Patients with hypovolemia usually need the administration of intravenous fluids. Current evidence points to the use of crystalloids since colloids produce increased adverse effects and human albumin has high cost. Among crystalloids, the use of balanced solutions, mainly Lactated Ringer’s, has been proposed as the infusate of choice since normal saline infusion leads to hyperchloremic metabolic acidosis and renal vasoconstriction. However, it should be mentioned that Lactated Ringer’s should not be infused in patients with severe metabolic alkalosis, lactic acidosis with decreased lactate clearance or severe hyperkalemia and in patients with traumatic brain injury or at risk of increased intracranial pressure. Moreover, the correction of any acid-base or electrolyte disorders that not infrequently co-exist with hypovolemia is crucial. Clinicians should target any co-existing disorders and accordingly determine infusate treatment in patients with hypovolemia.

**Keywords:** hypovolemia; crystalloids; colloids; isotonic; hypotonic; hypokalemia

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The use of intravenous fluids is necessary in many cases of hypovolemia in which fluid consumption by mouth is inadequate. However, current evidence shows that intravenous administration of fluids should follow certain rules.

A) The administration of colloids (mainly semisynthetic colloids) should be restricted since clinical trials and meta-analyses have shown that their administration is associated with a lack of clinical benefit, potential nephrotoxicity and increased cost [1, 2]. However, although it has increased cost, patients with severe sepsis may benefit from albumin administration [3].

B) Careful individualized infusate administration of crystalloids is indicated (Table 1) [4]. It has been recently suggested that balanced salt solutions, such as the Lactated Ringer’s solution, may be the infusate of choice especially in patients with coexistent hypokalemia and metabolic acidosis [5, 6]. This is especially relevant in surgical patients, in patients with trauma, in patients with burns as well as in patients with diabetic ketoacidosis [4-6].

On the contrary, the use of large amounts of normal saline is associated with a number of adverse events, including metabolic acidosis (dilutional acidosis), with its consequences (cellular dysfunction but also impaired coagulation and bleeding), and hyperchloremia leading to acidosis and adverse renal hemodynamic effects (renal vasoconstriction) resulting in an increased incidence of acute kidney injury and delayed restoration of glomerular filtration in patients with prerenal azotemia [4, 7, 8]. Furthermore,
isotonic saline infusions as compared with the balanced crystalloid fluids are associated with a greater increase in interstitial volume in renal tissue, with adverse hemodynamic effects of the kidney, and also in splanchic tissues leading to increased rate of splanchic and peripheral edema [9, 10]. However, it has recently been reported that the use of small to moderate amounts of isotonic sodium chloride solution does not increase the incidence of acute kidney injury [11].

On the other hand, Lactated Ringer’s solution is not indicated in patients with severe metabolic alkalosis (since lactate is rapidly metabolized to HCO₃⁻), lactic acidosis with decreased lactate clearance or severe hyperkalemia (since it contains small amounts of potassium) [4, 12]. Furthermore, this relatively hypotonic solution may be associated with increased cerebral pressure and edema especially in patients with compromised vascular endothelial barrier, such as in patients with brain injury or increased intracranial pressure [1, 13]. It should be also mentioned that the addition of calcium in Lactate Ringer’s solution may be associated with microthrombi when citrate–containing red cell transfusions are simultaneously administered [8].

C) In cases that Lactated Ringer’s is not indicated, saline solution in glucose solutions should be preferred to provide adequate amount of calories and to avoid endogenous catabolism [13].

D) It has recently been stressed that hypotonic fluids (including Lactated Ringer’s) should be avoided in critically ill patients who commonly exhibit stimuli for antidiuretic hormone (ADH) secretion that increase the risk of hyponatremia with its adverse results [13]. A number of conditions are known to be associated with nonosmotic release of ADH including baroreceptor–mediated ADH secretion in hypovolemic patients (including patients with edema who exhibit reduced effective arterial volume), nausea, vomiting, pain and stress, hypoxemia and hypercapnia, in the perioperative state, as well as in patients with cancer and pulmonary or central nervous system disease [13]. This is especially evident in children in whom an increased risk of hyponatremia-associated cerebral edema has been increasingly reported [14-18].

E) It should be acknowledged that normal saline solution may be associated with serum sodium disturbances depending on the presence of impaired renal concentration or dilution ability [19]. Thus, in patients with impaired urine diluting ability (due for example to thiazides administration), even isotonic saline infusates can result in water retention and hyponatremia, while in patients with abnormalities in urine concentrating ability (such as patients with sickle cell disease, obstructive or reflex uropathy, tubule interstitial disease or in patients receiving lithium) isotonic saline solution may be associated with hyponatremia; thus a rather hypotonic saline solution is preferred [10, 13].

It is worth mentioning that in patients with the syndrome of inappropriate ADH secretion (SIADH) and increased urine osmolality (>550 mosmol/kg), but also in neurosurgical patients, isotonic sodium chloride infusate is commonly associated with a decrease in serum sodium concentration (a desalination process); thus, a rather hypertonic saline is preferred [13].

F) Potassium balance should be also taken into account in the choice of infusates [4, 20]. It should be stressed that in cases of potassium depletion potassium solution (mainly potassium chloride) should be added to the administered fluids. However, to avoid fluid overload, potassium chloride should be added to hypotonic saline solutions (including Lactated Ringer’s), since potassium (and chloride) anions are
osmotically active and can substantially increase serum tonicity leading to water transfer from the cells to the extracellular fluid \[4\]. Thus, the addition of 60mEq of KCl to a 0.45% sodium chloride solution (N/2) is close to an isotonic sodium chloride solution. Moreover, the use of the relatively hypotonic Lactated Ringer’s solution (actual osmolality 254 mosmol/kg) may be useful in these cases with potassium deficit, since the addition of 20mEq of KCl renders it practically isotonic \[4\].

G) In selected patients with metabolic acidosis, sodium bicarbonate should be added to the infusates \[20\]. In this case, it is imperative to avoid hypertonic solutions leading to volume overload. Thus, 100ml of bicarbonate added in 400 ml sterile water plus 20mmol of potassium chloride could be administered in patients with metabolic acidosis with associated hypokalemia. Of note NaHCO_3 solution should not be added to solutions containing calcium, such as Lactated Ringer’s, since the combination of Ca^{2+} και HCO_3^{-} may result in the formation of the insoluble salt CaCO_{3} \[4, 13\].

Based on the above evidence, clinicians should target any co-existing disorders and accordingly determine infusate treatment in patients with hypovolemia.

**Conflicting interests**

The authors have declared that no conflict of interests exist.

**Author contributions**

T.F. wrote the review, M.E. edited and supervised the manuscript.

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