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Fluids and the neurosurgical patient

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The fluid management of neurosurgical patients presents special challenges for anesthesiologists and intensivists [1]. Neurosurgical patients often receive diuretics (eg, mannitol, furosemide) to treat cerebral edema and/or to reduce intracranial hypertension. Conversely, they may also require large amounts of intravenous fluids to correct preoperative dehydration and/or to maintain intraoperative and postoperative hemodynamic stability as part of therapy for vasospasm, for blood replacement, or for resuscitation.

For a long time restrictive fluid management has been the treatment of choice in patients with brain pathology, growing from fear that fluid administration could enhance cerebral edema [2]. It is well known that fluid restriction, if pursued to excess (hypovolemia), may result in episodes of hypotension, which can increase intracranial pressure (ICP) and reduce cerebral perfusion pressure, and the consequences can be devastating [3].

It is unfortunate that little substantial human data exist concerning the impact of fluids on the brain, or which can guide rational fluid management in neurosurgical patients. However, it is possible to examine those factors that influence water movement into the brain, and to make some reasonable recommendations.

This review will address some of the physical determinants of water movement between the intravascular space and the central nervous system (CNS). Subsequent sections will address specific clinical situations with suggestions for the types and volume of fluids to be administered.

Osmolality/osmolarity, osmotic and oncotic pressure, hemodilution

With intravenous fluid therapy, three properties of the blood can be manipulated: osmolality (owing to concentrations of large and small molecules), colloid oncotic pressure (COP; owing to large molecules only), and hematocrit.

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Osmotic pressure

This is the hydrostatic force acting to equalize the concentration of water on both sides of the membrane that is impermeable to substances dissolved in that water. Water will move along its concentration gradient. *Osmolarity* describes the molar number of osmotically active particles per *liter* of solution. In practice, the osmolarity of a solution can be "calculated" by adding up the mEq concentrations of the various ions in the solution. *Osmolality* describes the molar number of osmotically active particles per *kilogram* of solvent. This value is directly "measured" by determining either the freezing point or the vapor pressure of the solution. For most dilute salt solutions, osmolality is equal to or slightly less than osmolarity.

Colloid oncotic pressure

Osmolarity/osmolality is determined by the total number of dissolved "particles" in a solution, regardless of their size. COP is nothing more that the osmotic pressure generated by large molecules (eg, albumin, hetastarch, dextran). The COP becomes particularly important in biological systems where vascular membranes are often permeable to small ions, but not to large molecules.

Fluid movement between capillaries and tissues

As defined by the Starling equation [4], the major factors that control the movement of fluids between the intravascular and extravascular spaces are the transcapillary hydrostatic gradient, the osmotic and oncotic gradients, and the relative permeability of the capillary membranes that separate these spaces. The Starling equation is as follows:

$$\mathrm{FM} = k(P_c + p_i - P_i - p_c)$$

where FM = fluid movement, k = the filtration coefficient of the capillary wall (= how leaky it is), P_c = hydrostatic pressure in the capillaries, P_i = hydrostatic pressure (usually negative) in the interstitial space, and p_i and p_c are interstitial and capillary osmotic pressures, respectively. In a simplified fashion, fluid movement is proportional to the hydrostatic pressure gradient minus the osmotic gradient across a vessel wall. The magnitude of the osmotic gradient will depend on the relative permeability of the membrane.

In the periphery (muscle, lung, and other areas), the capillary endothelium has a pore size of 65 Å, and is freely permeable to small molecules and ions (Na^+, Cl^-), but not to large molecules, such as proteins [5] (Fig. 1A). Thus, in the periphery, 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 edema. In the cerebral capillaries, Fenstermacher [5] calculated the effective pore size to be only 7 to 9 Å. This small pore size of the blood–brain barrier (BBB) prevents not only the movement of proteins, but also

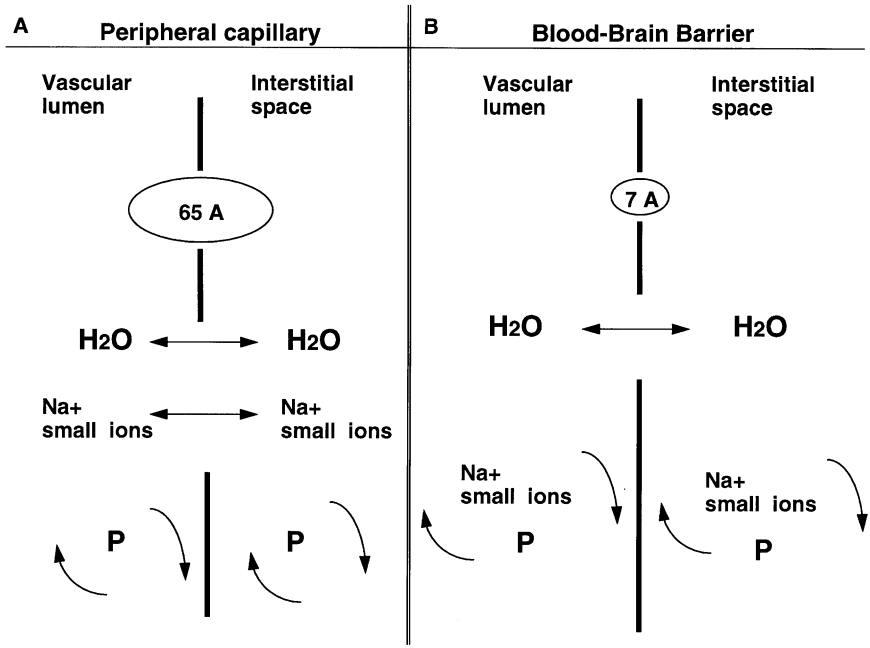

Fig. 1. Schematic diagram of capillary membrane in the periphery. (A) The vessel wall is permeable to both water (H_2O) and small ions, but not to proteins (P), in the brain. (B) The blood–brain barrier is permeable only to water.

sodium, chloride, and potassium ions [5] (Fig. 1B). The fluid movement across the BBB is determined by the "total" osmotic gradient, generated both by large molecules and small ions. Because there are so few protein molecules compared with the number of inorganic ions, their effect on total osmolality is minimal (normal COP $\approx$ 20 mmHg $\approx$ 1 mOsm/kg). Clearly, the influence of changes in osmolality on cerebral water distribution dwarfs the effects of alteration in COP. These differences explain why the administration of large volumes of isotonic crystalloids, with dilutional reduction of COP, results in peripheral edema, but does not increase brain water content and/or ICP [6–8].

When plasma osmolality decreases, the osmotic gradient drives water into the brain tissue. Even small changes in plasma osmolality ($<5\%$) increase brain water content and ICP [7].

The above scenario describes the situation in conditions of normal BBB. After a brain lesion, according to the severity of the damage (head trauma, tumor, seizure, abscess, or other damage), there can be varying degrees of BBB integrity, which can respond differently to the osmotic/oncotic changes. With complete breakdown of the BBB, no osmotic gradient can be established [9–11]. It is possible that with a less severe injury to the BBB, the barrier *may* function similarly to the peripheral tissue [12]. Finally, there is usually a significant

portion of the brain where the BBB is normal. The presence of a functionally intact BBB is essential if osmotherapy is to be successful [13].

Hematocrit and hemodilution

One common accompaniment of fluid infusion is a reduction in hemoglobin/hematocrit. This hemodilution is typically accompanied by an increase in cerebral blood flow (CBF) [7,14,15]. In the normal brain, the increase in CBF produced by hemodilution is an active compensatory response to a decrease in arterial oxygen content, and this response is essentially identical to that seen with hypoxia [16–18]. However, it should be stressed that in the face of brain injury, the normal CBF responses to hypoxia and to hemodilution are attenuated, and both changes may contribute to secondary tissue damage [19].

A hematocrit level of 30–33% gives the optimal combination of viscosity and O_2 carrying capacity, and may improve neurologic outcome [6,20,21]. However, marked hemodilution (Hct $<30\%$) exacerbates neurologic injury [20,22].

Fluids for intravenous administration

The anesthesiologists and the intensivists can choose among a variety of fluids suitable for intravenous administration, commonly categorized as crystalloids and colloids.

Crystalloids and cerebral effects of plasma osmolality

Crystalloid solutions do not contain any high molecular weight compound, and have an oncotic pressure of zero. Crystalloids may be hypo-osmolar, iso-osmolar or hyperosmolar, and may or may not contain glucose. Commonly used crystalloid solutions are illustrated in Table 1.

Hypo-osmolar crystalloids

Since the early years of the last century, scientists have known that fluid regimens provide free water (eg, 0.45% saline or 5% glucose in water, D5W), and cause a concomitant reduction in plasma osmolality, can cause cerebral edema. One of the first animal studies on the cerebral effects of fluid administration showed that hypotonic solutions expanded the brain [23]. The osmotic gradient drives water across the BBB into the cerebral tissue, increasing brain water content (= edema) and ICP. As a consequence, the use of fluid therapy that avoids excess free water has been a standard element of management in patients with brain and spinal cord damage.

Iso-osmolar crystalloids

Although some clinicians have long believed that iso-osmolar crystalloids induce and/or aggravate brain edema, the many attempts to demonstrate experi-

Table 1
Composition of commonly used intravenous fluids: Crystalloids

		mEq/l					g/l	
Intravenous fluids	MOsm/l[a]	Na^+	Cl^-	K	Ca	Mg	Lactate	Dextrose (g/l)
5% Dextrose in water (D5W)	278							50
5% Dextrose in 0.45% NaCl	405	77	77					50
5% Dextrose in 0.9% NaCl	561	154	154					50
5% Dextrose in Ringer's solution	525	130	109	4	3			50
Ringer's solution	309	147	156	4	4–4.5			
Lactated Ringer's solution	275	130	109	4	3		28	
5% Dextrose in Lactated Ringer's solution	525	130	109	4	3		28	50
Plasmalyte[b]	298	140	98	5		3		
0.45% NaCl	154	77	77					
0.9% NaCl	308	154	154					
3.0% Saline	1026	513	513					
5.0% Saline	1710	855	855					
7.5% Saline	2566	1283	1283					
20% Mannitol	1098							

[a] osmolarity = calculated value (osm/l = mg ÷ molecular weigh × 10 × valence).
[b] Acetate 27 mEq/l and gluconate 23 mEq/l.

mentally this phenomenon have not yielded scientifically convincing proof or have generated negative results [7–11,24–27]. Iso-osmolar solutions, with an osmolality ≈300 mOsm/L, such as plasmalyte, 0.9% saline, do not change plasma osmolality, and do not increase brain water content. The same does not apply to solutions that are not truly iso-osmolar with respect to plasma. For example, commercial lactated Ringer's solution has a calculated osmolarity of ≈275 mOsm/L, but a measured osmolality of ≈254 mOsm/kg, indicating incomplete dissociation [7]. The administration of large volumes of this solution (>3 l in humans) can reduce plasma osmolality and increase brain water content and ICP [7,28], as approximately 114 mL of free water is given for each liter of lactated Ringer's solution.

Hyperosmolar crystalloids

Crystalloids may be made hyperosmolar by the inclusion of electrolytes (eg, Na^+ and Cl^-, as in hypertonic saline), or low molecular weight solutes, such as mannitol (molecular weight 182), or glucose (molecular weight 180). Hyperosmolar solutions exert their beneficial effects by osmotically shifting water from the nervous tissue (intracellular and interstitial space) to the intravascular space. This effect has been demonstrated in brain tissue with normal a BBB [13,28–31], and is the cornerstone treatment of intracranial hypertension. Furthermore, the increased serum osmolality reduces cerebrospinal fluid (CSF) secretion rate, and this effect can contribute to improve the intracranial compliance [32–34].

Table 2
Composition of commonly used intravenous fluids: Colloids

Intravenous fluids	mEq/l				Osmolarity[a] (mOsm/l)	Oncotic pressure (mm Hg)
	Na^+	Cl^-	K	Ca		
Fresh-frozen plasma	168	76	3.2	8.2	≈ 300	21
5% Albumin					290	19
Dextran (10%) 40 in 0.9% saline	154	154			≈ 310	61
Dextran (6%) 70 in 0.9% saline	154	154			≈ 310	19
Hetastarch (6%) in 0.9% saline	154	154				31
Hetastarch (10%) in 0.9% saline	154	154			≈ 310	82

[a] Osmolarity = calculated value (osm/l = mg ÷ molecular weigh × 10 × valence).

Colloids and cerebral effects of colloid oncotic pressure

Colloid is the term used to denote solutions that have an oncotic pressure similar to that of plasma. Colloidal solutions share the presence of large molecules that are relatively impermeable to the capillary membranes. Frequently used colloids are illustrated in Table 2**.** Colloids include albumin, plasma, hetastarch (hydroxyethylstarch, molecular weight 450), pentastarch (a low molecular weight, 264, hydroxyethylstarch), and the dextrans (molecular weights 40 and 70). Dextran and hetastarch are dissolved in normal saline, so the osmolarity of the solution is approximately 290 to 310 mOsm/L, with a sodium and chloride content of about 154 mEq/L each.

Although it is accepted that a reduction in serum osmolality will cause cerebral edema [7,12,23], there is not uniform agreement about the potential effect of reduction in COP. Carefully conducted investigations have systematically sought a cerebral edema effect of COP reduction but have failed to identify one [6,8–11]. Only a recent and elegant study by Drummond et al. [12] has reported that COP reduction has the potential to aggravate brain edema. The different results can be explained by the nature and severity of the brain injury. In the study of Drummond et al. [12], the injury was deliberately mild. It seem reasonable to suspect that this type of mechanical injury made the BBB permeable to low molecular weight solutes while remaining impermeable to colloids.

From the above-mentioned studies we can postulate that, depending on the severity of the BBB damage, we will have brain areas where the osmotic/oncotic gradient is totally effective (normal BBB), areas where only the colloid oncotic gradient is effective (mild opening of the BBB, with pore size similar to the periphery), and areas where there is no osmotic/oncotic gradient effect (BBB breakdown).

The message is to avoid and/or correct, in patients with brain or spinal cord injury, a decrease in ''both'' serum osmolality and COP. This message, however, is part of the ''common clinical sense.'' As anesthesiologists and intensivists, we treat not only brains but patients, and a COP reduction, even if it could not directly affect brain water content, affects other organs and perfusion (eg, pulmonary edema) [35], which in turn, can influence brain homeostasis.

Glucose-containing solutions

Intravenous salt-free solutions containing glucose should be avoided in patients with brain and spinal cord pathology. Once glucose is metabolized, only free water remains only free water, which reduces serum osmolality and increases brain water content. Furthermore, several studies in animals as well as in humans have demonstrated that glucose administration increases neurologic damage and can worsen outcome from both focal and global ischemia [36–40], presumably because in ischemic areas glucose metabolism enhances tissue acidosis [40,41]. Glucose-containing solutions should be withheld in adult neurosurgical patients, with the exception of neonates and patients with diabetes, in whom hypoglycemia can occur very rapidly and be detrimental. It should be noted that this caveat does not appear to apply to the use of hyperalimentation fluids in neurosurgical patients, perhaps because these hyperglycemic fluids are typically started several days after the primary insult, and/or because concomitant insulin is used. In humans, it has not been carefully studied whether aggressive control of hyperglycemia with insulin will improve outcome, but laboratory evidence supports the concept that preischemic correction of hyperglycemia with insulin improves outcome.

In neurosurgical patients blood sugar level should be controlled frequently, and the goal should be to avoid either hypo-and hyperglycemia, and maintain sugar levels between 100 and 150 mg/dL.

Fluids to control ICP and brain swelling

Diuretics: mannitol and furosemide

Both mannitol and furosemide are extensively used to control ICP and brain swelling. Mannitol accomplishes this goal by establishing an osmotic gradient between the intravascular compartment and the cerebral parenchyma, in the presence of a relatively intact BBB. The increased plasma osmolality promotes removal of water from areas of normal brain [29,33]. Several issues related to mannitol have also been clarified in recent years. Mannitol can transiently elevate ICP. The mechanism of this effect is clearly due to the vasodilator effects of hyperosmolality, with a resultant increase in cerebral blood volume (CBV) [42,43]. However, it has been shown in both dogs and humans that this is a phenomenon that does not occur in the presence of intracranial hypertension, or when mannitol is given at moderate rates [42,43]. Thus, there is no important reason to avoid mannitol in most neurosurgical patients, other than in patients with significant cardiovascular disease, in whom the transient volume expansion might precipitate congestive heart failure.

The other important concern is the excessive and/or repeated use of the drug, because excessive hyperosmolality can be detrimental. In addition, mannitol does progressively accumulate in the interstitium with repeated doses, and may even aggravate brain edema [44,45]. If interstitial osmolality rises excessively, it is

possible that the normal brain–blood gradient might be reversed, with resultant worsened edema. Furthermore, if brain osmolality is increased, there is a risk of enhancing edema by subsequent normalization of serum osmolality.

Although mannitol is extensively used in patients with intracranial hypertension, a larger dose-finding study in humans has not been performed, and single doses of mannitol from 0.25 up to 2.27 g/kg have been reported in the literature. Marchall et al. [46] studied the effect of different mannitol doses in patients, and concluded that small doses (0.25 g/kg) were as effective as larger doses. At our institution mannitol is used at a dose range of 0.25–1.0 g/kg, and we always choose the smallest possible dose, which is infused in at least in 10–15 min.

The mechanism of furosemide's action remains controversial (although it certainly is related to the drug's ability to block Cl^- transport) [47]. Furosemide and similar drugs may also act primarily by reducing cell swelling, rather than by changing extracellular fluid volume. In several studies it has been demonstrated that furosemide decreases CSF production, and this effect can explain the synergism between mannitol and furosemide on intracranial compliance [48]. Furosemide's maximal effect is delayed compared with mannitol [49,50]. For this reason, mannitol probably remains the agent of choice for rapid ICP control.

Hypertonic saline solutions

Hypertonic salt solutions have been primarily used for small-volume resuscitation in patients with hemorrhagic shock. Because hyperosmolality is known to reduce brain volume [23], hypertonic saline may become part of standard resuscitation in patients with concomitant head injury. Laboratory and clinical data suggest that hypertonic solutions are effective for volume resuscitation, and result in a lesser degree of cerebral edema [51,52]. In humans, acute resuscitation from hemorrhagic shock with 7.5% hypertonic saline is associated with improved outcome in traumatized head-injured patients, and clinical studies suggest that hypertonic saline may be efficacious in hypotensive, brain-injured patients during transport to the hospital [53,54].

Various animal experiments have indicated that hypertonic saline solutions lower ICP and improve cerebral perfusion pressure [3,30,31,51]. The CNS effects of hypertonic saline are similar to mannitol [30,55]; however, the fact that hypertonic saline does not produce an osmotic diuresis simplifies perioperative fluid management. There are a number of case reports and a few controlled trials that suggest that hypertonic saline may produce significant and sustained reductions in ICP where mannitol has failed [56,57]. The mechanism by which hypertonic saline succeeded when mannitol failed, however, remains unclear.

The principal disadvantage of hypertonic saline is related to the possible danger of hypernatremia. In a recent study in neurosurgical patients during elective procedures, we have shown that equal volumes of 20% mannitol and 7.5% hypertonic saline reduce brain bulk and cerebrospinal fluid pressure to the same extent [55]. Serum sodium levels increased during the administration of hypertonic saline, and peaked at over 150 mEq/L at the end of the infusion [55].

However, initial concerns regarding the adverse nurologic sequelae of hypertonic saline appear to have been premature. First, the increment in serum sodium in response to addition of concentrated sodium is less than would be predicted [55]. Second, patients tolerate acute increases in serum sodium to 155–160 mEq/L, without apparent harm [53–55,58]. Third, central pontine myelolysis has not been observed in a clinical trial of hypertonic resuscitation [53]. One concern is that hypertonic saline solutions have the potential to cause rebound intracranial hypertension, similar to other osmotic agents [59,60].

Hypertonic/hyperoncotic solutions

More recent attention has been directed at hypertonic/hyperoncotic solutions (typically hypertonic hetastarch or dextran solutions). Because of the powerful hemodynamic properties of these fluids in circulatory shock, administration in patients with multiple traumas and head injury might be particularly advantageous for the prevention of secondary ischemic brain damage [58]. Small volumes of such solutions can restore normovolemia rapidly, without increasing ICP [28,61]. They have been successfully used to treat intracranial hypertension in head-injured patients and in patients with stroke [53,54,62,63].

Implications for patient care

The available information can be used to make a series of ''reasonable'' suggestions, useful either in the perioperative period as well as for fluid resuscitation.

Fluid restriction

Despite a lack of convincing experimental evidence that iso-osmolar crystalloids are detrimental, fluid restriction is still widely practiced in patients with mass lesions, cerebral edema, and/or at risk for intracranial hypertension. The only directly applicable data indicate that clinically acceptable fluid restriction has little effect on edema formation; however, there is some ''logic'' behind modest fluid restriction. One of the few human studies on fluid therapy in neurosurgical patients demonstrated that patients given standard ''maintenance'' amounts of intravenous fluids (eg, 2000 mL/day) in the postoperative period developed a progressive reduction in serum osmolality [2]. On the other hand, patients given half this volume over a period of about 1 week showed a progressive increase in serum osmolality, which could account for dehydration of the brain (Fig. 2) [55]. Although no CNS-related parameters were measured in this study, the results suggest that the maintenance fluids used (0.45% NaCl in 5% dextrose) contain excess-free water for the typical postoperative craniotomy patient. In this light, fluid restriction can be viewed as ''preventing'' hypoosmotically driven edema. This does not imply that even greater degrees of fluid

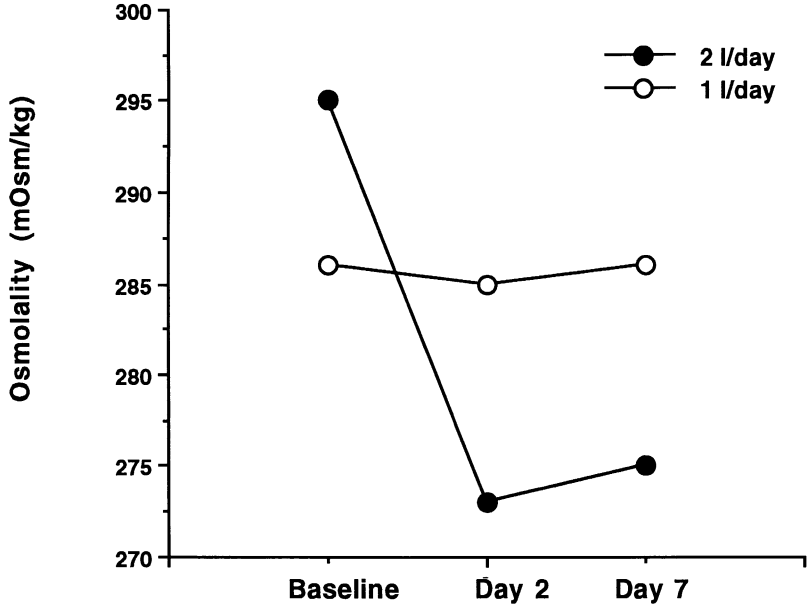

Fig. 2. Effect of fluid restriction (1 L/day) on serum osmolality in neurosurgical patients. (*From* Shenkin HA, Benzier HO, Bouzarth W. Restricted fluid intake: rational management of the neurosurgical patient. J Neurosurg 1976;45:432–6; with permission by Lippincott Williams & Wilkins ©.)

restriction are beneficial, or that the administration of a fluid mixture that does not reduce osmolality is detrimental.

Intraoperative volume replacement/resuscitation

As a general rule, intraoperative fluid administration should be given at a rate sufficient to replace the urinary output and insensible losses. Table 3 illustrates the intravascular volume expansion obtained with different types of fluids.

The available data indicate that volume replacement/expansion will have no effect on cerebral edema as long as normal serum osmolality and oncotic pressure are maintained, and as long as cerebral hydrostatic pressures are not markedly increased (eg, due to true volume overload and elevated right heart pressures). Whether this is achieved with crystalloids or colloids seems irrelevant. Serum osmolality should be checked repeatedly, with the goal being to maintain this value either as constant or slightly increased.

Table 3
Fluid replacement and intravascular volume

Fluid infused	Intravascular volume increase
1 liter isotonic crystalloid	≈ 250 ml
1 liter 5% albumin	≈ 500 ml
1 liter hetastarch	≈ 750 ml

Fluid administration that results in a reduction in osmolality should be avoided. Small volumes of Lactated Ringer's (not strictly iso-osmotic, measured osmolality 252–255 mOsm/kg) are unlikely to be detrimental, and can be safely used. If large volumes are needed (blood loss or other source of volume loss), a change to a more isotonic fluid is advisable. It is also important to remember that large and rapid infusion of 0.9% NaCl can induce a dose-dependent hyperchloremic metabolic acidosis [64,65]. Whether this acid-base abnormality is, in fact, harmful remains unclear, although animal studies suggest that hyperchloremia causes renal vasoconstriction [66]. If large volumes are needed, a combination of isotonic crystalloids and colloids may be the best choice. The combined use of these fluids can avoid reductions both is serum osmolality and COP. Hetastarch should be used with caution due to coagulation factor VIII depletion and possible coagulation difficulties encountered with volumes >1000 mL [67,68]. Pentastarch, a new formulation of hydrolyzed amylopectin, causes fewer effects on coagulation than hetastarch; it does not prolong the bleeding time, and has little effect on factor VIII [69]. Dextran 40 interferes with normal platelet function, and therefore is not advisable for patients with intracranial pathology, other than to improve rheology, such as in ischemic brain diseases.

These recommendations should not be interpreted as "give all the isotonic–iso-oncotic fluid you like." Volume overload can have detrimental effects on ICP, via increasing CBV or via hydrostatically driven edema formation.

Postoperative period

In the postoperative period, large fluid requirements should cease. In such cases, the recommendations of Shenkin et al. [2] are probably reasonable, and we recommend periodic measurements of serum osmolality, particular if neurologic status deteriorates. If cerebral edema does develop, further restriction is unlikely to be of value, and can result in hypovolemia. Specific treatment with mannitol, furosemide, and other drugs, combined with normovolemia achieved with fluids that will maintain the increased osmolality, appears to be reasonable.

Head injury

Prompt restoration of systemic pressure is essential in head-injuried patients. In patients in whom multiple trauma complicates head injury, no resuscitation fluid has proven ideal [70]. Hypotonic solutions (including Lactated Ringer's solutions) should be avoided, and therapy should rely on fluids with osmolalities around 300 mOsm/L. In cases of large-volume fluid administration, oncotic pressure should be checked, and colloid solutions administered as needed. Hypertonic saline solutions have been used successfully to treat hypovolemia and intracranial hypertension in these patients [51–54,62]. Glucose-containing solutions should be avoided, because hyperglycemia is associated with poorer neurologic outcome in head-injured patients [37,39].

Subarachnoid hemorrhage

When treating patients with subarachnoid hemorrhage two problems should be kept in mind: hyponatremia and hypovolemia.

In these patients, relative hypovolemia develops very often. The cause is multifactorial, and includes bed rest, negative nitrogen balance, decreased erythropoiesis, iatrogenic blood loss, and dysregulation of the autonomic nervous system. Hyponatremia appears to develop as the result of a central salt-wasting syndrome, and the causative factor seems to be an increased release of a natriuretic factor from the brain [71]. Excessive renal excretion of sodium precedes the development of ischemic symptoms [72], and patients appear to be at increased risk for delayed cerebral infarction [73]. Hyponatremia should not be a serious concern if electrolytes and type of fluids administered are carefully monitored. With the administration of a large volume of isotonic crystalloids and restriction of free water (hypotonic intravenous fluids and oral fluids) the severity of the fall in serum sodium concentration is ameliorated, and usually does not require further intervention. If hyponatremia is more severe or significant cerebral edema exists, the use of mild hypertonic fluids (1.25 or 1.5% saline) and strict avoidance of free water administration are usually successful in reversing the hyponatremia.

Fluid restriction should be abandoned, as it worsens volume contraction and exacerbates symptoms from vasospasm. Hypertensive/hypervolemic therapy is widely accepted to prevent/treat symptomatic cerebral vasospasm [74]. This therapeutic treatment, however, has never been carefully studied (control group with no therapy, or other treatments), and it is not clear whether hypertension and/or hypervolemia is the critical factor. Volume loading is usually performed with colloids, and great care is required to avoid reduction in serum osmolality, because this will increase brain water content in ischemic as well as normal cerebral regions [75].

Ischemic injury

The one situation where hemodilution may be beneficial is in the period immediately during/after a focal cerebral ischemic event. Several studies have shown that regional O_2 delivery in this situation may be increased (or at least better maintained) in the face of modest hemodilution (Hct $\approx$ 30%), and animal studies demonstrate improvement in CBF and some reductions in infarction volumes [20,76]. Unfortunately, several trials have failed to demonstrate any benefit of hemodilution in stroke, except in polycythemic patients [77–80].

Spinal cord injury

Although the literature lacks specific studies on the spinal cord effects of fluid therapy, in patients with acute spinal cord injury, a prevalence of hyponatremia much higher than in the general medical or surgical patient population has been reported [81]. This study did not elucidate the ethiology of hyponatremia, and did

not consider type and amount of fluids administered. However, the occurrence of hyponatremia after acute spinal cord injury stresses the importance of appropriate fluid management in these patients, mostly to prevent the consequences of reduced plasma osmolality, which might exacerbate spinal cord edema. Laboratory researches have demonstrated that hypertonic saline decreases spinal cord water content [13], and may provide protection after mechanical injury [82].

Water and electrolytes disturbances

Diabetes insipidus

Diabetes insipidus (DI) is a common sequelae of pituitary and hypothalamic lesions, but it can also occur after head trauma or intracranial surgery. Patients with brain death also commonly develop DI, and it should be remembered that DI may also occur during phenytoin use, in alcohol intoxication, and bacterial meningitis.

DI is a metabolic disorder due to a decreased secretion of antidiuretic hormone (ADH), resulting in failure of tubular reabsorbtion of water. Polyuria (>30 mL/kg/h or, in an adult, >200 mL/h), progressive dehydration, and hypernatremia subsequently occur. Diabetes insipidus is present when the urine output is excessive, the urine osmolality is inappropriately low relative to serum osmolality (above normal because of water loss), and the urine specific gravity is lower than 1.002 (Table 4).

Management of DI requires careful balancing of intake and output, mostly to avoid fluid overload

Each hour the patient should receive maintenance fluids plus three quarters of the previous hour's urine output, or plus the previous hour's urine output minus 50 mL. Half-normal saline and D5W are commonly used as replacement fluids,

Table 4
Principal water-electrolytes disorders

		DI	SIADH	CSWS
Etiology		Reduced secretion of ADH	Excessive release of ADH	Release of brain natriuretic factor
Urine	Output	> 30 ml/kg/h		
	specific gravity	< 1.002		
	Sodium	< 15 mEq/l	> 20 mEq/l	> 50 mEq/l
	Osmolality vs. serum osmolality	Lower	Higher	Higher
Serum	Sodium	Hypernatremia	Hyponatremia	Hyponatremia
	Osmolality	Hyperosmolality	Hypoosmolality	
Intravascular volume		Reduced	Normal or increased	Reduced

Abbreviations: ADH, antidiuretic hormone; CSWS, celebral salt-wasting syndrome; DI, Diabetes insipidus; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

with appropriate potassium supplementation. Serum sodium, potassium, and glycemic values should be checked frequently. In the presence of urine output higher than 300 mL/h, at least for 2 hours, it is now standard practice to administer aqueous vasopressin [5-10 IU, intramuscularly (i.m.), or subcutaneously (s.c.), q 6 h] or the synthetic analog of ADH, desmopressin acetate (DDAVP: 0.5–2 mg, intravenously (i.v.), q 8 h; or by nasal inhalation, 10–20 mg).

Syndrome of inappropriate antidiuretic hormone secretion

Various cerebral pathologic processes (mostly head trauma) can result in excessive release of ADH, which causes continued renal excretion of sodium, despite hyponatremia and associated hypo-osmolality. Urine osmolality is therefore high, relative to serum osmolality (Table 4). It should be remembered that the syndrome of inappropriate antidiuretic hormone secretion (SIADH) can also be the result of overadministration of free water (D5W) in patients who cannot excrete free water, because of excess of ADH.

Management

The mainstay of treatment of SIADH is fluid restriction, usually to about 1000 mL/24 h of an iso-osmolar solution. If hyponatremia is severe (lower than 110–115 mEq/L) administration of hypertonic (3–5%) saline and furosemide may be appropriate. Great care is required to avoid rapid correction of severe hyponatremia. A good rule is to restore serum sodium levels at a rate of about 2 mEq/L/h.

Cerebral salt-wasting syndrome

Cerebral salt-wasting syndrome (CSWS) is frequently seen in patients with subarachnoid hemorrhage, and is characterized by hyponatremia, volume contraction, and high urine sodium concentration (Table 4).

Management

The therapy is to reestablish normovolemia with the administration of sodium-containing solutions.

The distinction between SIADH and CSWS is very important, because fluid treatment of theses two syndromes is quite different (fluid restriction versus fluid infusion). It should be stressed that in patients with SAH, in whom normo/hypervolemia is advocated, fluid restriction (that is, further volume contraction) may be especially deleterious.

Conclusion

Fluid management has progressed rapidly in the last 3 decades. Current regimens are sufficient to restore systemic perfusion in the majority of patients undergoing surgery. However, important questions still remain to be answered regarding the frequency of complications of current fluid therapy

and the comparative advantages of different fluid formulations in a variety of clinical circumstances.

As neuroanesthesiologists/intensivists, we should always remember that we treat patients and not only brains. Thus, with the exception of patients with SIADH, the old dogma that states that patients with intracranial pathology should be kept "dry" ("run them dry") should be abandoned, and be replaced by "run them isovolemic, isotonic, and isooncotic."

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