

Fluid management during neurosurgical procedures

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INTRODUCTION

The perioperative fluid management of neurosurgical patients presents a special challenge to the neuroanaesthesiologists in the perioperative period. These patients receive diuretics such as mannitol and furosemide in the pre-operative period to reduce the intracranial pressure. During the intraoperative period, they may have vasodilatation due to administration of inhalational anaesthetics and depletion of intravascular volume as a result of severe blood loss. The development of diabetes insipidus (DI) or syndrome of inappropriate antidiuretic hormone secretion may further lead to haemodynamic instability. This review will summarise the physical determinants of water movement across the biological membranes and the practical considerations while administering fluids in various cerebral pathologies.

OSMOLALITY/OSMOTIC PRESSURE/ COLLOID ONCOTIC PRESSURE

The four colligative properties of a solution are vapour pressure, freezing point depression, boiling point elevation and osmolality. Osmolality is defined as the number of particles in a solution. Osmolality is the number of the milliosmoles (mOsm) per kilogram of solvent while as osmolarity is the number of milliosmoles per litre of solution. Osmolarity determines the fluid movement between the various physiologic compartments of the body. The movement continues until the solutions attain an equal osmolality on the two sides of the membrane.

Osmotic pressure is the hydrostatic force which acts to equalise the concentration of water on both sides of the

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membrane that is impermeable to solutes dissolved in that water. Colloid oncotic pressure (COP) is osmotic pressure generated by large molecules (e.g. albumin, hetastarch and dextran). COP is of clinical significance in vascular membranes in the biological systems which are permeable to small ions but not to large molecules.

Ernest Starling studied the forces that determine the movement of water between tissues and the intravascular space.^[1] Starling found that the three main factors controlling the movement of fluids between the intra- and extra-vascular spaces are:

- Transcapillary hydrostatic gradient,
- Osmotic and oncotic gradients, and
- The relative permeability of the capillary membranes between these separating spaces.

The Starling equation is stated as below:

$$FM = k (Pc + pi - Pi - pc)$$

Where FM = fluid movement, k = the filtration coefficient of the capillary wall (which determines the leakiness of the capillary wall), Pc = hydrostatic pressure in the capillaries, Pi = hydrostatic pressure (usually negative) in the interstitial space and pi and pc are interstitial and capillary osmotic pressures, respectively. The amount of fluid movement is proportional to the hydrostatic pressure gradient minus the osmotic gradient across a vessel wall.

The peripheral vasculature of the muscles and the pulmonary vasculature have a capillary endothelium with a pore size of around 65 Å. Small molecules and ions (Na⁺, Cl⁻) pass freely through these pores, but the large molecules such as proteins cannot pass through them. Hence, the movement of water is governed by the plasma concentration of large molecules (oncotic gradient). If COP is reduced, fluid will begin to accumulate in the interstitium, producing oedema. Fenstermacher and

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Johnson^[2] found that the cerebral capillaries have a very, small pore size of around 7–9 Å. This small pore size of the blood–brain barrier (BBB) prevents movement of both proteins and ions (sodium, chloride and potassium). Hence, the fluid movement across the BBB is determined by the ‘total’ osmotic gradient, generated both by large molecules and small ions. As the number of protein molecules is negligible compared with the number of inorganic ions, their effect on total osmolality is minimal.

With a normal BBB, when there is a decrease of the plasma osmolality, the osmotic gradient drives the water into the brain tissue. Tommasino *et al.* found that even very small changes in plasma osmolality (<5%) increase brain water content and intracranial pressure (ICP).^[3]

When the BBB is damaged as in head injury, tumour, seizure and abscess, there will be a variable response to the changes in plasma osmotic/oncotic pressures. With complete breakdown of the BBB, there will be no osmotic gradient that can be established.^[4] With a partial damage to the BBB, the barrier may behave in a similar way as the peripheral tissue.^[5] There is usually a significant portion of the brain where the BBB is normal, and the presence of this functionally intact BBB is essential for osmotherapy to be effective.^[6]

FLUIDS FOR INTRAVENOUS ADMINISTRATION

Crystalloids and cerebral effects of plasma osmolality

Crystalloid solutions contain small molecules that pass freely through cell membranes and vascular system walls. They have an oncotic pressure of zero. Crystalloids may be hypo-, iso- or hyper-osmolar.

Hypo-osmolar crystalloids

Fluids as 0.45% saline or 5% glucose in water are hypo-osmolar and when administered, cause a reduction in plasma osmolality. This osmotic gradient causes movement of water across the BBB into the cerebral tissue. This increases the brain water content resulting in oedema and an increase in the ICP.

One of the first animal studies conducted by Weed and McKibben on the cerebral effects of fluid administration showed that hypotonic solutions expanded the brain.^[7] Hence, the use of hypo-osmolar solutions should be avoided in patients with neurological and neurosurgical disorders.

Iso-osmolar crystalloids

The administration of iso-osmolar solutions (plasmalyte, 0.9% saline), which has an osmolality of around 300 mOsm/L, will not result in any changes in the plasma osmolality. Therefore, their administration results in

no increase in the brain water content. However, those solutions which are not truly iso-osmolar with respect to plasma as Ringer’s lactate solution (calculated osmolarity of 275 mOsm/L but a measured osmolality of 254 mOsm/kg due to incomplete dissociation) reduce the plasma osmolality and increase brain water content and ICP.^[3,8,9]

Hyper-osmolar crystalloids

Crystalloid solutions as hypertonic saline and mannitol shift the water from the nervous tissue (intracellular and interstitial space) to the intravascular space.^[10] This effect occurs in patients with a normal BBB^[6] and is the main mechanism by which the intracranial hypertension is reduced.

COLLOIDS AND CEREBRAL EFFECTS OF COLLOID ONCOTIC PRESSURE

Colloidal solutions as albumin, plasma, hetastarch, pentastarch and dextrans are composed of large molecules which are relatively impermeable to the capillary membranes. A study by Drummond *et al.*^[5] showed that COP reduction can aggravate brain oedema after a mild to moderate mechanical head injury. Another study by Jungner *et al.*^[11] showed that when given to the same intravascular volume expansion, isotonic crystalloids caused greater post-traumatic brain oedema than 5% albumin at 3 and 24 h after trauma.

Li *et al.*^[12] studied the effects of colloid infusions in patients undergoing surgery for intracranial tumours. They found that hydroxyethyl starch affected coagulation at lower volumes, with a more prominent effect on clot structure at the end of surgery. Albumin decreased platelet aggregation. The message from all these studies is that it is better to correct the changes in COP in patients with brain or spinal cord injury.

GLUCOSE-CONTAINING SOLUTIONS

The salt-free solutions which contain glucose are avoided in brain and spinal cord injuries due to several reasons:

- The metabolised glucose in 5% dextrose releases only free water remains. This causes a reduction in the serum osmolality and increases brain water content
- Glucose administration may increase neurologic damage and can worsen the outcome from both local and global ischaemia^[13] as in the ischaemic areas glucose metabolism may enhance the tissue acidosis.^[13,14]

A recent cerebral microdialysis study conducted by Magnoni *et al.* showed that a linear relationship between systemic glucose and brain glucose is preserved in

patients with traumatic brain injury (TBI).^[15] Hence, brain glucose in tissues with disturbed oxidative metabolism may decrease to dangerously low levels even with systemic glucose being in the lower limit of 'normal range'. The authors strongly recommend avoiding severe glycaemic reductions. The best practice seems to adopt a moderate range of target blood glucose control 140–180 mg/dl. The American Heart Association/American Stroke Association guidelines also recommend avoiding intraoperative hyperglycaemia minimising glucose variability and aggressive management of hypoglycaemia.^[16] Cinotti *et al.*^[17] found out that intensive insulin therapy (IIT) did not appear to alter the day-90 neurological outcome or Intensive Care Unit (ICU) morbidity in severe brain injured patients or ICU morbidity. IIT group experienced more episodes of hypoglycaemia ($P < 0.0001$). In the IIT group, 24 (26.6%) patients had a favourable neurological outcome (good recovery or moderate disability) compared to 31 (31.6%) in the control group ($P = 0.4$).

FLUIDS TO CONTROL INTRACRANIAL PRESSURE AND BRAIN SWELLING

Diuretics: Mannitol and furosemide

Mannitol causes an increase in the plasma osmolality. An osmotic gradient is established between the intravascular compartment and the cerebral parenchyma. Mannitol is less effective with larger lesions because of the damaged BBB. In case of deranged BBB, the mannitol may go down its concentration gradient into the brain leading to a rebound phenomenon with an increase in the brain oedema and increased ICP. Administration of mannitol may cause a triphasic haemodynamic response. Transient (1–2 min) hypotension may occur after rapid administration of mannitol.^[18,19] It is followed by an increase in blood volume, cardiac index and pulmonary capillary wedge pressure. At 30 min after mannitol administration, blood volume returns to normal and pulmonary capillary wedge pressure and cardiac index drop to below normal levels because of peripheral vascular pooling.^[18,19] The mechanism of furosemide's action is not clear. It is believed to act by blocking the chloride transport and reduce the cerebrospinal fluid production.

Hypertonic saline solutions

Hypertonic salt solutions were primarily used for small-volume resuscitation in trauma patients with haemorrhagic shock. However, it was found that when TBI patients were acutely resuscitated from haemorrhagic shock with 7.5% hypertonic saline, there was an improved outcome.^[20] It has been seen from various studies that hypertonic saline solutions lowers ICP and improve cerebral perfusion pressure.^[21] When compared to mannitol, it does not produce an

osmotic diuresis which makes the perioperative fluid management relatively simple. Prabhakar *et al.*^[22] did a Cochrane review on mannitol versus hypertonic saline for brain relaxation in patients undergoing craniotomy. The authors suggested from studying 6 randomised controlled trials comprising 527 participants that the hypertonic saline significantly reduces the risk of tense brain during craniotomy. A single trial suggested that ICU stay and hospital stay are comparable with the use of mannitol or hypertonic saline.

Hypertonic/hyperoncotic solutions

Hypertonic and hyperoncotic solutions (hetastarch or dextran) restore normovolaemia rapidly without increasing the ICP. They are beneficial in head-injured patients and in patients with stroke.^[23,24]

CLINICAL IMPLICATIONS

Intraoperative volume replacement/resuscitation

The intraoperative fluid administration should take into account the amount of intraoperative blood loss, urinary output and insensible losses. Fluids should be administered judiciously to maintain a normal or slightly increased serum osmolality and a normal plasma oncotic pressure. Fluid administration should be guided by the trends in the arterial blood pressures and central venous pressures.

Hypo-osmolar fluids should be avoided as they may reduce the plasma osmolality. Small volumes of Lactated Ringer's (measured osmolality 252–255 mOsm/kg) can be used without any detrimental physiological effects. In case of massive blood loss, isotonic fluids can be safely administered. However, large volumes of 0.9% NaCl result in hyperchloremic metabolic acidosis with a normal anion gap.^[25] In large volumes resuscitation, a combination of isotonic crystalloids, colloids and blood transfusion may be the best choice.

Pentastarch has little effect on Factor VIII in comparison to hetastarch infusion which in volumes >1l leads to factor VIII depletion.^[26,27]

Pituitary and spine surgery are other neurosurgical procedures that require special considerations so far the fluid management is concerned. In patients undergoing pituitary surgery, DI both during the intraoperative and post-operative period may be observed. Fluid balance needs close monitoring to avoid complications and disabling electrolyte imbalance and to avoid fluid overload. It is imperative to check serum osmolality frequently which guides the administration of amount and type of fluid.

Surgeries on the spine may be extensive involving many sections of the vertebral column, especially when instrumentation is planned. Massive blood loss and blood transfusions may be expected. It is important to maintain adequate fluid status without producing fluid overload, which may lead to venous congestion and at the same time compromising the blood flow and oxygenation of the spinal cord.

HEAD INJURY

A fluid which maintains or augments intravascular volume and does not increase cerebral oedema would be an ideal fluid in head injury patients. Isotonic saline is good choice for head injured patient as it has an osmolality of 308 mOsmol/L and therefore will not cause exacerbation of brain oedema. Hypertonic saline because of its higher osmolality (514 mOsmol/L) withdraws the fluid from the tissues and increases intravascular volume. There is an increase in the cardiac output and systolic arterial pressure resulting in a better perfusion of the brain.^[28] In addition, there may be a vasodilator effect in the microcirculation and a modulatory effect on the immune trauma response.^[29] Central pontine demyelination, seen after rapid correction of hyponatraemia, has not been reported with hypertonic saline resuscitation in head injured patients.^[30]

Colloids remain within the intravascular compartment due to large size of their molecules. They stabilise the systolic blood pressure and do not increase the cerebral oedema.

Despite the theoretical superiority of colloids, there is a limited scientific evidence to support their use. A meta-analysis of several studies suggests rather a slightly lower mortality with crystalloids.^[31]

The SAFE study which has looked into saline versus albumen fluid evaluation in head injury patients did not show any benefit with albumin. Albumin was rather found to increase mortality probably due to increased vasogenic oedema.^[32]

Blood is an ideal for resuscitation, with blood loss up to 20% of blood volume treated with crystalloids and colloids. A blood loss of 30% or more requires blood replacement. A haemoglobin of <9 g% is associated with increased mortality while as a transfusion trigger of >10 g% may be associated with thrombo-embolic complications.^[33] A haemoglobin value of greater than that should be maintained to improve the outcome.^[33]

SUBARACHNOID HEMORRHAGE

Hyponatraemia and hypovolaemia occur frequently in patients with subarachnoid haemorrhage (SAH).

Hypovolaemia is mainly due to bed rest, negative nitrogen balance, decreased erythropoiesis, iatrogenic blood loss and dysregulation of the autonomic nervous system. Hyponatraemia may be due to cerebral salt-wasting syndrome, and the causative factor seems to be an increased release of a natriuretic factor from the brain.^[34] Hyponatraemia is managed by the administration of a large volume of isotonic crystalloids and the restriction of free water.

The traditional management of delayed cerebral ischaemia (DCI) attempted to augment cerebral blood flow (CBF) with triple-H therapy defined by hypertension, hypervolaemia and haemodilution. Because the fundamental objective in managing DCI is maximising DO_2 and not CBF, haemodilution by reducing CaO_2 may actually be detrimental. Although avoiding hypovolaemia reduces the risk of DCI after SAH, prophylactic hypervolaemia has not been seen to offer any benefit with the incidence of symptomatic cerebral vasospasm similar in hypervolaemic and normovolaemic groups.^[35] A task force of neuroscientists recommended^[36] that in SAH (a) intravascular volume management should target euvolaemia and avoid prophylactic hypervolaemic therapy. In contrast, there is evidence for harm from aggressive administration of fluid aimed at achieving hypervolaemia (high quality evidence; strong recommendation), (b) isotonic crystalloid is the preferred agent for volume replacement (moderate quality evidence; weak recommendation) and (c) in patients with persistent negative fluid balance, use of fludrocortisone or hydrocortisone may be considered (moderate quality evidence; weak recommendation).

WATER AND ELECTROLYTES DISTURBANCES

Diabetes insipidus

DI is caused by decreased secretion (central/neurogenic DI) or action (nephrogenic DI) of antidiuretic hormone (ADH, vasopressin). The decreased secretion or action of ADH leads to failure of tubular reabsorption of water resulting in decreased urine specific gravity is (<1.002).

DI is seen commonly after head injury, pituitary and hypothalamic lesions. The main clinical features are polyuria (>5 mL/kg/h^[37] or in an adult, >200 mL/h), resulting in dehydration, and hypernatremia. Agha *et al.* diagnosed post-traumatic DI based on the combination of polyuria (>3.5 l/24 h) with dilute urine (urine/plasma osmolality <2), hypernatraemia (>145 mmol/L) and increased plasma osmolality (>300 mosm/kg).^[38]

Management

- The patient should receive maintenance fluids plus three-quarter of the previous hour's urine output in

each hour. Alternatively, the previous hour's urine output minus 50 mL should be administered. The fluids administered should have a low sodium load as half-normal saline and D5W. When the urine output is higher than 300 mL/h, at least for 2 h, aqueous vasopressin is given at 5–10 IU, intramuscularly or subcutaneously q 6 h. However, due to the lower duration of action and option of more frequent dose adjustment, the use of vasopressin has become limited. The synthetic analogue of vasopressin, 1-deamino-8-d-arginine-vasopressin (DDAVP) and desmopressin with minimal pressor effects is widely used for the management of central DI. DDAVP is used 0.5–2 mg, intravenously, q 8 h; or by nasal inhalation, 10–20 mg.

Syndrome of inappropriate antidiuretic hormone secretion

Head injury can result in excessive release of ADH leading to continuous renal excretion of sodium, despite hyponatraemia and associated hypo-osmolality. Urine osmolality is therefore high, relative to serum osmolality.

Management

Treatment involves fluid restriction. A volume of 1000 mL of an iso-osmolar solution is administered over 24 h. If hyponatraemia lower than 110 mEq/L, hypertonic saline may be administered along with furosemide.

Cerebral salt-wasting syndrome

It is seen mainly with SAH and is characterised by hyponatraemia, volume contraction and high urine sodium concentration due to release of natriuretic factor from the brain. Treatment involves to re-establish the normovolaemia with the administration of sodium-containing solutions.

CONCLUSION

The understanding of fluid management has improved in the last decade. However, the comparative advantages and disadvantages of different fluid regimens are still poorly understood. As neuro-intensivists we should keep our patients isovolaemic, isotonic and iso-oncotic except for SIADH patients where fluid administration should be used cautiously.

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