Associations of Dialysate Bicarbonate with Mortality: Results from the Dialysis Outcomes and Practice Patterns Study

F Tentori¹, J Zhang¹, A Sen², H Morgenstern², B Robinson¹,², H Rayner³, R Fissell⁴, R Vanholder⁵, T Tomo⁶, F Port¹,²

¹Arbor Research Collaborative for Health, Ann Arbor, USA; ²University of Michigan, Ann Arbor, USA; ³Birmingham Heartlands Hospital, Birmingham, United Kingdom; ⁴Cleveland Clinic Foundation, Cleveland, USA; ⁵University Hospital Gent, Gent, Belgium; ⁶Oita University, Yufu, Japan
Acknowledgements

The DOPPS would not be possible without the generous financial support of the following companies who have demonstrated their strong commitment to independent scientific research to improve patient care:

- Amgen (since 1996)
- Kyowa Hakko Kirin (since 1999, in Japan)
- Abbott Laboratories (since 2009)
- Genzyme (since 2009)
- Baxter Healthcare (since 2011)

Support from DOPPS sponsors is provided without restrictions on publications.
Background

• Pre-dialysis metabolic alkalosis has been associated with elevated mortality risk in patients on maintenance hemodialysis (HD) [e.g. Bommer AJKD 2004]

• We hypothesized that use of high dialysate bicarbonate (DB), which could result in severe post-dialysis metabolic alkalosis, may adversely affect clinical outcomes
Methods

• Study population:
  – Exclusions: Patients in centers using non-bicarbonate dialysate (<1%)

• Outcome: all-cause mortality

• Covariates:
  – Age, sex, BMI, vintage, 13 comorbidities, albumin, hemoglobin, serum bicarbonate, SBP, residual kidney function, catheter use, and spKt/V

• Model:
  – Cox models stratified by country and study phase, and accounting for facility level clustering
Bicarbonate vs. Total Base Concentration

- ‘Bicarbonate’ dialysate often also contains acetate at 2-4 (up to 8) mEq/L

- Study coordinators were asked to provide the prescribed dialysate base/buffer concentration as sum of acetate and bicarbonate if combined

- In this presentation, concentration of ‘dialysis bicarbonate’ refers to total base concentration

- Some misclassification of total base concentration was possible (if acetate content was not appreciated)
Dialysate Bicarbonate by Country

% of patients

D.B (mEq/L)

- D.B > 37
- D.B 34-37
- D.B < 34

<table>
<thead>
<tr>
<th>Country</th>
<th>N patients</th>
<th>Mean D.B</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANZ</td>
<td>1172</td>
<td>35.2</td>
</tr>
<tr>
<td>BE</td>
<td>1313</td>
<td>34.5</td>
</tr>
<tr>
<td>CA</td>
<td>1110</td>
<td>36.3</td>
</tr>
<tr>
<td>FR</td>
<td>1391</td>
<td>34.9</td>
</tr>
<tr>
<td>GE</td>
<td>1402</td>
<td>32.1</td>
</tr>
<tr>
<td>IT</td>
<td>1235</td>
<td>34.0</td>
</tr>
<tr>
<td>SP</td>
<td>1531</td>
<td>35.4</td>
</tr>
<tr>
<td>SW</td>
<td>1361</td>
<td>34.4</td>
</tr>
<tr>
<td>UK</td>
<td>881</td>
<td>35.3</td>
</tr>
<tr>
<td>US</td>
<td>4318</td>
<td>36.8</td>
</tr>
<tr>
<td>ALL</td>
<td>15714</td>
<td>35.2</td>
</tr>
</tbody>
</table>

* % of facilities where ≥ 90% of patients use a single D.B concentration
Source: DOPPS 2-3 data; Japan not shown due to possible misclassification issues
Mortality is Positively Associated with Dialysate Bicarbonate Concentration

Hazard Ratio (95% CI)

- D.B < 34
- D.B 34-37
- D.B > 37

*(Ref.)*

All patients

Individualized* D.B facilities

Non-Individualized* D.B facilities

*Non-individualized defined as ≥90% of patients in a facility prescribed the same D.B; All other facilities defined as Individualized.

Source: DOPPS 2-3 data; Cox model stratified by phase and region, adjusted for age, sex, vintage, BMI, 13 comorbidities, albumin, hemoglobin, SBP, vascular access, residual kidney function, Kt/V, serum bicarbonate, and facility clustering.

Adapted from Tentori et al. ASN 2011 abstract
Many Facilities Use A Single Dialysate Bicarbonate Concentration

% of facilities that do not individualize D.B*

* % of facilities where ≥ 90% of patients use a single D.B concentration
Source: DOPPS 2-3 data; Japan not shown due to possible misclassification issues
Dialysate Bicarbonate Concentration Varies, Even Between ‘Non-Individualized’ Facilities

% of patients

- **All patients**
  - > 37 mEq/L: 27%
  - 34-37 mEq/L: 54%
  - < 34 mEq/L: 20%

- **Individualized* D.B facilities**
  - > 37 mEq/L: 29%
  - 34-37 mEq/L: 48%
  - < 34 mEq/L: 23%

- **Non-individualized* D.B facilities**
  - > 37 mEq/L: 18%
  - 34-37 mEq/L: 57%
  - < 34 mEq/L: 25%

*Non-individualized defined as ≥90% of patients in a facility prescribed the same D.B; All other facilities defined as Individualized; Source: DOPPS 2-3 data
Mortality is Positively Associated with Dialysate Bicarbonate Concentration

Hazard Ratio (95% CI)

- **D.B < 34**: p=0.005
- **D.B 34-37**: p=0.08
- **D.B > 37**: p=0.04

All patients

Individualized* D.B facilities

Non-Individualized* D.B facilities

*Non-individualized defined as ≥90% of patients in a facility prescribed the same D.B; All other facilities defined as Individualized;
Source: DOPPS 2-3 data; Cox model stratified by phase and region, adjusted for age, sex, vintage, BMI, 13 comorbidities, albumin, hemoglobin, SBP, vascular access, residual kidney function, Kt/V, serum bicarbonate, and facility clustering; P-values represent the effect of D.B as a continuous variable

Adapted from Tentori et al. ASN 2011 abstract
Dialysate Bicarbonate and Mortality, by Serum Bicarbonate

Hazard Ratio (95% CI)

Source: DOPPS 2-3 data; Cox model stratified by phase and region, adjusted for age, sex, vintage, BMI, 13 comorbidities, albumin, hemoglobin, SBP, vascular access, residual kidney function, Kt/V, serum bicarbonate, and facility clustering; P-values represent the effect of D.B as a continuous variable

Adapted from Tentori et al. ASN 2011 abstract
Additional Analyses

• The association of higher DB with higher mortality did not vary appreciably by level of serum or dialysate potassium, or serum or dialysate calcium.

• Findings did not differ appreciably when excluding Japan.

• Similar findings were observed using an upper cutpoint of >35 mEq/L (rather than >37 mEq/L).
Summary / Conclusion

• High dialysate bicarbonate ( >37 mEq/L):
  – Is quite common, especially in US
  – Is associated with higher mortality

• This association is most apparent among patients with low predialysis serum bicarbonate

• Dialysate composition can easily be modified, and avoidance of high DB may have a beneficial impact on survival

• This novel finding, and mechanisms such as the possible role of post dialysis alkalosis, deserve further study