Author's response to reviews

Title: Differential effects of phosphate binders on pre-dialysis serum bicarbonate in end-stage kidney disease patients on maintenance haemodialysis

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Author's response to reviews: see over
Reviewer:
The authors have addressed my comments adequately, although a number of minor typographical errors remain.

Response:
We have corrected some minor typographical errors we have identified. Some of these may be special character errors by the system when the article is uploaded. Please let us know if there are any specific typographical errors of concern remaining in the manuscript.

Reviewer:
However, the covering letter also deals with the question of oral or dialysis fluid supplementation of bicarbonate. This introduces another layer of complexity.

1. Is there any evidence that all patients had supplementary bicarbonate if venous levels fell below 18mmol/L?
2. Was application of this policy uniform and unbiased? In an observational study this seems unlikely.
3. Can the authors tell us how many patients had oral supplements versus dialysis fluid supplementation versus no supplements, and what was the breakdown by type of phosphate binder?
4. If the patient changed binder, was the venous bicarbonate supplementation reviewed? Were there criteria for stopping the supplement at a certain level of venous bicarbonate?

Response Q1&2:
Both Western & Melbourne Health Nephrology units have the same monthly blood audit policy. It was a standard practice to supplement bicarbonate by increasing dialysate bicarbonate concentration from 35 mmol/L to 40 mmol/L and not supplement oral bicarbonate at monthly blood audit in both units when serum bicarbonate fell below 18mmol/L. The audits were conducted by the same clinician in the respective centres during the period. In order to avoid post-dialysis alkalemia, dialysate bicarbonate concentrations were modified back to 35mmol/L when pre-dialysis serum bicarbonate was ≥24 mmol/L, irrespective of phosphate binders used.
Response Q3:
Majority (approximately 90-95%) remained on the same binders at each of the 6 month study period. Both Melbourne and Western Health units phased out oral bicarbonate supplementation. During the study period, auditors identified only 2% of the cohort who remained on oral sodium bicarbonate and terminated the treatment completely. Patients who required an increased dose of dialysate bicarbonate are summarized in table 4. Compared to Group (A) Ca/Al, Group B (SH) and Group D (SH plus Ca/AL) received more alkali supplementation by increasing dose of dialysate bicarbonate. We have added above information in the article. This if anything would have biased our results toward a negative effect. (Please see page 6 and table 4)

Table 4: Number of patients (%) who required increased dose of dialysate bicarbonate

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<thead>
<tr>
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<tbody>
<tr>
<td>Group A (Ca &amp; Al)</td>
<td>10/108</td>
<td>5/83</td>
<td>6/81</td>
</tr>
<tr>
<td>Group B (SH)</td>
<td>21/80</td>
<td>17/76</td>
<td>6/68</td>
</tr>
<tr>
<td>Group C (LC)</td>
<td>0/24</td>
<td>0/22</td>
<td>1/21</td>
</tr>
<tr>
<td>Group D (SH &amp; Ca/Al)</td>
<td>19/60</td>
<td>13/59</td>
<td>5/50</td>
</tr>
<tr>
<td>Group E (LC &amp; Ca/Al)</td>
<td>1/20</td>
<td>2/20</td>
<td>3/17</td>
</tr>
<tr>
<td>P Value (B&amp;D cf. A)</td>
<td>&lt;0.001</td>
<td>&lt;0.004</td>
<td>0.67</td>
</tr>
</tbody>
</table>

Group A (Calcium and/or Aluminum binders);
Group B (Sevelamer hydrochloride alone);
Group C (Lanthanum carbonate alone);
Group D (Sevelamer hydrochloride and Calcium and/or Aluminum binders);
Group E (Lanthanum carbonate and Calcium and/ Aluminum binders)

Response Q4: As mentioned in response to Q1 and 2, the bicarbonate baths were changed in response to monthly blood tests as a part of routine and consistent audit and not to changing phosphate binders.
We appreciate the reviewer’s concerns and we have added our audit policy of correcting acidosis and terminating alkali therapy in the Material & Method section of the article. (Please see page 4 & 5)