Transient decrease of serum bicarbonate levels with Sevelamer hydrochloride as the phosphate binder

To the Editor: Calcium carbonate is widely used as a phosphate binder: it reduces phosphate absorption by the intestine and it ameliorates metabolic acidosis, but increases plasma calcium concentrations. The limitations of currently available aluminum-based and calcium-based phosphate binding agents and the impact of uncontrolled phosphorus levels on the morbidity and mortality of patients with kidney disease [1] have prompted the search for new therapeutic approaches of hyperphosphatemia in dialysis patients. Sevelamer hydrochloride (RenaGel®; GelTex Pharmaceuticals, Waltham, MA; distributed by Genzyme Corporation, Cambridge, MA, USA) is a novel calcium- and aluminum-free polymer [cross-linked polyallylamine hydrochloride]. It contains multiple amines (40% amine hydrochloride) separated by one carbon from the polymer backbone and it is not absorbed by the intestine. These amines are partially protonated and interact with phosphate molecules through ionic and hydrogen bonding, therefore reducing phosphate absorption and lowering serum phosphate concentration [2].

Previous studies showed a trend toward lowered serum bicarbonate concentrations during administration of Sevelamer HCl that were not statistically significant [3]. We studied the effects of substituting Sevelamer HCl for calcium carbonate on metabolic acidosis in 16 clinically stable chronic hemodialysis patients. Following a two-week phosphate binder washout period, patients previously treated with calcium carbonate at the mean (± SD) dose of 3.2 ± 1.1 g/day were treated with Sevelamer HCl for 6 weeks. The treatment period was followed by two additional weeks of washout.

Starting doses of Sevelamer HCl (capsules, 403 mg) varied depending on the patient’s degree of hyperphosphatemia at the end of the first washout period. Patients with serum phosphate levels between 5.5 and 6.5 mg/dL received 5 capsules per day (1+2±2 capsules with meals); between 6.5 and 7.5 mg/dL, 7 capsules per day (1+3+3); and over 7.5 mg/dL, 9 capsules per day (1+4+4). All patients were treated with a bicarbonate concentration of 34 mmol/L in the dialysis fluid, and the duration of dialysis was 3 to 4 hours (mean ± SD: 3.7 ± 0.5 hours).

During the six weeks of treatment with Sevelamer HCl a significant reduction of serum phosphate (from 7.3 ± 1.6 to 5.5 ± 0.8 mg/dL, P < 0.001) and of calcium × phosphate product (from 64.6 ± 15.9 to 48.1 ± 7.7 mg²/dL², P < 0.001) was observed, confirming its excellent efficacy as a phosphate binder. Results regarding the change in serum bicarbonate concentration after discontinuation of calcium carbonate and during treatment with Sevelamer HCl are illustrated in Table 1. At the end of the two-week washout period, the serum bicarbonate decreased by a mean of 1.9 mmol/L, from 20.1 ± 2.6 to 18.2 ± 3.1 mmol/L. A further reduction to 17.3 ± 3.2 mmol/L was observed in the first week of treatment with Sevelamer HCl, but bicarbonate levels remained stable during the following weeks of treatment and during the two-week washout after discontinuation of Sevelamer HCl. Analysis of variance (ANOVA) failed to detect significant variations of bicarbonate levels. However, the decrease observed at three weeks after discontinuation of calcium carbonate was significant (P < 0.05) at the individual posttest when compared to baseline values.

Acidemia in patients with chronic renal failure should be avoided because bone buffering of some of the excess hydrogen ions is associated with the release of calcium and phosphate from bone [4]. Preventing this change may minimize the degree of negative calcium balance and prevent or delay the progression both of osteopenia and of hyperparathyroid bone disease. In this short term study, no clinically significant changes in bicarbonate levels could be observed after discontinuation of calcium carbonate and during treatment with Sevelamer HCl in hemodialysis patients. However, a transient decrease was observed in the first three weeks after discontinuation of calcium carbonate. Such a reduction appears to be dependent on the withdrawal of calcium carbonate (and the consequent reduced intake of alkali) rather than on treatment with Sevelamer HCl. Bone buffering could have prevented further decreases of bicarbonate levels. This hypothesis underscores the need for further studies on acid-base balance during long-term treatment with Sevelamer HCl, in patients who discontinue calcium salts.

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REFERENCES
**Table 1.** Weekly determinations of predialysis serum bicarbonate levels (mean ± standard deviation) during the study

<table>
<thead>
<tr>
<th>Week</th>
<th>Wash-out</th>
<th>Treatment with Sevelamer HCl</th>
<th>Wash-out</th>
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<tbody>
<tr>
<td></td>
<td>w.o. -2</td>
<td>w.o. -1</td>
<td>0</td>
</tr>
<tr>
<td>Mean</td>
<td>20.05</td>
<td>18.9</td>
<td>18.2</td>
</tr>
<tr>
<td>SD</td>
<td>2.56</td>
<td>3.15</td>
<td>3.07</td>
</tr>
</tbody>
</table>

Abbreviations are: w.o., wash-out; Rx, treatment with Sevelamer HCl (begun at time 0).

<sup>a</sup> P < 0.05 by the uncorrected ANOVA post-test vs. baseline values

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