Best Practices in Dialysate Composition: 
The New 45x Concentrate Series

Fresenius NaturaLyte® and GranuFlo®
Acid Concentrate
Topics

• Background in Concentrates Selection
• Best Practices in Dialysate Composition:
  – Dextrose 100 mg/dL for physiologic glucose balance
  – Magnesium 1.0 mEq/L for intradialytic hemodynamic stability
  – Sodium 100 mEq/L in the acid portion for prescriptive consistency
• Potential Clinical Benefits of Improved Dialysate:
  – Less frequent and severe hypoglycemic episodes\textsuperscript{1}
  – Lower amounts of glucose lost in effluent dialysate\textsuperscript{1}
  – Less fatigue\textsuperscript{5}
  – Helps prevent vascular calcification in hemodialysis patients\textsuperscript{2,4}
  – Less intradialytic hypotension\textsuperscript{3,4}
  – Potentially lower mortality risk\textsuperscript{6}

While maintaining patient quality outcomes to potentially improve quality of life
Background in Concentrate Selection

1943 to 1960
• Bicarbonate-based solution used in batch containers, but precipitation & bacterial contamination remained problematic

1964 to 1985
• Acetate-based solutions widely used world-wide
• 200 mg/dL dextrose added in ~1978 to prevent hypoglycemia & hypotension
• In many parts of the world, dextrose was not added due to additional cost & risk of bacterial contamination

1978 to present
• Bicarbonate-based solutions used only
• 100 - 200 mg/dL dextrose offered in 3 series due to machine limitations

2009 to present
• Fresenius standardizes use of best practice dialysate composition in one series

1. Reference
2. Reference
The new 45X Series acid standardizes:

- Dextrose concentration to 100 mg/dL
- Magnesium concentration to 1.0 mEq/L
- Sodium concentration to 100 mEq/L
Dextrose
For Physiologic Glucose Balance
The Importance of Glucose in Dialysate

- Prevents hypoglycemia
  - Hypoglycemia frequently occurs in patients on HD\(^1\-^3\)
  - More frequent among diabetics if glucose is not added to the dialysate\(^2,^3\)
  - During a glucose-free dialysis session, 15 to 30 g of glucose is lost in the effluent dialysate\(^4\)

- Achieves hypertonicity and increases UF\(^2,^5\) in the early days of HD

- Prevents hypotension
  - Some studies suggest that glucose in the dialysate helps prevent hypotension through increased extracellular osmolality and prevention of IV fluid loss into the intracellular compartment.\(^1,^2\)

- Helps to prevent disequilibrium syndrome\(^3,^4\)

- Provides additional calories
Best Practices in Dialysate Composition

Glucose Helps Reduce Number & Severity of Hypoglycemic Episodes

Background: Burmeister et al compared glucose free and glucose dialysate for HD in 42 subjects in sequential 1 week periods

Results:
- Mean blood glucose level was higher in the 90 mg/dL glucose period than in the glucose-free period (p = 0.0392)
- The effect of glucose containing dialysate was significant in diabetic subjects (DM) (p= 0.0067), and non-significant in non-diabetics (NDM) (p = 0.06)

Authors Conclusion:
- Glucose-added dialysate at 90 mg/dl significantly reduced the number and severity of HG episodes
- Glucose in dialysate advisable in all patients despite higher mean blood glucose in DM patients during HD
Prevent Inappropriate Loss of Glucose in Effluent

Result:

- Burmeister et al also noted that glucose lost in effluent dialysate was significantly lower when using glucose-added dialysate ($p < 0.0001$)
  - All patients: $16.7 \pm 10.9$ g/h with 90 mg/dL glucose dialysate; $5.2 \pm 2.9$ non-glucose dialysate
  - DM patients: $18.5 \pm 10.6$ with glucose dialysate; $8.5 \pm 4.9$; non-glucose dialysate; $p < 0.001$
  - NDM patients: $15.4 \pm 12.0$ with glucose dialysate; $2.2 \pm 0.3$ non-glucose dialysate; $p < 0.000$
Glucose Balance According to Dialysate Concentration

Based on the available literature, we should expect the following glucose gains and losses according to dialysate glucose concentration:

<table>
<thead>
<tr>
<th>Dialysate Glucose Concentration</th>
<th>Anticipated Glucose Gains / Losses*</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg/dL</td>
<td>g/tx</td>
</tr>
<tr>
<td>Zero(^1,2)</td>
<td>- 50 to - 60</td>
</tr>
<tr>
<td>90(^2)</td>
<td>- 15 to – 20</td>
</tr>
<tr>
<td>100(^3)</td>
<td>- 5 to + 10</td>
</tr>
<tr>
<td>200(^3)</td>
<td>+ 20 to + 30</td>
</tr>
</tbody>
</table>

A net of ~ zero

* Based on 3 – 4 hr treatments
Reasons to Avoid High Glucose Dialysate (>100 mg/dL)

- Excessive caloric load may increase risk of obesity\(^1\)
- Increases risk of hyperglycemia in diabetic patients\(^2\)
- Increases risk of hyperinsulinemia\(^3\)
- Potential interference with potassium and phosphorus removal\(^2\)
- Potential causative factor in the inflammation associated with ESRD\(^3\)
Less Fatigue With Use of 100 mg/dL Dextrose

Background: Raimann et al studied the difference in fatigue in chronic HD patients treated with 100 mg/dL versus 200 mg/dL dialysate dextrose.

Results:

• Fatigue Severity Score was higher with 200 mg/dL dextrose dialysate especially for diabetic patients
• Fatigue is more prominent using a dialysate dextrose of 200 mg/dL as compared to 100 mg/dL

Authors Conclusion:

• Dialysate dextrose concentration of 100 mg/dL is potentially advantageous.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Dextrose 200 mg/dL</th>
<th>Dextrose 100 mg/dL</th>
<th>P-Value (D100 vs D200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetics</td>
<td>13</td>
<td>4.97 ± 1.0 *</td>
<td>4.23 ± 1.13 *</td>
<td>0.016</td>
</tr>
<tr>
<td>Non-Diabetics</td>
<td>14</td>
<td>3.46 ± 1.87 *</td>
<td>3.0 ± 1.55 *</td>
<td>0.234</td>
</tr>
<tr>
<td>All Patients</td>
<td>27</td>
<td>4.19 ± 1.68</td>
<td>3.6 ± 1.48</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Fatigue index as assessed by the Fatigue Severity Scale

* Indicates p<0.05 between diabetics and non-diabetics

Magnesium
For Intradialytic Hemodynamic Stability
Magnesium is Important for ESRD Patients

**Magnesium:***
- Controls serum phosphate
- Controls hyperthyroidism

**Magnesium:***
- ↓ serum PTH levels
- ↓ vascular calcification
- ↓ left ventricular hypertrophy
- ↓ mortality

**Magnesium Suppresses Inflammation:**
- ↓ Immune response
- ↓ Constitutive nitric oxide synthase

**Magnesium Regulates:**
- Vascular tone
- Heart rhythm
- Blood pressure

**Magnesium Prevents:**
- Thrombosis
- Atherosclerosis
- Arrhythmias
- Osteoporosis
- Insulin Resistance


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Higher Serum Mg Levels May Prevent Vascular Calcification

Background:
• Vascular calcification, significantly increases cardiovascular and other causes of mortality, and is highly prevalent in HD patients.¹
• Ishimura et al examined the association between serum Mg levels and vascular calcification in 390 NDM hemodialysis patients.

Results:
Serum Mg was significantly lower in patients with vascular calcification than in those without (2.69 ± 0.28 vs. 2.78 ± 0.33 mg/dL, \( p < 0.05 \) after adjustments for age, gender, duration of HD, Ca, PO4, and intact parathyroid hormone concentrations.

Conclusion:
• Higher serum Mg concentrations may play an important protective role in the development of vascular calcification in HD patients.
• Mg concentration of dialysis fluid may need to be reconsidered in view of preventing vascular calcification in HD patients.

Mg Important For Intradialytic Hemodynamic Stability

**Background:**

- Intradialytic hypotension continues to be a problem in up to 20% of HD treatments.\(^1\)
- Mg exerts a direct modulatory action on cardiac excitability and vascular smooth muscle contraction and relaxation.
- Hypomagnesemia has been shown to contribute significantly to cardiac morbidity and mortality.\(^1\)
- Kyriazis et al evaluated the effect of dialysate magnesium levels upon blood pressure in a blinded, two-part study of 8 HD patients in study A, 14 patients in study B.

**Study A:** Used four combinations of dialysate Mg of 0.25 (low) or 0.75 (high) mmol/L and Ca of 1.25 (low) or 1.75 (high) mmol/L.

**Study A Results:**

- Blood Pressure, Mean Arterial Pressure, Cardiac Index, and Stroke Index all fell to a greater extent in group IV dialyzing on the low Mg and low Ca solution.
- Total Peripheral Resistance Index remained unchanged in group IV indicating that the hypotensive effect was due primarily to the changes in cardiac output through changes in stroke volume.

Mg Important For Intradialytic Hemodynamic Stability

_Study B:_ Held the Ca constant at 1.25 mmol/L while randomly varying the dialysate Mg to:

- Low: 0.25 mmol/L
- Medium: 0.50 mmol/L
- High: 0.75 mmol/L

_Study B Results:_

- Less symptomatic hypotension in the high Mg treatments
- Fewer episodes of asymptomatic and total hypotension in the high Mg treatments as compared to the low and medium Mg treatments

<table>
<thead>
<tr>
<th>Symptom</th>
<th>HdMg N (%)</th>
<th>LdMg N (%)</th>
<th>MdMg N (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic hypotension</td>
<td>7 (4.2)</td>
<td>18 (10.7)</td>
<td>13 (7.7)</td>
<td>0.019</td>
</tr>
<tr>
<td>Asymptomatic hypotension</td>
<td>11 (6.5)</td>
<td>26 (15.4)</td>
<td>24 (14.3)</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Total hypotension</td>
<td>18 (10.7)</td>
<td>44 (26.2)</td>
<td>37 (22.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Authors Conclusions:**

1. **Treatment with a combination of low Ca and low Mg dialysate should be avoided** especially in the hypotensive-prone patients with impaired cardiovascular function.
2. **Use of high Mg dialysate may be an easy way to prevent hypotension** in patients treated with low Ca dialysate.


Best Practices in Dialysate Composition
Higher Serum Mg Levels Associated With Lower Mortality Risk

**Background:**
- Lacson et al evaluated the effect of magnesium levels on mortality risk in a contemporary cohort of 27,544 HD patients.

**Results:**
- There is a linear trend with lower mortality risk associated with increasing Mg levels.
- Compared to mid-normal values (Mg = 1.6 – 1.89 mEq/L), the unadjusted hazard ratio drops significantly at Mg ≥ 1.9, to as low as 0.68 for Mg > 2.3 (p < 0.001).

**Authors Conclusion:**
- High normal and elevated serum magnesium levels were associated with lower risk of mortality in prevalent HD patients.

Maintaining Patient Quality Outcomes
Less Intradialytic Saline Administered (Surrogate for Hypotension)

**Background:** Comparison of 2,978 patients using 100 mg/dL dextrose dialysate to 9,295 standard or 200 mg/dL dextrose dialysate patients.

**Results:** The average volume of fluids given was ~10% lower in the 100 mg/dL dextrose patients.

**Conclusion:** Suggests that some patients may have experienced less frequent or less pronounced intradialytic hypotension.
Patient Quality Outcomes Maintained

**Background:**
Diabetic and non-diabetic HD patients were compared for those being treated with dialysate containing 100 mg/dL dextrose versus those being treated with dialysate containing 200 mg/dL dextrose.

<table>
<thead>
<tr>
<th>Number of Patients by Group:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic patients</td>
</tr>
<tr>
<td>100 dex</td>
</tr>
<tr>
<td>n = 1,478</td>
</tr>
<tr>
<td>Non-diabetic patients</td>
</tr>
<tr>
<td>100 dex</td>
</tr>
<tr>
<td>n = 1,320</td>
</tr>
<tr>
<td>Diabetic patients</td>
</tr>
<tr>
<td>200 dex</td>
</tr>
<tr>
<td>n = 4,928</td>
</tr>
<tr>
<td>Non-diabetic patients</td>
</tr>
<tr>
<td>200 dex</td>
</tr>
<tr>
<td>n = 4,367</td>
</tr>
</tbody>
</table>

**Results:**
No clinically significant differences in patient quality outcomes were noted between the patient groups. The following patient quality outcomes were maintained:

- eKt/V $\geq 1.2$
- Bicarbonate 22-26 mEq/L
- HgB $\geq 11$ g/dL
- TSAT $\geq 20$
- Albumin $\geq 3.8$ g/dL
- Ferritin 100-500 ng/mL
- Phosphorus $\leq 5.5$ mg/dL
- I-PTH 150-300 pg/mL (over 12 mos)

**Conclusion:**
Diabetic and non-diabetic patients were able to adequately maintain quality outcomes after switching to the 100 mg/dL dextrose dialysate.

Data Source: FMS Data Warehouse
Summary

• **Best Practices in Dialysate Composition:**
  – Dextrose 100 mg/dL for physiologic glucose balance
  – Magnesium 1.0 mEq/L for intradialytic hemodynamic stability
  – Sodium 100 mEq/L in the acid portion for prescriptive consistency

• **Potential Clinical Benefits of Improved Dialysate:**
  – Less frequent and severe hypoglycemic episodes\(^1\)
  – Lower amounts of glucose lost in effluent dialysate\(^1\)
  – Less fatigue\(^5\)
  – Helps prevent vascular calcification in hemodialysis patients\(^2,4\)
  – Less intradialytic hypotension\(^3,4\)
  – Potentially lower mortality risk\(^6\)

*While maintaining patient quality outcomes to potentially improve quality of life*