

## EDITORIAL VIEWS

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## Hyperchloremic Metabolic Acidosis Is a Predictable Consequence of Intraoperative Infusion of 0.9% Saline

IN this issue of *ANESTHESIOLOGY*, Scheingraber *et al.*<sup>1</sup> quantify two phenomena that are important to anesthesiologists and other clinicians caring for perioperative patients: (1) intravenous infusion of 0.9% saline in patients undergoing gynecologic surgery results in hyperchloremic metabolic acidosis and (2) intravenous infusion of either 0.9% saline or lactated Ringer's solution results in hypoproteinemia and a decreased anion gap. Although neither of these observations is surprising, no other data define so clearly the expected effects of conventional intravenous therapy in a population of patients undergoing

common procedures of intermediate magnitude. Clarification of these effects is important in interpreting perioperative acid-base changes and in assessing the need for treatment to modify those changes.

A brief review of the key observations of this study is necessary to appreciate its importance. Scheingraber *et al.*<sup>1</sup> randomized 24 women to receive either 0.9% saline or lactated Ringer's solution while undergoing elective gynecologic lower abdominal surgery. During surgical procedures averaging slightly more than 2 h in duration, subjects lost a mean volume of approximately 850 ml blood, received a mean volume of either of the two crystalloids of almost 70 ml/kg, and excreted a mean volume of almost 900 ml urine. During the first 2 h of saline infusion, the serum bicarbonate concentration ( $\text{HCO}_3^-$ ), calculated from the Henderson-Hasselbalch equation) decreased from  $23.5 \pm 2.2$  mM to  $18.4 \pm 2.0$  mM. The anion gap concentration decreased from  $16.2 \pm 1.2$  mM to  $11.2$  mM, and the mean serum chloride concentration ( $\text{Cl}^-$ ) increased from 104 to 115. During the same interval,  $\text{HCO}_3^-$  in the group receiving lactated Ringer's solution remained similar ( $23.8 \pm 2.0$  mM and

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23.2  $\pm$  1.7 mm), the anion gap decreased from 15.2  $\pm$  1.4 mm to 12.1 mm, and the mean Cl<sup>-</sup> increased from 104 mm to 106 mm.

The occurrence of hyperchloremic acidosis in the saline group, although consistent with the anecdotal experience of clinicians who have infused large volumes of saline intraoperatively,<sup>2-4</sup> appears to contradict traditional thinking about acid-base balance, *i.e.*, that saline infusion alone is unlikely to significantly alter HCO<sub>3</sub><sup>-</sup>. Perhaps the most striking experimental evidence supporting that concept is that of Rosenbaum *et al.*,<sup>5</sup> who infused 50, 75, and 100 ml/kg 0.9% saline over 30 min in anephric dogs and demonstrated decreases in HCO<sub>3</sub><sup>-</sup> of only 2.4  $\pm$  0.7, 2.5, and 3.0 mm, respectively, 1 h after infusion. They concluded that the relatively slow infusion rate, coupled with "appropriate cellular buffering," explained the small changes and that the "clinical significance of acute extracellular expansion with saline is moot." In contrast, Scheingraber *et al.*<sup>1</sup> infused 70 ml/kg of saline over 120 min in patients with normal renal function and reported decreases in HCO<sub>3</sub><sup>-</sup> that were twice as large. Apart from the obvious difference in species, no reasons for the disparate findings are apparent.

Curiously, the general concept of hyperchloremic acidosis was infrequently discussed in the anesthesiology literature before 1994. Subsequently, clinical reports described this entity as a consequence of administration of unusually large volumes of saline, most often during prolonged procedures, such as major hepatobiliary or pancreatic surgery,<sup>6</sup> anterior spinal fusion,<sup>3</sup> and bilateral nephrectomy.<sup>4</sup> In the latter two case reports, preexisting urinary tract disease was a possible confounding variable. Miller *et al.*<sup>2,7</sup> responded to each of these case reports with letters to the editor emphasizing the pathogenetic role of large volumes of saline and extensive surgery. In contrast to previous reports, Scheingraber *et al.*<sup>1</sup> provide unequivocal evidence that hyperchloremic acidosis is a predictable accompaniment of saline administration during procedures of even moderate duration.

One might argue that this study is misleading because the total fluid infused by Scheingraber *et al.*<sup>1</sup> was excessive for surgical procedures of intermediate magnitude. Patients in the saline group received a total of almost 5,000 ml during the first 120 min of their procedures. However, using conventional crystalloid: blood replacement ratios of 3:1 or 5:1 to replace a mean blood loss of 962  $\pm$  332 ml would require comparable volumes.

Therefore, these data should apply to routine clinical practice.

Moreover, in nonsurgical circumstances involving fluid resuscitation with saline, the occurrence of hyperchloremic acidosis has long been recognized. Because 0.45% and 0.9% saline conventionally are used for fluid resuscitation of patients with diabetic ketoacidosis, hyperchloremic acidosis routinely develops during treatment of the hypovolemia associated with this disorder.<sup>8</sup> Of course, in diabetic ketoacidosis, additional factors contributing to ketoacidosis include the consumption of HCO<sub>3</sub><sup>-</sup> in buffering of ketoacids and the loss in the urine of ketoacids that otherwise would be converted to HCO<sub>3</sub><sup>-</sup> in the liver.

The study by Scheingraber *et al.*<sup>1</sup> also elucidates the influence of perioperative protein dilution on the calculated anion gap. In the two groups, serum proteins decreased from 6.2 to 4.3 g/dl in association with the previously noted decreases in the anion gap. The anion gap is a useful, if imperfect, tool for distinguishing metabolic acidoses, such as ketoacidosis, lactic acidosis, and uremic acidosis, that increase the anion gap from hyperchloremic acidosis, in which the anion gap does not increase.<sup>9</sup> These observations by Scheingraber *et al.*<sup>1</sup> show both the usefulness of assessing the anion gap in managing postoperative metabolic acidosis and the influence of hypoalbuminemia on the anion gap. Because approximately 75% of the normal anion gap is composed of the negatively charged albumin molecule,<sup>9</sup> both the chronic hypoalbuminemia that accompanies critical illness and the acute dilutional hypoalbuminemia that accompanies rapid crystalloid infusion effectively reduce the upper limit of the normal range of the anion gap. Recently, Figge *et al.*,<sup>10</sup> based on analysis of blood samples from 9 healthy subjects and 152 critically ill patients, demonstrated that a reduction in serum albumin of 1 g/dl reduced the anion gap by 2.5 mEq/l. Although Scheingraber *et al.*<sup>1</sup> do not separate total protein measurements into serum albumin and other proteins, their results are generally consistent with a change of similar magnitude during acute dilutional hypoalbuminemia.

What these data fail to address is the influence, if any, of acute hypoalbuminemia on acid-base balance in this study. An assumption, based in part on the Stewart approach to acid-base interpretation,<sup>11</sup> is that hypoalbuminemia produces metabolic alkalosis that can be reversed by infusion of albumin. Although *in vitro* data show a linear correlation between albumin concentration and HCO<sub>3</sub><sup>-</sup>,<sup>12</sup> the effects of a decrease in total protein of only 2 g/dl, of which a little more than half presumably would represent a decrease in serum albu-



## EDITORIAL VIEWS

min, would not be expected to cause a clinically important decrease in  $\text{HCO}_3^-$ .

The most important question posed by this study is whether these data should prompt any alteration in clinical management. Mathematically, these data suggest that lactated Ringer's solution is preferable to 0.9% saline because it causes less acid-base disturbance. However, the changes in serum sodium concentration ( $\text{Na}^+$ ) also merit discussion. One theoretical reason to use 0.9% saline rather than lactated Ringer's solution in patients at risk for intracranial hypertension is that an increase in  $\text{Na}^+$  will tend to reduce brain water, whereas a decrease in  $\text{Na}^+$  will tend to increase brain water.<sup>13</sup> At 120 min into the study by Scheingraber *et al.*,<sup>1</sup>  $\text{Na}^+$  was  $\geq 3.5$  mM greater in the saline group. This equates to a difference in serum osmolality of  $\geq 7.0$  mOsm/kg and in serum osmotic pressure of  $\geq 135$  mmHg. Theoretically, a difference of this magnitude should influence brain water and intracranial pressure.

Is hyperchloremic metabolic acidosis hazardous? Most evidence suggests that it is not. However, correct treatment is absolutely dependent on differentiation of hyperchloremic acidosis from lactic acidosis. Aggressive attempts to improve organ perfusion, based on misdiagnosis of lactic acidosis, could prove harmful. These data show the value of using the anion gap to support the diagnosis of acute dilutional hyperchloremic acidosis. However, they also provide the caveat that the anion gap must be interpreted in light of any accompanying acute hypoalbuminemia. In the presence of an acute decrease in serum albumin, the anion gap should be decreased proportionately; if it is not, other causes of metabolic acidosis should be considered.

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