Hidden Phosphorus: It’s Impact on the Renal and General Populations

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Today’s Discussion

- Discuss the consequences of hyperphosphatemia in the general and Chronic Kidney (CKD) population
- Identify the uses for phosphate additives in foods and the foods containing phosphate additives
- Suggest ways to improve phosphate control.
- Introduce the concept of the Kidney Friendly shelf

Source: Canadian Organ Replacement Register, CIHI.
Expected Remaining Lifetimes (years)

USRDS 1995

USRDS 2002

<table>
<thead>
<tr>
<th></th>
<th>Age 45-54</th>
<th>Age 55-64</th>
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<td>7.0</td>
</tr>
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<td>12.8</td>
<td>5.1</td>
</tr>
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US Resident, Colon Cancer, ESRD
Cardiovascular Disease (CVD) Mortality
General Population vs ESRD Patients

Cardiovascular Calcification in Stage 5 Chronic Kidney Disease Patients on Dialysis

Identification, Prevalence and Outcomes
EBCT Scores and Cardiovascular Risk in the General Population

<table>
<thead>
<tr>
<th>EBCT Score</th>
<th>Plaque Burden</th>
<th>Implication for CV Risk</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>Minimal</td>
<td>Low</td>
<td>Reassurance, education</td>
</tr>
<tr>
<td>11-100</td>
<td>Definite, mild</td>
<td>Moderate</td>
<td>Counseling for primary prevention; daily ASA</td>
</tr>
<tr>
<td>101-400</td>
<td>Definite, moderate</td>
<td>Moderately high</td>
<td>Institute risk factor modification and secondary prevention</td>
</tr>
<tr>
<td>&gt;400</td>
<td>Extensive</td>
<td>High</td>
<td>Institute aggressive risk factor modification</td>
</tr>
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</table>

EBCT=Electron Beam Computed Tomography  
CV=Cardiovascular  
Coronary Artery Calcification Score and Survival in Chronic Hemodialysis

Survival rate

Median CACS = 200

\[ P = 0.015 \]
\[ N = 104 \]

CACS = Coronary Artery Calcification Score

Cardiac Calcification in Adult Hemodialysis Patients

Figure 2.
The prevalence of atherosclerotic vascular disease by coronary artery calcium score category

ASVD = atherosclerotic vascular disease

N = 205
83% positive CACS
Median CACS = 595

p = < 0.0001

Categories of coronary calcium score

Risk of Cardiovascular Calcification is Increased in Dialysis Patients

Mean coronary artery calcium score*

- Nondialysis, No CAD (N=22)
- Nondialysis, CAD (N=80)
- Dialysis (N=49)

Age (years)

- 28-39
- 40-49
- 50-59
- 60-69

Very high CV risk†

* Determined by EBT
CAD=coronary artery disease

Rapid (<1Year) Progression of Valvular Calcification in Dialysis Patients

Median calcium score

<table>
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<th>Aortic Baseline occurrence: 55%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcification Score</td>
</tr>
<tr>
<td>1st measurement</td>
</tr>
<tr>
<td>2nd measurement</td>
</tr>
</tbody>
</table>

| Mitral Baseline occurrence: 59% |

- 40-49
- 50-59
- 60-69

**Elevated Serum Phosphorus Increases Mortality Risk**

N = 40,538
< 0.0001

*Multivariable adjusted*

**Association of Elevated Serum PO₄ with Cardiac Mortality Risk in Chronic Hemodialysis Patients**

Relative Risk of Death

- CAD: 1.41
- Sudden: 1.20
- Other Cardiac: 1.18
- CVA: 1.26
- Infect.: 1.20
- Other Known: 1.07
- Unknown: 1.25
- Missing: 1.27

**N=12,833**

2 year f/u

RR=1.21 for all causes combined

*P<0.0005; †P<0.005; ††P<0.05 compared with RR of 1.0

CAD=coronary artery disease; CVA=cerebrovascular accident

RR=relative risk of mortality (for serum PO₄>6.5 mg/dL vs. 2.4-6.5 mg/dL; eight Cox models)

Current Strategies for PO4 control

- **Phosphate binders**
  - Aluminum based
  - Calcium based
  - Lanthanum carbonate
  - Sevelamer hydrochloride

- **Education:**
  - Avoid high phosphorus foods: dairy, legumes, nuts, cola, “pepper” style beverages
  - Choose low PO4 protein sources
Phosphate Salt Additives
Common Phosphate Additives

- Phosphoric Acid
  - Beverages
- Calcium Phosphate
  - Calcium supplement
- Sodium Phosphate
  - Polyphosphates have many uses
**Phosphate Salt Additives**

- **Stabilizer**
  - Adjusts pH: buffer and acid
  - Emulifies

- **Protectant**
  - Flavor
  - Color
  - Spoilage
  - Product integrity
  - Prevents and promotes coagulation
Phosphate Salt Additives

- Leavening agent
- Conditioner
  - Meltability and pliability
- Enhancer
  - Flavor
    - Distinctive flavors associated with a brand
  - Color
Phosphate Salt Additives

- Tenderizer
- Supplement
  - Calcium, Phosphorus, Magnesium
Food Sources

- Beverages: canned and plastic-bottled iced teas, fruit drinks, punch drinks, flavored waters, bottled lemonade
- Restructured meats: chicken patties/nuggets
- “Instant” products: sauces and puddings
- Refrigerated bakery products
- Breakfast cereals and breakfast bars
- Enhanced meat products
Phosphate Additives Impact on the Renal Population

- Additives are HIGHLY absorbable
  - Normal diet only 60% of PO4 is absorbed
  - Additives are close to 100% absorbed

- Increased need for binders
  - Diet high in PO4 additives, more PO4 absorbed

- Limits food choices
**Strategies for PO4 control:**

**Phosphate Load**

- **Binder dosing**
  - Based on Serum level or phosphate load?
  - Individualized for meals?

- **Better control with calculating phosphate load and individualizing binder needs/ meal**
Strategies for PO4 control: Phosphate Load

*Binder capacity:*
- **CaCO3**
  - 39 mg PO4/1 gm CaCO3
- **CaAcetate**
  - 45 mg PO4/1 gm CaAcetate
- **Mg**
  - Unknown
- **Al**
  - 22.3 mg PO4/5 ml
- **Sevelamer**
  - 64 mg PO4/800 mg
- **Lanthanum Carbonate**
Strategies for PO4 control: Education

- READ LABELS!
- “Do Not Buy” Poster
- Detailed Diet Recalls: Include where food is purchased and brands used.
- Grassroots effort to bring more attention to Kidney Friendly foods and the “Kidney Friendly Shelf”
The Kidney Friendly Shelf

- Grassroots effort started by Dr. William Pordy and other nephrologist to bring “Kidney Friendly” food to the millions who have CKD
- Had advantage to both the consumer and the grocer
- Increase demand in Kidney Friendly foods may help reduce PO4 additive containing foods
Strategies for PO4 Control: Dialysis

- Average HD session removes 800 mg PO4
- Daily dialysis increases PO4 removal
- Nocturnal Dialysis remove the most PO4 with the need for additional PO4 supplementation
Alterations in Ca:P ratio in the General Population
1988:
MS Calvo, R Kumar, H Heath 3rd
- 1st study: 8 men, 8 women
- 8 days of 820 mg Ca, 930 mg P diet
- Test diet: 420 mg Ca, 1660 mg P
- Used common grocery store foods
- RESULTS: For test diet: increase in PTH, PO4, plasma 1,25-dihydroxyvitamin D, and urinary hydroxyproline.
Effect of Phosphorus on the General Population

1990:
MS Calvo, R Kumar, H Heath 3rd

– 2nd study: 15 young women
– Basal diet: 800 mg Ca, 900 mg P for 28 days
– 10 Test diet: 400 mg Ca, 1700 mg PO4 for 28 days
– RESULTS: significant increase in PTH levels of Test diet subjects.
Effects on the General Population

- Stephen Onufrak, et al, Phosphorus levels are associated with subclinical atherosclerosis in the general population, Atherosclerosis (2007)

- Analyzed data from Atherosclerosis Research in Community (ARIC) study to investigate relationship between serum P levels and carotid intima-media thickness (cIMT)
Subclinical Atherosclerosis

- Subjects 45-64 years of age from 4 regions of US between 1987-1989
- In this analysis, 10,688 subjects with normal renal function and dietary intake data
- Prior studies have shown that as cIMT increases, the risks for MI and stroke also increase
Carotid Intima-media Thickness

![Graph showing the relationship between Serum Phosphorus (mg/dl) and Carotid IMT in different adjusted states: Age/Sex Adjusted, Multivarient Adjusted, GFR Adjusted. The graph indicates higher Carotid IMT with increasing serum phosphorus levels, with distinct bars for each adjusted state across different phosphorus ranges.]
Conclusions
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- Phosphorus is not only a problem for the Renal population, but there is growing evidence that alterations in C:P intake may also cause long term problems in the general population.
- The increase use of phosphate additives makes it harder for the patient and clinician to know which foods to limit in the renal population and increases the general population’s exposure to excess phosphorus.
Conclusions

Strategies for improving PO4 control incorporate all of the healthcare team

- Detailed diet recalls
- Adjusting binder dose for PO4 load
- Utilizing the multiple binders if necessary
- Increasing the frequency of dialysis if necessary
Conclusions

✨ Not enough can be said about reading labels!!
QUESTIONS?