Nutritional Management of CKD-MBD

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DISCLOSURES

Member, Work Group for Development of Practice Guidelines for CKD-MBD

Amgen Speakers Bureau
Overview

• Discussion of 2017 guideline changes and rationale pertaining to nutrition
  • Phosphate lowering therapy.
  • Dietary phosphate modification

• Review of key messages

• Q&A
Time is short....

It is impossible to impart the wealth of information that was reviewed, discussed, and eventually agreed upon for the guidelines in this short period of time. I urge you to read the guidelines and rationale which can be accessed at the KDIGO website below.

www.kdigo.org
http://www.kisupplements.org
www.annals.org
• Geoffrey Block (USA)
• Pieter Evenepoel (Belgium)
• Masafumi Fukagawa (Japan)
• Charles A. Herzog (USA)
• Linda McCann (USA)
• Sharon M. Moe (USA)
• Rukshana Shroff (UK)
• Marcello A. Tonelli (Canada)
• Nigel D. Toussaint (Australia)
• Marc G. Vervloet (The Netherlands)

Guideline Work Group
Markus Ketteler (Germany) – Co-chair
Mary B. Leonard (USA) – Co-chair

Evidence Review Team
Johns Hopkins University
Karen A. Robinson, Casey Rebholz,
Lisa M. Wilson, Ermias Jirru,
Marisa Chi Liu, Jessica Gayleard,
Allen Zhang

The Work Group included individuals with expertise in internal medicine, adult and pediatric nephrology, cardiology, hematology, oncology, hypertension, NUTRITION, pathology, pharmacology, epidemiology, and endocrinology. The ERT consisted of physician-methodologists with expertise in nephrology and evidence-based clinical practice guideline development, along with support staff, from Johns Hopkins University.
## Chapter 4.1 Treatment Guideline Changes

<table>
<thead>
<tr>
<th>2017</th>
<th>2009</th>
<th>Update Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1.6 CKD 3a-5D receiving P-lowering tx, <strong>suggest restrict Ca</strong>&lt;sup&gt;++&lt;/sup&gt; binders. <em>(2B)</em> Peds base choice on serum Ca**&lt;sup&gt;++&lt;/sup&gt;** (Not graded)</td>
<td>4.1.5 CKD 3a-5 &amp; hyper P, rec restricting dose of Ca**&lt;sup&gt;++&lt;/sup&gt;** binders and/or dose active D w/persist/recur hyperCa**&lt;sup&gt;++&lt;/sup&gt;** (1B) arterial calcification (2C), ABD (2C), persist low PTH (2C)</td>
<td>New evidence (3 RCTs) support more general recommendation to restrict Ca**&lt;sup&gt;++&lt;/sup&gt;** binders in all stages of CKD – no caveats.</td>
</tr>
</tbody>
</table>

DRI for calcium is 1000 to 1200 mg/day

**Tolerable Upper limit for calcium is 2000 mg for adults > 50, 2500 for young adults** *(Tolerable upper intake level, which is the maximum intake that is unlikely to pose risks of adverse health effects in almost all individuals. 2010)*

May be important to ensure that patient is not taking other supplemental calcium or ingesting calcium enhanced foods or beverages.

It also may be helpful to make sure your dietitian is aware of the symptoms of hypercalcemia to identify risk in patients who are in the upper ranges.
<table>
<thead>
<tr>
<th>Year</th>
<th>Recommendation</th>
<th>Update Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>4.1.8 CKD 3a-5D suggest limiting dietary P intake in tx of hyper P alone or in combo with other tx (2D)</td>
<td>Absence of data that dietary restr improves outcomes in CKD G3a-G4. New data on phosphate sources and bioavailability were deemed to be an important additional qualifier to the previous recommendation.</td>
</tr>
<tr>
<td>2009</td>
<td>4.1.7 CKD 3-5D suggest limit dietary P in tx of hyper P alone or in combo with other tx (2D)</td>
<td></td>
</tr>
</tbody>
</table>
Public review had some strong opinions...
Reasoning

• 2 RCTs eligible; both studied the impact of intensified vs routine diet counseling over 6 months; intensified counseling was more successful in reaching lab targets, but no hard end points were documented, thus it was considered weak evidence.

• Re-analysis of MDRD/NHANEs dietary restriction showed little effect on serum levels in CKDG3-G4/normal as evidenced by urinary excretion and/or diet recall.

• Speculate that compensatory mechanisms maintain serum P until late stages regardless of intake.

• A recent Cochrane review concluded there is low-quality evidence that dietary interventions positively affect CKD-MBD markers.
Reasoning

• Logical to try to minimize hyperphosphatemia vs having to aggressively treat, but reasonable/realistic goals individualized to the patient are needed.

• Qualifier calls attention to the impact of different sources of phosphorus
  • Multiple studies have shown differences in the bioavailability of phosphate from different foods based on organic versus inorganic forms.
  • Individual patients have may different ability to digest different sources as well.
  • Multiple studies have shown food additives have a profound effect on phosphate load
  • Moe, et al. demonstrated that a vegetable-based diet showed significantly lower phosphate absorption than a meat-based diet with similar phosphorus content.
Phosphorus/Phosphate

What is the difference between Phosphorus and Phosphate?

– Phosphorus is a single atom and phosphate is a polyatomic anion.
– Phosphorus is not stable as an element, but phosphate is stable.
– Phosphorus has the capability to form cations, but phosphate is an anion.
– We take phosphorus into our bodies in the form of phosphates.

Terminology is often used as interchangeably in the literature.
Phosphorus/Phosphate

• One of most common elements in the body; used in a variety of metabolic/enzymatic processes
• Normal PO$_4$ levels in plasma: 2.5–4.5 mg/dL
• Total body PO$_4$ content: 500–700 g (85% in bone)
• Dietary Reference Intake (DRI) = 700 mg
• Daily Value (used on food labels) = 1000 mg
• Upper tolerable limit = 4000 mg (3000 for those > 70) (Has not been revisited since 1996)
• Increased emphasis on lower Na intake likely has increased the use of phosphate food additives.
Phosphorus Absorption

• Dietary phosphates are absorbed in the small intestine (passive paracellular diffusion and actively across cells by luminal sodium phosphate cotransporters).

• Principal factors determining net GI absorption: amount of phosphate present in the food, bioavailability of phosphate, and presence of natural/pharmacologic phosphate binders.

• Unlike calcium the intestinal absorption of phosphorus is not controlled according to the body needs.

• Phosphorus is predominantly absorbed as inorganic phosphate and absorption is enhanced by vitamin D.
Not all phosphorus is created equal!

**Organic Phosphorus**
- Example: Phytate
  - Absorbed at slow rate
  - 40-60% animal source abs
  - 10-30% veg source abs
  - Generally low bioavailability
  - Bioavailability can increase if degraded by enzyme action/processing

**Inorganic Phosphate Salts**
- Example: Food Additives
  - High digestibility (> 90%)
  - Absorbed rapidly
  - Not bound to fats/CHO
  - No enzyme action needed


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Phytates: Good, Bad, Ugly?

Major storage form of phosphorus in cereals, legumes, seeds, nuts, rice

**Good:** Anti-oxidant, anti-cancer properties, may increase immunity

**Good-Bad:** Anti-nutrient, hinders absorption of minerals
- Helps deter phosphorus availability from these foods in CKD allowing a more liberal choice of foods. (Good)
- Could lead to deficiencies especially in countries that don’t have access to varied diets with other sources of minerals (Bad)

**Ugly**
## Dietary Phosphate Availability

<table>
<thead>
<tr>
<th>Inorganic</th>
<th>Food Additives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organic</td>
<td></td>
</tr>
<tr>
<td>Animal</td>
<td>Dairy Derived</td>
</tr>
<tr>
<td>Meat/Fish</td>
<td>High Phos to protein ratio</td>
</tr>
<tr>
<td></td>
<td>Low Phos to protein ratio</td>
</tr>
<tr>
<td>Plant</td>
<td>Plant Derived</td>
</tr>
</tbody>
</table>

Processing (soaking, sprouting, fermenting) of foods can break down phytate and make phosphorus more available for absorption.
# Phosphorus: Organic and Inorganic

<table>
<thead>
<tr>
<th>Organic</th>
<th>Serv</th>
<th>Phos mg</th>
<th>Phos:Pro</th>
<th>GI absorb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk, skim</td>
<td>8 oz</td>
<td>247</td>
<td>29:1</td>
<td>40-60%</td>
</tr>
<tr>
<td>Yogurt, plain nonfat</td>
<td>8 oz</td>
<td>385</td>
<td>27:1</td>
<td>40-60%</td>
</tr>
<tr>
<td>Cheese, Mozzarella</td>
<td>1 oz</td>
<td>131</td>
<td>20:1</td>
<td>40-60%</td>
</tr>
<tr>
<td>Egg</td>
<td>1 large</td>
<td>86</td>
<td>14:1</td>
<td>40-60%</td>
</tr>
<tr>
<td>Beef, cooked</td>
<td>3 oz</td>
<td>173</td>
<td>7:1</td>
<td>40-60%</td>
</tr>
<tr>
<td>Chicken</td>
<td>3 oz</td>
<td>155</td>
<td>8:1</td>
<td>40-60%</td>
</tr>
<tr>
<td>Fish</td>
<td>3 oz</td>
<td>250</td>
<td>11:1</td>
<td>40-60%</td>
</tr>
<tr>
<td>Almonds</td>
<td>1 oz</td>
<td>134</td>
<td>23:1</td>
<td>10-30%</td>
</tr>
<tr>
<td>Peanuts</td>
<td>1 oz</td>
<td>107</td>
<td>15:1</td>
<td>10-30%</td>
</tr>
<tr>
<td>Lentils</td>
<td>½ cup</td>
<td>178</td>
<td>20:1</td>
<td>10-30%</td>
</tr>
<tr>
<td>Chocolate</td>
<td>1.4 oz</td>
<td>142-216</td>
<td>27:1</td>
<td>10-30%</td>
</tr>
<tr>
<td>Cola</td>
<td>12 oz</td>
<td>40</td>
<td>NA</td>
<td>80-100%</td>
</tr>
</tbody>
</table>
Hidden Phosphate

The diagram shows the phosphorus/protein content in various meat products. The x-axis represents different meat products: Pork Chops, Pork Loin Ribs, Strip Steak, Sirloin, Bacon, and Chicken Drumsticks. The y-axis represents the phosphorus/protein content in milligrams per gram. The bars indicate the content levels across different categories.
Other sources of phosphate

• Phosphate-containing excipients, largely inert salts used in the formulation of drugs found in ~11% of frequently used medications without any indication of the concentration (buffers, dilutants, density for the preparation)

• Example: phosphate content of a single 20-mg tablet of paroxetine may be as high as 296 mg, while 10 mg of amlodipine may have up to 165 mg. Many other commonly prescribed CKD medications contain at least some phosphorus.

• Even tap water may need to be scrutinized because phosphate salts are often added to soften hard water in the United States and Europe.

Calvo M, Sherman RA, Uribarri J. AJKD, 2019; 73(4)542–551
Estimates of Dietary Intake

• Average daily dietary intake of phosphorus is about 1550 mg (males) and 1000 mg (females) but is reportedly increasing as phosphates are added to a large number of processed foods including meats, cheeses, dressings, beverages, and bakery products.

• Depending on the food choices, additives may increase phosphorus intake by as much as 1 g/day.

• Nutrient composition tables usually do not include the phosphorus from these additives, resulting in an underestimate of the dietary load of phosphorus.
Contribution of Additives

• Est that > 50% of Phos in Western diet is from additives

• Estimated that intake of Phos from additives has increased from 500 mg/day to > 1000 mg/day since 1990

• Foods containing phosphorus additives contained 70% more phosphorus than similar foods without additives. Example: Boiled ham w/additives has 66% more P

  Cupusti A et al. JREN, Nov 2012

• Products that reported use of additives had average phosphate-protein ratio 28% higher than additive free products.

• Most, but not all foods with additives reported the additives (unquantified) on the label; 8 of 25 enhanced products did not list the additives

Prevalence of Additives in Grocery Items

- 44% “best-selling grocery” items had phos additives.
- Additives were particularly common in prepared frozen foods (72%), dry food mixes (70%), packaged meat (65%), bread and baked goods (57%), soup (54%), and yogurt (51%).
- Phos additive-containing foods averaged 67 mg phosphorus/100 g more than matched nonadditive-containing foods (P = .03).
- Sample meals w/phos additive-containing foods had 736 mg more phos/day than meals using only additive-free foods.
- Phosphorus additive-free meals cost an average of $2.00 more per day.
- Commonly used for moisture retention, leavening, flavoring, emulsification, coloring, etc.


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Fast Food and Phosphorus Additives

• Examined nutrition labels/ingredient lists provided by 15 fast-food chains.

• Each entrée/side dish was assessed according to traditional criteria (Na, K, and naturally occurring phosphorus content), and then according to the presence of a phosphorus-containing additive.

• Conclusion - Only a small proportion of fast-food entrees and side dishes are compatible with reduction in dietary phosphate.

Role for dietary P modification in CKD?

CKD
• Scarcity of research, minimal change in serum levels
• Most research based on protein restriction and extrapolated to P
• Can maintain nutrition status with careful monitoring requiring significant RD staffing

CKD Stage 5D
• Necessary to use diet modification in conjunction with traditional thrice weekly dialysis as adjunct therapy along with binders
• Can maintain nutrition status with careful monitoring requiring significant RD staffing
• Phosphate control is easier with multifaceted treatment of abnormal labs including increased dialysis clearance and control of hyperparathyroidism

Long term adherence is challenging!
Barriers to Dietary Phosphorus Control

- Multiple long-term diet modifications
- Professional resources (time/staffing for counseling)
- Binder non-adherence
- Reliance on processed/fast foods w/additives
- Limited/confusing/incomplete info on food labels
- Socioeconomic/education/language/physical barriers
- Lack of coordinated care – remembering the interaction of all therapies –
  - Uncontrolled PTH makes it almost impossible to control serum levels of phosphate (bone release)
  - Use of calcium binders adds to calcium load and may require more than the TUL in some patients to lower serum phosphorus
It is almost impossible for average consumer to identify acceptable foods due to the complexity of food labels and lack of quantitative information about phosphates.

Chemical Cuisine
Learn about Food Additives

Shopping was easy when most food came from farms. Now, factory-made foods have made chemical additives a significant part of our diet.
Use fresh foods, avoid prepared/fast foods, and additives:

A day in the life.....
Changes in Dietary Counseling

• Teach label reading – look for the PHOS

• Educate on ALL P sources
  • Natural or organic
  • Inorganic/additives
  • Supplements (vitamins/minerals)

• Identify “better choices”

• Fresh vs fast/convenience foods

• IDT reinforcement/same message

• Recognize clinically significant changes in serum level changes, not “targets”

• Ongoing education and follow-up
Dietary Modification- ancillary aides

• Health literacy (education, culture, language, etc.)

• Patient Engagement/ Motivational Interviewing

• Abilities (hearing, seeing, etc.)

• Critical to know what is important to the patient, consider their goals, understand their limitations.
Prioritize and simplify instructions!

Diet Plan
You can eat 1/3 cup of pinto beans unless your phosphorus is high, then you should eat ½ cup of potatoes, unless your potassium is high, then you should eat lots of protein, unless your BUN or phosphorus is high, then you should drink clear broth unless your fluid weight gain is high, then you should eat hard candy unless your glucose is high.... Any questions?
Key Messages

• Choose phosphate lowering medications with consideration of potential side effects and patient specific profile.

• Avoid hypercalcemia.

• It is reasonable to identify and modify excess dietary intake of phosphorus considering all sources, different absorption rates, and “hidden” sources such as additives – without compromising levels of other nutrients

• Tailor diet counseling to the individual patient