Fluid Management in Neurocritical Care

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Roop Kishen

CIT: 'The quantity (of fluid) necessary to be injected will probably be found to depend upon quantity of serum lost, the object of the practice being to place the patient in nearly his ordinary state as to the quantity of blood circulating in the vessels'

—Dr. Robert Lewins,

Contents

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IFA Commentary (MLNGM)

This chapter is a summary of the key learning objectives and take-home messages related to fluid therapy management in patients with neurological injury. The chapter emphasises the importance of understanding the basic physiological and pathological considerations in brain-injured patients and the role of cerebral blood flow in maintaining cerebral homeostasis. It also stresses the need to maintain euvolaemia and avoid both hypovolaemia and hypervolaemia in these patients. The take-home messages highlight the use of isotonic crystalloids as first-line fluids for resuscitation and maintenance, while hypotonic fluids should be avoided due to the risk of brain oedema. Colloids, glucose-containing hypotonic solutions, 4% albumin, and hypertonic 20% albumin are not recommended for resuscitation or maintenance fluids. The use of hypertonic saline (HTS) solutions as resuscitation fluids is also discouraged. The chapter recommends a multimodal approach to monitor fluid therapy, including integration of more than one haemodynamic parameter, arterial blood pressure, and fluid balance. Central venous pressure alone as a fluid management monitoring parameter is discouraged. This chapter also recommends monitoring electrolytes and measured osmolality as safety end points and using mannitol or HTS to reduce intracranial pressure in neuro-intensive care patients. For patients with diffuse cerebral injury, fluid boluses are recommended, and the use of multimodal monitoring of their efficacy is suggested. Overall, this chapter provides a concise and informative overview of the key considerations and recommendations related to fluid therapy management in neurologically injured patients. The emphasis on individualised patient care, multimodal monitoring, and careful evaluation and management of electrolyte abnormalities is particularly notable. The take-home messages provide practical guidance for clinicians involved in the care of these patients.

Suggested Reading

1. Oddo M, Poole D, Helbok R, Meyfroidt G, Stocchetti N, Bouzat P, Cecconi M, Geeraerts T, Martin-Loeches I, Quintard H, Taccone FS, Geocadin RG, Hemphill C, Ichai C, Menon D, Payen JF, Perner A, Smith M, Suarez J, Videtta W, Zanier ER, Citerio G. Fluid therapy in neurointensive care patients: ESICM consensus and clinical practice recommendations. Intensive Care Med. 2018;44(4):449-463. https://doi.org/10.1007/s00134-018-5086-z.

Learning Objectives

After reading this chapter, you will have:

1. Briefly revised the basic physiological and pathological considerations in brain-injured patients.

2. Understood the importance of cerebral blood flow and its role in maintaining cerebral homeostasis.
3. Understood the importance of fluid resuscitation and maintenance of 'normal' intravascular volume status in brain-injured patients as well as understood the important differences between these and non-brain-injured patients as far as the fluid resuscitation is concerned.
4. Have a good knowledge of which fluids to use and which to avoid in these patients with regard to fluid content and fluid osmolality.
5. Understood the principles of monitoring fluid resuscitation and management of further fluid infusion in these patients.
6. Have a knowledge of some specific electrolyte abnormalities encountered in NIC patients and their brief management.
7. Have knowledge of the latest 'clinical practice recommendations' of an expert group of European Society of Intensive Care Medicine.

Case Vignette

Mr. C, aged 38 years, is brought to the emergency department (ED) by an ambulance after being hit by a car on his right side while crossing a busy road. He was thrown about 5 m from the collision site and was found unconscious at the scene by paramedics. His injuries are closed right femoral fracture, pelvic ramus fracture, and bruising over the abdomen. He has been evaluated by emergency physicians, surgeons, and intensivists. His vital observations, at the time of presentation to ED, are BP 85/65 mmHg, HR 123/min, and RR of 24 breaths/min. He has received 3 litres of Plasma-Lyte and two units of blood. His Glasgow Coma Scale (GCS) score was 7 (eyes 2, motor 3, verbal 2) at presentation and has not improved since. He was intubated and ventilated in the ED and reassessed after resuscitation (BP 114/70 mmHg, HR 96/min). He had a full-body computerised tomography (CT) scan that showed a right mid-shaft femoral fracture and base of skull fracture but no mass lesion in the brain except for several small cerebral contusions. No thoracic or internal abdominal injuries were identified on CT. He was transferred to the operating theatre and his femoral fracture was reduced and stabilised with an external fixator. He was transferred to the intensive care unit, where he is now on a ventilator with stable vital signs. He is still unconscious, requiring minimal sedation.

Questions

Q1. What fluids should Mr. C receive now and how should his fluid therapy/balance be monitored?

Introduction

All critically ill patients require fluids during the course of their illness, neurocritical care (NIC) patients being no exception. Fluids are administered orally or intravenously (IV). Orally administered fluids have different systemic effects compared to IV fluids. IV fluids are required during resuscitation of acutely ill patients in shock and in correcting volume deficits, and once normality is established, fluids are necessary for maintenance of volume status. The main objectives of fluid therapy during resuscitation are to maintain organ perfusion by improving cardiac output (CO) and thereby tissue oxygen delivery(DO_2). After achieving stabilisation, oral intake may be adequate in a minority of patients without requiring any further IV fluids; in majority of the patients however, IV fluids will needed for continued volume maintenance, drug carriage, and occasionally parenteral nutrition. As all these fluids contribute to overall fluid intake, and unless care is taken, fluid accumulation can easily occur. Both hypervolaemia and hypovolaemia are detrimental to NIC patients, euvolaemia being the best clinical practice standard [1]. This chapter focuses on the use of IV fluids in NIC patients. This chapter will focus on adult patients, and more information on fluid therapy in children can be found in Chap. 20. Some other chapters will discuss fluids in specific populations: sepsis (Chap. 14), heart failure (Chap. 15), trauma (Chap. 16), perioperative setting (Chap. 18), burns (Chap. 19), liver failure (Chap. 21), abdominal hypertension (Chap. 22), and COVID-19 (Chap. 26).

Physiological Considerations

The objectives of fluid resuscitation in brain-injured patients are to improve and optimise cerebral blood flow (CBF) and cerebral DO_2. Whereas general physiological principles of improving CO and tissue DO_2 with fluid resuscitation apply equally to the central nervous system (CNS) as to other organs, fluid management in NIC patients has some unique features which are different from non-brain-injured patients [1]. These relate to the effects of fluid infusion on CBF, intracranial pressure (ICP), and cerebral perfusion pressure (CPP). Thus, it is essential to understand CBF autoregulation and blood–brain barrier (BBB) physiology, both of which are designed to preserve the integrity of the brain cellular fluid and cerebral interstitial fluid (ISF) composition as well as homeostasis, which is important for proper functioning of the CNS. Both CBF autoregulation and BBB function can be disturbed in the critically ill NIC patients, causing alterations in CBF and ICP and ultimately affecting mortality as well as functional neurological recovery [2].

Under normal physiological conditions, the brain receives about 20% of the CO. CBF, like blood flow to any other organ system in the body, is a function of blood volume, CO,

and peripheral vascular resistance and therefore systemic blood pressure(BP). In addition, cerebral vascular resistance (CVR) influenced by cerebral autoregulation also determines CBF [3]. These ensure that, under normal physiological conditions with intact autoregulation, CBF is maintained constant over a wide range of BP (mean arterial pressure [MAP] 60–180 mmHg). Beyond these limits, CBF is pressure dependent. This means that there is a risk of cerebral ischaemia because of low CBF at lower MAP and a risk of cerebral hyperaemia causing possible increase in ICP at higher MAP. Cerebral autoregulation responds to and alters CBF according to the demands of cerebral metabolism and is disrupted by trauma, infarction, brain haemorrhage, both subarachnoid (SAH) as well as intracerebral (ICH), and possibly by local and systemic infections [4].

The BBB is a complex physiological entity resulting from interrelationship between cerebral blood vessels, their endothelium, vascular wall smooth muscle cells, perivascular tissue, and a variety of neuronal cells (e.g. astrocytes, microglia). The endothelial cells have 'tight junctions' allowing movement of gases, water, and nutrients by facilitated diffusion (a type of energy-independent carrier-mediated transport) into the cerebrospinal fluid (CSF) and brain ISF [4, 5]. Evidence is emerging that BBB integrity may also be affected by dysfunction of the endothelial glycocalyx [6]. BBB prevents toxic molecules and electrolytes from entering the brain substance, and its normal physiological 'opening' is regulated by locally mediated molecules [5]. Under pathological processes, such as trauma, ischaemic stroke, haemorrhage (ICH, SAH), infections, and inflammation, the BBB opens with tight junctions becoming more 'permeable' to water, cytokines, electrolytes, etc. [5, 7]

CPP is determined by MAP and ICP, with some minimal contribution from cerebral venous pressure. In simple terms:

$$\text{CPP} = \text{MAP} - \text{ICP}$$

Thus, in hypotensive patients, CPP will be lower despite normal ICP. Conversely, CPP may be inadequate if ICP is high with a 'normal' CBF and MAP. Inadequate CCP is detrimental for brain perfusion and linked to further brain damage, especially in traumatic brain injury (TBI) [8]. Maintenance of optimal CPP, with fluid infusion and inotropes/vasopressors to maintain adequate CO and cerebral DO_2, forms the standard management guideline of the Brain Trauma Foundation (BTF) [9]. It is, therefore, traditional and logical to optimise ' blood pressure to target CPP >70 mmHg [8]. The BTF guidelines suggest maintaining CPP between 50 and 70 mmHg with the caution that lower or higher CPP values are associated with complications [9]. It is also accepted that CPP values need to be individualised for the best outcomes [10].

The effect of fluid management on CBF, CPP, and cerebral oxygenation is complex as illustrated in Fig. 17.1.

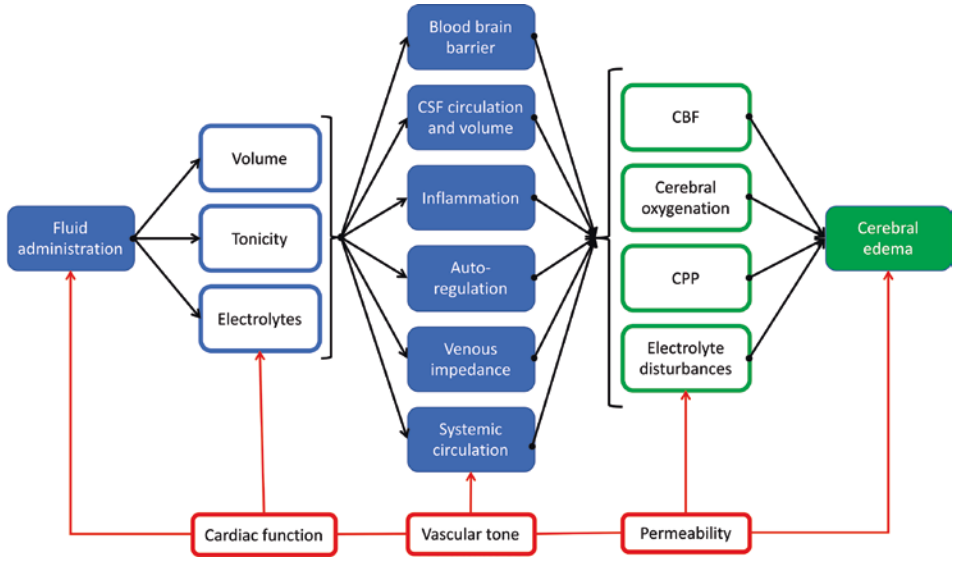

Fig. 17.1 The effect of fluid management on cerebral blood flow (CBF), cerebral perfusion pressure (CPP), and cerebral oxygenation is complex because many intermediate variables exist that should be taken into account to fully appreciate possible cause and effect relationships. (Adapted from Van der Jagt M. under the Open Access CC BY Licence 4.0 [1]) *CBF* cerebral blood flow, *CSF* cerebrospinal fluid, *CPP* cerebral perfusion pressure

What Kind of Fluid Is Appropriate in NIC Patients?

Available literature and major guidelines suggest crystalloids as the primary choice for fluid resuscitation and maintenance in NIC patients; [9, 10] however, the type of crystalloid is not specified. As has been discussed in Chap. 9, some concerns have emerged about excess chloride content of 0.9% saline (NS) resulting in hyperchloraemic metabolic acidosis(HCMA) with potentially increased risk of acute kidney injury, need for renal replacement therapy, increased inflammation, as well as increased mortality. However, randomised control trials in general ICU patients have produced conflicting results when NS is compared with balanced salt solutions, and there is still no definitive consensus for or against using NS versus balanced crystalloids in general ICU patients.

It is difficult to extrapolate these findings to NIC patients because of two major reasons: (1) relatively smaller number of TBI patients were included in these studies (because of the concerns among clinicians that relative hypotonicity of balanced crystalloids may increase ICP) and (2) because of poor understanding of the effects of HCMA on neurological recovery. For example, in the SMART study, a large, single-centre randomised study comparing effects of balanced fluid versus NS, only 17.3% of patients had TBI

(8.8% in balanced crystalloid group and 8.5% in NS group), and clinicians were also free to use NS in TBI group [11]. The concerns about the effects of the tonicity of fluid on ICP are addressed in the next section.

Colloids have been used in the past (and are still being used) with the 'physiological rationale' that their use allows resuscitation with a smaller volume of infused fluid. However, this perceived benefit of colloids has not been proven in randomised studies and meta-analyses [12]. Colloids are discussed in greater detail in Chaps. 10 and 11.

Albumin, a natural colloid, has been the subject of much research and discussion. The SAFE study showed that 4% albumin (compared to NS) had detrimental effects on TBI [13]. In a post hoc analysis of the SAFE study, 460 well-matched patients with TBI, who received albumin, had increased mortality at 24 months after injury when compared to resuscitation with NS [14]. Some researchers have also explored the possible neuroprotective effect of albumin in patients with SAH. In a multicentre dose-ranging study, Suarez and colleagues found that 25% albumin at a dose of 1.25 g/kg/day for 7 days had the best neuroprotective effect in SAH patients with the best clinical outcome at 3 months without producing adverse effects like heart failure or anaphylaxis [15].

Does Tonicity of the IV Fluids Matter in NIC Patients?

BBB is designed to preserve CNS homeostasis. Under normal physiological conditions, osmolalities of plasma and CSF are equal. As BBB is water-permeable, hypotonic fluids can cause water to shift into CSF and brain substance; conversely, hypertonic fluids can cause brain dehydration whether BBB is intact or disrupted [5, 7]. Under normal conditions, neurons maintain their homeostasis by solute depletion and the ability of the BBB and neurovascular unit cells to expel water into the intravascular compartment [16]. Whereas peripheral vascular endothelium is highly permeable to electrolytes, with oedema formation roughly proportional to the infused volume of isotonic fluid, an intact BBB does not allow free passage of electrolytes and thus protects the brain from oedema even when large volumes of isotonic fluids are administered to the patients [16]. This ability to control water and electrolyte homeostasis is locally abolished by disruption of BBB function; fluid shifts become more dependent on the pressure difference between intravascular and extravascular compartments and the prevailing osmolality of the former [5, 7, 16]. Thus, hypo-osmolar fluids, by reducing plasma osmolarity, can cause brain oedema, especially in presence of functional BBB disruption [16].

In a single-centre RCT, 36 patients with SAH were randomised to receive NS and hydroxyethyl starch (HES) in NS or Ringer's lactate (RL) and HES in RL. NS-based fluid therapy was associated with hyperchloraemia, increased tonicity, and more positive fluid balance than balanced fluids. In contrast, the balanced fluids group did not have more hyponatraemia or hypotonicity [17]. However, this is a small study, and the findings need to be validated in a larger trial.

Hyperosmolar Therapy in NIC Patients

Small-volume hypertonic saline (HTS) infusions (usually around 4 mL/kg/15 min) have been used for resuscitation in TBI. In a blinded RCT, 229 severe TBI patients (GCS < 9) with hypotension (systolic BP <100 mmHg) were randomised to receive a 250 ml bolus of either Ringer's lactate or 7.5% HTS in the prehospital phase, in addition to other resuscitation fluids. All patients, regardless of assigned prehospital fluid group, were adequately resuscitated (as judged by normal post-resuscitation BP) upon arrival into the hospital. However, there was no difference in survival to hospital discharge and neurological function as measured by Glasgow Outcome Scale (GOS) at 6 months between the groups [18].

Another indication for hyperosmolar fluid therapy in brain-injured patients is in the management of raised ICP. Mannitol has been popular for a long time as the first-line IV fluid to treat raised ICP in TBI as well as in patients with SAH, ICH, and acute ischaemic stroke (AIS) [19]. Recently, HTS has been gaining popularity over mannitol [19] and a recently published meta-analysis of 12 RCTs showed that HTS was better than mannitol in controlling raised ICP in TBI, though there was no difference in neurological outcome as determined by GOS [20]. Evidence for the beneficial use of hyperosmolar therapies in ICH and AIS is even more sparse. Hyperosmolar therapy does reduce ICP in these conditions; however, its effect on clinical outcome is unclear. A post hoc analysis of the data from one study (Ethnic/Racial Variation of Intracerebral Haemorrhage, ERICH) showed that both mannitol and HTS were associated with unfavourable outcomes at 3 months [21]. It is also worth noting that recently there have been reports of increased in-hospital mortality associated with hyperchloraemia in patients with ICH receiving continuous infusions of 3% HTS and NS [22, 23]. The commonest causes of raised ICP in SAH include hydrocephalus, ICH with intraventricular haemorrhage, and global cerebral oedema. Cerebral oedema can also occur from diffused cerebral injury (DCI) and standard hyperosmolar strategies apply in these patients as well. A systemic review of five observational studies (n = 175) showed that HTS was similar to mannitol in reducing ICP. However, it was unclear if it had any effect on outcome nor could an optimum dose for HTS be recommended in SAH [24].

End Points of Fluid Therapy Management in Neurocritical Care: How Much Fluid Is Enough?

The goal of fluid therapy in NIC patients is to optimise cerebral perfusion and, therefore, cerebral DO_2 while at the same time minimising further/secondary brain injury [6]. Studies have adequately stressed the adverse effects of hypo- as well as hypervolaemia in NIC patients [1]. Unfortunately, achieving euvolaemia in brain-injured patients without sophisticated cardiovascular and brain monitoring is not always possible. Besides, euvolaemia is subject to individual interpretation [1]. Positive fluid balance in NIC patients has been associated with vasospasm (proven on angiography), increased hospital stay, poor

neurological outcome, and adverse cardiovascular side effects [25]. In SAH, hypervolaemia has not been shown to be of benefit in terms of neurological outcome [26]. In another RCT, SAH patients were randomised to prophylactic triple-H (hypervolaemia, hypertension, and haemodilution) therapy versus normovolaemia [27]. Patients in the normovolaemic group received about 3 L/day, while the triple-H group received about 4–5 L/day of fluids. Clinical outcomes were similar in both groups, while the triple-H group had more complications like haemorrhagic diathesis, congestive heart failure, arrhythmias, and extradural haematomata [27]. However, hypovolaemia is also harmful especially in TBI, despite ICP control [28].

Monitoring Fluid Therapy in NIC Patients

As the dangers of under- or over-resuscitation have been repeatedly emphasised, it is of utmost importance that fluid management should be carefully monitored. Monitoring of fluid resuscitation in NIC patients should involve multimodal parameters, [29] which include non-invasive or invasive blood pressure monitoring, neurological function assessment, invasive haemodynamic monitoring (thermodilution CO measurement, global end-diastolic volume index [GEDI], stroke volume variation, and other invasive and non-invasive modalities), CBF assessment (e.g. with transcranial doppler), and measurement of ICP/CPP and brain tissue oxygenation (jugular venous oximetry). Assessing the middle cerebral artery mean velocity (MCA MV) in response to fluid infusion, with Transcranial Doppler, may turn out to be another method to assess fluid management in these patients; however, larger studies and more robust data are required [30]. Routine monitoring of brain tissue oxygenation or CBF is not recommended as a standard. Central venous pressure (CVP) monitoring is not useful; fluid management should not be guided by CVP readings or its response to fluid infusion. Hourly urine output is a time-honoured parameter; it can be used in some patients but cannot be universally applied. Finally, it cannot be overemphasised that fluid management and its monitoring must be individualised..

A Note on Common Electrolyte Disturbances in NIC Patients

General Considerations

(See Table 17.1).

Electrolyte disturbances are frequently seen in critically ill patients. Although not a direct remit of this chapter, a reference is made to these disturbances in NIC patients here, especially those of sodium (Na^+), as they may affect the type of fluid infused and rate of its administration. Disturbances of sodium (Na^+) and potassium (K^+) are the commonest abnormalities seen in NIC patients. Some syndromes are specific to TBI/SAH, with hyponatraemia being more commonly associated with SAH. However, aggressive use of

Table 17.1 Electrolyte disorders in NIC patients at a glance (Please see text for details)

Disorder	Defining parameters (sub-types)	Aetiology	Clinical management
Hyponatraemia	Serum $Na^+ < 135$ mmol/L Mild, moderate, severe Acute or chronic	Diuretics Hyperosmolar fluid use SIADH[a] CSWS[b]	IV 150 mL 3.0% saline over 20 min Recheck serum Na^+ Repeat if necessary, till serum $Na^+ > 130$ mmol/L
Hypernatraemia	Serum $Na^+ > 150$ mmol/L Mild, moderate, severe	Hyperosmolar fluid use Hypovolaemia Diabetes insipidus Low intake of H_2O	IV balanced electrolyte solutions Careful rehydration
Hyperchloraemia	Serum $cl^- > 110$ mmol/L	Excessive use of high Cl^- containing fluids (NS, HTS)	IV balanced electrolyte solutions Spontaneous resolution
Hypokalaemia	Serum $K^+ < 3.5$ mmol/L	Diuretics Hyperosmolar fluid use Low K^+ containing fluid use	Replacement of K^+ with supplements in fluids
Hypomagnesaemia	Serum $Mg^{++} < 0.6$ mmol/L	Diuretics Hyperosmolar fluids use Poor GI absorption	1–4 g (4–16 mmol) of IV magnesium sulphate over 15–20 min Repeat, if required 5–15 g (20–60 mmol) per hour

[a]SIADH, syndrome of inappropriate secretion of antidiuretic hormone
[b]CSWS, cerebral salt wasting syndrome

osmotically active fluids (e.g. mannitol) and other diuretics, which is one of the common causes of hyponatraemia in these patients to control raised ICP, must not be overlooked. Detailed description of these electrolyte disturbances is outside the scope of this chapter.

Both hypo- and hypernatraemia are common in NIC patients.

Hyponatraemia

Hyponatraemia is defined as a serum $Na^+ < 135$ mmol/L. Depending on serum Na^+ levels, hyponatraemia is classified as mild (serum Na^+ 134–131 mmol/L), moderate (serum Na^+ 130–125 mmol/L), or severe (serum $Na^+ < 125$ mmol/L). Apart from common aetiological factors (e.g. overuse of diuretics), two syndromes resulting in hyponatraemia are specifically associated with NIC patients [31–33]:

(a) Syndrome of Inappropriate secretion of antidiuretic hormone (SIADH).
(b) Cerebral salt wasting syndrome (CSWS).

The distinction between the two can be difficult and requires measurement of several plasma and urine biomarkers and osmolalities [31, 32]. However, which of the two syndromes is responsible for observed hyponatraemia may still not be clear, even after extensive laboratory workup. Some authorities believe that a) CSWS does not exist as a separate entity but is a variant of SIADH with apparent Na^+ loss consequent upon 'unrecognised' volume expansion and/or excessive use of HTS [34], b) is a relatively rare cause of hyponatraemia [33, 35], and c) hyponatraemia in itself is not diagnostic of CSWS [33, 36]. Hyponatraemia can exist as two subtypes: hypotonic hyponatraemia (which can be hypovolaemic, euvolumaeic, or hypervolaemic) and iso- or hypertonic hyponatraemia [31, 32]. For clinical relevance and management, it is also classified as acute (<48 h in development) and chronic (developing over >48 h).

Regardless of aetiology, hyponatraemia needs prompt evaluation and treatment. Clinical management involves careful evaluation of the patient, neurological symptoms, as well as volume status (which usually requires invasive or other cardiovascular monitoring). Chronic hyponatraemic patients can tolerate fairly low levels of serum Na^+, often of the order of <125 mmol/L, because of the adaptive mechanisms to prevent cerebral oedema [33]. However, all NIC patients with hyponatraemia, in whom it is almost always of acute origin (<48 h), should be treated as 'symptomatic, acute hyponatraemic' patients and considered a medical emergency because of a high risk of increasing or worsening cerebral oedema [33]. Suggested treatment is an immediate infusion of 150 mL of 3% hypertonic saline over 20 min. Serum Na^+ must be re-checked and 150 ml of 3% saline may be repeated twice till there is a rise of at least 4–6 mmol/L in serum Na^+ [33, 36, 38, 39], as experience with hypertonic saline, in these situations, has shown that an increase of ≈5 mmol/L in serum Na^+ reduces ICP and risk of cerebral herniation in ≈50% of the patients within 1 h [37]. Once a desired increase in serum Na^+ is achieved, NS should be substituted for 3% saline [33, 38, 39], a search for the underlying cause should be made, and treatment instituted, if possible (e.g. stopping aggressive hyperosmolar therapy). Further correction of serum Na^+ should be slower (10 mmol in the first 24 h and 8 mmol in subsequent 24-h periods, thereafter), till serum Na^+ level is 130 mmol/L. Further infusions of 3% saline may have to be continued, to increase the Na^+ level by 1 mmol/L/h, in patients who are still symptomatic, till there is an improvement in symptoms or serum Na^+ has increased by 10–12 mmol/L or reached 130 mmol/L. Subsequent management is as for mild hyponatraemia [38, 39]. Serum Na^+ corrections of >12 mmol/L in 24 h or > 25 mmol/L in 48 h result in osmotic demyelination syndrome. It is thought to be caused by a rapid swelling of brain tissue and some patients may be more vulnerable to it. However, it is thought that patients with acute hyponatraemia are less prone to develop osmotic demyelination syndrome [33] and immediate treatment should not be withheld in these patients, especially as cerebral herniation is a real concern. It cannot be overemphasised that frequent patient evaluation with respect to volume status and neurological symptoms are of utmost importance in managing these patients. It is also suggested that acute deficiency of glucocorticoids is, in part, responsible for hyponatraemia seen in NIC patients; a trial of glucocorticoids has been suggested, after careful patient evaluation [33].

Hypernatremia

Hypernatraemia is another electrolyte abnormality seen in NIC patients, can adversely affect their mortality and morbidity, as well as prolong their hospital stay. Hypernatremia is defined as a serum Na+ >150 mmol/L and can be mild (serum Na^+ 150–155 mmol/L), moderate (serum Na^+ 155–160 mmol/L, or severe (serum $Na^+ > 160$ mmol/L). It occurs in ≈50% of NIC patients, consequent upon treatment with hyperosmolar fluids (mannitol, hypertonic saline), hypovolaemia, diabetes insipidus, or low intake of water (because of reduced thirst). Management of hypernatraemia involves careful volume assessment of the patient and replacement of any deficit volume with IV fluids, preferably balanced salt solutions [32]. Care must be taken not to overhydrate the patients and half the fluid deficit should be replaced over 12–24 h and the other half over the next 24 h. Serum Na^+ should be reduced slowly, over 24–48 h to avoid acute osmotic shifts.

Hyperchloraemia

Hyperchloraemia has already been mentioned. It is mostly iatrogenic, caused by infusion of high Cl^- containing fluids (NS, HTS). It is defined as serum chloride level of ≥110 mmol/L. Hyperchloraemia causes HCMA and may adversely affect renal blood flow. Mostly, it needs no treatment and usually corrects itself overtime.

Other Electrolyte Disturbances

Other commonly seen electrolyte abnormality is hypokalaemia (serum $K^+ < 3.5$ mmol/L). This can, again, be a consequence of diuretic/high osmolar fluid use or replacement with low potassium (K^+) containing fluids. Hypokalaemia can cause arrythmias and is managed simply by adequate replacement of K^+.

A relatively less well-known electrolyte abnormality, hypomagnesaemia, defined as serum magnesium (Mg^{++}) < 0.6 mmol/L (1.5 mg/dL) is probably more common than realised, as Mg^{++} measurements are not routinely performed. Hypomagnesaemia occurs due to reduced absorption of Mg^{++} in gut but in NIC patients is mostly due to use of hyperosmolar solutions (mannitol, HTS) and diuretics (all used in control of ICP) as well as certain antibiotics (aminoglycosides) [40, 41]. Hypomagnesaemia can cause ECG changes (appearance of U waves, prolonged QT interval, ventricular arrhythmias, and *torsade de pointes*) and decreased or impaired responsiveness to inotropes/vasoactive drugs [40–42]. Hypomagnesaemia also causes various neurological symptoms (weakness, paraesthesia, tremors, seizures, etc.). Its management requires careful patient evaluation (particularly

with regard to neurological condition, other electrolyte abnormalities, e.g. hypercalcaemia and hypokalaemia, which often accompany it) and replacement therapy. One to 4 g (4–16 mmol) of IV magnesium sulphate over 15–20 min, in repeated doses, or as an infusion of 5–15 g (20–60 mmol) per hour is acceptable standard therapy to keep serum Mg^{++} at 1.0–1.5 mmol/L [40, 41].

Fluid Therapy Management in Neurocritical Care: Clinical Practice Recommendations

A consensus committee of 22 international experts considered various aspects of fluid management in NIC patients. These experts met in 2014 and subsequently deliberated for more than a year in face-to-face meetings and teleconferences, considering various questions about fluid therapy management in NIC patients. They looked at all the available evidence and came up with a consensus and clinical practice recommendations. These recommendations have been published recently as 'Consensus and Clinical Practice Recommendations' (JC-2018) [10]. Their main/broad recommendations for clinical practice are listed at the end under take-home messages (it should be noted that not all recommendations are backed by irrefutable evidence).

Case Vignette

In the case vignette, Mr. C should receive NS in adequate amounts, with monitoring of fluid balance to keep MAP around 80–90 mmHg and UO at about 0.5 mL/kg/h (30–40 mL/h) as these are immediately available parameters in this patient. If available, ultrasound-guided monitoring may be instituted as well to ensure that hypervolaemia does not occur. As there are likely to be no facilities for monitoring ICP in this ICU, it is difficult to make allowances for raised ICP in this patient; a target MAP of 80–90 mmHg will ensure that a CPP of at least 50–60 mmHg is achieved even if ICP begins to rise. Monitoring pupillary size and reaction may warn of impending rise in ICP; however, it should be remembered that pupillary dilatation is rather a late sign of raised ICP. Should there be a suspicion of increased ICP, mannitol or HTS (according to local protocol) can be used to lower it. The best management for this patient is monitoring and care in an appropriate setting.

Conclusion

Fluid therapy management in NIC patients is a complex issue. Whereas the general principles of fluid therapy management in other critically ill patient groups also apply, issues particular to NIC patients require special care. Crystalloids are the first-line fluids for resuscitation as well as maintenance in NIC patients, isotonic crystalloids like NS being in common and frequent use. Concerns are emerging about the effects of high chloride containing fluids on plasma electrolytes, acid–base balance and the possible harmful effect of hyperchloraemia on the injured brain. Hypotonic fluids are not recommended for use in NIC patients as brain oedema is likely to occur. There is a consensus on avoiding colloids in brain-injured patients. Maintaining euvolaemia is the clinical practice standard; both hypovolaemia and hypervolaemia are to be assiduously avoided. Monitoring fluid therapy in NIC patients entails multimodal monitoring parameters and clinicians should not rely on just one individual parameter. Various electrolyte abnormalities are often seen in NIC patients, hypo- and hypernatraemia being common. These electrolyte abnormalities need careful patient evaluation and appropriate fluid management. Finally, as no two patients are similar, fluid management should be individualised.

Take Home Messages

- Isotonic crystalloids should be first-line fluids for resuscitation as well as maintenance. There are no recommendation as yet on balanced crystalloids. In this context, solutions with an osmolality of <260 mosmol/kg are considered hypotonic.
- Colloids, glucose-containing hypotonic solutions, 4% albumin, and high concentration (20–25%) albumin (especially in AIS) are not recommended for resuscitation or as maintenance fluids.
- Hypertonic saline solutions are not recommended as resuscitation fluids either.
- Normovolaemia is suggested as a clinical practice standard.
- For ‘achieving’ normovolaemia and for general fluid management, a multimodal approach to monitor fluid therapy is strongly recommended. These parameters include, but are not limited to:
  - Integration of more than one haemodynamic parameter.
  - Arterial BP and fluid balance as the main parameters.
  - Other variables like CO, mixed venous oxygen saturation (SvO_2), blood lactate, and urine output should be used/considered.
  - CVP alone as a fluid management monitoring parameter is strongly discouraged.
  - Fluids should not be restricted to achieve a negative fluid balance.
- Negative fluid balance is not recommended in NIC patients.
- Monitoring of electrolytes as well as measured osmolality as a safety end point is recommended.

- Mannitol or HTS can be used as agents to reduce ICP in NIC patients.
  - Serum osmolality and effect of hyperosmolar therapy on BP and fluid balance should be monitored.
- For DCI (Diffused Cerebral Injury) patients, fluid boluses are recommended, as is the use of multimodal monitoring of their efficacy.
  - Transcranial doppler-assessed CBF velocities may be used as secondary end points.

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