Kidney International, Vol. 56, Suppl. 72 (1999), pp. S-37–S-40

Acid-base balance and substitution fluid during continuous hemofiltration

PETER HEERING, KATRIN IVENS, OLIVER THÜMER, MATTHIAS BRAÜSE, and BERND GRABENSEE

Department of Nephrology, Heinrich-Heine-University of Düsseldorf, Düsseldorf, Germany

Acid-base balance during continuous hemofiltration in patients with acute renal failure. Critically ill patients with acute renal failure usually present with an unstable acid-base balance, often leading to cardiovascular complications and multi-organ failure. Therefore, to prevent metabolic acidosis, acid-base balance must be normalized and maintained; these patients are primarily treated with continuous hemofiltration techniques using different replacement fluids to influence the acid-base values. Dialysate solutions can be an acetate-based, lactate-based, citrate-based or bicarbonate-based buffer. This article discusses the strengths and weaknesses of each type of hemofiltration replacement fluid.

Acute renal failure (ARF) complicating the course of critical illness continues to be associated with a high mortality, despite many advances made over the last decades in the care of the critically ill patients. The majority of these patients suffer from multiple- rather than single-organ failure. Continuous venovenous hemofiltration (CVVH) has become common as a renal replacement therapy, which is often better tolerated than intermittent hemodialysis at facilitating extracellular fluid volume control and reducing cardiovascular disturbances [1, 2]. During continuous renal replacement therapies (CRRTs), alkali administration, either in the replacement fluid or by diffusive uptake from the dialysate, must replace not only the bicarbonate lost in the buffering of endogenous acid production, but also the bicarbonate lost across the hemodiafilter. In most patients with ARF, a buffer concentration of approximately 30 to 35 mmol/liter and an ultrafiltration rate (or dialysate flow rate) approaching or exceeding 1 liter/hr can be expected to normalize the acid-base status within one or two days. In individuals with ARF and lactic acidemia, the buffer load may need to approach ≥50 mmol/liter to correct the associated metabolic acidemia. Acetate, bicarbonate, citrate, and lactate are the possible choices for bicarbonate or bicarbonate-equivalent administration during CRRT. Acetate- and lactate-based physiological solutions have the advantage of being commercially available. Under normal conditions, acetate and lactate are metabolized rapidly to bicarbonate. In addition, the administration of large amounts of lactate may result in increased urea generation (abstract; Olbricht et al, *Int Soc Blood Purif* 10:48, 1992). Bicarbonate has the major advantage of being the most physiologic anion. Unfortunately, the production of a commercially available bicarbonate-based physiologic solution is difficult because of the loss of bicarbonate from the solution or the formation of calcium and magnesium salts. Persistent acidosis has been demonstrated to be an indicator of poor prognosis [3]. Acetate, as well as lactate, must be metabolized in the organism in order to compensate for the loss of endogenous bicarbonate. Acetate is converted on a 1:1 basis to bicarbonate by both the liver and skeletal muscle. Lactate is converted in the liver on a 1:1 basis to bicarbonate, and each type of anion is capable of providing an alkali load sufficient to correct the acidemia of ARF. Previous studies have suggested that the metabolism of acetate and lactate was impaired in critical illness and might be able to produce acidosis [2, 4]. Furthermore, it was suggested that lactate and acetate might act as a cardiovascular depressant [4]. The correction of metabolic acidosis is a primary aim for renal replacement therapy. Depending on the type of dialytic modality employed, the buffer balance is influenced by several factors; among those, the type of buffer employed influences not only acid-base correction, but possibly also clinical outcomes. In this brief review, the importance of different buffers applied is reviewed under the topic of ARF in intensive care medicine.

DIALYTIC TECHNIQUES

The buffer balance depends on buffer losses with ultrafiltrate and buffer gain with replacement fluid. When continuous venous-venous hemofiltration is applied to reduce the patient's fluid overload, huge volumes of bicarbonate are lost and this bicarbonate loss has to be

Key words: critical care, multi-organ failure, metabolic acidemia, acidosis, dialysate buffer.

replaced. When metabolic acidosis needs to be corrected, the amount of buffer in the replacement fluid must exceed the amount lost in ultrafiltrate, thus providing a positive balance of buffer. Several observations have reported that the loss of bicarbonate in the ultrafiltrate exceeds that of plasma so that a sieving coefficient of higher than 1 can be calculated (between 1.1 and 1.25) [5]. Because of their greater stability compared with bicarbonate, acetate or lactate is used in the buffer of commercial fluids. The natural buffer, bicarbonate, precipitates as an insoluble salt when sterilized together with divalent cations, calcium, and magnesium. Recent technological advances have enabled this problem to be overcome. A double chamber bag with two separate compartments, one containing bicarbonate and the other calcium and magnesium, allows the bicarbonate solution to be sterilized and stored. Bicarbonate is the most physiologic of the possible anions available for use in CRRT. Based on our experience and that of other investigators, normalization of the acid-base balance in patients with metabolic acidemia resulting only from ARF can be accomplished within 24 to 48 hours using these rates of bicarbonate gain.

CLINICAL FINDINGS

Few clinical studies have been performed in critically ill patients treated with CVVH in order to assess the efficacy of acidosis correction and to compare the differently buffered replacement solutions. However, a great deal of information could be derived from the treatment of chronic patients or from intermittent treatments of critically ill patients. The effect on acid-base status depends on the buffer concentration in the fluid and on the type of buffer used. In general, each type of anion is capable of providing an alkali load sufficient to correct the acidemia of ARF.

However, there are clinical conditions that might influence the clinician's decision to chose a particular buffer. Hyperacetatemia has a peripheral vasodilating effect and a myocardial depressant effect and is able to increase oxygen consumption as a result of acetate metabolism [4]. In a recent study on critically ill patients treated with CVVH and a 35 mmol/liter acetate replacement solution, no substantial increase in blood bicarbonate concentration was recorded (Fig. 1) (abstract; Heering et al, *J Am Soc Nephrol* 8:159, 1997). In this study, the correction of metabolic acidosis occurred much more rapidly and completely in patients who were treated with CVVH and lactate- or bicarbonate-based replacement therapy. Lactate is a powerful peripheral vasodilator, affects myocardial contractility, and reduces blood pressure. It has been demonstrated that the use of lactate-buffered replacement solution was associated with a higher serum urea concentration and urea generation

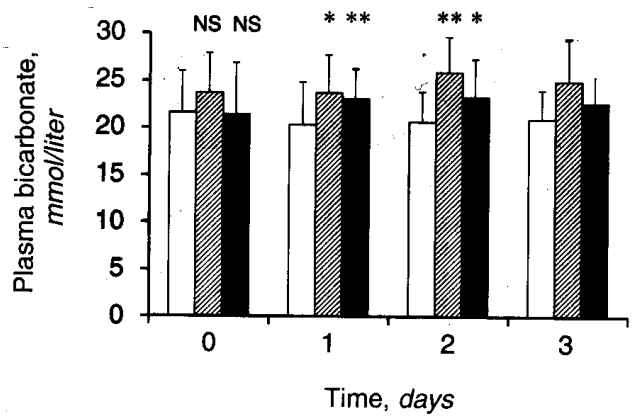

Fig. 1. Plasma bicarbonate levels in patients treated with lactate (▨), acetate (□) or bicarbonate (■) based buffer in continuous venous-venous hemofiltration (CVVH). (Data are from: abstract; Heering et al, *J Am Soc Nephrol* 8:159, 1997).

and had a presumably higher protein catabolic rate (abstract; Olbricht et al, *Int Soc Blood Purif* 10:48, 1992).

The use of lactate-based hemofiltration/hemodiafiltration solutions is generally well tolerated in most patients undergoing continuous therapies. Most commercially available solutions are buffered with approximately 40 to 45 mmol/liter of lactate. The resulting exogenous lactate load is capable of being cleared by the liver even in the setting of fulminant hepatic failure. However, there are complications that may arise from the use of lactate-based replacement fluids in critically ill patients. The administration of large amounts of lactate without its redox partner pyruvate can possibly result in an increased protein catabolic rate and myocardial depression. The administration of lactate in patients with severe hypoxia, liver impairment, or pre-existing lactic acidemia can result in a worsening of lactic acidemia. In critically ill patients with shock and liver failure, the use of lactate-based fluids in CRRTs may be associated with a paradoxical worsening of acid-base balance. If lactate-based fluids are to be used in these individuals, close attention to the patient's catabolic rate, acid-base status, and arterial lactate levels may be necessary. If hemodynamic instability worsens, an assessment of myocardial function and—if indicated—inotropic support may be appropriate. In addition, serial measurements of the serum anion gap may be necessary to detect the accumulation of D-lactate, which is not measured by standard laboratory methodology. Continuous lactate-based buffer is still the treatment of choice. The exceptions are impairment of liver function and lactic acidosis [2].

When oxidizable anions are used in the replacement fluids, the anion (acetate or lactate) must be completely oxidized to CO_2 and H_2O in order to generate an equimolar amount of bicarbonate. If the metabolic conversion of nonbicarbonate anions proceeds without accumulation, the buffering capacity of them is equal to that of bicar-

replaced. When metabolic acidosis needs to be corrected, the amount of buffer in the replacement fluid must exceed the amount lost in ultrafiltrate, thus providing a positive balance of buffer. Several observations have reported that the loss of bicarbonate in the ultrafiltrate exceeds that of plasma so that a sieving coefficient of higher than 1 can be calculated (between 1.1 and 1.25) [5]. Because of their greater stability compared with bicarbonate, acetate or lactate is used in the buffer of commercial fluids. The natural buffer, bicarbonate, precipitates as an insoluble salt when sterilized together with divalent cations, calcium, and magnesium. Recent technological advances have enabled this problem to be overcome. A double chamber bag with two separate compartments, one containing bicarbonate and the other calcium and magnesium, allows the bicarbonate solution to be sterilized and stored. Bicarbonate is the most physiologic of the possible anions available for use in CRRT. Based on our experience and that of other investigators, normalization of the acid-base balance in patients with metabolic acidemia resulting only from ARF can be accomplished within 24 to 48 hours using these rates of bicarbonate gain.

CLINICAL FINDINGS

Few clinical studies have been performed in critically ill patients treated with CVVH in order to assess the efficacy of acidosis correction and to compare the differently buffered replacement solutions. However, a great deal of information could be derived from the treatment of chronic patients or from intermittent treatments of critically ill patients. The effect on acid-base status depends on the buffer concentration in the fluid and on the type of buffer used. In general, each type of anion is capable of providing an alkali load sufficient to correct the acidemia of ARF.

However, there are clinical conditions that might influence the clinician's decision to chose a particular buffer. Hyperacetatemia has a peripheral vasodilating effect and a myocardial depressant effect and is able to increase oxygen consumption as a result of acetate metabolism [4]. In a recent study on critically ill patients treated with CVVH and a 35 mmol/liter acetate replacement solution, no substantial increase in blood bicarbonate concentration was recorded (Fig. 1) (abstract; Heering et al, *J Am Soc Nephrol* 8:159, 1997). In this study, the correction of metabolic acidosis occurred much more rapidly and completely in patients who were treated with CVVH and lactate- or bicarbonate-based replacement therapy. Lactate is a powerful peripheral vasodilator, affects myocardial contractility, and reduces blood pressure. It has been demonstrated that the use of lactate-buffered replacement solution was associated with a higher serum urea concentration and urea generation

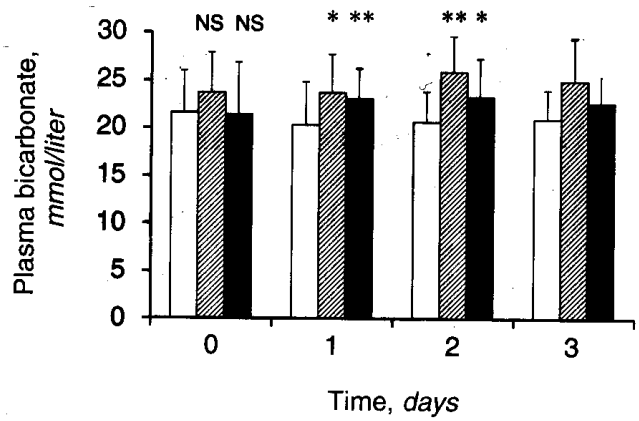

Fig. 1. Plasma bicarbonate levels in patients treated with lactate (▨), acetate (□) or bicarbonate (■) based buffer in continuous venous-venous hemofiltration (CVVH). (Data are from: abstract; Heering et al, *J Am Soc Nephrol* 8:159, 1997).

and had a presumably higher protein catabolic rate (abstract; Olbricht et al, *Int Soc Blood Purif* 10:48, 1992).

The use of lactate-based hemofiltration/hemodiafiltration solutions is generally well tolerated in most patients undergoing continuous therapies. Most commercially available solutions are buffered with approximately 40 to 45 mmol/liter of lactate. The resulting exogenous lactate load is capable of being cleared by the liver even in the setting of fulminant hepatic failure. However, there are complications that may arise from the use of lactate-based replacement fluids in critically ill patients. The administration of large amounts of lactate without its redox partner pyruvate can possibly result in an increased protein catabolic rate and myocardial depression. The administration of lactate in patients with severe hypoxia, liver impairment, or pre-existing lactic acidemia can result in a worsening of lactic acidemia. In critically ill patients with shock and liver failure, the use of lactate-based fluids in CRRTs may be associated with a paradoxical worsening of acid-base balance. If lactate-based fluids are to be used in these individuals, close attention to the patient's catabolic rate, acid-base status, and arterial lactate levels may be necessary. If hemodynamic instability worsens, an assessment of myocardial function and—if indicated—inotropic support may be appropriate. In addition, serial measurements of the serum anion gap may be necessary to detect the accumulation of D-lactate, which is not measured by standard laboratory methodology. Continuous lactate-based buffer is still the treatment of choice. The exceptions are impairment of liver function and lactic acidosis [2].

When oxidizable anions are used in the replacement fluids, the anion (acetate or lactate) must be completely oxidized to CO_2 and H_2O in order to generate an equimolar amount of bicarbonate. If the metabolic conversion of nonbicarbonate anions proceeds without accumulation, the buffering capacity of them is equal to that of bicar-

seem to occur during the treatments that are linked to the use of different buffers. The choice of the hemofiltration replacement fluid is essential for influencing acid-base values. Although lactate- and bicarbonate-based replacement fluids lead to a remarkable elevation in serum bicarbonate and arterial pH, acetate-based replacement fluid has been reported to compensate metabolic acidosis insufficiently. An absence of an increase in serum bicarbonate and arterial pH can be seen as a poor prognosis for the outcome in lactate- and bicarbonate-based but not in acetate-based hemofiltration. However, in patients with multiple-organ failure, the physiological buffer bicarbonate is preferable because of its lack of metabolic interference. Future studies are needed to prove that the application of bicarbonate-buffered hemofiltration fluid does not only improve acid-base metabolism, but also the overall prognosis of patients treated with CVVH.

Reprint requests to Peter Heering, M.D., Department of Nephrology and Rheumatology, Heinrich-Heine-University, 40001 Düsseldorf, Germany.

REFERENCES

1. Agazia B, Ferrari G, Santoro A: Acid-base balance during hemofiltration with bicarbonate substitution fluid: A prospective multicenter trial, in *Istituto Italiano Per Gli Studi Filosofici Acid Base and Electrolyte Balance*, edited by De Santo NG, Capasso G, Editoriale Bios, Cosenza, 1995, pp 341–346
2. Davenport A, Will EJ, Davidson AM: Improved cardiovascular stability during continuous modes of renal replacement therapy in critically ill patients with acute hepatic and renal failure. *Crit Care Med* 21:328–338, 1993
3. Wendon J, Smithies M, Sheppard M, Bullen K, Tinker J, Bihari DJ: Continuous high, venous-venous hemofiltration in acute renal failure. *Intensive Care Med* 15:358–363, 1989
4. Jacob AD, Elkins N, Reiss O, Chan L, Shapiro JI: Effects of acetate on energy metabolism and function in the isolated perfused rat heart. *Kidney Int* 52:755–760, 1997
5. Feriani M, Dell'Aquila R: Acid-base balance and replacement solutions in continuous renal replacement therapies. *Kidney Int* 66(Suppl):156–159, 1998
6. Macias W: Choice of replacement fluid/dialysate anion in continuous renal replacement therapy. *Am J Kidney Dis* 28(Suppl 3):S5–S20, 1996
7. Hakim RM, Pontzer MA, Tilton D, Lazarus JM, Gottlieb M: Effects of acetate and bicarbonate dialysate in stable chronic dialysis patients. *Kidney Int* 28:535–540, 1985
8. Heering P, Ivens K, Thümer O, Morgera S, Heintzen M, Passlick-Reetjen J, Willers R, Strauber BE, Grabensee B: The use of different buffers during continuous filtration in critically ill patients with acute renal failure. *Intensive Care Med* (in press)
9. Thomas AN, Guy JM, Kishen R, Geraghty IF, Bowles BMJ, Vadgama P: Comparison of lactate and bicarbonate buffered hemofiltration fluids: Use in critically ill patients. *Nephrol Dial Transplant* 12:1212–1217, 1997
10. Nimmo GR, Mackenzie SJ, Walker S, Grant IS: Acid base response to high, hemofiltration in the critically ill patient. *Nephrol Dial Transplant* 8:854–857, 1993
11. Kierdorf H, Leue C, Heintz B, Riehl J, Melzer H, Sieberth HG: Continuous venovenous hemofiltration in acute renal failure: Is a bicarbonate or lactate buffered substitution better? in *Continuous Extracorporal Treatment in Multiple Organ Dysfunction Syndrome.* Contrib Nephrol, vol. 116, edited by Sieberth HG, Stummvoll HK, Kierdorf H, Karger, 1995, pp 38–47
12. Santoro A, Ferrari G, Bolzani R, Spongano M, Zucceli P: Regulation of base balance in bicarbonate hemofiltration. *Int J Artif Organs* 17:27–36, 1994
13. Locatelli F, Pontoriero G, Di Filippo S: Electrolyte disorders and substitution fluid in continuous renal replacement therapy. *Kidney Int* 66(Suppl):151–155, 1998
14. Wakabayashi Y, Ohwada T, Kikawada R: Hemodialysis/hemofiltration using sodium bicarbonate depresses cardiac function in critically ill patients with acute renal failure. *Jpn Circ J* 58:81–86, 1994