EFFECTS OF IONIZED SODIUM CONCENTRATIONS ON ULTRAFILTRATION RATE IN PERITONEAL DIALYSIS USING LACTATE AND LACTATE/BICARBONATE SOLUTIONS

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Objective: To investigate the possible effects of different concentrations of ionized sodium (NaI) on peritoneal ultrafiltration (UF) rate using lactate (Lac) and lactate/bicarbonate (Lac/Bic) dialysis solutions.

Design: Two random consecutive (after an interval of 48 hours) peritoneal equilibration tests (PETs) were performed in 13 patients (4 males and 9 females) on regular continuous ambulatory peritoneal dialysis (PD) treatment for at least 3 months. Two different PD solutions containing anhydrous glucose 3.86% were used: a 40 mmol/L Lac solution and a 15/25 mmol/L mixed Lac/Bic solution. Concentrations of total sodium (NaT) and NaI were measured by flame photometer and direct ion-selective electrode respectively.

Results: Dialysate concentrations of NaT were not different during PETs using Lac and Lac/Bic. Dialysate concentrations of NaI in fresh PD solutions were different (133.3 ± 1.7 vs 128.2 ± 3.9 mmol, p < 0.0001); however, these differences disappeared just after the end of the infusion of the fresh solutions. Peritoneal UF rate was not significantly different during PETs using Lac versus Lac/Bic (609 ± 301 mL vs 542 ± 362 mL). The dialysate-to-plasma ratios of sodium concentrations at 60 minutes of the PETs (which are expressions of free water transport) were not different using Lac versus Lac/Bic (0.89 ± 0.04 vs 0.89 ± 0.04 respectively, p = 0.96). All the other classical parameters of the PET were not different between Lac and Lac/Bic.

Conclusions: The higher dialysate concentrations of NaI due to lower dialysate pH and consequently the higher effective osmolality of the fresh Lac PD solutions did not influence peritoneal UF rate, probably because of the fast reduction of NaI concentrations due to rapid correction of dialysate pH at the end of the infusion of Lac solutions into the peritoneal cavity.

KEYWORDS: Total sodium concentration; ionized sodium concentration; pH; dialysis fluid; ultrafiltration rate; lactate; bicarbonate.

The low pH of conventional peritoneal dialysis (PD) solutions, especially in combination with lactate (Lac), seems to cause vasodilatation, recruitment of microvessels, increased glucose disappearance, and, finally, a reduction in peritoneal ultrafiltration (UF) rate. In order to improve the biocompatibility of PD solutions, new solutions characterized by more physiological pH and containing bicarbonate only or a mixture of lactate and bicarbonate (Lac/Bic) as buffer and less glucose degradation product (GDP) have recently been introduced (1–3).

The results of several studies evaluating the effects of these novel more biocompatible solutions on peritoneal UF rate are in conflict. Some studies report a higher peritoneal UF rate (4,5), others a similar (2,6–8) or a paradoxically lower peritoneal UF rate (9–11). Other biocompatible solutions with less GDP and a more physiological pH but containing Lac as buffer show a lower (12,13) peritoneal UF rate.

Generally, the solutions containing Lac have a very low pH, which allows total dissociation of sodium to ionized sodium (NaI) (14,15), the osmotically active form of sodium, so that the osmotic pressure due to sodium is maximal and the concentration of NaI is nearly the same as the concentration of total sodium (NaT). In solutions with a neutral pH containing only bicarbonate or a mix of Lac/Bic, sodium is not totally dissociated and some sodium ions are complexed with various anions; thus the NaI concentration is lower than NaT and the osmotic pressure due to sodium is not the maximum. Theoretically, the total dissociation of sodium should not greatly influence the osmotic pressure of a PD solution. However, the dissociation of sodium using PD solutions with different pH has never been quantified experimentally and it is still unknown whether the higher dialysate pH and consequently the lower con-
concentration of NaI of the Lac/Bic solutions can influence peritoneal UF rate.

The aim of the present study was to verify whether different NaI concentrations due to the dialysate pH can influence peritoneal UF rate.

PATIENTS AND METHODS

Two random consecutive (after an interval of 48 hours) peritoneal equilibration tests (PETs) were performed in patients that had been on regular continuous ambulatory peritoneal dialysis (CAPD) treatment for at least 3 months and that had been peritonitis-free for at least 1 month. All patients gave written informed consent before participating in the study.

The PET performed in the study differed from the classical method (16) insofar as two different PD solutions containing anhydrous glucose 3.86% were used: a 40 mmol/L Lac solution and a 15/25 mmol/L mixed Lac/Bic solution. Both solutions had the same nominal osmotic activity (483 mOsm/kg H₂O), nominal concentration of sodium (132 mmol/L), and nominal concentration of other solutes. In all cases, the dwell prior to the PET (overnight PET) was performed using a PD solution containing a glucose concentration of 1.36%. According to the design of the study, two different PETs using the two different solutions (Lac and Lac/Bic) had to be consecutively performed in a randomly determined order for each patient participating in the study.

Blood samples were drawn at the start, at 60 minutes, and at 240 minutes of the tests. Fresh PD solution samples were taken from the bag at the end of the infusion. After complete infusion of the PD solution, 20-mL dialysate samples were taken at 1, 60, 120, and 180 minutes after 30 mL of dialysate had been flushed back. After 240 minutes, the dialysate was collected by gravity for at least 20 minutes and a sample was taken. The volumes of the fresh PD solution and the drained dialysate were measured by weighing the bag and subtracting the weight of the empty bag; no corrections were made for differences in the specific weight of the solutions. In all the PETs, the volume of the “flush-before-fill” was 30 mL.

Plasma and dialysate creatinine, total protein, and glucose concentrations were analyzed using a Hitachi 717 instrument (Hitachi, Tokyo, Japan); an enzymatic method was used to analyze creatinine in order to eliminate the effect of the high dialysate glucose concentration on the measurement of creatinine concentrations in the dialysate. Concentrations of NaT and NaI in blood, fresh peritoneal fluids, and dialysate samples were measured by flame photometer (IL 943; Instrumentation Laboratory, Milan, Italy) and by direct ion-selective electrode (Stat Profile 4; Nova Biomedical, Waltham, MA, USA) respectively. The pH of the PD fluid and dialysate was also measured using the Stat Profile 4.

CALCULATIONS

The ratio D/D₀ was calculated by dividing the dialysate glucose concentrations at the end of each PET by that of the fresh PD solution. The dialysate-to-plasma ratios (D/P) for creatinine and for urea were calculated at the end of each PET (16). The plasma water concentrations of creatinine and urea were considered (17). Mass transfer area coefficients of creatinine, urea, and glucose were calculated using Garred’s simplified model (18). For D/P Na at 60 minutes, dialysate Na concentration was divided by plasma Na concentration.

Sodium removal (NaR) was calculated as follows:

\[ \text{NaR} = \frac{\text{Na}_d \text{Out} \times V \text{Out} - \text{Na}_d \text{In} \times V \text{In}}{V} , \]

where \( V \) is the volume of the PD solution in liters and \( \text{Na}_d \) is the concentration of sodium in PD solution in millimoles per liter.

STATISTICAL METHODS

Results are expressed as mean ± standard deviation (SD). The differences in variables are expressed as mean ± SD. Repeated measure of variance was used to assess variations in Na concentrations and pH during the PETs. The paired t-test was used for normally distributed variables to compare differences between groups. A \( p \) value less than 0.05 was considered statistically significant.

RESULTS

Thirteen patients (4 males and 9 females) participated in the study. Mean age of patients was 57.1 ± 13.7 years. Mean time on CAPD was 39.9 ± 28.7 months.

Peritoneal UF rate and NaR were not different during PETs using Lac or Lac/Bic solutions. The D/P Na at 60 minutes, an indirect expression of peritoneal free water transport, was not different between Lac and Lac/Bic. Also, all the other classical parameters were not different between PETs performed with Lac and with Lac/Bic (Table 1). Peritoneal UF rate was only slightly higher during the PET with Lac but this difference was not different statistically. Concentrations of NaT in the fresh PD fluids and in all the dialysate samples were not different between Lac and Lac/Bic [Figure 1(a)].
Concentrations of NaI were higher in the fresh Lac solutions compared to Lac/Bic solutions (133.3 ± 1.7 vs 128.2 ± 3.9 mmol, \( p < 0.0001 \)) [Figure 1(b)], but just after completion of infusion of the solutions this difference disappeared due to the rapid correction of the acidic pH (Figure 2); concentrations of NaI became similar during the PETs with Lac and Lac/Bic.

**DISCUSSION**

The present study did not show any difference in peritoneal UF rate comparing two PD solutions, one containing Lac and one containing Lac/Bic. Peritoneal UF rate was slightly higher during the PETs with Lac but this difference was not different statistically.

The main result of this study is that the peritoneal UF rate was not influenced by the higher NaI concentration of the PD solution containing Lac. The higher NaI concentration is due to the fact that Lac solutions have lower pH than Lac/Bic solutions. Theoretically, a higher NaI concentration in a PD solution could stimulate higher UF because NaI is the active (also osmotically active) form of sodium. However, the pH of the Lac PD solution was rapidly corrected during infusion of the solution into the peritoneal cavity, thus the concentrations of NaI became similar in the Lac and Lac/Bic solutions. This rapid correction of NaI concentrations does not allow prolonged action of osmotic pressure of the active sodium ions. The result is that peritoneal UF rate is similar during a PET performed with a PD solution containing Lac or Lac/Bic. Thus, it can be excluded that the higher dissociation of sodium in the fresh Lac solution was able to stimulate a higher peritoneal UF rate.

In the present study, we did not find any difference in peritoneal UF rate or in the other parameters of peritoneal small solutes when performing PETs with the two different solutions, even if it cannot be excluded that such differences might arise after prolonged treatments. These findings confirm the results of other authors (2,6,7). However, studies on biocompatible solutions show conflicting results, perhaps because of different methodological approaches; moreover, it is not always reported whether the correction for flush-before-fill (19) or for the over filling of PD bags (20) has been performed. Different solutions were used and UF was evaluated considering either the daily UF or the UF of a fraction of 1 day.

**TABLE 1**

Peritoneal Ultrafiltration (UF) and Small Solute Transport During Peritoneal Equilibration Tests (PETs) with Peritoneal Dialysis (PD) Solutions Containing Lactate (Lac) or Lactate/Bicarbonate (Lac/Bic)

<table>
<thead>
<tr>
<th></th>
<th>Lac</th>
<th>Lac/Bic</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UF (mL)</td>
<td>609±301</td>
<td>542±362</td>
<td>0.611</td>
</tr>
<tr>
<td>( D/D_0 )</td>
<td>0.19±0.03</td>
<td>0.19±0.02</td>
<td>0.986</td>
</tr>
<tr>
<td>( D/P ) urea</td>
<td>0.87±0.04</td>
<td>0.86±0.04</td>
<td>0.889</td>
</tr>
<tr>
<td>( D/P ) creatinine</td>
<td>0.73±0.09</td>
<td>0.72±0.09</td>
<td>0.867</td>
</tr>
<tr>
<td>MTAC glucose (mL/min)</td>
<td>18.4±2.4</td>
<td>18.1±1.5</td>
<td>0.711</td>
</tr>
<tr>
<td>MTAC urea (mL/min)</td>
<td>21.2±2.9</td>
<td>20.4±3.6</td>
<td>0.580</td>
</tr>
<tr>
<td>MTAC creatinine (mL/min)</td>
<td>12.2±4.2</td>
<td>11.9±4.1</td>
<td>0.838</td>
</tr>
<tr>
<td>( D/P ) Na( ^{a} )</td>
<td>0.89±0.04</td>
<td>0.89±0.04</td>
<td>0.960</td>
</tr>
<tr>
<td>NaR (mmol)</td>
<td>70±28</td>
<td>62±38</td>
<td>0.556</td>
</tr>
</tbody>
</table>

\( D/D_0 \) = ratio of dialysate glucose concentration at the end of the PET to that of fresh PD solution; \( D/P \) = dialysate-to-plasma ratio of solute concentrations calculated at the end of the PET; MTAC = mass transfer area coefficient; NaR = sodium removal.

\( ^{a} \) Calculated at 60 minutes of the PET.

**Figure 1** — Concentrations total sodium (A) and ionized sodium (B) in fresh peritoneal dialysis fluid (time 0 minutes) and dialysate during peritoneal equilibration test using lactate (L) and lactate/bicarbonate (L/B) solutions are shown.

**Figure 2** — pH during peritoneal equilibration test using lactate (L) and lactate/bicarbonate (L/B) peritoneal dialysis solutions is shown. *\( p < 0.01 \) L/B versus L.
of treatment, and with PETs lasting 4 hours but using solutions with different glucose concentrations. The use of a solution with glucose concentration 2.5%, low GDP, and a pH of 6.3 did not show a higher overnight (10 hours) peritoneal UF rate compared with a standard solution with glucose concentration 2.5% and a pH of 5.5 (13). Recently, Williams et al. (12) compared a standard Lac-buffered PD solution with high GDP and a pH of 5.5 with a Lac-buffered PD solution with low GDP and a pH of 7.0: the use of the more biocompatible solution caused a higher permeability of peritoneal membrane to small solutes and a loss of daily peritoneal UF rate compared with the standard solution. In fact, a high Lac concentration, independent of pH, is known to act as a vasodilator (21) and the result could be a higher permeability (times surface area) of peritoneal membrane and a reduction of peritoneal UF capacity.

The use of a PD solution containing only bicarbonate as buffer showed similar daily peritoneal UF (6). However, Montenegro et al. reported a lower daily peritoneal UF rate in two studies (9,10).

The high extracellular pCO$_2$ produced when the intraperitoneal bicarbonate concentration is higher than 30 mmol/L, leading to rapid intracellular diffusion of CO$_2$, may cause intracellular acidosis (22); a high extracellular CO$_2$ level with concomitant intracellular acidosis is a classic vasodilator in the microcirculation (23) and the result could be similar to that of the low-GDP solutions containing Lac.

Finally, the use of a mixture of Lac/Bic as buffer seems to be the best way to avoid the possibility of overdosing of either lactate or bicarbonate, but studies show contrasting results in this area also. Some studies reported a higher daily peritoneal UF rate when using Lac/Bic solutions (4,5), while others showed a similar (2,7,8) or a paradoxically lower peritoneal UF rate (11).

In the present study, we considered peritoneal UF during a PET lasting 4 hours and performed with a 3.86% glucose concentration. In all the studies — except one (7) — that assessed peritoneal UF with PETs lasting 4 hours (performed with glucose concentrations of 1.36% – 3.86%), the peritoneal UF observed using Lac/Bic solutions was similar to that observed using Lac solutions with the same glucose concentrations. However, after prolonged treatments with Lac/Bic solutions, the resulting daily peritoneal UF was similar or increased. We conclude that acute use of Lac/Bic solutions seems to have little or no effect on peritoneal UF rate, while prolonged treatment seems associated with higher peritoneal UF rate, perhaps because these more biocompatible solutions, having less inflammatory effect on the peritoneal membrane, lead to lower vasodilatation.

In the present study, we found that peritoneal UF rate was not influenced by the concentration of NaI in fresh PD solutions. The mechanisms of variable peritoneal UF rate using more biocompatible PD solutions are still unclear.

CONCLUSIONS

In a single dwell, solutions with acid pH containing Lac and those with physiologic pH containing a mixture of Lac/Bic do not influence peritoneal UF capacity, free water transport, or the transport of small solutes across the peritoneal membrane. The higher NaI concentration of the solution containing Lac seemed not to influence peritoneal UF capacity.

DISCLOSURE

The authors declare no conflict of interest.

REFERENCES


