In acute renal failure (ARF) in the setting of a pediatric intensive care unit, most authors report the use of frequent cycles of (often low-volume) high-glucose solutions. That approach results in appropriate H₂O ultrafiltration, but not in appropriate sodium removal, as a consequence of the sieving coefficient of sodium. That in turn leads not only to inefficient treatment of intravascular fluid overload, but also frequently to hypernatremia. The problem can be resolved by the use of low-sodium (127 mmol/L) dialysis solution.

In the present prospective study in children, we performed peritoneal dialysis using a pharmacy-made solution containing 127 mmol/L sodium and 3.86% glucose, comparing that solution with conventional glucose solution. We calculated the ultrafiltration rate and the sodium removal. We observed no statistical difference in ultrafiltration rate, but a significantly increased sodium extraction.

Children with acute overload during ARF may benefit if low-sodium solution is used in place of conventional dialysate. A low-sodium solution does not attenuate the pure ultrafiltration rate, but does result in higher sodium extraction, reducing intravascular volume and plasma sodium levels.

**Key words**
Sieving coefficient of sodium, low-sodium dialysis solution, acute renal failure, HCO₃⁻-buffered dialysis solution, ultrafiltration

**Introduction**
Acute renal failure (ARF) in young children is a special condition demanding a special dialysis attitude.

The major causes of ARF in infants in pediatric intensive care units (PICUs) are multi-organ failure and the aftereffects of cardiac surgery. Although in some countries hemolytic uremic syndrome has a comparably high incidence, the affected children rarely need intensive care and are therefore not considered in the present discussion.

Dialysis techniques must deliver adequate ultrafiltration (UF) and sodium extraction, removal of acute toxic elements such as potassium, correction of acidosis, and removal of several uremic toxins, all without interfering with cardiorespiratory and hemodynamic stability. In this paper, we concentrate on the problem of sodium extraction.

The total amount of sodium present in the body conditions the extracellular volume. In ARF, sodium and water balance both become positive, and the extracellular volume inflates, possibly leading to hypertension, cardiac decompensation, ascites, and pulmonary edema (“wet lung”). Although maintenance of a neutral fluid and sodium balance is one of the basic goals in a PICU, that goal is often not achievable. To keep the various monitoring lines open, to deliver vasopressors continuously, and to supply appropriate nutrition, fluid administration exceeds by far basic needs. Correction of acidosis by NaHCO₃ and various colloid solutions leads to a high sodium load.

Conventional peritoneal dialysis (PD) with its 4 daily exchanges is inappropriate for UF and for dialysis adequacy with regard to small solutes such as potassium, especially in PICU patients, in whom only small fill volumes are often tolerated because of cardiorespiratory and hemodynamic instability. The introduction of frequent exchanges of hypertonic 3.86% glucose solution may lead to a higher UF rate, better
potassium removal, and correction of acidosis, but the effect on sodium removal is limited because of the sieving characteristics of sodium. The result may therefore be inefficient treatment of intravascular fluid overload—even aggravation of hypernatremia—and a subsequent decrease in the UF rate.

For those reasons, the tendency to continuous renal replacement therapy (CRRT) is increasing, even in pediatrics. Although CRRT definitely has benefits for some indications, deficient sodium removal may not be one of those reasons, provided that the problem can otherwise be resolved. And the problem can be resolved by using low-sodium (127 mmol/L) dialysis solution.

In patients on acute PD, we have used HCO₃⁻-buffered, low-sodium (128 mmol/L) dialysis solution and have reported low serum sodium values in the study group (1). Our aim in the present prospective study was to document the sodium removal benefit with a low-sodium dialysis solution.

**Patients and methods**

*Dialysis protocol*

All patients were started on day 1 with a PD regimen of 25 mL/kg fill volume and 5-minute inflow, 20-minute dwell time, and 5-minute outflow (30-minute) cycles with a PAC-Xtra cycler (Baxter Healthcare SA, Castlebar, Ireland).

Group A was started on day 1 with Dianeal 3.86% (Baxter Healthcare SA). Group B received a pharmacy-made solution based on the Bieffe CRRT solution bags (Bieffe Medital, Lugano, Switzerland), to which 50% glucose solution was added to achieve a glucose concentration of 3.86%. The addition of glucose led to a dilution of the sodium concentration to 127 mmol/L. The other major difference between the two solutions (besides the sodium level) is that the Bieffe-based solution is buffered with 38 mmol/L HCO₃⁻; the Dianeal contains lactate.

To avoid dilution by the volume in the tubes, dialysate samples were obtained from an injection port in the cycler set after at least 3 hours of automated PD (APD), during an outflow phase, once 50% of outflow volume was reached.

*Statistical analysis*

Because the dialysis regimen in infants depends on body size, all values are normalized to body weight [BW (kg)] or fill volume (mL/kg BW), as appropriate. Data are presented as mean ± one standard deviation. Statistical differences were calculated using the Mann–Whitney U-test. Statistical significance was accepted at p < 0.05.

**Study population**

Between 1997 and 2003, 17 children were entered into the study. For data analysis, 1 patient in each group had to be excluded, because the dialysis regimen had had to be adapted so that it no longer adhered to the prescribed standardized regimen. Of the remaining 15 patients (6 girls, 9 boys; age: 4 days – 2 years), 7 had had cardiac surgery, and 8 had experienced multi-organ failure because of sepsis. Patients in an unstable hemodynamic condition, with severe lactate acidosis (lactate > 40 mg/dL), or with a need for high intravenous HCO₃⁻ administration (>2 mmol/kg daily) were excluded. Patients in whom the dialysis regimen was likely to require adaptation were also excluded.

**Results**

No statistical differences in sex, body weight, or age were observed between the two study groups. Table I shows several dialysis parameters for the two groups. Plasma sodium levels were not different between the two study groups. Although the dialysate-to-plasma (D/P) ratio of sodium of the dialysis solutions at 0 minutes was statistically different (because of the study design), that significance was lost in the effluent at 30 minutes, pointing to significantly higher sodium removal with the low-sodium solution.

**TABLE 1 Dialysis parameters in the study groups**

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma sodium (mmol/L)</td>
<td>143.7±3.9</td>
<td>145.1±3.1</td>
<td>0.520</td>
</tr>
<tr>
<td>Dialysate sodium (mmol/L)</td>
<td>128.9±2.0</td>
<td>126.2±1.8</td>
<td>0.310</td>
</tr>
<tr>
<td>UF rate (mL/kg/cycle)</td>
<td>2.39±0.54</td>
<td>2.73±0.64</td>
<td>0.521</td>
</tr>
<tr>
<td>UF rate/fill volume (%)</td>
<td>10±2</td>
<td>11±3</td>
<td>0.521</td>
</tr>
<tr>
<td>D/P sodium (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t0min</td>
<td>91.9±2.5</td>
<td>88.3±2.5</td>
<td>0.017⁴</td>
</tr>
<tr>
<td>t30min</td>
<td>89.4±1.7</td>
<td>88.3±2.1</td>
<td>0.214</td>
</tr>
<tr>
<td>Sodium removal (mmol/kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Per cycle</td>
<td>0.23±0.08</td>
<td>0.35±0.09</td>
<td>0.037⁴</td>
</tr>
<tr>
<td>In 24 hours</td>
<td>11.0±3.7</td>
<td>17.0±4.5</td>
<td>0.037⁴</td>
</tr>
</tbody>
</table>

UF = ultrafiltration.
Discussion
Studies in children, especially in intensive-care situations, are difficult to perform—not only from a practical point of view, but because of the multiple variables that may be involved. These logistic and population limitations required us to concentrate on a rather homogeneous group of children, which is why it took several years to collect sufficient data.

The use of low-sodium PD solutions in infants with ARF demonstrates a clear sodium extraction benefit. But comparing our results with the literature remains difficult, because the existing data come exclusively from adults on chronic PD [continuous ambulatory PD (CAPD) or APD], with a conventional fill volume (2). Understanding our results and correctly interpreting the data, while preventing premature extrapolation to the chronic PD situation in both children and adults, requires a full literature survey (2,3).

Evidence from adult studies is promising, but limited, despite the fact that the concept of using lower-sodium dialysis solution to remove more sodium from the patient is not new. Three decades ago, Ahearn and Nolph (4) used low-sodium dialysis solution to manage hypernatremia in PD patients. Those authors demonstrated that a dialysis solution containing 7% dextrose and 100 – 130 mmol/L sodium removed more sodium per exchange than did a standard 7% solution containing 140 mmol/L sodium. But their idea was lost during the subsequent two decades, and no studies using low-sodium dialysis solution were published.

More recently, stimulated by the work on sodium-sieving by groups led by Krediet (5) and Lindholm (6,7), small studies in PD patients have shown that low-sodium dialysis solution increases sodium removal and improves blood pressure control. The current sodium concentration in PD solutions is ±132 mmol/L. Further lowering that concentration enhances sodium removal by means of diffusion. Clinical experience with low-sodium solutions is limited, but promising.

Short-dwell studies have been performed using dialysates with a lower sodium concentration than that found in conventional dialysates (5,8). For example, Imholz et al. (5) compared two dialysis solutions with similar osmolality, but different sodium concentrations (129 mmol/L and 102 mmol/L, respectively) during two peritoneal permeability tests. Peritoneal sodium and chloride losses increased, and plasma sodium, chloride, and osmolality decreased in conjunction with a fall in plasma volume. Nakayama et al. (9) observed a significant reduction in body weight and mean arterial blood pressure with the use of a solution containing 98 mmol/L sodium for 1 week in 6 patients with fluid overload.

As compared with CAPD, APD imposes additional demands on the optimal composition of a PD solution. Electrolyte concentrations should be adjusted to the shorter dwell times in APD. A solution with a lower sodium concentration is needed to enhance sodium removal by diffusion both during rapid hypertonic exchanges and in patients with a high salt intake. It has recently been shown that, because of the short dwell times in APD, absolute removal of sodium is less than in CAPD (10). This negative effect of APD on sodium balance is largely overcome when a daytime dwell with Extraneal (Baxter Healthcare) is introduced, a technique that is not an option in acute dialysis.

The clinical safety and efficacy of low-sodium dialysate has been tested (although still not sufficiently) by clinical trials for patients with chronic renal failure on APD (10). A recent study by Ortega et al. (11) reported better control of hypertension with CAPD than with APD and attributed that result to the higher 24-hour sodium removal with CAPD. Because the number of prevalent APD studies related to sodium concentration in the dialysis fluid is very small, more evidence is needed to confirm that a dialysate sodium concentration of 125 – 130 mmol/L is beneficial for anuric PD patients. Despite the apparently convincing results, some caveats are definitely required. Many patients on CAPD and APD have a rather low plasma sodium level, which reflects fluid overload more than sodium overload. Chronic use of a low-sodium PD solution may therefore lead to symptomatic hyponatremia. Studies in children on chronic PD are absent.

In ARF, especially in children, the intensive care situation often forces inventive adaptation of dialysis therapy. The safety questions are obviously different, because the patient and the patient’s fluid status and plasma electrolytes are monitored many times daily, and oral sodium restriction is impossible. In the past, we presented preliminary data on the advantages of low-sodium bicarbonate solution over the standard lactate solutions for acute APD in children (1). Over a period of 24 hours, we used a solution with 128 mmol/L sodium and a bicarbonate concentration of 38 mmol/L in study patients. Although serum concentrations of sodium before the start of the study on
day 1 and after 24 hours of standard fluid on day 2 were not different, they were significantly lower in the study group on day 4. The mean serum sodium concentrations were 148 mmol/L in the study group (range: 137 – 156 mmol/L) and 154 mmol/L in the control group (range: 142 – 165 mmol/L). Those findings demonstrated a higher sodium extraction with low-sodium APD solution in children with ARF, which may be important for infants with fluid overload, especially after cardiac surgery. But the study was limited in that (A) the control group was a retrospective study population, so that interference of changing attitudes about PICU care could not be excluded, and (B) we concluded from the reduced plasma sodium levels that sodium extraction was increased, when reduced intravenous HCO₃ administration in patients on HCO₃ dialysis might also explain the phenomenon.

The present study tries to resolve that problem by tracking a control population simultaneously with a study population, and by calculating the sodium extraction in the dialysate. The data cannot be compared to the previous study because of patient selection: In the previous study, most of the patients had severe lactate acidosis and therefore a greater need for HCO₃ substitution. The situation of ARF in children is also entirely different from the chronic dialysis situation in adults, and therefore our results are obviously difficult to compare with results in adults.

Children in a PICU are often cardiorespiratorily and hemodynamically unstable, which limits epuration techniques such as conventional intermittent hemodialysis and CAPD with 4 exchanges of 1200 mL/m² body surface area. Normalized for body size, huge amounts of fluid are given to children in a PICU (to keep lines open, to deliver vasopressors at a continuous rate, to administer other drugs, or to give total parenteral nutrition). Although hypotension may be present, hypotension is not unusual because of the relatively high sodium administration in the various solutions; because of the greater perspiration (higher respiration rate, relatively higher body surface area, thinner skin, artificial heating lamp); and especially because of the correction of acidosis with sodium bicarbonate. The tendency to hypernatremia is aggravated when PD is initiated with frequent exchanges of small volumes of hypertonic solution.

Children in a PICU are often on artificial ventilation and are hemodynamically unstable; they do not support the abdominal fill rate well. The fill volume therefore often remains lower than 30 mL/kg of body weight. The major epuration needs are reduction of potassium, maintenance of UF, and correction of acidoses. Frequent exchanges (every 30 minutes) with small volumes of hypertonic (3.86%) glucose solution and use of a cycler are therefore often introduced. Although such a regimen may be less optimal for larger molecules such as phosphate, that concern is minor during acute treatment. In adults, such a strategy would definitely lead to inadequate dialysis efficiency, but in infants, this seems not to be the case. One possible explanation may be that most of these patients are in cardiac decompensation and an inflammatory state, leading to maximal dilation of the intraperitoneal vessels (a state of larger dialysis surface area and hyperpermeability), although increased venous pressure will stimulate UF (as proven by the often pre-existing ascites).

Extrapolation of our data to conventional chronic dialysis remains difficult. Although the D/P ratio after 30 minutes is comparable to those reported in the literature (6,7), that ratio is obtained mainly by higher plasma sodium levels than by dilution of the PD fluid by UF (±10%). Although such a finding may look surprising, part of it can be explained by fluid recycling (even in pediatric cycler sets) and a significant relative (though not absolute) residual volume with small fill volumes and short outflow time (5 minutes). Although that situation might make extrapolation to adults difficult, it does not change the statistical significance, because both groups in the present study received the same PD regimen.

The UF rate was not significantly higher in the HCO₃-based solution (group B), and so did not contribute per se to the higher sodium extraction. Also, the plasma sodium levels—and therefore the plasma/dialysate gradients—were not significantly different between the two study groups, and therefore do not explain the sodium losses. Although the sodium concentration in the PD effluent remained lower after 30 minutes in group B, the initial concentration difference of 4 mmol/L (132 mmol/L to 128 mmol/L) was reduced to ±2 mmol/L, clearly indicating higher sodium losses.

**Conclusions**

Infants with ARF can be treated with PD. The use of low-sodium PD solutions may increase sodium
removal, especially during continuous APD with frequent cycles using hypertonic glucose solutions.

References

Corresponding author:
Johan Vande Walle, MD, Renal Unit, University Hospital, 185 De Pintelaan, B-9000 Gent, Belgium.
E-mail: Johan.VandeWalle@Ugent.be