ADVANCES IN THE NUTRITIONAL MANAGEMENT OF HYPERPHOSPHATEMIA AMONG HEMODIALYSIS PATIENTS

Rana G. Rizk, PhD, MPH, LD
Maastricht University, The Netherlands

October, 2017
Learning objectives

• Review the guidelines and available treatment options for hyperphosphatemia among hemodialysis patients

• Examine the traditional approach to dietary management of hyperphosphatemia

• Recognize the importance of differentiating between sources of dietary phosphate in hyperphosphatemia management

• Discuss the best approach to dietary management of hyperphosphatemia
Phosphate homoeostasis in humans

1500 mg
Food
20 mg kg⁻¹ day⁻¹

1100 mg
Total absorbed intestinal phosphorus
16 mg kg⁻¹ day⁻¹

200 mg
Digestive juice phosphorus
3 mg kg⁻¹ day⁻¹

200 mg
Bone
Formation
3 mg kg⁻¹ day⁻¹
Resorption
3 mg kg⁻¹ day⁻¹

600 mg
Feces
7 mg kg⁻¹ day⁻¹

900 mg
Kidney
Urine
13 mg kg⁻¹ day⁻¹
Phosphorus pool

Phosphate homoeostasis in CKD

Hruska et al., Kidney Int. 2008; 74(2): 148-57
Hyperphosphatemia in hemodialysis

- Jordan: 41%
- Egypt: 69.1%
- Lebanon: 40.4%

Most common single mineral deviation from KDOQI guidelines

<table>
<thead>
<tr>
<th>Phosphate binder type</th>
<th>Qatar</th>
<th>Saudi Arabia</th>
<th>UAE</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium-based only</td>
<td>100%</td>
<td>57%</td>
<td>84%</td>
<td>65%</td>
</tr>
<tr>
<td>Sevelamer only</td>
<td>0%</td>
<td>13%</td>
<td>15%</td>
<td>3%</td>
</tr>
<tr>
<td>Calcium + sevelamer only</td>
<td>0%</td>
<td>23%</td>
<td>2%</td>
<td>33%</td>
</tr>
<tr>
<td>Other binder or combination</td>
<td>0%</td>
<td>7%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>
Why do we even care?! Hyperphosphatemia & mortality

“Silent killer of hemodialysis patients”

What is the evidence?

Hyperphosphatemia & adverse outcomes

Hyperphosphatemia

↑ hospitalizations

↓ physical functioning

↑ pill burden

↑ cost

↓ QOL

Other

Blayney & Tentori, 2009; Bover et al., 2009; Danese et al., 2008; Floege et al., 2011; Heymann et al., 2012; Hruska et al., 2011; Johansen & Chertow, 2007; Lee et al., 2007; Moorthie & Moe, 2011; Naves-Diaz et al., 2011; Roman-Garcia et al., 2009; Tentori et al., 2008; Young et al., 2004; Young et al., 2005
Hyperphosphatemia management

Table 1  Phosphorus balance in HD patients

Recommended dietary intake
1000 mg/day × 7 = 7000 mg/week
Assumed gastrointestinal absorption (60%)
7000 mg/week × 0.6 = 4200 mg/week
Average elimination by hemodialysis (HD)
800 mg/HD × 3 = 2400 mg/week
Phosphorus balance = 1800 mg/week
Phosphorus mass to be bound by phosphate binders
1800 mg: 7 days = 250 mg/day

KDIGO, 2009; KDOQI, 2003
Traditional dietary phosphate restriction

20 years ago dietitians emphasized controlling hyperphosphatemia by absolute dietary phosphate restriction

... and this dish is totally phosphorus-free!
What is the evidence?

**Dietary phosphate restriction & mortality**

- *Post hoc* analysis of data from the Hemodialysis Study (*n*=1751)
- More restrictive phosphate prescription → **poorer indices of nutritional status**

Traditional dietary phosphate restriction

Did we miss anything?!

Estimated phosphate intake (mg/dl) calculated from daily protein intake (g/d) in hemodialysis patients from the NIED study (n=107)

Phosphorus Estimation Equation \( \leftrightarrow \) Protein Intake (assuming minimal additives)

\[
\text{Dietary phosphorus (milligrams)} = 78 + 11.8 \times \text{(protein intake [grams])}
\]

\( r = 0.91, \ P < 0.001 \)

Kalantar-Zadeh et al., CJSN. 2010; 5:519-30
What is the evidence?

**Dietary phosphate, protein & mortality**

![Graph showing the relationship between phosphorus intake and death rate ratio.]

- The risk of controlling serum phosphate by restricting protein intake may outweigh the benefit of controlled phosphate intake.
- May ↑mortality.
- ↑protein intake → ↑survival.
- ↑↑survival with simultaneous ↓serum phosphate.

Traditional dietary phosphate restriction

Did we miss anything?! 

The efficacy of traditional phosphate restriction has not been established

Absolute dietary phosphate restriction does not distinguish between types of phosphate

Could result in protein restriction

This restriction may lead to a lower intake of nutrient dense foods, and result in restriction of other nutrients, such as dietary fiber

Fouque et al., AJKD. 2014;64(1):143-50; Kalantar-Zadeh et al., CJASN. 2010; 5:519-30; KDOQI, 2003; Noori et al., IJKD. 2010;4:89-100
# Phosphorus-to-protein ratio

<table>
<thead>
<tr>
<th>P-to-Protein Ratio &lt; 5</th>
<th>P-to-Protein Ratio 10 &lt; 15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg white, large</td>
<td>Egg substitute, ¼ c.</td>
</tr>
<tr>
<td>Orange roughy, 3 oz.</td>
<td>Salmon-sockeye, 3 oz.</td>
</tr>
<tr>
<td><strong>P-to-Protein Ratio 5 &lt; 10</strong></td>
<td>Bagel, 4”</td>
</tr>
<tr>
<td>Lamb, 3 oz.</td>
<td>Cheeseburger, fast food</td>
</tr>
<tr>
<td>Tuna, water packed, 3 oz.</td>
<td>Bologna, 2 slices</td>
</tr>
<tr>
<td>Chicken drumstick</td>
<td>Cottage cheese, ½ c.</td>
</tr>
<tr>
<td>Beef, 3 oz.</td>
<td>Tuna, oil packed, 3 oz.</td>
</tr>
<tr>
<td>Ground beef, 3 oz.</td>
<td>Tempeh, ½ c.</td>
</tr>
<tr>
<td>Chicken breast, 3 oz.</td>
<td>Tofu raw, ½ c.</td>
</tr>
<tr>
<td>Turkey, 3 oz.</td>
<td>Peanut butter, 1 T.</td>
</tr>
<tr>
<td>Pork sausage, 2 links</td>
<td>Whole egg, large</td>
</tr>
<tr>
<td>Taco, fast food</td>
<td>Frankfurter, beef, 1</td>
</tr>
<tr>
<td>Soy protein isolate, 1 oz.</td>
<td>Lima beans, ½ c.</td>
</tr>
</tbody>
</table>
Phosphorus-to-protein ratio

• Advantages
  • Simultaneous representation of dietary phosphate & protein
    • Helps in selecting foods with desirable ratio & not solely based upon phosphate content
    • Emphasize foods with high amount of phosphate additives but having similar amount of dietary protein
  • Does not depend on the food portion being served

• Disadvantages
  • Sometimes difficult to calculate
    • Variations & inaccuracies in estimations of phosphate content
  • Does not give any information about phosphate bioavailability

KDOQI, 2003
What is it with phosphate sources?!

- **Inorganic**
  - Food additives

- **Organic Animal**
  - Dairy derived
  - Meat or fish derived:
    - High phosphate: protein ratio
    - Low phosphate: protein ratio

- **Plant**
  - Plant derived

Phosphorus bioavailability:
- ≈100%
- 40-80%
- 20-40%

What is it with phosphate bioavailability?! 

The role of Phytate

Phosphate in meat is easily hydrolyzed & readily absorbed

Phosphate in plants is mostly in phytic acid or phytate form (75%)

Humans do not express phytase (low phosphate bioavailability: <50%)

↓ intestinal phosphate absorption per gram of plant vs. animal-based protein

Urinary phosphate excretion: meat >>> plant-based diet

Plant foods are less likely to ↑ phosphate burden

Kalantar-Zadeh et al., CJASN. 2010; 5:519-30
What is it with phosphate bioavailability?! The role of Phytate

The traditional approach of totally restricting intake of beans, peas, seeds & chocolate is of no major relevance?

• Important considerations
  • Even with ↓ fractional rate of intestinal absorption,
    ↑ intake can still lead to excessive phosphate burden
  • Some seeds & beans ↑ potassium → hyperkalemia
  • Yeast-based phytase in whole grains:
    ↑ absorption of phosphate in leavened breads than cereals or flat breads
  • Unclear effect of probiotics on phosphate absorption

Kalantar-Zadeh et al., CJASN. 2010; 5:519-30
What is it with protein digestibility?!

*Ratio adjusted for digestion & absorption*

Considers digestibility of protein & bioavailability of phosphate

### Protein digestibility

**Animal proteins:** 95%

**Plant proteins:** 85%

**Mixed meals:** 85% to 95%

#### Table: Ratio of mg Phosphorus to g Protein vs Ratio Adjusted for Digestion/Absorption

<table>
<thead>
<tr>
<th>Food Category</th>
<th>Ratio of mg Phosphorus to g Protein</th>
<th>Ratio Adjusted for Digestion/Absorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg white</td>
<td>1.4</td>
<td>1</td>
</tr>
<tr>
<td>Meat</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Tofu</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Egg</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Legumes</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td><strong>Lentils</strong></td>
<td><strong>20</strong></td>
<td><strong>12</strong></td>
</tr>
<tr>
<td>Nuts</td>
<td>25</td>
<td>15</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Food</th>
<th>Amount</th>
<th>Actual Content of Phosphorus (mg)</th>
<th>Actual Content of Protein (g)</th>
<th>Ratio of mg Phosphorus to g Protein</th>
<th>Phosphorus Content (mg) Adjusted for Bioavailability</th>
<th>Protein Content (g) Adjusted for Digestibility</th>
<th>Ratio of mg Phosphorus to g Protein Adjusted for Digestion and Absorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk/Dairy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cottage cheese, nonfat</td>
<td>1 cup</td>
<td>151</td>
<td>25</td>
<td>6.0</td>
<td>106</td>
<td>23.8</td>
<td>4.4</td>
</tr>
<tr>
<td>Cottage cheese, regular</td>
<td>1 cup</td>
<td>297</td>
<td>28</td>
<td>10.6</td>
<td>208</td>
<td>26.6</td>
<td>7.8</td>
</tr>
<tr>
<td>Cottage cheese, 2%</td>
<td>1 cup</td>
<td>340</td>
<td>31</td>
<td>11.0</td>
<td>238</td>
<td>29.5</td>
<td>8.1</td>
</tr>
<tr>
<td>Milk, soy, unfortified</td>
<td>1 cup</td>
<td>126</td>
<td>8</td>
<td>1.6</td>
<td>88</td>
<td>7.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Cheese</td>
<td>2 Tbsp</td>
<td>30</td>
<td>2</td>
<td>1.6</td>
<td>21</td>
<td>1.9</td>
<td>1.9</td>
</tr>
<tr>
<td>Cheese, mozzarella</td>
<td>1 oz</td>
<td>100</td>
<td>6</td>
<td>16.6</td>
<td>70</td>
<td>5.7</td>
<td>12.2</td>
</tr>
<tr>
<td>Cheese, cheddar</td>
<td>1 oz</td>
<td>145</td>
<td>7</td>
<td>20.7</td>
<td>102</td>
<td>6.7</td>
<td>15.3</td>
</tr>
<tr>
<td>Cheese, swiss</td>
<td>1 oz</td>
<td>171</td>
<td>8</td>
<td>21.4</td>
<td>120</td>
<td>7.6</td>
<td>15.8</td>
</tr>
<tr>
<td>Sour cream</td>
<td>1 Tbsp</td>
<td>32</td>
<td>2</td>
<td>26.7</td>
<td>12</td>
<td>1.1</td>
<td>19.7</td>
</tr>
<tr>
<td>Yogurt, regular</td>
<td>4 oz</td>
<td>107</td>
<td>4</td>
<td>26.8</td>
<td>75</td>
<td>3.8</td>
<td>19.7</td>
</tr>
<tr>
<td>Yogurt, lowfat</td>
<td>4 oz</td>
<td>162</td>
<td>6</td>
<td>27.0</td>
<td>113</td>
<td>5.7</td>
<td>19.9</td>
</tr>
<tr>
<td>Light cream</td>
<td>1 cup</td>
<td>192</td>
<td>6</td>
<td>27.4</td>
<td>134</td>
<td>6.7</td>
<td>20.2</td>
</tr>
<tr>
<td>Ice cream, vanilla</td>
<td>1 cup</td>
<td>138</td>
<td>8</td>
<td>27.6</td>
<td>97</td>
<td>4.8</td>
<td>20.3</td>
</tr>
<tr>
<td>Milk, whole</td>
<td>1 cup</td>
<td>227</td>
<td>8</td>
<td>28.4</td>
<td>159</td>
<td>7.6</td>
<td>20.9</td>
</tr>
<tr>
<td>Milk, 2%</td>
<td>1 cup</td>
<td>232</td>
<td>8</td>
<td>29.0</td>
<td>162</td>
<td>7.6</td>
<td>21.4</td>
</tr>
<tr>
<td>Milk, 1%</td>
<td>1 cup</td>
<td>235</td>
<td>8</td>
<td>29.4</td>
<td>165</td>
<td>7.6</td>
<td>21.7</td>
</tr>
<tr>
<td>Yogurt, nonfat</td>
<td>4 oz</td>
<td>177</td>
<td>6</td>
<td>29.5</td>
<td>124</td>
<td>5.7</td>
<td>21.7</td>
</tr>
<tr>
<td>Heavy cream</td>
<td>1 cup</td>
<td>149</td>
<td>8</td>
<td>29.8</td>
<td>104</td>
<td>4.8</td>
<td>22.0</td>
</tr>
<tr>
<td>Milk, nonfat</td>
<td>1 cup</td>
<td>247</td>
<td>8</td>
<td>30.9</td>
<td>173</td>
<td>7.6</td>
<td>22.8</td>
</tr>
<tr>
<td>Milk, chocolate</td>
<td>1 cup</td>
<td>255</td>
<td>7</td>
<td>36.4</td>
<td>179</td>
<td>6.7</td>
<td>26.8</td>
</tr>
<tr>
<td>Hot fudge sundae</td>
<td>1 small</td>
<td>227</td>
<td>6</td>
<td>37.8</td>
<td>159</td>
<td>5.7</td>
<td>27.9</td>
</tr>
</tbody>
</table>
Focus on avoiding phosphate additives

- Consumption of phosphate additives: ≈ 1000 mg/day
  - 2 servings of additive-containing chicken products: 880 mg

- Difficult to precisely determine
  - Food industry is not required to report the quantity used
  - Only listing the additives used in the ingredient list

- Concerns of underestimation of dietary phosphate intake

- Processed foods
  - ↑ inorganic phosphate load
  - ↓ nutritional value
  - Often paired with sodium & potassium additives

Biruete et al., *J Ren Nut.* 2017;31:62-70
Many packaged foods have added phosphorus. Look for phosphorus, or for words with PHOS, on ingredient labels, like the one below. Choose a different food when the ingredient list has PHOS on the label.

**Ingredients:** Potatoes, Vegetable Oil (Partially Hydrogenated Soybean Oil), Salt, Dextrose, Disodium Dihydrogen Pyrophosphate...
International survey of renal care professionals

- Consumption of food made from fresh ingredients
- Consumption of fast food
- Consumption of food containing phosphorus-based additives
- Patient awareness of the phosphorus content of food

Fouque et al., J Ren Nut. 2014;24:110-5
Focus on avoiding phosphate additives

- Cluster RCT
- n=279; with serum phosphorus levels >5.5 mg/dL
- Counseling on avoiding phosphate additives vs. standard recommendations

### Table 2: Primary and Secondary Outcomes Among 145 Intervention and 134 Control Participants

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>Difference in Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phosphorous level, mg/dL</strong></td>
<td>7.2 (1.2)</td>
<td>7.1 (1.0)</td>
<td>-0.6 (-1.0 to -0.1)</td>
</tr>
<tr>
<td><strong>Food knowledge score</strong></td>
<td>67 (16)</td>
<td>66 (16)</td>
<td>3 (-1 to 7)</td>
</tr>
<tr>
<td><strong>Reads ingredient list</strong></td>
<td>53 (36)</td>
<td>62 (35)</td>
<td>22 (15 to 30)</td>
</tr>
<tr>
<td><strong>Reads nutrition facts label</strong></td>
<td>57 (36)</td>
<td>59 (39)</td>
<td>9 (1 to 17)</td>
</tr>
</tbody>
</table>

Executive summary of the 2017 KDIGO CKD-MBD Guideline update: What’s changed and why it matters

Limiting phosphate intake with phosphate sources as additional qualifier

Not all Phosphate is created equal

KDIGO, 2017
Cooking techniques to reduce phosphate content

- Boiling of sliced food using pressure cooker & discarding water
- Soaking in cold water (4°C) for 1 hour before thermal processing
- Significant reduction of phosphate content while preserving protein content

Ando et al., J Ren Nut. 2015;25:504-9
Cooking techniques to reduce phosphate content

<table>
<thead>
<tr>
<th>Milligrams of Potassium, Phosphorous, and Sodium per 100 g of Sample</th>
<th>0 Time</th>
<th>1 Hr</th>
<th>4 Hr</th>
<th>8 Hr</th>
<th>Total % Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>K</td>
<td>P</td>
<td>Na</td>
<td>K</td>
<td>P</td>
</tr>
<tr>
<td><strong>Legumes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Great Northern beans (C)</td>
<td>214</td>
<td>84</td>
<td>ND</td>
<td>38</td>
<td>51</td>
</tr>
<tr>
<td>Kidney beans (D)</td>
<td>215</td>
<td>104</td>
<td>ND</td>
<td>95</td>
<td>98</td>
</tr>
<tr>
<td>Lima beans (C)</td>
<td>306</td>
<td>70</td>
<td>ND</td>
<td>84</td>
<td>51</td>
</tr>
<tr>
<td>Peanuts (D)</td>
<td>549</td>
<td>310</td>
<td>ND</td>
<td>364</td>
<td>257</td>
</tr>
<tr>
<td>Soybeans (D)</td>
<td>1010</td>
<td>367</td>
<td>ND</td>
<td>116</td>
<td>184</td>
</tr>
<tr>
<td><strong>Processed meats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ham (C)</td>
<td>292</td>
<td>250</td>
<td>1104</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Hot dogs</td>
<td>155</td>
<td>222</td>
<td>1379</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Tuna (C)</td>
<td>136</td>
<td>92</td>
<td>219</td>
<td>5</td>
<td>51</td>
</tr>
</tbody>
</table>

- Patients’ feedback
  - Straightforward processing instructions
  - Product satisfactory vis-à-vis texture & visual appeal, slightly "bland" taste
  - "Demineralization" rated positively; "Leaching" & "dialyzing" rated "somewhat negative", "unappealing"

Jones, J Ren Nut. 2001;11:90-6
The “phosphorus pyramid”: a visual tool for dietary phosphate management in dialysis and CKD patients

Claudia D’Alessandro, Giorgina B Piccoli and Adamasco Cupisti
The “Phosphorus Pyramid”

D’Alessandro et al., BMC Nephrol. 2015;16:9
The “Phosphorus Pyramid”

D’Alessandro et al., BMC Nephrol. 2015;16:9
The “Phosphorus Pyramid”

D’Alessandro et al., BMC Nephrol. 2015;16:9
Self-adjustment of phosphate binder dose

1. A typical meal is depicted
2. Patients are instructed to eye-estimate the phosphate content of meal components using Phosphate Units (PU) (1 PU = 100 mg/serving)
3. Summing up PUs of each meal component to have the total meal PU
4. Adjusting phosphate binder pills to total meal PU based on prescribed number of pills per 1 PU (binder/unit ratio)

Ahlenstiel et al., Nephrol Dial Transplant. 2010;25:3241–9
Self-adjustment of phosphate binder dose

‘Phosphate Education Program’ (PEP); n=16 children with CKD

Suggested as first concept applying the idea of patient empowerment to the management of hyperphosphatemia in hemodialysis patients in binder use

Clinical studies are needed to establish its practical value

Re-channeling dietary counseling

Judicious dietary phosphate restriction while maintaining adequate dietary protein intake

*Individualize therapy*

Greater focus on identifying sources of added phosphate
& better appreciating that natural (organic) phosphate is not well absorbed

Phosphate content
Phosphate bioavailability
Phosphorus-to-protein ratios

Dietary phosphate restriction

Toussaint et al., *Nephrology*. 2017;22, (Suppl. 2):36–41
Take-home message

1. **Natural, unprocessed** foods with ↓ phosphorus-to-protein ratios
   - Adequate protein content

2. Identify added phosphate in processed foods

3. Choose commercial food items prepared **without phosphorus-containing additives**

4. Prepare foods at home, using wet cooking methods such as **boiling** (discard water)

5. **Substitute** commonly eaten high-phosphorus foods with nutritionally equivalent foods ↓ in bioavailable phosphate
   - Consistent with acceptable palatability

6. Take **phosphate binders** diligently

Take-home message

- **Nutrition education**
  - Patient education & open patient/team dialogue
  - Regular monitoring of phosphate & protein intake

- **Empower your patients**
  - Glossaries of additives used
  - Label-reading
  - Food charts with phosphate content, acceptable & less-acceptable choices
  - Phosphate-lowering cooking methods

---

DOI 10.1186/s41100-017-0095-x

---

Let's reduce phosphorus intake!

**Point 1: How to prepare instant noodles before eating**
- A lot of phosphorus food additives containing phosphorus are included in instant noodles.
- When preparing instant noodles, throw away the hot water after boiling the noodles, and soak the soup with new hot water.
- Similarly for cup noodles, throw away the hot water used for boiling the noodles, and soak the soup with new water. Add the packet preserving to the new hot water.
- Phosphorus additives melt in the hot water used for boiling noodles.
- You can reduce the amount of phosphorus additive by throwing away the hot water.
- Leave behind any excess soup!
- You can reduce your consumption of harmful excess salt, water and phosphorus additives which are harmful by doing this.

**Point 2: How to prepare processed food**
- Ham, Bacon
  - Let’s boil it.
- Fish jelly product
  - Slice it, and let’s boil it.
- Phosphorus food additives will dissolve in hot water.
- Canned food
  - Throw away the juice.
  - Because phosphorus additives are often added to the juice of the canned food, throw out the juice before cooling.
Thank you!

“REST IN REASON; MOVE IN PASSION.”

~ KHALIL GIBRAN