Artificial Organs
25(2):99–108, Blackwell Science, Inc.

Better Correction of Metabolic Acidosis, Blood Pressure Control, and Phagocytosis with Bicarbonate Compared to Lactate Solution in Acute Peritoneal Dialysis

*Visith Thongboonkerd, *Dusit Lumlertgul, and †Volaluck Supajatura

**Renal Division, Department of Medicine; and †Department of Microbiology, Faculty of Medicine, Chiang Mai University, Chiang Mai,Thailand*

Abstract: Lactate solution has been the standard dialysate fluid for a long time. However, it tends to convert back into lactic acid in poor tissue-perfusion states. The aim of this study was to evaluate the efficacy of magnesium (Mg)- and calcium (Ca)-free bicarbonate solution compared with lactate solution in acute peritoneal dialysis (PD). Renal failure patients who were indicated for dialysis and needed acute PD were classified as shock and nonshock groups, and then were randomized to receive either bicarbonate or lactate solution. Twenty patients were enrolled in this study (5 in each subgroup). In the shock group, there were more rapid improvements and significantly higher levels of blood pH (7.40 ± 0.04 versus 7.28 ± 0.05, $p < 0.05$), serum bicarbonate (23.30 ± 1.46 versus 18.37 ± 1.25 mmol/L, $p < 0.05$), systolic pressure (106.80 ± 3.68 versus 97.44 ± 3.94 mm Hg, $p < 0.05$), mean arterial pressure (80.72 ± 2.01 versus 73.28 ± 2.41 mm Hg, $p < 0.05$), percentages of phagocytosis of circulating leukocytes (65.85% ± 2.22 versus 52.12% ± 2.71, $p < 0.05$), and percentages of positive nitroblue tetrazolium (NBT) reduction test without and with stimulation (14.43 ± 1.93 versus 9.43 ± 2.12, $p < 0.05$ and 65.08 ± 6.80 versus 50.23 ± 4.21, $p < 0.05$, respectively) in the bicarbonate subgroup compared with the lactate subgroup. In the nonshock group, blood pH, serum bicarbonate, and phagocytosis assays in both subgroups were comparable. Lactic acidosis was more rapidly recovered and was significantly lower with bicarbonate solution for both shock and nonshock groups (3.63 ± 0.37 versus 5.21 ± 0.30 mmol/L, $p < 0.05$ and 2.92 ± 0.40 versus 3.44 ± 0.34 mmol/L, $p < 0.05$, respectively). Peritoneal urea and creatinine clearances in both subgroups were comparable for both shock and nonshock groups. There was no peritonitis observed during the study. Serum Mg and Ca levels in the bicarbonate subgroup were significantly lower, but no clinical and electrocardiographic abnormality were observed. We concluded that Mg- and Ca-free bicarbonate solution could be safely used and had better outcomes in correction of metabolic acidosis, blood pressure control, and nonspecific systemic host defense with comparable efficacy when compared to lactate solution. It should be the dialysate of choice for acute PD especially in the poor tissue-perfusion states such as shock, lactic acidosis, and multiple organ failure. **Key Words:** Acute peritoneal dialysis—Bicarbonate—Lactate—Phagocytosis—Metabolic acidosis—Magnesium- and calcium-free dialysate.

Hemodialysis (HD) and other modalities of blood purification cannot be performed in every renal failure patient who needs dialysis therapy. Treatment is limited by contraindication for HD, especially hemodynamic instability. Some centers have no facility to perform this procedure as promptly as required, and some patients cannot afford the expense. Peritoneal dialysis (PD) is then an important tool for these situations.

Received May 2000; revised October 2000.
Address correspondence and reprint requests to Dr. Dusit Lumlertgul, Professor of Medicine, Renal Division, Department of Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand. E-mail: dlumlert@mail.med.cmu.ac.th

Lactate solution has been the standard dialysate solution for more than 15 years. It can be converted to bicarbonate by using a pyruvate dehydrogenase enzyme in the tissues of mainly the liver and muscles (1,2). Bicarbonate then is diffused throughout the blood circulation system. Thereafter, serum bicarbonate is elevated, and metabolic derangement, such as metabolic acidosis and hyperkalemia, also are improved.

However, poor tissue-perfusion states are considered problematic in the conversion of lactate to bicarbonate (1,2) that, instead, tends to convert back into lactic acid, which then accumulates in the blood stream and worsens metabolic acidosis. Therefore,

the application of lactate solution for PD in patients with shock or other poor tissue-perfusion states should be debated.

Bicarbonate solution is dated and is limited in its use by precipitation of magnesium (Mg) and calcium (Ca) salts (3). However, it has been revived recently in continuous ambulatory peritoneal dialysis (CAPD)without causing a precipitation problem when using a 2 chambered bag system (4,5). Several studies, in vitro and in vivo, have shown the advantages of bicarbonate solution in the correction of metabolic acidosis and local peritoneal host defense (6–8). However, acute PD usually is introduced to acute renal failure (ARF) patients with hypercatabolic states, in which Mg and Ca are prone to be at high levels. Moreover, acute PD is usually performed in the ICU for a short period of time, usually 1 week during the critical period, when HD is contraindicated. Consequently, hypomagnesemia and hypocalcemia are uncommon, and due to close monitoring and the availability of safe intravenous replacement of both substances, Mg- and Ca-free dialysate solutions may be useful for short-term acute PD in the ICU.

The aims of this study were to evaluate the effects of bicarbonate solution on metabolic acidosis, hemodynamics, and systemic host defense in a poor tissue-perfusion state compared with lactate solution. Also, the usefulness and complications of Mg- and Ca-free bicarbonate solution in acute PD for renal failure patients are examined.

MATERIALS AND METHODS

Patients

The study was conducted in the ICU of Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University, Thailand. Renal failure patients with hypercatabolic states and intractable metabolic acidosis, which were contraindicated or could not be treated with HD, were enrolled in this study. They were classified as shock and nonshock groups and were randomized to receive either lactate or bicarbonate solution. Patients with a history of abdominal surgery or abdominal infections were excluded.

Dialysate solutions

The compositions of lactate and Mg- and Ca-free bicarbonate solutions are shown in Table 1. The bicarbonate solution was made in Maharaj Nakorn Chiang Mai Hospital by the adjustment of glucose and sodium chloride concentrations to achieve the same osmolarility as lactate solution for a comparison of efficacy. The amount of bicarbonate was adjusted for a pH level of 7.8, which differed from the pH level of 5.5 for the lactate solution. To avoid bacterial colonization, bicarbonate was added to the solution immediately before use.

Protocols

Acute PD was mandated by the Japan Medical Supply (JMS, Tokyo, Japan) peritoneal dialysis administration set. The dialysate volume for each cycle was 1 L for patients whose body weight was 50 kg or less and 1.5 L for those weighing more than 50 kg. The solution was retained inside the peritoneal cavity for 30 min during each cycle to study clearance of the solutes. Outflow volume was recorded for every cycle. Blood and outflow dialysate for urea, creatinine (Cr), bicarbonate, and lactate, and blood only for pH, Mg, and Ca were measured after every 6 cycles. Blood for phagocytic assays was collected after every 12 cycles. Blood pressure was recorded routinely in the ICU.

Blood and dialysate chemistry

Urea, Cr, bicarbonate, lactate, Mg, Ca, and pH levels were measured by automated methods.

Phagocytic assays

Preparation for Candida albicans suspension

Candida albicans colonies from Sabouraud dextrose agar were isolated in sterile normal saline solution and centrifuged 5 times at 1,000 rpm for 5 min at room temperature. The concentration of suspension was adjusted to 2.0×10^9 cells/L by sterile phosphate buffered saline (PBS) solution pH 7.4.

Preparation for nitroblue tetrazolium solution

Nitroblue tetrazolium (NBT) solution was prepared by 1 mg of NBT salt in 1 ml of sterile PBS solution pH 7.4.

Test for phagocytic capacity

Heparinized whole blood at 1.0 ml was mixed with 0.2 ml of *C. albicans* suspension. The mixture then was incubated at 37°C for 5 min, smeared on the slides, and stained with Wright's stain. The percentage of phagocytosis was evaluated by counting

TABLE 1. *Compositions of the dialysate solutions*

Solutes	Lactate	Bicarbonate
Sodium (mmol/L)	150	135
Chloride (mmol/L)	100	91
Bicarbonate (mmol/L)	0	44.6
Lactate (mmol/L)	55.5	0
Calcium (mmol/L)	2.6	0
Magnesium (mmol/L)	2.6	0
Glucose (%g)	1.5	2.125
Osmolarity (mOsm/L)	380	380
pH	5.5	7.8

phagocytic cells with ingested *C. albicans* in vacuoles and comparing them with 200 white blood cells.

NBT reduction test

Heparinized whole blood at 1.0 ml was mixed with 0.2 ml of NBT solution. The mixture was incubated at 37°C for 15 min and then at room temperature for 10 min. Thick smears were stained with Wright's stain. Dark-blue precipitations could be seen in the cytoplasm of NBT positive cells from reduced NBT by peroxidase enzyme of the leukocytes. The percentage of NBT positive cells was calculated by comparing them with a total of 200 white blood cells.

NBT reduction test with stimulation by C. albicans

Heparinized whole blood at 1.0 ml was mixed with 0.2 ml of NBT solution and 0.2 ml of *C. albicans* suspension. The mixture was incubated at 37°C for 15 min and then at room temperature for 10 min. Thick smears were stained with Wright's stain. Dark-blue precipitation could be seen in the cytoplasm of NBT positive cells from reduced NBT. The percentage of NBT positive cells was calculated by comparing them with a total of 200 white blood cells.

Peritoneal solute clearance

Peritoneal solute clearance of each cycle was calculated by the following equation:

$$\text{Peritoneal solute clearance (ml/min)} = (D \times P)/(V_d \times T) \quad (1)$$

where D is the dialysate concentration of solutes (mmol/L), P is the plasma concentration of solutes (mmol/L), V_d is the drained dialysate volume (ml), and T is the duration of each cycle of acute PD (min).

Statistical analysis

All parameters were presented as mean ± SEM. Comparisons between 2 subgroups at each time point were assessed by Wilcoxon's method while comparisons of overall values of each parameter were assessed by the unpaired t test. A p value of <0.05 was considered statistically significant.

RESULTS

Patients

Twenty renal failure patients were enrolled in this study. The number, age, serum albumin, and APACHE II scores were comparable for each subgroup (Table 2). All patients in the shock group suffered from septic shock and multiple organ failure. The volume of dialysate, which was used in this study, was almost 1.5 L except for 1 patient each in the shock-bicarbonate subgroup, the shock-lactate subgroup, and the nonshock-bicarbonate subgroup. The number of cycles performed in each subgroup was comparable (Table 2).

Blood pH

All patients in this study had severe metabolic acidosis. Baseline pH levels in the lactate and bicarbonate subgroups were comparable to both the shock and nonshock groups. In the shock group, blood pH levels in the bicarbonate subgroup improved more rapidly and were significantly better during Cycles 6–42 compared with the lactate subgroup, but they reached comparable levels thereafter. However, the overall levels of blood pH were significantly better in the bicarbonate subgroup (Table 3, Fig. 1A). In the nonshock group, there were no significant differences between the 2 subgroups (Table 4, Fig. 1B).

Serum bicarbonate

As in blood pH, all patients previously had low levels of serum bicarbonate. The baseline levels in both subgroups were comparable. In the shock group, the levels in the bicarbonate subgroup improved more rapidly and were significantly better for most of the cycles, except for Cycles 36 and 42. The overall levels in the bicarbonate subgroup also were significantly higher (Table 3, Fig. 1C). In the nonshock group, only Cycles 12, 30, and 54 showed any significant differences. However, overall levels were comparable between both subgroups (Table 4, Fig. 1D).

Blood lactate

In the shock group, the baseline lactate levels in the bicarbonate subgroup were higher than those in the lactate subgroup. Conversely, they were signifi-

TABLE 2. *Patient characteristics, volume of dialysate used, and number of cycles performed for each patient*

Group	Lactate subgroup	Bicarbonate subgroup	p values
Shock (n)	(5)	(5)	
Age (years)	48.0 ± 10.2	44.8 ± 10.0	0.828
Albumin (g/L)	31.5 ± 1.6	30.7 ± 1.8	0.760
APACHE II score	26.0 ± 3.0	23.3 ± 1.7	0.459
Volume of dialysate (L)	1.40 ± 0.01	1.40 ± 0.01	1.000
Number of cycles	19.0 ± 1.8	18.8 ± 1.1	0.785
Nonshock (n)	(5)	(5)	
Age (years)	43.5 ± 9.5	39.3 ± 12.6	0.797
Albumin (g/L)	33.5 ± 1.6	32.0 ± 1.4	0.502
APACHE II score	24.8 ± 1.7	26.5 ± 0.5	0.350
Volume of dialysate (L)	1.50 ± 0.00	1.40 ± 0.01	0.317
Number of cycles	18.3 ± 1.7	18.8 ± 0.9	1.000
Total number	10	10	

APACHE II: Acute Physiologic Assessment and Chronic Health Evaluation (a classification system of disease severity).

TABLE 3. *Blood pH, serum bicarbonate, blood lactate, phagocytic assays, peritoneal solute clearance, serum Mg, and serum Ca during dialysis in the shock group*

Parameters	Subgroup	Cycle 0	Cycle 12	Cycle 24	Cycle 36	Cycle 48	Cycle 60	Cycle 72	Overall
Blood pH	Lactate	7.03 ± 0.05	7.05 ± 0.04	7.27 ± 0.04	7.35 ± 0.05	7.40 ± 0.06	7.46 ± 0.05	7.47 ± 0.05	7.28 ± 0.05
	HCO_3	7.04 ± 0.04	7.30 ± 0.03[a]	7.46 ± 0.06[a]	7.48 ± 0.03[a]	7.45 ± 0.03	7.46 ± 0.04	7.48 ± 0.04	7.40 ± 0.04[a]
Serum HCO_3 (mmol/L)	Lactate	10.0 ± 1.6	14.3 ± 1.3	19.2 ± 1.2	22.5 ± 1.4	22.6 ± 1.6	19.4 ± 2.7	21.2 ± 2.5	18.3 ± 1.3
	HCO_3	11.3 ± 1.6	21.2 ± 1.8[a]	24.3 ± 1.3[a]	25.5 ± 1.5	27.4 ± 1.7[a]	28.0 ± 2.2[a]	27.4 ± 2.4[a]	23.3 ± 1.5[a]
Blood lactate (mmol/L)	Lactate	4.9 ± 0.4	6.3 ± 0.4	6.5 ± 0.4	4.9 ± 0.5	4.4 ± 0.7	4.3 ± 0.4	4.0 ± 0.5	5.2 ± 0.3
	HCO_3	6.3 ± 0.5[a]	5.2 ± 0.5[a]	3.8 ± 0.8[a]	3.3 ± 0.6[a]	2.6 ± 0.6[a]	2.5 ± 0.6[a]	2.0 ± 0.5[a]	3.6 ± 0.4[a]
%Phagocytic cells with *C. albicans*	Lactate	39.3 ± 3.8	41.1 ± 2.2	52.3 ± 3.3	59.5 ± 4.2	39.1 ± 3.7	81.2 ± 3.6	NA	52.1 ± 2.7
	HCO_3	33.8 ± 4.4	54.5 ± 2.1[a]	78.2 ± 3.2[a]	61.3 ± 3.8	78.2 ± 3.5[a]	89.1 ± 4.0[a]	NA	65.8 ± 2.2[a]
%Phagocytic cells with reduced NBT	Lactate	7.3 ± 0.9	7.3 ± 0.6	4.0 ± 0.9	8.1 ± 0.7	11.1 ± 0.5	19.0 ± 0.9	NA	9.4 ± 0.6
	HCO_3	7.0 ± 0.8	11.3 ± 0.5[a]	14.3 ± 1.0[a]	18.0 ± 0.8[a]	16.0 ± 0.6[a]	20.1 ± 0.8	NA	14.4 ± 0.7[a]
%Phagocytic cells with reduced NBT and *C. albicans*	Lactate	45.6 ± 3.2	36.3 ± 4.6	50.5 ± 5.0	50.2 ± 5.0	51.2 ± 3.4	68.3 ± 4.1	NA	50.2 ± 3.2
	HCO_3	35.2 ± 2.4[a]	58.5 ± 5.1[a]	74.2 ± 4.7[a]	73.1 ± 3.5[a]	68.2 ± 3.3[a]	82.3 ± 4.2[a]	NA	65.1 ± 3.7[a]
PD urea clearance (ml/min)	Lactate	20.0 ± 4.2	25.3 ± 3.5	30.0 ± 4.2	28.4 ± 2.3	41.9 ± 5.8	28.0 ± 3.5	22.0 ± 2.3	29.8 ± 2.8
	HCO_3	14.5 ± 4.1	23.2 ± 4.1	36.0 ± 3.1	31.0 ± 2.2	32.2 ± 1.8[a]	35.0 ± 4.4	50.3 ± 6.1[a]	32.4 ± 3.0
PD Cr clearance (ml/min)	Lactate	14.4 ± 3.3	31.6 ± 2.0	30.5 ± 3.0	25.3 ± 4.0	34.4 ± 2.2	24.2 ± 3.0	27.1 ± 1.6	25.0 ± 1.5
	HCO_3	17.1 ± 3.0	22.1 ± 1.8[a]	26.6 ± 4.4	30.3 ± 3.3	31.6 ± 3.0	23.1 ± 2.0	28.7 ± 1.8[a]	26.2 ± 1.2
Serum Mg (mmol/L)	Lactate	0.66 ± 0.02	0.91 ± 0.03	1.11 ± 0.03	1.15 ± 0.04	0.91 ± 0.03	1.03 ± 0.04	1.15 ± 0.03	0.97 ± 0.02
	HCO_3	0.82 ± 0.03[a]	0.91 ± 0.04	0.74 ± 0.03[a]	1.11 ± 0.04	0.91 ± 0.04	0.82 ± 0.03[a]	0.78 ± 0.03[a]	0.85 ± 0.03[a]
Serum Ca (mmol/L)	Lactate	1.35 ± 0.15	1.78 ± 0.15	1.53 ± 0.15	1.83 ± 0.13	1.80 ± 0.08	1.83 ± 0.18	1.80 ± 0.10	1.68 ± 0.04
	HCO_3	1.40 ± 0.18	1.33 ± 0.13[a]	1.55 ± 0.18	1.43 ± 0.10[a]	1.33 ± 0.1[a]	1.40 ± 0.15[a]	1.45 ± 0.13[a]	1.42 ± 0.06[a]

[a] $p < 0.05$ in comparison between lactate and bicarbonate subgroups.
Mg: magnesium, Ca: calcium, NBT: nitroblue tetrazolium, PD: peritoneal dialysis, Cr: creatinine, HCO_3: bicarbonate, NA: not applicable.

cantly lower for most of the cycles, except for Cycle 6 (Table 3, Fig. 1E). In the nonshock group, the baseline levels in both subgroups were comparable. The levels in the bicarbonate subgroup were significantly lower for Cycles 12, 36, 42, 48, and 60. The overall levels in the bicarbonate subgroup also were significantly lower than in the lactate subgroup (Table 4, Fig. 1F).

TABLE 4. *Blood pH, serum bicarbonate, blood lactate, phagocytic assays, peritoneal solute clearance, serum Mg, and serum Ca during dialysis in the nonshock group*

Parameters	Subgroup	Cycle 0	Cycle 12	Cycle 24	Cycle 36	Cycle 48	Cycle 60	Cycle 72	Overall
Blood pH	Lactate	7.10 ± 0.03	7.28 ± 0.04	7.41 ± 0.02	7.47 ± 0.02	7.45 ± 0.03	7.46 ± 0.03	7.46 ± 0.03	7.38 ± 0.03
	HCO_3	7.11 ± 0.02	7.31 ± 0.03	7.42 ± 0.03	7.48 ± 0.02	7.47 ± 0.04	7.46 ± 0.03	7.46 ± 0.04	7.40 ± 0.03
Serum HCO_3 (mmol/L)	Lactate	13.5 ± 1.5	16.0 ± 1.3	23.5 ± 1.5	27.1 ± 1.7	29.3 ± 2.0	29.6 ± 1.6	32.0 ± 1.6	24.0 ± 1.4
	HCO_3	15.0 ± 1.9	20.2 ± 1.2[a]	23.3 ± 1.6	26.2 ± 1.8	28.4 ± 1.5	30.5 ± 2.6	30.3 ± 2.2	25.1 ± 1.5
Blood lactate (mmol/L)	Lactate	5.4 ± 0.8	5.3 ± 0.3	3.8 ± 0.3	3.5 ± 0.3	2.9 ± 0.3	2.3 ± 0.3	2.0 ± 0.4	3.5 ± 0.2
	HCO_3	5.6 ± 0.6	4.3 ± 0.4[a]	3.4 ± 0.3	2.5 ± 0.4[a]	1.8 ± 0.3[a]	1.5 ± 0.4[a]	1.4 ± 0.3	2.9 ± 0.2[a]
%Phagocytic cells with *C. albicans*	Lactate	65.6 ± 4.2	63.6 ± 4.1	58.4 ± 3.0	72.0 ± 4.0	72.5 ± 4.5	83.2 ± 3.2	NA	68.1 ± 2.4
	HCO_3	65.0 ± 3.3	60.5 ± 4.2	68.5 ± 3.1[a]	55.0 ± 4.2[a]	76.5 ± 3.4	83.1 ± 3.0	NA	69.2 ± 2.2
%Phagocytic cells with reduced NBT	Lactate	10.2 ± 0.5	10.6 ± 0.9	18.3 ± 0.7	14.5 ± 0.5	13.1 ± 0.8	11.5 ± 0.6	NA	13.0 ± 0.7
	HCO_3	5.5 ± 0.6[a]	12.5 ± 0.8	12.1 ± 0.8[a]	12.0 ± 0.5[a]	13.0 ± 0.6	14.1 ± 0.5[a]	NA	14.4 ± 0.7
%Phagocytic cells with reduced NBT and *C. albicans*	Lactate	69.6 ± 5.2	68.6 ± 3.1	67.6 ± 4.2	77.0 ± 5.1	66.0 ± 2.3	80.5 ± 4.5	NA	71.6 ± 3.0
	HCO_3	69.5 ± 5.0	72.0 ± 4.2	70.1 ± 4.3	80.5 ± 5.3	83.5 ± 3.2[a]	75.0 ± 5.0	NA	75.1 ± 3.3
PD urea clearance (ml/min)	Lactate	34.3 ± 3.0	35.0 ± 6.1	32.0 ± 4.1	33.6 ± 4.1	38.3 ± 2.4	27.6 ± 1.8	26.8 ± 3.1	30.0 ± 2.4
	HCO_3	25.0 ± 2.6[a]	29.3 ± 4.4	26.5 ± 4.0	26.6 ± 3.2	27.0 ± 2.3[a]	19.4 ± 2.0[a]	25.0 ± 3.2	26.2 ± 2.5
PD Cr clearance (ml/min)	Lactate	16.8 ± 2.2	22.0 ± 1.8	30.5 ± 2.2	19.0 ± 2.8	37.0 ± 2.3	24.2 ± 2.4	20.7 ± 2.0	23.3 ± 1.6
	HCO_3	14.7 ± 3.0	23.8 ± 2.0	21.3 ± 2.4[a]	21.8 ± 3.1	29.6 ± 2.4[a]	14.8 ± 2.2[a]	23.0 ± 3.0	21.1 ± 1.6
Serum Mg (mmol/L)	Lactate	0.86 ± 0.03	0.82 ± 0.03	1.19 ± 0.04	1.15 ± 0.03	1.07 ± 0.03	0.99 ± 0.04	0.99 ± 0.03	0.98 ± 0.02
	HCO_3	0.91 ± 0.04	0.70 ± 0.03[a]	0.66 ± 0.04[a]	0.53 ± 0.03[a]	0.53 ± 0.04[a]	0.62 ± 0.03[a]	0.58 ± 0.03[a]	0.64 ± 0.03[a]
Serum Ca (mmol/L)	Lactate	1.48 ± 0.15	1.50 ± 0.23	1.83 ± 0.20	1.88 ± 0.13	1.68 ± 0.10	1.80 ± 0.18	1.80 ± 0.13	1.70 ± 0.04
	HCO_3	1.40 ± 0.18	1.33 ± 0.20	1.25 ± 0.15[a]	1.30 ± 0.15[a]	1.40 ± 0.13[a]	1.45 ± 0.15[a]	1.40 ± 0.10[a]	1.35 ± 0.06[a]

[a] $p < 0.05$ in comparison between lactate and bicarbonate subgroups.
Mg: magnesium, Ca: calcium, HCO_3: bicarbonate, NBT: nitroblue tetrazolium, PD: peritoneal dialysis, Cr: creatinine, NA: not applicable.

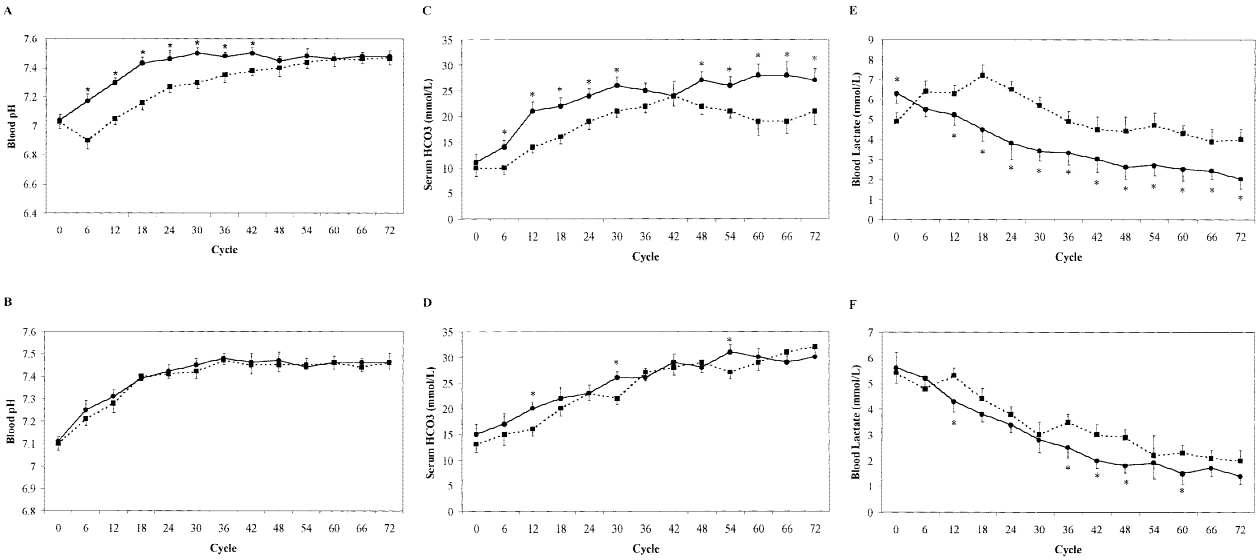

FIG. 1. The graphs show blood pH in the shock **(A)** and nonshock **(B)** group, serum bicarbonate in the shock **(C)** and nonshock group **(D)**, and blood lactate in the shock **(E)** and nonshock group **(F)** (---■--- lactate subgroup, —●— bicarbonate subgroup; *p < 0.05 in comparison between the lactate and bicarbonate subgroups).

Blood pressure

The effects of different dialysate solutions on hypotension in the shock group were analyzed in this study. Systolic pressure levels in the bicarbonate subgroup were significantly higher for most of the time points. The overall systolic pressure levels were 106.80 ± 3.68 mm Hg in the bicarbonate subgroups versus 97.44 ± 3.94 mm Hg in the lactate subgroup, $p < 0.05$ (Fig. 2A). Mean arterial pressure (MAP) levels in the bicarbonate subgroup were significantly higher for some time points. However, the overall MAP levels in the bicarbonate subgroup were significantly higher than in the lactate subgroup (80.72 ± 2.01 mm Hg versus 73.28 ± 2.41 mm Hg, $p < 0.05$) (Fig. 2B).

Phagocytosis assays

Phagocytic capacity

In the shock group, the baseline percentages of phagocytic cells in both subgroups were comparable. The percentages in the bicarbonate subgroup were significantly higher than those in the lactate subgroup for Cycles 12, 24, 48, and 60. The overall percentages in the bicarbonate subgroup also were significantly higher (Table 3, Fig. 3A). In the nonshock group, the percentages in the bicarbonate subgroup were higher for Cycle 24, but lower for Cycle 36. Other time points and overall percentages in both subgroups were comparable (Table 4, Fig. 3B).

NBT reduction test

In the shock group, the percentages of NBT positive cells in both subgroups were comparable, but were significantly higher in the bicarbonate subgroup for Cycles 12, 24, 36, and 48. The overall percentages in the bicarbonate subgroup also were significantly higher (Table 3, Fig. 3C). In the nonshock group, there were crossing interactions between both subgroups. The overall percentages in both subgroups were comparable (Table 4, Fig. 3D).

NBT reduction test with stimulation by C. albicans

In the shock group, the percentages of NBT positive cells in the bicarbonate subgroup were significantly higher for Cycles 12–60 (Table 3, Fig. 3E). In the nonshock group, the percentages of NBT positive cells in the bicarbonate subgroup were higher than those in the lactate subgroup only for Cycle 48. The overall percentages in both subgroups were comparable (Table 4, Fig. 3F).

Peritoneal solute clearance

Peritoneal urea and Cr clearance had many crossing interactions during dialysis. The overall peritoneal urea and Cr clearance in both subgroups were comparable for both shock and nonshock groups (Tables 3 and 4).

Serum Mg and Ca

Serum Mg and Ca levels in the bicarbonate subgroup were significantly lower than those in the lactate subgroup for both the shock and the nonshock groups. However, no clinical signs or symptoms of hypomagnesemia and hypocalcemia were observed during the lower levels of these solutes, and electrocardiographic studies showed no abnormalities (Tables 3 and 4, Fig. 4).

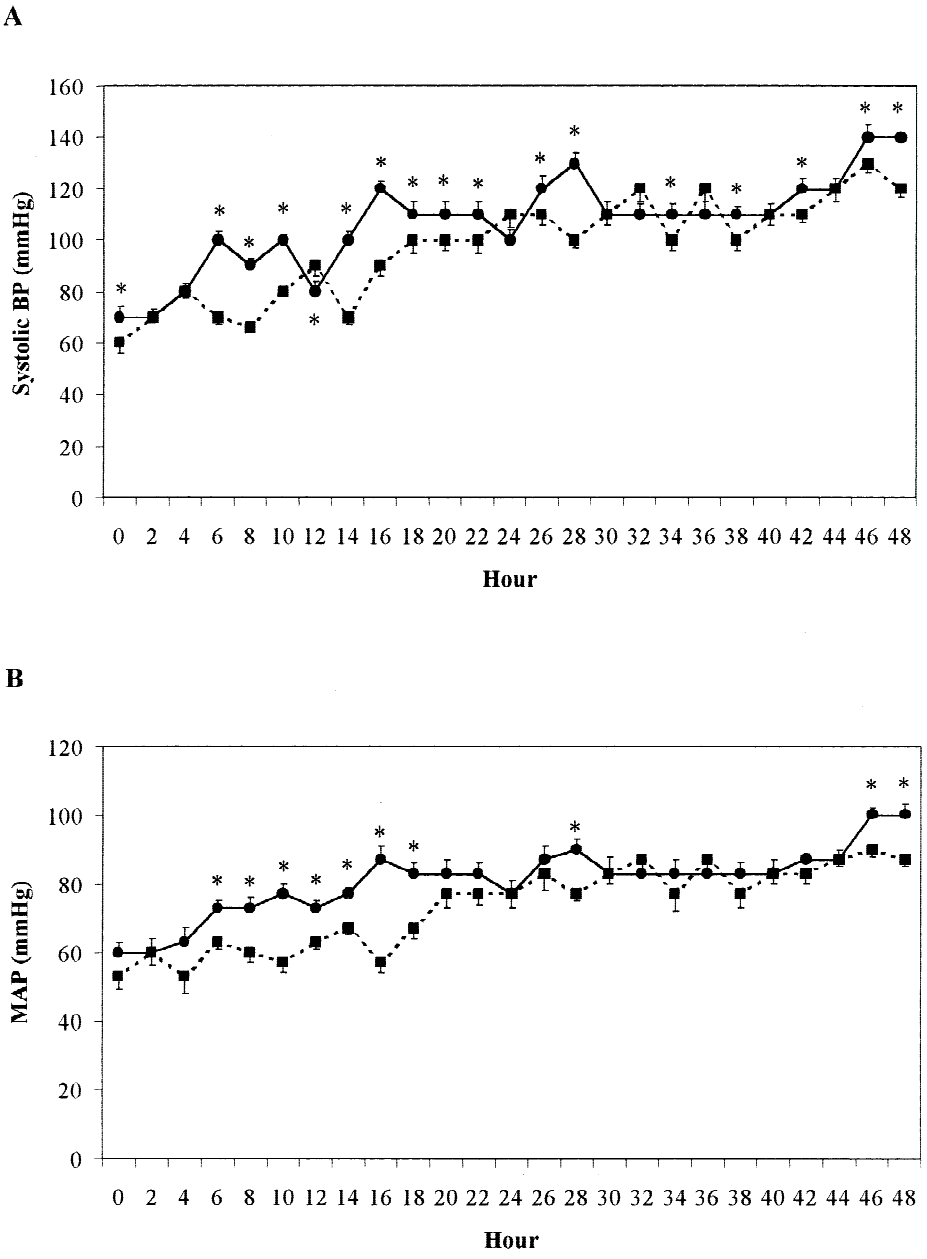

FIG. 2. Shown are systolic blood pressure **(A)** and MAP **(B)** in shock patients during peritoneal dialysis (---■--- lactate subgroup, —●— bicarbonate subgroup; *$p < 0.05$ in comparison between the lactate and bicarbonate subgroups).

Mortality

Three patients died in the shock group (2 in the lactate subgroup and 1 in the bicarbonate subgroup) because of intractable sepsis and septic shock from falciparum malaria, cellulitis, and septic arthritis 48 h after admission. No patients died in the nonshock group.

DISCUSSION

The roles of bicarbonate solution have been studied extensively in CAPD for chronic renal failure (CRF) patients (9,10). PD with bicarbonate solution is strongly associated with better outcomes in peritoneal macrophage, monocyte, mesothelial, and fibroblast cell functions (11,12). Most of these reports have studied PD in vitro. They reported that inhibitory effects on interleukin-1β stimulated an interleukin-6 release from the human peritoneal mesothelial cell, which was observed as being less by using bicarbonate rather than lactate solution (11). Tumor necrotic factor-α generation of peritoneal macrophage was significantly increased by bicarbonate or bicarbonate combined with lactate solution compared to lactate solution alone (7). Biocompatibility also was better by bicarbonate solution (8,11). The rate

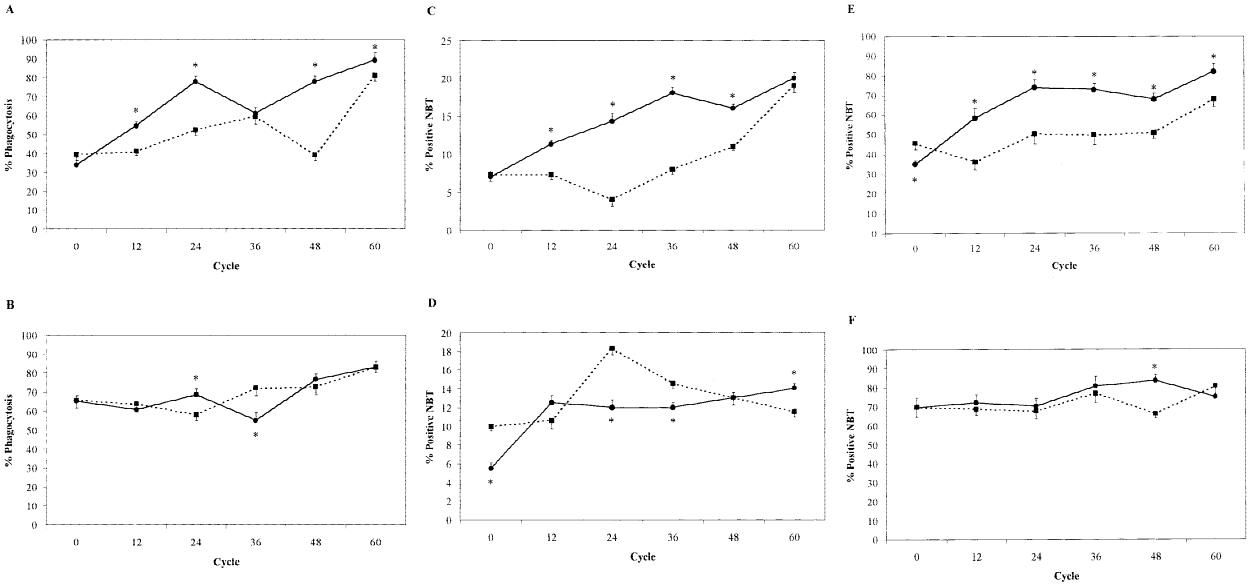

FIG. 3. The phagocytic test in the shock **(A)** and nonshock **(B)** group, the NBT tube test in the shock **(C)** and nonshock group **(D)**, and the NBT tube test with stimulation by *C. albicans* in the shock **(E)** and nonshock group **(F)** are depicted (---■--- lactate subgroup, —●— bicarbonate subgroup; *p < 0.05 in comparison between the lactate and bicarbonate subgroups).

of cell necrosis after 15 min of incubation was increased mostly with glucose/lactate, but not with glucose/bicarbonate and amino acid/bicarbonate solution (13).

The in vivo study by Feriani et al. (9) showed a significant improvement of metabolic acidosis and plasma bicarbonate levels during treatment by bicarbonate solution while no significant change was observed in acidotic patients treated with the conventional lactate-buffered solution.

The pH of dialysate solutions for acidotic patients should be debated. Conventional lactate solutions have pH levels between 5.2 and 5.5 while blood pH levels of the critically acidotic patients are about 6.8 to 7.2. The ordinary target of corrected blood pH is 7.35 to 7.45. This gap can be closed only if lactate converts to bicarbonate normally. In this instance, the correction of metabolic acidosis by dialysate solution alone takes time and mostly benefits PD in

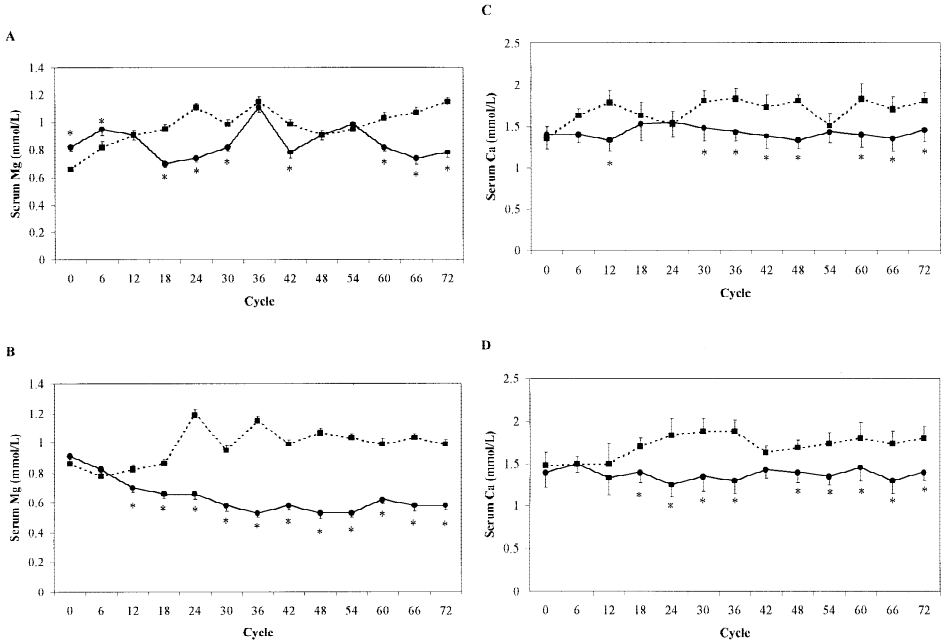

FIG. 4. Shown are serum Mg in the shock **(A)** and nonshock **(B)** group, and serum Ca in the shock **(C)** and nonshock group **(D)** (---■--- lactate subgroup, —●— bicarbonate subgroup; *p < 0.05 in comparison between the lactate and bicarbonate subgroups).

normal tissue-perfusion states, but not for PD in poor tissue-perfusion states. For the latter, the dialysate should be bicarbonate based and should have a higher pH than the conventional lactate solution. Several studies evaluated conventional lactate solution pH 5.2 to 5.5 versus lactate solution pH 7.4 to 7.5 and versus bicarbonate solution pH 7.4 to 7.5 on peritoneal cell functions. They concluded that bicarbonate solution is best regarding cell metabolism, viability, and cytokine release, and lactate solution pH 7.4 to 7.5 was superior to standard lactate solution pH 5.2 to 5.5 (6,13).

Several studies have described the effects of different dialysate solutions on local peritoneal host defenses in CAPD as mentioned perviously. However, there is no information currently available regarding the potential impact of dialysate solution on the systemic host defense, and no study has been documented in acute PD.

Acute PD is still widely used in many areas as mentioned before. Its application is mostly for acute renal failure patients with hypercatabolic states and intractable metabolic and fluid derangement who cannot be treated with PD. It is also used for CRF patients with the same indications. It is usually prescribed in such cases for up to 3 days with a rigid PD catheter. However, for a longer duration with a Tenckhoff catheter, HD can be prescribed instead of the PD catheter.

This research reported on a pilot study comparing bicarbonate with lactate solution on the correction of metabolic acidosis, hemodynamics, and systemic host defense in acute PD. The rationale is that lactate cannot normally convert to bicarbonate, but converts back to lactic acid in poor tissue-perfusion states. The accumulation of lactic acid and its inability to normally correct metabolic acidosis may have some effect on systemic host defense and hemodynamics. This study divided the patients into shock and nonshock groups in order to evaluate these differences.

A poor tissue-perfusion model in this study was septic shock. The number of patients, their age, nutritional status, severity index, number of cycles, and volume of each cycle were comparable for each subgroup. While improvement of blood pH by lactate solution was slower to reach the same final levels as bicarbonate solution in the shock group, there were comparable levels of blood pH for every time point in the nonshock group. This difference might be explained by the impairment of lactate conversion. Therefore, it took quite a long duration for a gradual improvement in blood pH in shock patients who received lactate solution. Nonshock patients received normal lactate conversion as expected. Therefore, the blood pH in the lactate subgroup could be improved as well as that in the bicarbonate subgroup. The changes in serum bicarbonate levels were in concordance with the changes in blood pH and could be explained by the same reason.

Blood lactate levels in the lactate subgroup were significantly higher for both shock and nonshock groups. This implied that, despite the normal conversion of lactate to bicarbonate in the tissues, higher lactate loading caused a greater accumulation of lactate in the blood circulation.

All phagocytosis assays showed significantly better phagocytic capacity and peroxidation in the shock patients using the bicarbonate solution. While phagocytic capacity was evaluated by *C. albicans,* which phagocytes attacked and ingested into their phagosomes, the peroxidation of phagocytes was evaluated by the NBT reduction test (14,15). Reduced NBT by peroxidase enzyme was seen as a blue color. The NBT reduction test, with stimulation by *C. albicans,* then was used to evaluate both phagocytic capacity and the peroxidation of phagocytes. These phagocytic tests referred to a nonspecific systemic host defense that differed from those in previous studies, which were mainly evaluated in local peritoneal host defenses. Despite the initially low phagocytic capacity of the shock group compared to the nonshock group, these percentages were improved rapidly and reached the same final levels at Cycle 60. This benefit might be helpful for infectious renal failure patients for whom early dialysis with proper dialysate solution could improve the nonspecific systemic host defenses that are necessary to eradicate the organisms.

Better blood pH and serum bicarbonate levels might be the correct way to explain the improvement in nonspecific systemic host defense and hemodynamics in the bicarbonate subgroup. However, several factors such as antibiotics, inotropic agents, difference in dialysate sodium, Mg, and Ca should be debated. All septic shock patients had been prescribed antibiotics and/or antimalarial and inotropic agents, which could have affected the systemic host defense as well as the hemodynamics. Further studies of systemic host defense in poor tissue-perfusion states should include conditions other than septic shock. Hypomagnesemia could cause peripheral vasoconstriction, which might increase the blood pressure levels in the bicarbonate subgroup (16). However, hypocalcemia could lower the blood pressure, and lower dialysate sodium has been known as a factor introducing hypotension (16–18). Thus, these counterbalance effects might abolish the effect of

hypomagnesemia. Extracellular calcium has played an important role in phagocytic capacity (19,20). Mg also has a minor effect on the induction of phagocytosis (21). However, phagocytic assays in the bicarbonate subgroup of this study improved conversely with hypocalcemia and hypomagnesemia. This could strengthen the benefits of the bicarbonate solution.

The efficacy of acute PD was determined by peritoneal solute clearance. There was no significant difference between both dialysate solutions used in this study.

PD ordinarily removed Mg and Ca via peritoneal transport (22,23). The most suitable method for replacing these substances is to continually add them into each bag of the dialysate solution at an appropriate concentration (24,25). The 2 chambered bag system, which contains Mg and CaCl, is then necessary for CAPD to prevent hypomagnesemia and hypocalcemia. For acute PD, which is usually performed in ARF patients with hypercatabolic states, a 2 chambered bag may not be necessary. Even if signs and symptoms of hypomagnesemia and hypocalcemia occur, slow intravenous replacement of Mg and Ca can be used safely for the correction of hypomagnesemia and hypocalcemia in the ICU with electrocardiographic (ECG) monitoring.

Despite serum Mg and Ca levels being significantly lower in the bicarbonate subgroup, no clinical signs or symptoms of hypomagnesemia and hypocalcemia were observed. No ECG abnormality of hypomagnesemia or hypocalcemia was seen during the study. Therefore, Mg- and Ca-free bicarbonate solution could be safely used in short-term (up to 72 h) PD.

To avoid bacterial colonization by a high concentration of bicarbonate, bicarbonate was injected into the solution bag immediately before use. No clinical sign or symptom of peritonitis was observed during the study. This technique should be reasonable for patients with acute PD in the ICU, but not for ambulatory patients.

CONCLUSIONS

This study introduced Mg- and Ca-free bicarbonate solution to acute PD in shock patients and found that it had better outcomes in the correction of metabolic acidosis, blood pressure control, and nonspecific systemic host defense compared to lactate solution, which suggested a poor tissue-perfusion state.

Bicarbonate solution provided a comparable efficacy with lactate solution. There was no bacterial colonization or peritonitis seen during the study. Without Mg and CaCl, which can be precipitated with carbonate in bicarbonate solution, this solution could be used safely for short-term (up to 3 days) PD without any clinical signs or symptoms of hypomagnesemia and hypocalcemia. Therefore, this dialysate should be chosen for acute PD, especially in poor tissue-perfusion states such as shock, lactic acidosis, and multiple organ failure.

However, further large-scale, controlled trials should be conducted in renal failure patients who are contraindicated or incapable of being treated with HD for a period of time. There should be much more concern when using acute PD during this critical period.

REFERENCES

1. Kreisberg RA. Lactate homeostasis and lactic acidosis. *Ann Intern Med* 1980;92:227–37.
2. Madias NE. Lactic acidosis. *Kidney Int* 1986;29:752–74.
3. Feriani M, Biasioli S, Borin D, Bragantini L, Brendolan A, Chiaramonte S, Dell'Aquila R, Fabris A, Ronco C, La Greca G. Bicarbonate buffer for CAPD solution. *Trans Am Soc Artif Intern Organs* 1985;31:668–72.
4. Feriani M, Dissegna D, La Greca G, Passlick-Deetjen J. Short-term clinical study with bicarbonate-containing peritoneal dialysis solution. *Perit Dial Int* 1993;13:296–301.
5. Sundaram S, Cendoroglo M, Cooker LA, Jaber BL, Faict D, Holmes CJ, Pereira BJ. Effect of two-chambered bicarbonate lactate-buffered peritoneal dialysis fluids on peripheral blood mononuclear cell and polymorphonuclear cell function in vitro. *Am J Kidney Dis* 1997;30:680–9.
6. Dobos GJ, Bohler J, Kuhlmann J, Elsner J, Andre M, Passlick-Deetjen J, Schollmeyer PJ. Bicarbonate-based dialysis solution preserves granulocyte functions. *Perit Dial Int* 1994;14: 366–70.
7. MacKenzie RK, Holmes CJ, Moseley A, Jenkins JP, Williams JD, Coles GA, Faict D, Topley N. Bicarbonate/lactate- and bicarbonate-buffered peritoneal dialysis fluids improve ex vivo peritoneal macrophage TNF-alpha secretion. *J Am Soc Nephrol* 1998;9:1499–506.
8. Pedersen FB. Biocompatibility studies with bicarbonate-based solutions. *Adv Perit Dial* 1994;10:245–50.
9. Feriani M, Kirchgessner J, La Greca G, Passlick-Deetjen J. Randomized long-term evaluation of bicarbonate-buffered CAPD solution. *Kidney Int* 1998;54:1731–8.
10. Passlick-Deetjen J, Kirchgessner J. Bicarbonate: The alternative buffer for peritoneal dialysis. Perit Dial Int 1996;16(Suppl 1):S109–13.
11. Jorres A, Bender TO, Finn A, Witowski J, Frohlich S, Gahl GM, Frei U, Keck H, Passlick-Deetjen J. Biocompatibility and buffers: Effect of bicarbonate-buffered peritoneal dialysis fluids on peritoneal cell function. *Kidney Int* 1998;54:2184–93.
12. Fischer FP, Schenk U, Kiefer T, Hubel E, Thomas S, Yatzidis H, Mettang T, Kuhlmann U. In vitro effects of bicarbonate- versus lactate-buffered continuous ambulatory peritoneal dialysis fluids on peritoneal macrophage function. *Am J Kidney Dis* 1995;26:924–33.
13. Plum J, Lordnejad MR, Grabensee B. Effect of alternative peritoneal dialysis solutions on cell viability, apoptosis/ necrosis and cytokine expression in human monocytes. *Kidney Int* 1998;54:224–35.
14. Csato M, Dobozy A, Simon N. Study of phagocytic function with a quantitative nitroblue-tetrazolium (NBT) reduction test in diabetes mellitus. *Arch Dermatol Res* 1980;268:283–8.
15. Herzer P, Lemmel EM. Inhibition of granulocyte function by prednisolone and non-steroid anti-inflammatory drugs. Quan-

titative evaluation with NBT test and its correlation with phagocytosis. *Immunobiology* 1980;157:78–88.
16. Narins RG, ed. *Clinical Disorders of Fluid and Electrolyte Metabolism.* New York: McGraw-Hill, 1994.
17. Nakayama M, Yokoyama K, Kubo H, Matsumoto H, Hasegawa T, Shigematsu T, Kawaguchi Y, Sakai O. The effect of ultra-low sodium dialysate in CAPD. A kinetic and clinical analysis. *Clin Nephrol* 1996;45:188–93.
18. Leypoldt JK, Charney DI, Cheung AK, Naprestek CL, Akin BH, Shockley TR. Ultrafiltration and solute kinetics using low sodium peritoneal dialysate. *Kidney Int* 1995;48:1959–66.
19. Gabler WL, Creamer HR, Bullock WW. Role of extracellular calcium in neutrophil responsiveness to chemotactic tripeptides. *Inflammation* 1986;10:281–92.
20. Ballarin L, Cima F, Sabbadin A. Calcium homeostasis and yeast phagocytosis in hemocytes of the colonial ascidian *Botryllus schlosseri. Comp Biochem Physiol A Physiol* 1997;118: 153–8.
21. Roschger P, Graninger W, Klima H. Magnesium-dependent induction of phagocytosis-associated chemiluminescence of adherent human polymorphonuclear leukocytes by non-opsonized zymosan. *J Biolumin Chemilumin* 1990;5:31–6.
22. Markell MS, Altura BT, Sarn Y, Delano BG, Ifudu O, Friedman EA, Altura BM. Deficiency of serum ionized magnesium in patients receiving hemodialysis or peritoneal dialysis. *ASAIO J* 1993;39:M801–4.
23. Takahashi S, Okada K, Yanai M. Magnesium and parathyroid hormone changes to magnesium-free dialysate in continuous ambulatory peritoneal dialysis patients. *Perit Dial Int* 1994;14: 75–8.
24. Merchant MR, Hutchinson AJ, Butler SJ, Boulton H, Hintchliffe R, Gokal R. Calcium, magnesium mass transfer and lactate balance study in CAPD patients with reduced calcium/ magnesium and high lactate dialysis fluid. *Adv Perit Dial* 1992;8:365–8.
25. Hutchison AJ, Merchant M, Boulton HF, Hinchcliffe R, Gokal R. Calcium and magnesium mass transfer in penitoneal dialysis patients using 1.25 mmol/L calcium, 0.25 mmol/L magnesium dialysis fluid. *Perit Dial Int* 1993;l3:219–23.