Alkalosis and hypomagnesaemia: unwanted effects of a low-calcium CAPD solution

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Abstract. We studied 43 CAPD patients for 4 months during the change from a high-calcium dialysis fluid (Baxter PD1) to a low-calcium fluid (Baxter PD4), which also contained low magnesium (0.25 mmol/l) and high lactate concentrations (40 mmol/l). Serum calcium fell significantly as did the incidence of hypercalcaemia, whilst the proportion of patients taking calcium-containing phosphate binders increased. There was a non-significant increase in serum i-PTH levels but the proportion with i-PTH >150 pg/ml (normal range 10–65 pg/ml) increased significantly. There was a significant fall in serum magnesium level and seven patients developed hypomagnesaemia. Serum bicarbonate increased significantly and progressively and 17 patients were alkalotic at 4 months, five severely (bicarbonate 35–40 mmol/l). One patient developed recurrent episodes of painful subcutaneous and periarticular calcification, which may have been related to the alkalosis. Initial serum bicarbonate levels correlated significantly with dialysis adequacy assessed by daily Kt/V (r = 0.458, P = 0.002). The relationship to adequacy was abolished during the period of use of the high-lactate dialysis fluid. Use of low-magnesium CAPD fluids must be supported by regular monitoring of serum magnesium levels. The high lactate concentration in such fluids may not be appropriate and is potentially hazardous when individualization of dialysis dose demands the use of relatively high exchange volumes. We therefore studied the effects of changing from a high-calcium dialysis fluid (Baxter PD1) to such a low-calcium dialysis fluid (Baxter PD4) in an unselected group of such CAPD patients.

Subjects and methods

Patients

All 43 CAPD patients (26 males, 17 females) dialysing at Lister Renal Unit and using high-calcium fluid (Baxter PD1) on 1 November 1993 were studied. Ages ranged from 32 to 83 years (mean ± SD = 58.8 ± 14.5). Duration of dialysis ranged from 1 to 51 months (19.9 ± 12).

Drug therapy

Twenty-six patients were taking phosphate binders (19 calcium carbonate or acetate and 7 aluminium hydroxide). Seven patients were taking calcitriol or alfacalcidol; 35 were on various antihypertensive treatments.

Dialysis technique

Systems. All patients dialysed using disconnect systems. Adequacy. Dialysis adequacy was monitored 3-monthly and the prescribed dialysis fluid, exchange volume and cycle frequency adjusted to attempt to maintain a daily Kt/V >0.25. The daily Kt/V was calculated as detailed elsewhere [5,6] from:

\[ K(\text{ml/min}) = \text{the sum of dialysis and residual renal urea clearance, calculated from simultaneous 24-h collections of urine and CAPD fluid effluent and a blood sample.} \]
Alkalosis and hypomagnesaemia with low-calcium CAPD

Table 1. Composition of dialysis fluids. Concentrations expressed in mmol/l

<table>
<thead>
<tr>
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<th>PD1</th>
<th>PD4</th>
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<tr>
<td>Sodium</td>
<td>132</td>
<td>132</td>
</tr>
<tr>
<td>Calcium</td>
<td>1.75</td>
<td>1.25</td>
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<tr>
<td>Magnesium</td>
<td>0.75</td>
<td>0.25</td>
</tr>
<tr>
<td>Chloride</td>
<td>102</td>
<td>95</td>
</tr>
<tr>
<td>Lactate</td>
<td>35</td>
<td>40</td>
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\[ T = \text{number of minutes/day} \]
\[ V = 1000(2.447 - 0.09516A + 0.1074H + 0.3362W) \text{ml} \] (males)
\[ V = 1000(-2.097 + 0.1069H + 0.2466W) \text{ml} \] (females)
where \( A = \text{age (years)}, H = \text{height (cm)}, W = \text{weight (kg)} \) [7].

Dialysis fluid composition. All patients were dialysed using a high-calcium dialysate (Baxter PD1) (Table 1) and had been stable on this regime for at least 1 month.

Protocol

All 43 patients were switched to a low-calcium, low-magnesium dialysate (Baxter PD4) (Table 1) and had been stable on this regime for at least 1 month.

Biochemical methods

Urea, calcium, phosphate, and bicarbonate levels were measured using a Hitachi 717 autoanalyzer. Serum magnesium was measured by a modified xylidyl blue-1 method (Wako Chemicals GmbH). Serum i-PTH was measured by an immunoradiometric method detecting the intact molecule (Biocode Technology).

Statistical methods

The paired Student’s \( t \) test, the Chi-squared test with Yates’ correction, and the calculation of the Pearson correlation coefficient were used as appropriate.

Results

Ten patients did not complete the 4-month study. The reasons for withdrawal are shown in Table 2.

Table 2. Reasons for withdrawal from the study

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<tr>
<td>5</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>1</td>
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<td>1</td>
</tr>
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</table>

six patients were restudied at 1 month and 33 at 4 months. The effects of the change of dialysis fluid on the measured biochemical markers are shown Table 3.

Calcium. The mean serum calcium concentration at 1 month was significantly reduced and remained so at 4 months (Table 3). None of the patients was initially hypocalcaemic (<2.15 mmol/l) but four were hypocalcaemic at 1 month \((P<0.05)\) and two at 4 months. Eleven patients were initially hypercalcaemic, which had reduced to three by 1 month and four by 4 months \((P<0.05\) in both cases). These changes are depicted in Figure 1.

Phosphate. The mean serum phosphate at 1 month but not 4 months was significantly higher than the mean initial value \((P<0.01)\).

Parathyroid hormone. There was no significant difference between initial and final mean serum i-PTH levels. However, 14 patients had low or normal initial levels (up to 65 pg/ml) compared with only four at the end of the study \((P<0.01)\). Eight patients had initial i-PTH levels greater than three times the upper limit of normal, whilst 16 patients had such levels at the end \((P<0.01)\). These changes are depicted in Figure 2.

Changes in i-PTH levels during the study correlated significantly with changes in the serum calcium level \((r=0.505, P = 0.005)\), but not with changes in the serum magnesium.

Magnesium. The mean serum magnesium level was
significantly lower at 1 and 4 months than the mean initial level \( (P<0.001 \text{ in both cases}) \). Sixteen patients had initial mild hypermagnesaemia \( (> 1.1 \text{ mmol/l}) \). This had reduced to six at 1 month (not significant) and three at 4 months \( (P<0.025) \). In contrast none of the patients was initially hypomagnesaemic \( (<0.7 \text{ mmol/l}) \) but six were at 1 month and seven at 4 months \( (P<0.005 \text{ in both cases}) \). Four patients developed profound hypomagnesaemia with levels of 0.44, 0.46, 0.57, 0.58 mmol/l. These changes are depicted in Figure 3.

**Bicarbonate.** The mean serum bicarbonate at 1 and 4 months was higher than the mean initial level \( (P<0.001 \text{ in both cases}) \). The mean level at 4 months was also significantly higher than the mean 1 month level \( (P<0.001) \). Two patients were initially mildly acidotic \( (<22 \text{ mmol/l}) \) but none was during the subsequent course of the study. None of the patients was initially alkalotic \( (> 29 \text{ mmol/l}) \) but nine were at 1 month and 17 at 4 months \( (P<0.001 \text{ in both cases}) \). The incidence of alkalosis at 4 months was significantly more than that at 1 month \( (P<0.01) \). By the end of the study five patients were severely alkalotic with serum bicarbonate levels ranging from 35–40 mmol/l. These changes are depicted in Figure 4. There was a weak but significant correlation between the initial serum bicarbonate level and the daily \( Kt/V \) estimated immediately before the study \( (r=0.458, P=0.002, \text{ Figure 5}) \). However, daily \( Kt/V \) did not correlate with serum bicarbonate levels at 1 and 4 months. In addition five of the nine patients whose dialysis adequacy was suboptimal (daily \( Kt/V <0.25 \) had initial serum bicarbonate levels <24 mmol/l, whilst 29 of the 34 patients with adequate dialysis by this criteria had initial bicarbonate concentrations above this level \( (P<0.005) \).

**Exchange volume.** The mean exchange volume at the commencement of the study was \( 9.6 \pm 1.6 \text{ litres} \). It did not change significantly during the study, being \( 9.8 \pm 1.7 \text{ litres} \) at completion.

**Changes in drug therapy.** The proportion of patients taking calcium-containing phosphate binders (calcium carbonate or acetate) increased significantly during the study ... daily \( Kt/V \) did not correlate with serum bicarbonate levels at 1 and 4 months. In addition five of the nine patients whose dialysis adequacy was suboptimal (daily \( Kt/V <0.25 \) had initial serum bicarbonate levels <24 mmol/l, whilst 29 of the 34 patients with adequate dialysis by this criteria had initial bicarbonate concentrations above this level \( (P<0.005) \).
study (Table 4). There was also a decrease in the proportion taking aluminium hydroxide and an increase in the proportion taking alfacalcidol or calcitriol, but these changes were not statistically significant.

**Clinical problems.** One patient developed multiple episodes of painful subcutaneous and periarticular calcification beginning 1 month after the start of the study, during which her serum calcium fell from 2.62 to 2.53 mmol/l, phosphate from 2.32 to 2.12 mmol/l, and magnesium from 1.05 to 0.74 mmol/l. Serum bicarbonate rose from 28 to 34 mmol/l and i-PTH from 92 to 269 pg/ml. In the 3 months after switching back to PD1 at the conclusion of the study she has had no further episodes, the i-PTH had fallen to 136 pg/ml and the bicarbonate had fallen to 26 mmol/l.

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<thead>
<tr>
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<th>% on treatment</th>
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<tr>
<td>Calcium-containing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>phosphate binders</td>
<td>44</td>
<td>70*</td>
</tr>
<tr>
<td>Aluminium-containing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>phosphate binders</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Vitamin D compounds</td>
<td>12</td>
<td>21</td>
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* P < 0.05 between initial and final values.

**Discussion**

This study has confirmed some of the reported benefits of changing from a high-calcium CAPD fluid to a low-calcium fluid [2,3]. These included a significant reduction in the incidence of hypercalcemia in spite of a significant increase in the proportion of patients taking calcium-containing phosphate-binding agents, and a reduction in the proportion of patients requiring aluminium-containing phosphate binders. There was also a slight increase in the proportion of patients taking vitamin D compounds. Some of the previously reported problems [8] associated with this manoeuvre were also apparent, including a significant increase in the incidence of hypocalcaemia, and hyperparathyroidism. The increase in phosphate one month after changing to the low-calcium fluid may have been related to the increase in i-PTH, possibly by mobilizing phosphate from bone.

We also encountered a number of other problems not directly related to the reduced calcium content of the dialysis fluid but stemming from other changes in its composition. These were a significant reduction in the serum magnesium level giving rise in a number of patients to profound hypomagnesaemia, and a significant and sustained increase in the serum bicarbonate level such that over half the patients who completed the study were alkalotic, and five patients severely so. These changes may have been exaggerated by the use of relatively high exchange volumes but nevertheless may have important implications.

Hypomagnesaemia was not seen in a previous study using the same low-calcium, low-magnesium dialysate [2,9], which advocated the use of these solutions for the control of hypermagnesaemia. None of our patients, though, had significant hypermagnesaemia initially. The significant incidence of severe hypomagnesaemia we encountered may be a high price to pay for the correction of mild hypermagnesaemia, since magnesium depletion may predispose to cardiac arrhythmias [10]. It is fair to say, though, that hypermagnesaemia has been implicated in the pathogenesis of renal osteodystrophy and visceral calcification [11,12]. Hypomagnesaemia can be avoided by the use of magnesium salts as phosphate binders [13]. Nevertheless it would seem wise to monitor plasma magnesium levels when using low-magnesium dialysis fluids.

Mild alkalosis in a minority of patients has also been reported in a previous study using this CAPD fluid [2]. In contrast we have found that the majority of patients developed an alkalosis that was severe in a significant proportion. Furthermore, the incidence of alkalosis rose significantly between 1 and 4 months, suggesting that with continued use the incidence may rise further. In addition the clinical course of the patient we described who developed multiple painful episodes of metastatic calcification during this study, suggests that alkalosis may have been a contributory factor. Alkalosis has been thought to play a role in the pathogenesis of metastatic calcification in haemodialysis patients [14].

This study demonstrates that in CAPD patients using the 'standard' dialysis fluid lactate concentration of 35 mmol/l, acidosis is a marker of inadequate dialysis. By changing to a higher lactate-containing fluid the acidosis is abolished without increasing Kt/V and the relationship between bicarbonate to adequacy is lost. In our patients, in whom adequacy is optimized by increasing exchange volume and frequency to compensate for declining residual renal function [6], the incidence of acidosis is minimal on the 'standard' lactate solution. Furthermore one of the aims of using low-calcium CAPD fluids is to allow the more liberal use of calcium carbonate as a phosphate binder, which may also contribute to alkalosis. In this setting, use of the higher-lactate fluid seems unnecessary, and possibly hazardous. At the very least it masks an important indicator of inadequate dialysis. It is conceivable that the high incidence of hypomagnesaemia observed in this study is also a reflection of the use of high exchange volumes to preserve adequacy.

In conclusion, the benefits of using a low-calcium CAPD fluid were tempered by a high incidence of hypomagnesaemia and alkalosis. Use of low-magnesium CAPD fluids must be supported by regular monitoring of serum magnesium levels. We suggest that the high lactate concentration in such fluids is unjustified and potentially hazardous. Low serum bicarbonate levels in CAPD patients reflect inadequate dialysis, which use of these fluids serves to mask.
References


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