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Print Post approved: PP381867/00481
Original Article

Calcium acetate versus calcium carbonate: Phosphate absorption studies in chronic renal failure

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Summary: The aim of this study was to compare the alimentary phosphate-binding capacity of calcium acetate to calcium carbonate in stable chronic renal failure patients who were not on haemodialysis. Intestinal absorption of phosphate and calcium was measured on three occasions in five patients with chronic renal failure who were not on maintenance haemodialysis. During each test period they received either no drug, calcium carbonate or calcium acetate (both containing 1g elemental calcium) in a randomized manner, along with a standardized meal. Intestinal contents were recovered after 10h by whole gut lavage, and phosphorus and calcium measured in meal and intestinal contents. Faecal excretion of ingested phosphorus increased from 13.85% in the absence of drug to 29.91% after calcium carbonate administration. Phosphorus excretion was significantly higher after calcium acetate (43.92%) compared to calcium carbonate (P < 0.05). Less calcium was absorbed from calcium acetate than from equimolar amounts of calcium carbonate (P < 0.05). In patients with stable renal failure, calcium acetate is a better alimentary phosphate binder than calcium carbonate and binds more phosphorus for each mol of calcium absorbed.

Keywords: calcium acetate, phosphate binder, renal failure.

INTRODUCTION

Aluminium hydroxide, commonly used as a phosphate binder to combat the phosphate retention of advanced renal failure, produces toxicity after long-term use in these patients.1 Calcium salts, carbonate and acetate have been used as alternative phosphate binders. Based on phosphorus absorption studies in normal subjects and in patients with chronic renal failure on haemodialysis calcium acetate appears to bind more phosphate than carbonate.1,2 Haemodialysis has a variable effect on phosphate balance and there have been no previous studies of phosphorus balance in patients not on dialysis. The present study was carried out to compare the relative phosphate binding efficacy of calcium acetate and calcium carbonate in patients with stable chronic renal failure who were not on haemodialysis. Absorption of calcium from both the salts was also quantitated.

METHODS

Subjects

Five patients (three male) with chronic renal failure, none of whom were on dialysis, were included in this study.

All the subjects had stable chronic renal failure and hyperphosphataemia with a serum creatinine greater than 5 mg/dL and serum phosphorus between 6 and 12 mg/dL. Their mean (s.d.) age was 41.4 (19.3) years. Two of the patients had diabetic nephropathy while three were diagnosed to have chronic glomerulonephritics. Their urea and creatinine values (mean ± s.d.) were 137.6 ± 30.7 mg/dL and 6.1 ± mg/dL, respectively. Their immunoreactive parathyroid hormone (iPTH) values were 134.6 ± 50.3 ng/dL (mean ± s.d.; normal range 0–27). Patients on dialysis were excluded since dialysis has a variable influence on phosphate balance. The following were excluded: patients with severe hyperphosphataemia (serum phosphorus greater than 12 mg/dL) who were treated with aluminium hydroxide; patients receiving vitamin D supplementation antacids or other phosphate binders; those with co-existent gastrointestinal diseases or acute infection; and those on antibiotic therapy.

Study protocol

The study was approved by the research committee of the Christian Medical College, Vellore, India. Informed consent was obtained from all subjects. The subjects were studied while they were fasting and after they had ingested a standard test meal which consisted of a vegetarian diet ordinarily recommended with a conservative therapy of chronic renal failure (i.e. daily intake of 35 kcal/kg, 0.6 gm protein/kg, 60–80 mmol sodium, 40–60 mmol
Table 1 Amount of phosphorus ingested, absorbed and excreted during the three test periods

<table>
<thead>
<tr>
<th></th>
<th>No drug</th>
<th>Calcium carbonate</th>
<th>Calcium acetate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphorus ingested (mg/day)</td>
<td>431.6 ± 16.8</td>
<td>436 ± 27.4</td>
<td>445 ± 20.0</td>
</tr>
<tr>
<td>Amount of ingested phosphorus excreted (mg/day)</td>
<td>59.8 ± 12.2</td>
<td>130.4 ± 16.7&quot;</td>
<td>195.4 ± 16.8&quot;</td>
</tr>
<tr>
<td>%</td>
<td>13.85</td>
<td>29.91'</td>
<td>43.92'</td>
</tr>
<tr>
<td>Amount of ingested phosphorus absorbed (mg/day)</td>
<td>371.8 ± 22.3</td>
<td>305.6 ± 11.3&quot;</td>
<td>249.6 ± 4.8&quot;</td>
</tr>
<tr>
<td>%</td>
<td>86.15</td>
<td>70.09&quot;</td>
<td>56.08&quot;</td>
</tr>
</tbody>
</table>

All values shown are mean ± s.e.m. *P < 0.05 compared to control. **P < 0.05 compared to calcium carbonate.

Calculations

Intake of phosphorus during each test period was obtained by analysis of the duplicate test meal. The amount of dietary phosphorus excreted during the study period was calculated by subtracting fasting effluent phosphorus (representing endogenous losses) from the effluent phosphorus after the test meal. The amount of dietary phosphorus that was absorbed was calculated as ingested phosphorus minus excreted phosphorus. Calcium intake was calculated on the basis of the calcium content of the duplicate meal plus calcium in the duplicate capsules. Calcium absorption was calculated as calcium intake minus calcium recovered in rectal effluent. The amount of calcium (mg) absorbed for each mg of phosphorus bound was also calculated and the ratio of absorbed calcium to bound phosphorus (as mmol of ion) was calculated as described by Mai et al.3

Statistics

All values were expressed as mean ± s.e.m. The significance of differences between study groups was determined using the two-tailed Wilcoxon signed ranks sum.

RESULTS

The intake of phosphorus in the meal was comparable between the three test periods as shown in Table 1. In the absence of administered drug, the mean (s.e.) phosphorus absorption was 371.8 ± 22.3 mg of phosphate which was 86.15% of the ingested phosphate. As shown in Table 1, absorption of meal phosphorus was significantly reduced to 70.09% (P < 0.05) after administration of calcium carbonate, while it was further reduced to 56.08% after calcium acetate (P < 0.05 compared to calcium carbonate).

Calcium intake in the absence of administered drug
was 608 ± 27 mg (mean ± s.e.m.), while it was 1588 ± 40 mg in the calcium carbonate studies and 1622 ± 24 mg in the calcium acetate studies. In the absence of administered drug, these patients absorbed 154.6 ± 19.3 mg (mean ± s.e.m.) calcium, representing 25% of the dietary intake. Calcium absorption was higher after administration of calcium carbonate (827 ± 39.5 mg, mean ± s.e.m., 53% of intake) than after administration of calcium acetate (709 ± 31.6 mg, 43.7% of intake; P < 0.05). The amount of calcium (mg) absorbed for each mg of phosphorus bound was significantly higher for calcium carbonate (6.36 mg) compared to calcium acetate (3.62 mg; P < 0.05). A calcium level of 2.94 mmol was absorbed for each 1 mmol of phosphorus bound when calcium carbonate was administered, whereas the corresponding amount of calcium absorbed with calcium acetate was 1.26 mmol.

**DISCUSSION**

The single meal phosphorus balance technique used in this study has been validated earlier. The present study in non-dialysed chronic renal failure patients demonstrates that calcium acetate is a significantly better phosphate binder than equimolar doses of calcium carbonate. It also reconfirms that calcium acetate has a better therapeutic index, because significantly less calcium is absorbed from it for each mol of phosphorus bound.

Hyperphosphataemia is a problem in patients with chronic renal failure. Since dietary phosphate intake is usually not adequately reduced in these patients, and because they may absorb 75–80% of ingested phosphate, it is necessary for these patients to ingest a phosphate-binding agent. Although calcium carbonate was shown to be effective in reducing hyperphosphataemia three decades ago, aluminium salts had been used as the binders of choice until the recognition of aluminium toxicity led to the use again of calcium carbonate. Factoring phosphorus binding for the dose of calcium administered (50 mmol) and assuming that phosphate is present as HPO\(^{4-}\), in the intestinal lumen, the phosphorus binding capacity of calcium in calcium acetate is 0.18 mmol compared to 0.09 mmol for calcium as the carbonate. Thus although calcium acetate is a better phosphate binder than the carbonate, only a small proportion of the calcium in the salt (18% for calcium acetate) actually serves to bind meal phosphate.

There is also evidence from clinical studies to suggest that calcium acetate is better than the carbonate in the management of hyperphosphataemia. In a limited number of patients with chronic renal failure on haemodialysis, predialysis serum phosphorus levels were lower during calcium acetate treatment than during calcium carbonate treatment. Calcium acetate was also shown to be better than calcium carbonate in preventing the rise in serum phosphorus levels after withdrawal of aluminium therapy in patients on haemodialysis. The major shortcoming of calcium carbonate is hypercalcaemia due to the imbalance between the dose necessary to achieve a good control in serum phosphorus levels and the amount of elemental calcium absorbed from it. The lower ratio of calcium absorbed and ratio of phosphorus bound, which is observed with calcium acetate, is likely to be advantageous especially in patients with secondary hyperparathyroidism who are at risk of developing hypercalcemia.

**REFERENCES**