—**Original**—

Effect of Bicarbonated Ringer's Solution on the Acid-base Balance in Patients Undergoing Abdominal Aortic Aneurysm Repair

Yoichi Shimada[1], Akira Kitamura[2], Kazuhiro Nakanishi[2], Takashi Hongo[2], Chol Kim[2] and Atsuhiro Sakamoto[2]

[1]Department of Anesthesiology, Nippon Medical School Second Hospital
[2]Department of Anesthesiology, Nippon Medical School Hospital

Abstract

Aim: The present study was designed to assess whether prophylactic use of bicarbonated Ringer's solution ameliorates metabolic acidosis in patients undergoing aortic surgery.

Methods: Twenty patients undergoing elective infrarenal aortic aneurysm repair were randomly assigned to receive either bicarbonated Ringer's solution or acetated Ringer's solution. The pH, $PaCO_2$, and base excess (BE) were measured before surgical incision (T0), 5 min before reperfusion (T1), 5 min after reperfusion (T2), and 30 min after reperfusion (T3). Data were compared between the two groups.

Results: Both pH and BE initially showed a slight decrease in both groups during clamping. After unclamping of the aorta, an additional decrease in pH was observed in both groups (T0 to T2, and T3). There were no significant differences in pH between the groups throughout the study period.

Conclusions: Aortic cross-clamping leads to the development of metabolic acidosis, with a decrease in pH and BE. The effect of administration of bicarbonated infusion fluid during elective abdominal aortic surgery had not significant compared with that of acetated Ringer's solution with respect to acid-base homeostasis.
(J Nippon Med Sch 2005; 72: 364–369)

Key words: bicarbonated Ringer's solution, acetated Ringer's solution, acid-base balance

Introduction

Hartmann's solution is widely available today, and it contains lactate or acetate as a substitute for bicarbonate[1,2]. The alkalizing effects of both lactate and acetate depend on these substances undergoing metabolism. Bicarbonate is a natural buffer that corrects acidosis through chemical neutralization, and it was the unquestioned agent for the treatment of metabolic acidosis until two decades ago. However, because the high concentration of sodium bicarbonate leads to instability before administration, it is impossible to sterilize a sodium bicarbonate solution before it is added to Ringer's solution. During autoclaving for sterilization, carbon dioxide gas is lost. Degradation of sodium bicarbonate occurs at room temperature, producing sodium carbonate, carbon dioxide, and water. Furthermore, sodium bicarbonate can form a sediment with calcium or magnesium. For these reasons, bicarbonated Ringer's solution has not been

Correspondence to Yoichi Shimada, MD, Department of Anesthesiology, Nippon Medical School Second Hospital, 1–396 Kosugi-cho, Nakahara-ku, Kawasaki, Kanagawa 211–8533, Japan
E-mail: megu@nms.ac.jp
Journal Website (http://www.nms.ac.jp/jnms/)

Table 1 Composition of solutions (Unit: mEq/L)

	Na^+	K^+	Ca^{2+}	Mg^{2+}	Cl^-	Others
Bicarbonate Ringer's solution	135	4	3	1	113	$Bicarbonate^-$ 25, $Citrate^-$ 5
Acetate Ringer's solution	130	4	3	0	109	$Acetate^-$ 28

marketed.

However, a new bicarbonated Ringer's solution that controls the above-mentioned problems chemically has been developed and approved in Japan. Preclinical studies of this solution in animal hemorrhagic shock models revealed improvement of the acid-base balance compared with alternatives, such as lactated, acetated, or non-buffered Ringer's solution[3].

The present study was designed to assess whether prophylactic infusion of bicarbonated Ringer's solution could ameliorate metabolic acidosis in patients undergoing aortic surgery. This population of patients was considered to be appropriate for examining the effects of such an intravenous fluid because these patients have several characteristics that could amplify any differences in fluid efficacy. For example, these patients receive large volumes of crystalloid fluid and they all undergo invasive monitoring at our institution. Because of the invasiveness of the operative procedure, the patients sometimes have complications related to the acid-base balance. Therefore, the patients were considered to offer an excellent opportunity to detect differences that might be caused by different intravenous fluids.

Patients and Methods

The subjects were 20 patients who were scheduled for elective surgery on infrarenal aortic aneurysms from June 2003 through May 2005. Patients were excluded if they had severe hepatic, renal, or pulmonary dysfunction or congestive heart failure, or were classified as physical status IV according to the American Society of Anesthesiologists. The surgical exclusion criterion was suprarenal clamping. The patients were randomly assigned to receive either bicarbonated Ringer's (BR) solution (Ajinomoto Pharmaceutical Co. Ltd., Tokyo, Japan) or acetated Ringer's (AR) solution (Veen F, Nikken Chemicals Co. Ltd., Tokyo, Japan). The researchers were not included in the anesthetists in charge of the surgery. The composition of both solutions is shown in **Table 1**. The BR solution used in this study is a new product, which has been used since 2002 as an experimental intravenous fluids during abdominal surgery with the approval of IRB of Nippon Medical School Hospital. The dosage of the fluid was that used in previous laboratory studies. Informed consent was obtained from each patient before surgery.

Patients were not premedicated. After arrival in the operating theater, monitors were applied and a lumbar epidural catheter was inserted in some patients for postoperative pain management. General anesthesia was induced with intravenous propofol, fentanyl, and vecuronium, and was maintained with sevoflurane (1 to 2.5%), while additional doses of vecuronium and fentanyl were administered as appropriate. Mechanical ventilation was performed to maintain the PaO_2 at 150 to 200 mmHg and the $PaCO_2$ as close as possible to 40 mmHg. A two-line central venous catheter was placed in the right internal jugular vein. Intraoperative parameters for monitoring included the end-tidal $PaCO_2$, electrocardiogram, arterial blood pressure (ABP), central venous pressure (CVP), pulse oximetry, urinary bladder temperature, and arterial blood gases. During the operation, the patient's temperature was kept constant with fluid warmers and warming blankets.

The rate of fluid replacement was adjusted according to the CVP, ABP, and urine volume. Intraoperatively, we aimed to maintain the CVP between 6 and 12 mmHg by using colloid and each crystalloid fluid. Packed red blood cells were transfused when the hemoglobin fell below 10 g/dL. Dopamine (3～5 μg/kg/min) was administered when systolic ABP was fall below 80 mmHg.

Table 2 Patient characterics

	BR Group (n = 10)	AR Group (n = 10)
Age (yrs)	68.6 ± 4.7	69.2 ± 4.1
Weight (kg)	56.6 ± 7.5	68.2 ± 10.9
ALT/AST	27.5 ± 7.5/29.7 ± 8.6	28.7 ± 8.5/29.5 ± 6.6
Creatinine	0.96 ± 0.38	0.97 ± 0.25
Duration of surgery (mins)	295 ± 73	270 ± 88
Aortic clamping (mins)	115 ± 22	108 ± 26
Cases of dopamine use (n)	3	2

BR: bicarbonated Ringer's solution
AR: acetated Ringer's solution
ALT: alanine aminotransferase
AST: asparate aminotransferase

Table 3 Hemodynamic changes during surgery

	T0	T1	T2	T3
SBP (BR group)	110 ± 15	111 ± 7	94 ± 7	108 ± 16
(AR group)	113 ± 18	108 ± 8	91 ± 8	103 ± 15
CVP (BR group)	7 ± 3	9 ± 4	6 ± 3	7 ± 3
(AR group)	7 ± 4	8 ± 4	5 ± 4	6 ± 3

BR: bicarbonated Ringer's solution
AR: acetated Ringer's solution
SBP: systolic blood pressure
CVP: central venous pressure

An arterial blood sample was withdrawn to measure baseline values (T0) under stable anesthetic conditions before surgical incision. The pH and $PaCO_2$ (standard electrodes) were measured with a bloodgas analyzer (Radiometer ABL 625, Radiometer, Copenhagen, Denmark), and the base excess (BE) was calculated with the Henderson-Hasselbach equation and the formula of Siggaard-Andersen. Subsequent blood samples were obtained 5 min before reperfusion (T1), 5 min after reperfusion (T2), and 30 min after reperfusion (T3). Urine output and body temperature were measured, and the volume of blood loss was estimated. The cardiovascular variables, urine output, and body temperature were monitored and recorded during anesthesia.

Statistical analysis. Statistical analysis was performed using Statview Version 5 (Abacus Concepts, Berkeley, CA, USA). The measured and calculated parameters all showed a normal distribution and are presented as the mean ± SD, unless otherwise indicated. Student's *t*-test for unpaired data was used for analysis of differences between the groups. Differences among repeated measures were assessed with analysis of variance and Scheffe's F test. A p value < 0.05 was considered statistically significant.

Results

The clinical characteristics of the subjects are presented in **Table 2**. There were no significant differences in age, weight, duration of surgery, the values of aminotransferases or creatinine, or aortic clamping time between the groups. The target CVP was maintained throughout the investigation period. There were no significant differences between the groups with regard to systolic ABP, CVP, urine output, or body temperature at any time (**Table 3**). The fluids infused in each group and the pre-unclamp and total infusion volumes are summarized in **Table 4**. There were no significant differences in the total volume of crystalloid or colloid infused, or the amount of blood transfused. Furthermore, there were no significant differences between the groups with respect to estimated blood loss and urine output (**Table 4**).

Table 4 Operative fluid balance

	BR Group (n = 10)	AR Group (n = 10)
Volume of Crystalloid infusion (pre-unclamp) (ml)	856 ± 186	866 ± 210
(total) (ml)	4,480 ± 857	4,061 ± 871
Volume of Colloid infusion (pre-unclamp) (ml)	605 ± 121	625 ± 178
(total) (ml)	777 ± 342	825 ± 334
Cell salvaged blood (pre-unclamp) (ml)	0	0
(total) (ml)	620 ± 268	766 ± 316
Blood transfusion (pre-unclamp) (ml)	0	0
(total) (ml)	448 ± 225	364 ± 158
Estimated blood loss (pre-unclamp) (ml)	90 ± 45	95 ± 38
(total) (ml)	531 ± 325	645 ± 225
Urine production (pre-unclamp) (ml)	90 ± 36	95 ± 40
(total) (ml)	645 ± 125	548 ± 245

BR: bicarbonated Ringer's solution
AR: acetated Ringer's solution

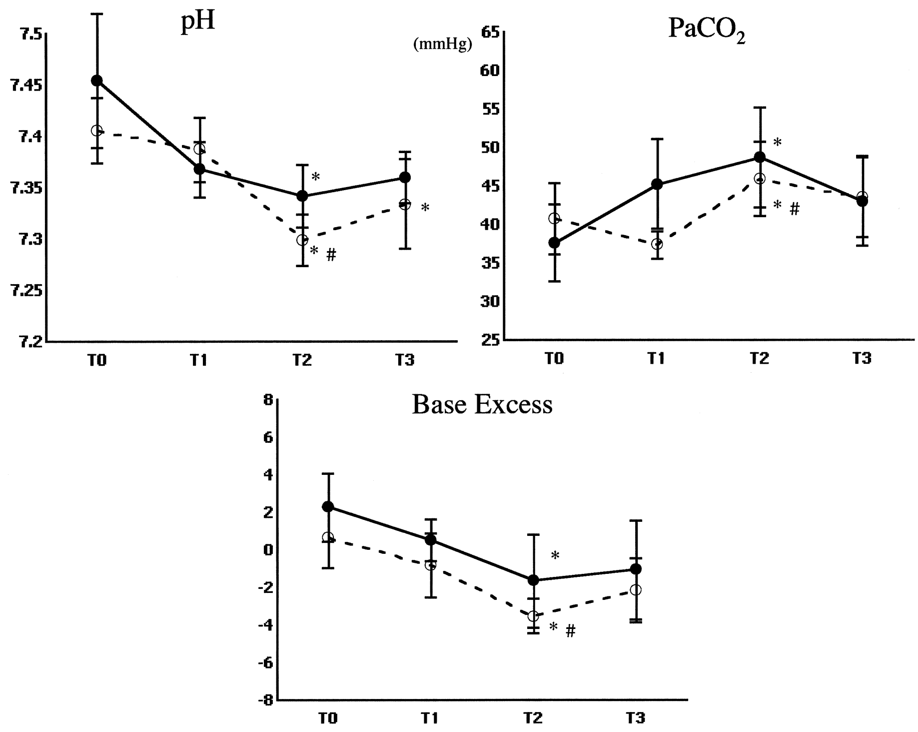

Fig. 1 Measured and calculated values (mean ± SD) at the different measuring points. Open circles, acetated Ringer's solution group; filled circles, bicarbonated Ringer's solution group. *Intragroup differences (compared with T0), # (compared with T1), $P<0.05$. There were no significant differences in pH or base excess between the groups throughout the study period.

Fig. 1 shows the pH, $PaCO_2$, and BE data obtained at the four time points. Somewhat unexpectedly, there were no significant differences in pH between the groups throughout the study period. The pH initially showed a slight decrease in both groups. After unclamping of the aorta, an additional decrease in pH was observed in both groups (T0 to T2). The $PaCO_2$ did not show major variations from baseline values throughout the study period, except for a slight increase at T2 in both groups. Changes in BE were similar to those in pH.

No adverse drug reactions occurred in either group.

Discussion

There were no significant differences in the acid-base balance between patients infused with Ringer's solution containing bicarbonate or acetate during elective infrarenal aortic aneurysm repair, although the pH and BE of the BR group were persistently higher than those of the AR group after unclamping of the aorta.

HCO_3^- is the physiological buffer of the body, and thus is the most effective buffer to compensate for metabolic acidosis, but bicarbonated Ringer's solution had not been available until recently because HCO_3^- formed a sediment with calcium or magnesium in the solution. The bicarbonated Ringer's solution used in this study is a new product that contains chelated calcium citrate and chelated magnesium citrate to prevent the formation of a sediment with bicarbonate at normal temperatures[3]. Lactate has been traditionally accepted as the best substitute for bicarbonate in the treatment of metabolic acidosis since the early 1930s[2]. Lactate must be metabolized to bicarbonate in the liver before it acts as a buffer. However, infused lactate is significantly slower at increasing the bicarbonate level than is infused acetate or pyruvate, indicating that additional metabolic steps are required. Furthermore, administration of lactate has several disadvantages, including its accumulation in patients with decreased liver perfusion or hepatic dysfunction[4], as well as the increase in lactate caused by anaerobic glycolysis in hemorrhagic shock[5].

More recently, acetate has been used instead of lactate because it can be metabolized in organs other than the liver and kidney[4], and is converted to bicarbonate more readily than to lactate. Therefore, it is considered that acetated Ringer's solution should be more effective than a lactated solution in patients with liver dysfunction. However, bicarbonated Ringer's solution showed a more rapid buffering action than acetated Ringer's solution in a previous study[3], probably because of the delay until acetate is converted to bicarbonate. Furthermore, it has been reported that the acetate utilization rate is reduced by about one-third in diabetic ketoacidosis and after hepatectomy, indicating that its metabolism is not always complete[6]. Some studies have suggested that acetate has a vasodilatory effect and exerts a depressant action on the cardiovascular system[7–10]. There is also evidence that high concentrations of acetate can decrease ATP production and reduce tissue ATP concentrations, which will ultimately result in impaired myocardial contraction[11]. Unlike lactate and acetate, the effect of bicarbonate that is administered directly does not depend on its metabolism[2]. In this study, it might be possible that acetate has the good buffering effect, because no significant differences were in pH or BE between the BR and AR groups. However, the decrease in pH in the AR group was significant at T2 compared with T1, and that was not significant in the BR group. Moreover, no patient with severe liver or renal dysfunction or heart failure was included, and aortic clamping time was 100 to 120 min in each group in this study. More study is needed in the event of critical conditions or a longer cross-clamping time.

In this study, aortic cross-clamping was associated with the development of metabolic acidosis and decreases in pH and BE. Arterial PCO_2 increased after aortic unclamping, along with further decreases in pH and BE. These changes indicate that the patients had significant metabolic academia, which may have been due to the accumulation of lactic acid and other anaerobic metabolic by-products, including CO_2. Persistent severe metabolic acidosis is associated with a poor prognosis[12,13], and clinicians routinely use bicarbonate in order to stabilize the acid-base balance. However, the administration of sodium bicarbonate as a bolus or infusion for treating metabolic acidosis is controversial. There is little evidence of any benefit when bicarbonate is used for lactic acidosis or ketoacidosis[14]. Meanwhile, various studies have demonstrated a correlation between the elevation of lactate, the base deficit, and mortality in critically ill patients[15–17]. It has been suggested that non-survivors might show a decreased ability to correct metabolic acidosis[18]. More study will be needed to clarify the effectiveness of bicarbonate therapy in improving outcomes.

The bicarbonated Ringer's solution used in this study contains citrate to chelate bivalent ion for stability in the solution. Citrate infused rapidly can cause citrate intoxication, which is not caused by the citrate ion but because citrate binds calcium, leading to coagulatory dysfunction. In general, because citrate given intravenously is rapidly metabolized by the liver and excreted in the urine, less citrate remains in the blood. Oi et al.[3] have reported no difference in serum calcium and non-significant shortening in prothrombin time and activated partial thromboplastin time among conventional acetated or lactated Ringer's solution or new solution groups in a hemorrhagic shock model[3], indicating that the concentration of citrate in this solution is not high enough to produce bleeding problems.

It is unclear whether the choice of intravenous fluid has a major influence on the acid-base balance. The administration of bicarbonated Ringer's solution during elective abdominal aortic surgery did not have a significant effect compared with acetated Ringer's solution on acid-base homeostasis. Because the number of patients in our study was small, we were not able to demonstrate any difference between fluids with respect to mortality. It is possible that bicarbonated Ringer's solution would have advantages in more critical situations, when massive fluid infusion is needed, or in the postoperative state. Further studies are needed to determine whether administration of bicarbonate-buffered fluid will improve the acid-base balance and the prognosis of treated patients.

References

1. Hartmann AF, Senn JE: Studies in the metabolism of sodium r-lactate. I. Response of normal human subjects to the intravenous injection of sodium r-lactate. J Clin Invest 1932; ii: 327–335.
2. Schwartz WB, Waters WC: Lactate versus bicarbonate: A reconsideration of the therapy of metabolic acidosis. Am J Med 1962; 32: 831–834.
3. Oi Y, Terajima K, Kobayashi N, Matsuura A, Sato K, Ogawa R: Effects of bicarbonated Ringer's solution on acid-base status in hemorrhagic shock. Jap J Reanimatology 2004; 23: 73–80.
4. Schumer W, Moss GS, Nyhus LM: Metabolism of lactic acid in the Macacus rhesus monkey in profound shock. Am J Surg 1969; 118: 200–205.
5. Schumer W: Localization of the energy pathway block in shock. Surgery 1968; 64: 55–59.
6. Harper PV, Neal WB, Halavasek GR: Acetate utilization in the dog. Metabolism 1953; 2: 62–68.
7. Ling CS, Lowenstein JM: Metabolic control of the circulation. Effects of acetate and pyruvate. J Clin Invest 1978; 62: 1029–1038.
8. Kirkendol RL, Person JE, Bower JD, Holbert RD: Myocardial depressant effects of sodium acetate. Cardiovasc Res 1978; 12: 127–136.
9. Olinger GN, Werner PH, Bonchek LI, Boerboom LE: Vasodilator effects of the sodium acetate in pooled protein fraction. Ann Surg 1979; 190: 305–311.
10. Hakim RM, Pontzer MA, Tilton D, Lazarus JM, Gottlieb M: Effects of acetate and bicarbonate dialysate in stable chronic dialysis patients. Kidney Int 1985; 28: 535–540.
11. 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 1997; 52: 755–760.
12. Aggarwal S, Kang Y, Freman JA, Fortunato JA, Pinsky MR: Postreperfusion syndrome: cardiovascular collapse following hepatic reperfusion during liver transplantation. Transplant Proc 1987; 19: 54–55.
13. Nakasuji M, Bookallil MJ: Pathophysiological mechanisms of postrevascularization hyperkalemia in orthotopic liver transplantation. Anesth Analg 2000; 91: 1351–1355.
14. Forsythe SM, Schmidt GA: Sodium bicarbonate for the treatment of lactic acidosis. Chest 2000; 117: 260–267.
15. Rutherford EJ, Morris JA, Reed GW, Hall KS: Base deficit stratifies mortality and determines therapy. J Trauma 1992; 33: 417–423.
16. Husain FA, Martin MJ, Mullenix PS, Steele SR, Elliott DC: Serum lactate and base deficit as predictors of mortality and morbidity. Am J Surg 2003; 185: 485–491.
17. Singhal R, Coghill JE, Guy A, Bradbury AW, Adam DJ, Sciven JM: Serum lactate and base deficit as predictors of mortality after ruptured abdominal aortic aneurysm repair. Eur J Vasc Endvasc Surg 2005; 30: 263–266.
18. Nimmo GR, Mackenzie SJ, Walker S, Grant IS: Acid base response to high volume hemofiltration in the critically ill patient. Nephrol Dial Transplant 1993; 8: 854–857.

(Received, September 9, 2005)
(Accepted, October 25, 2005)