Considerable attention has been given to so-called “balanced solutions” (such as Ringer’s lactate, and more recent derivatives) as alternatives to the less physiological “abnormal” 0.9% saline. Colloids prepared in “balanced” electrolyte solutions have also been developed, alongside similar colloids in saline. This is a consequence of the observation that excessive use of saline will result in hyperchloremic acidosis, which has been identified as a potential side-effect of saline-based solutions. There is debate about the extent of the morbidity associated with this condition, although the risk is probably quite low. It has been suggested that the use of balanced solutions may avoid this effect.

A recent consensus guideline for intravenous fluid therapy in adult surgical patients recommend the use of “balanced” crystalloids rather than saline. However, there are no specific recommendations regarding colloids, implying that they could be suspended in either saline or balanced salt preparations. However, these recommendations have been challenged on the basis that there is little evidence that hyperchloremic acidosis is harmful to patients.

Physiological background

The Stewart hypothesis proposes that plasma pH is affected by three independent factors: $PCO_2$, the strong ion difference (SID), which is the difference between the charge of plasma strong cations (sodium, potassium, magnesium and calcium) and strong anions (chloride, sulphate, lactate and others); and $A_{sat}$, the total plasma concentration of non-volatile buffers (albumin, globulins, phosphate). Since the SID of isotonic saline is 0, the infusion of large quantities will dilute the normal SID of plasma, decreasing pH. Hyperchloremic metabolic acidosis (HCMA) is a decrease in SID associated with an increase in chloride. Infusions of isotonic saline will also dilute albumin and decrease $A_{sat}$, which increases pH. A balanced solution with a physiological SID of 40 mEq/L would induce a metabolic alkalosis, and the ideal balanced solution should have a SID of 24 mEq/L in order to avoid this. Balanced solutions using organic anions (such as lactate, acetate, gluconate, pyruvate or malate) have an in vitro SID equal to 0, similar to that of saline. In vivo, the metabolism of these anions increases the SID to a degree dependent on the extent and rate of metabolism of the included anion. There is currently no clinical research that establishes the comparative effects of the different anions on acid-base balance.

Clinical effects

There is an inverse linear relationship between chloride load and base excess, such that a decrease in base excess of 10 mmol/L would require a rise of plasma chloride of 20 mmol/kg, equivalent to the infusion of around 9 L of isotonic saline. In patients given 6 L of 0.9% isotonic saline over two hours, SID decreased from 40 to 31 mEq/L, chloride increased from 105 to 115 mmol/L and base excess decreased by 7 mmol/L. In the context of colloid infusions, the recommended limit of 50 ml/kg of HES 130/0.4 in saline would reduce base excess by a maximum of 3.5 mmol/L. This suggests that, when patients are treated with a combination of saline-based colloids and balanced crystalloids, the effects on acid-base equilibrium are limited.
in cardiac surgery, the difference in chloride concentration at the end of surgery was 110 mmol/L versus 112 mmol/L, and base excess differed by 2 mmol/L between groups. The difference was statistically significant, but not clinically relevant.

Large volumes of saline will increase chloride concentration and reduce base excess in a dose-dependent manner, but these disturbances return to normal within one or two days. It is possible that patients with pre-existing metabolic acidosis, especially with hepatic or renal dysfunction, may be more affected due to a reduced buffering capacity. Transient isotonic saline-induced reduction of base excess should be considered when interpreting acid-base status in unstable patients.

Renal function

Animal studies suggest that chloride induces renal vasoconstriction, increases renal vascular resistance, decreases glomerular filtration rate and decreases renin activity. However, at normal and slightly high concentrations these effects are small. In human volunteers, there was a significant delay in the mean time to urination after infusion of large volumes of saline compared to Ringer’s lactate that could be partly explained by the decreased serum osmolality in the Ringer’s group. A similar study confirmed the shorter time to first micturition with Ringer’s, but in this study, plasma osmolality was similar between the groups. The isotonic saline group retained a greater proportion of the sodium load than did the Ringer’s lactate group. These results emphasise that differences in osmolality between balanced solutions and isotonic saline must be taken into account in the interpretation of renal function parameters like time to micturition and urine output, but suggest that sodium clearance may be less effective in the face of hyperchloraemia.

In patients undergoing renal transplantation, saline caused greater acidosis and higher potassium concentrations than did Ringer’s lactate. This is the consequence of an acidosis mobilising potassium from the intracellular space in patients where renal function is unable to compensate for these changes. It is worth noting that no adverse effect of saline on renal function was shown. There is no evidence of this effect in other studies comparing saline to balanced salt crystalloids, and this risk of increased potassium with saline may only apply where renal function is already impaired.

From a renal perspective, the lower osmolality of Ringer’s lactate may result in earlier clearance of a sodium load, but this effect could also be attributed to decreased renal blood flow produced by increasing chloride where saline-based fluid regimes are used. In surgical patients, there are no current studies demonstrating any clinically different renal outcomes between saline or balanced salt preparations.

Coagulation

In vitro studies suggest that balanced solutions, particularly when used as suspending fluids for colloids, may have fewer negative effects on coagulation than saline solutions. However, limitations including calcium dilution and the absence of the endothelium, make it difficult to extrapolate in vitro data into the clinical situation.

In patients undergoing aortic aneurysm repair, a comparison of Ringer’s lactate with isotonic saline found that there was an increase in the need for platelets and the total volume of all blood products administered in the saline group. No significant difference in morbidity or mortality was reported. In the recent Trauma Trial, there was no evidence that saline impaired coagulation.

In conclusion, there is little evidence that large volumes of saline compared to balanced salts have a significantly detrimental effect on coagulation, blood loss or transfusion.

Gastrointestinal function

Williams et al reported that healthy volunteers receiving saline experienced more frequent abdominal discomfort than those receiving Ringer’s lactate. Wilkes et al investigated the effects of 6% hetastarch in a balanced carrier plus Ringer’s lactate, versus hetastarch in saline plus isotonic saline, in elderly surgical patients. They found a significantly greater gastric CO₂ gradient in the saline group that may suggest better gastric mucosal perfusion in the Ringer’s lactate group. A non-significant trend to more nausea and vomiting was observed in the saline group. However, Moretti et al, comparing hetastarch in isotonic saline, hetastarch in balanced solution and Ringer’s lactate, found no significant difference in the incidence of nausea and use of antiemetics between the hetastarch groups, which were both significantly lower than in the Ringer’s lactate group. The authors concluded that intraoperative fluid resuscitation with colloids, compared with crystalloids, improved postoperative recovery with regard to postoperative nausea and vomiting. These results suggest that fluid volume may be more important than fluid composition.
In conclusion, there is insufficient evidence from the available literature to suggest that dilutional-hyperchloraemic acidosis has a clinically relevant effect on gastrointestinal function. However, some degree of intraoperative crystalloid restriction and targeted colloid use may be associated with an improvement in gastrointestinal function and outcome.

**Mortality**

While metabolic acidosis is often associated with adverse outcomes, the underlying cause seems more important than the acidosis itself. An animal study on experimental sepsis showed an increase in inflammatory markers associated with hyperchloraemic acidosis. A retrospective study of critically ill patients found that 64% had a metabolic acidosis, related to either lactate, strong ion gap or hyperchloraemia. Mortality was highest in patients with lactic acidosis (56%). In patients with dilutional-hyperchloraemic acidosis, mortality was the same as in the control group without metabolic acidosis. From this observational study, it may be concluded that patients with hyperchloraemic acidosis were not associated with an increased risk of mortality compared to critically ill patients without metabolic acidosis.

In paediatric intensive care following cardiac surgery, dilutional-hyperchloraemic acidosis was associated with reduced requirement for adrenaline therapy, and the authors suggested hyperchloraemic acidosis was a benign phenomenon that should not prompt escalation of haemodynamic support. Other studies comparing hyperchloraemic acidosis with acidosis from other causes in critical illness found significantly fewer deaths in the hyperchloraemic group than in the remaining patients. The authors concluded that hyperchloraemic acidosis is a common cause of base deficit in the surgical intensive care unit and is associated with lower mortality than base deficit secondary to another cause.

**Conclusions**

Hyperchloraemic metabolic acidosis is a common side-effect of the use of saline-based solutions. While some animal and human experimental data suggest that this may be associated with diminished gastro-intestinal and renal function, there are little clinical data to support this. Large volumes of crystalloid may produce clinically relevant hyperchloraemia and this can be diminished by the appropriate use of colloid solutions. It must also be borne in mind that Ringer’s-type crystalloid with a saline-based colloid may be the most appropriate strategy for most surgical patients. However, where massive bleeding is anticipated, there is a strong argument for the use of an appropriately balanced colloid preparation, but there is currently no clinical evidence to confirm that this will change patient outcome.

Do we need a colloid in a balanced salt solution? Yes, provided that the balanced salt solution has been demonstrated to be a safe alternative, and there is lack of good evidence regarding the safety of many of the anions included in many such solutions. For most purposes, where relatively small volumes of saline-based colloids are to be administered, there is little evidence that switching to a balanced salt-suspending solution will offer significant advantages. However, basic common sense suggests that, where large-volume colloid resuscitations are to be used, a balanced salt preparation does appear to be a logical fluid management choice, even though conclusive clinical evidence is currently absent.

**References**


