Making Bones Strong and More: Vitamin D, Calcium, and Phosphorus

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Disclosure

- Support from Abbott Laboratories for clinical studies of Calcijex and Zemplar
- Consultant for Abbott Laboratories
Objectives

- Identify risk factors for nutritional vitamin D deficiency.
- Explain the difference between a nutritional vitamin D supplement and active vitamin D.
- Plan the treatment of a patient with an elevated serum phosphorus level.
- List 2 potential complications of treatment with calcium supplements.
Rickets
Rickets?

- Does it occur in 2013?
- What are the 2 most common groups in the United States?
  - Breast fed infants (African American)
  - Chronic kidney disease patients
Rickets: Clinical Features

- Frontal bossing
- Delayed dentition and carries
- Rachitic rosary
- Enlargement of wrists and ankles
- Valgus or varus deformities
- Fractures
- Respiratory infections and pulmonary atelectasis
Windswept Deformity
Calcium and Phosphate Metabolism

Skin
- Vitamin D

Liver
- 25-Vit D
- Phosphate loss

Gut
- 1,25-Vit D
- Calcium retention

PTH
- Calcium retention
- Phosphate loss

Bone
- Vitamin D

Pi

25-Vit D
1,25-Vit D
Vitamin D Deficiency

Skin

Liver

Gut

PTH

Bone

Ca++

Phosphate loss

Calcium retention
Vitamin D From Sunlight

7-dehydrocholesterol

↓

Cholecalciferol

(Vitamin D₃)
A Lack of Sunshine

- Exposure to sun
  - Less time outside
  - Latitude/season
  - Sunscreen

- Skin
  - Melanin slows vitamin D synthesis
  - Uremia decreases
Vitamin D From Diet

- Food sources limited
- Vitamin D added to milk/breakfast cereal
- Formula: 400 IU/L Vitamin D
- Human milk (12-60 IU/L)
Nutritional Vitamin D Deficiency

- Common
- Increased in CKD patients
- Other risk factors
  - African Americans
  - Decreased sun exposure
  - Poor intake
Nutritional Vitamin D Deficiency

- Definitions
  - Severe deficiency: <5 ng/mL
  - Mild deficiency: 5-15 ng/mL
  - Insufficiency: 16-30 ng/mL

- Common
Why Treat Nutritional Vitamin D Deficiency?

- Hyperparathyroidism
- Beyond bone
  - Local synthesis of 1,25-Vitamin D (including vascular smooth muscle and endothelial cells)
  - Receptors: vascular smooth muscle, myocytes, lymphocytes, osteoblasts
  - Fractures, autoimmune disease, CHF, hypertension, diabetes, inflammation, arterial calcification, atherosclerosis, cancer
### Treatment

<table>
<thead>
<tr>
<th>Level</th>
<th>Dose</th>
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</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>8,000/d x 4 wks or 50,000/wk x 4 weeks; then 4,000/d or 50,000 2x/month x 2 months</td>
</tr>
<tr>
<td>5-15</td>
<td>4,000/d or 50,000 q 2 weeks x 12 wks</td>
</tr>
<tr>
<td>16-30</td>
<td>2,000/d or 50,000 q 4 weeks x 12 weeks</td>
</tr>
</tbody>
</table>

- Preparations: 10,000 units/ml or 50,000 unit capsules
- Recheck level in 3 months
Unanswered Questions

- Measurement
  - Elevated PTH?
  - Repeat?
- Suppresses PTH?
- Maintenance dosing?
- Nephrotic syndrome?
Chronic Kidney Disease

Skin

Vitamin D

Liver

Phosphate loss

Liver

25-Vit D

Gut

Calcium retention

Gut

1,25-Vit D

Bone

Pi

Ca++

Pi

PTH

+
Metabolic Bone Disease: Goals

Healthy Bones

Optimize Growth

Avoid Vascular Calcifications
Vascular Calcifications: Electron-Beam CT

27-year-old male hemodialysis patient with extensive calcification in all 3 coronary arteries and aorta.
Coronary Artery Calcifications

Older and longer dialysis

Phosphorus

Ca x Pi

Daily calcium intake
Why Vascular Calcifications?

- Disordered mineral metabolism
- Treatment
  - Calcium-containing binders
  - Active vitamin D
  - Suppression of PTH below recommended targets
  - Calcium transfer during dialysis
Management of Metabolic Bone Disease

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Approach</th>
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</thead>
</table>
| Phosphorus  | 1. Diet  
              2. Binders |
| Calcium     | 1. Active vitamin D  
              2. Calcium |
| PTH         | 1. Lower phosphorus  
              2. Correct nutritional vitamin D deficiency  
              3. Active vitamin D  
              4. Correct hypocalcemia  
              5. Cinacalcet (Sensipar)  
              6. Parathyroidectomy |
Phosphorus

Skin

Vitamin D

Liver

25-Vit D

Calcium retention

Phosphate loss

PTH

Pi

Pi

+ -

+ -

1,25-Vit D

Bone

Gut

Ca++

+ -

+ -

1,25-Vit D

Pi
Hyperphosphatemia: Treatment

- **Diet**
  - PTH increased: dietary reference intake (DRI)
  - PTH increased and phosphorus increased: 80% DRI

- **Binders**
  - Calcium (avoid > 2x DRI or >2500 mg/day)
  - Non-calcium
    - Sevelamer hydrochloride (Renagel)
    - Sevelamer carbonate (Renvela)
    - Lanthanum (Fosrenol)
  - Aluminum (short-term; avoid citrate)

- **Dialysis**
Active Vitamin D

Skin

Vitamin D

Liver

25-Vit D

Gut

Ca++

Pi

Bone

PTH

1,25-Vit D
### Active Vitamin D

<table>
<thead>
<tr>
<th>Compound</th>
<th>Preparations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcitriol (Rocaltrol and others)</td>
<td>IV (Calcijex) Capsules (0.25 and 0.5 mcg) Liquid (1 mcg/ml)</td>
</tr>
<tr>
<td>Paricalcitol (Zemplar)</td>
<td>IV Capsules (1, 2, and 4 mcg)</td>
</tr>
<tr>
<td>Doxercalciferol (Hectorol)</td>
<td>IV Capsules (0.5, 1, 2.5 mcg)</td>
</tr>
</tbody>
</table>
Vitamin D and Mortality

Wolf et al KI 72 1004 2007
Calcium: Treatment

- Target: normal level (corrected for albumin)
- High calcium
  - Stop calcium-containing binders
  - Stop active vitamin D
  - Decrease dialysate calcium
- Low calcium
  - Calcium
  - Active vitamin D
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