability to capillary membranes are called colloids. Among the most commonly used we have: hydroxyethyl starch, dextran, gelatin (polygeline), albumin and plasma. Drummond et al, demonstrated that the reduction of colloid osmotic pressure can aggravate cerebral oedema after moderate head trauma. Another study by Jungner et al, demonstrated that, when the same expansion of intravascular volume is administered, isotonic crystalloids cause greater post-cerebral oedema traumatic when compared to 5% albumin.¹⁴

Albumin is a natural colloid available in concentrations of 5 and 20%. This is an effective, plasma expander with no effect on blood clotting and associated allergic reactions. With a molecular weight between 66,000-69,000 Daltons, it is extracted from various donors. In addition, the risk of transmitting infections is eliminated by heat treatment at 60 degrees for 10 hours and ultrafiltration. It is approximately 5 times more expensive than synthetic colloids, such as hetastarch. Although the 4% hypo-osmolar albumin solution (274 mOsm/L) has been associated with worsening cerebral oedema, based on empirical experience, albumin is a reasonable choice in neurosurgical patients in certain situations, but it must have its volume carefully limited. The other colloids, such as dextran, are less used due to the association with anaphylactic reactions and coagulation abnormalities, since they directly interfere with platelet function and factor VIII complex, and therefore its use should be caution in neurosurgery.

Solutions based on hydroxyethyl starch have their safety questioned. Inhibitory effects on platelet function and thromboelastography changes have been described, although the increase in blood loss has not been proven in clinical studies. A recent review of anaemia and transfusion in intracranial surgeries recommended avoiding the use of these solutions as a potentially beneficial measure in this population^{15,16,17}

Hemodynamic parameters to guide fluid therapy

The value of goal-directed fluid therapy (GDT) in neurosurgical patients, where brain swelling is a major

concern, is unknown, but various parameters have been used to guide fluid therapy. Various parameters have been used to guide fluid therapy. End points such as urine output, peripheral perfusion, and capillary refill time had all been suggested, but they are neither sensitive nor specific for evaluating fluid status as the signs of hypovolemia including tachycardia, hypotension, and oliguria may be present in euvoletic patients and absent during hypovolemia.¹⁸

Predictors of fluid responsiveness, such as Pulse Contour Analysis (PCA), offer a continuous analysis of cardiac output and fluid responsiveness with good correlation to the pulmonary artery catheter (PAC) under normovolemic states, but they lack accuracy as rapid changes in peripheral arterial resistance take place and when facing haemodynamic instability. They also require frequent recalibration to remain accurate in their measurements.

Although various parameters have been used to guide fluid therapy, such as static measurements like central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP), they are not fully reliable upon. CVP, for instance, suffers wide variations from intrathoracic pressures and Pulmonary Artery Occlusion Pressure (PAOP) is too invasive and thus, not recommended for intracranial surgery.

In recent years, an impressive number of studies have demonstrated that the pulse pressure variation (PPV), which is derived from the analysis of the arterial waveform, the stroke volume variation (SVV), derived from pulse contour analysis, and the variation of the amplitude of the pulse oximeter's plethysmographic waveform, are highly predictive of fluid responsiveness.¹⁹

Monitoring systems such as PPV and SVV (so-called 'dynamic indices of fluid responsiveness')²⁰ are more accurate on fluid responsiveness prediction. The ability of SVV is obtained with Vigileo/FloTrac system to monitor fluid responsiveness in mechanically ventilated patients.²⁰ SVV Stroke volume variation could be a predictor of fluid responsiveness in patients undergoing airway pressure release ventilation, but still, they still require patients to be anesthetized and on mechanical ventilation, with a tidal volume of at least 6ml/kg, with closed chest, sinus rhythm and normal intraabdominal pressure.²¹

Echocardiography is a tool that can help in the management of fluid responsiveness by evaluating cardiac systolic function. In the post-operative intensive care unit, the trained physician may perform transthoracic echocardiogram for evaluation of hypovolemia; with measurement of the left ventricular internal diameter at the end of diastole and evaluation of the diameter of the inferior vena cava along with its collapsibility index. The performance of echocardiogram during the surgery is difficult due to the positioning of the surgical fields, but it is an excellent tool for the diagnosis of air embolism.²³

Goal directed fluid therapy in neurosurgery

Individualised 'Goal-directed fluid therapy' has been shown to improve outcomes after surgery.²⁴ However, the limitations of each dynamic index must be considered. The presence of fluid responsiveness is not an indication for fluid administration; the final decision to give fluid must be supported by the clear need for hemodynamic improvement, presence of fluid responsiveness, and absence of associated risk. Goal-directed therapy has been shown to improve the outcome of patients undergoing major surgery. Current knowledge regarding the effect of fluid management on patient-orientated outcomes in neurosurgery is limited.²⁵

Discussion

Several studies have assessed the effect of a 'liberal' vs a 'restrictive' perioperative fluid regimen on post-operative outcome. The literature was reviewed in order to provide recommendations regarding perioperative fluid regimens. For many years the principles of fluid and electrolyte hydration management in neurosurgery were restrictive. The fear of excess fluid leading to perioperative cerebral oedema and postoperative intracranial hypertension has always been overestimated. Being liberal in relation to hydration in neurosurgery was to assume the risks above. However, many studies have shown that being restrictive in hydration in neuro-anaesthesia had a price in increasing mortality. We will still need further studies to make hydration more flexible in neurosurgery, but it is clear that a slightly more liberal approach reduces the risk of the most feared complication in neurosurgery, the perioperative cerebral ischemia. Perhaps at this point, goal-oriented therapy will meet expectations.^{26,27,28,29,30}

Conclusion

Fluid balance management is paramount to neurosurgical patients, and the consequences of fluid administration may be significant, since both, hypovolaemia and hypervolemia are known to cause increased perioperative morbidity and mortality. Therefore, assessment of the patient's actual haemodynamic status can guide appropriate therapy, especially in neurosurgery.

Postoperative ischaemia is catastrophic and is often due to excessive fluid restrictions associated with unmeasured bleeding. In recent times, mounting evidence demonstrates that outcomes may be improved if fluid therapy is individualized and based on objective feedback on the patient's individual fluid responsiveness.

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