Renal Dietitians on the Front Line: The Role of Calcium-based Phosphate Binders for Attainment of K/DOQI™ Bone Guidelines Part 1

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Overview
Renal Dietitians and Nurses are often on the front lines of treating hyperphosphatemia and work as a team to effectively manage patients with end-stage renal disease. This condition is not only a major factor in the development of secondary hyperparathyroidism and renal osteodystrophy, but is also independently associated with an increased risk of death. The mechanism whereby hyperphosphatemia increases mortality risk is unknown but it may promote cardiovascular calcification. The current recommendation is that dialysis patients be treated to maintain serum phosphorus and calcium-phosphorus product in the normal range. As dietary restriction of phosphorus and conventional dialysis do not adequately control serum phosphorus in the majority of patients, the use of dietary phosphate binders is often unavoidable. The most commonly used phosphate binders worldwide are calcium acetate in the United States and calcium carbonate in Europe. Although calcium-based binders are clinically efficacious and cost-effective, their long-term safety has recently become the subject of intense debate.

The objective of this two-part accredited CD series is to critically examine these issues and provide rational guidelines for the use of calcium-based phosphate binders in patients with end-stage renal disease in the context of the recently published K/DOQI™ guidelines for bone and mineral metabolism in patients with chronic kidney disease. In addition, we will examine the role of renal dietitians and nurses as clinical partners in the management of ESRD, and the importance of patient-focused care in the treatment paradigm.

Intended Audience
This activity will be of interest to renal dietitians, nurses, and technicians, who treat patient with end-stage renal disease.

Learning objectives
Upon completion of this activity, participants will be able to:

1. Describe patient types that are appropriate for therapy with calcium-based phosphate binders.
2. Correlate the role of dietary restriction of phosphorus in the treatment of patients with ESRD and the balance between diet and drug therapy.
3. Describe the risk factors for cardiac calcification in patients with ESRD and discuss the issues surrounding the use of calcium based phosphate binders in this patient population.
4. Review and discuss current studies of calcium acetate and sevelamer hydrochloride and their impact on patient care.
5. Review current K/DOQI™ bone guidelines and describe the clinical role of the renal dietitian in attaining these guidelines.

This program is sponsored by The American Academy of CME, Inc.

This program is supported by an unrestricted educational grant from Nabi Biopharmaceuticals.

Introduction and Overview
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Portland, OR
Challenges in Meeting the K/DOQI Guidelines
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Adjunct Faculty
Buffalo State College, Buffalo, NY

Phosphate Binder Efficacy: A Clinical Trial Review
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University of Texas Health Sciences Center at San Antonio
Organ Transplant Program, San Antonio, TX

Conflict of Interest Disclosure
Dr. Nolan has received financial support and has participated in a Consultant/Advisor’s Bureau/Advisory Board for Nabi Biopharmaceuticals.

Ms. Sturtevant does not have any relevant financial relationships with any commercial interests.

Ms. Murphy-Gutekunst has received financial support and has participated in a Consultant/Advisor’s Bureau/Advisory Board for Amgen.

This activity has been peer-reviewed for fair balance.

Accreditation
Registered Dietitians (RD) and registered dietetic technicians (DTR) will receive 1.0 Continuing Professional Education Units (CPEUs) for completion of this program. Continuing Professional Education Provider Accreditation does not constitute endorsement by CDR of a provider, program, or materials.

The American Academy of CME, Inc. (Academy) is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center’s Commission on Accreditation.

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Directions for Program Completion
1. Listen to the audio CD and read accompanying guide.
2. Circle the Posttest answers on page 23.
3. Complete the Post Program Self-assessment on pages 23–24. Complete all other requested information on the form, detach, fax or stamp, and mail (address and fax number on form).

Release Date: February 1, 2006
Expiration Date: February 1, 2008

K/DOQI™ is a trademark of the National Kidney Foundation, Inc.
Introduction and Overview

Learning Objectives
- Describe patient types that are appropriate for therapy with calcium-based phosphate binders.
- Correlate the role of dietary restriction of phosphorus in the treatment of patients with ESRD and the balance between diet and drug therapy.
- Describe the risk factors for cardiovascular calcification in patients with ESRD and discuss the issues surrounding the use of calcium-based phosphate binders in this patient population.
- Review and discuss current studies of calcium acetate and sevelamer hydrochloride and their impact on patient care.
- Review current K/DOQI™ bone guidelines and describe the clinical role of the renal dietitian in attaining these guidelines.

Program Objective
- The objective of this program is to provide rational guidelines for helping patients with end-stage renal disease meet the recently published K/DOQI™ guidelines for bone and mineral metabolism.
- We will examine the role of renal dietitians as clinical partners in the management of ESRD, and the importance of patient-focused care in the treatment paradigm.
K/DOQI™ Guidelines
Kidney Disease Outcomes Quality Initiative
- Multidisciplinary expert panel
- Scientifically rigorous
- Peer reviewed
- Evidence based

Clinical Significance of Hyperphosphatemia
- Secondary hyperparathyroidism
- Renal osteodystrophy
- Vascular calcification
- Increased risk of death

NKF-K/DOQI™ Bone Guidelines

<table>
<thead>
<tr>
<th>Parameter</th>
<th>K/DOQI™ Goal</th>
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<tbody>
<tr>
<td>Serum P</td>
<td>3.5 to 5.5 mg/dL</td>
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<tr>
<td>Ca x P Product</td>
<td>&lt;55mg²/dL²</td>
</tr>
<tr>
<td>Intact PTH (iPTH)</td>
<td>150 to 300 pg/mL</td>
</tr>
<tr>
<td>Serum HCO₃</td>
<td>&gt;22 mEq/L</td>
</tr>
<tr>
<td>Corrected total serum Ca</td>
<td>8.4 to 9.5 mg/dL</td>
</tr>
</tbody>
</table>
The Role of Calcium-based Phosphate Binders for Attainment of K/DOQI™ Bone Guidelines

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Binder Adherence

- Ensure prescriptions are clearly written
- Check patient understanding of Rx
- Ask open-ended questions
- Obtain a dietary recall

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Challenges in Meeting the K/DOQI™ Guidelines

Lisa Murphy-Gutekunst MSEd, RD, CSR, CDN

Unique Challenges in Calcium Control

- Diet driven: hidden sources
  - Beverages: fruit juices, energy drinks
  - Breakfast cereals and bars
  - OTC medications
- Patient driven: change in lifestyle
  - Unaware of dangers of calcium based antacids
  - Mistiming of calcium based binders
  - Arbitrarily increasing calcium binders
The Role of Calcium-based Phosphate Binders for Attainment of K/DOQI™ Bone Guidelines

Challenges of Adherence with PO4 Binder Prescription

- “Selective Amnesia”
- Written prescription
  - MD writes for binders t.i.d.
  - No binders for snacks
- Multiple adjustments
  - Binders may be adjusted based on serum level without checking for adherence with current Rx.

Conclusion

- Continual, on-going education
  - Diet restrictions
  - Hidden dietary sources
  - Binders
- Label reading
  - Hidden sources of calcium and phosphorus
- Partnership with physician
  - Binder and diet adherence
  - Binder needs

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Phosphate Binder Efficacy: A Clinical Trial Review

Charles R. Nolan, MD

The Role of Calcium-based Phosphate Binders for Attainment of K/DOQI™ Bone Guidelines

Renal Dietitians on the Front Line


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The Role of Calcium-based Phosphate Binders for Attainment of K/DOQI™ Bone Guidelines


Which Mineral Metabolism Profile is Preferred?

<table>
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<tr>
<th>Phosphorus</th>
<th>Calcium Acetate</th>
<th>Sevelamer</th>
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</thead>
<tbody>
<tr>
<td>5.2 mg/dL</td>
<td>6.0 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>9.6 mg/dL</td>
<td>8.3 mg/dL</td>
</tr>
<tr>
<td>Ca x P Product</td>
<td>50 mg/dL&lt;sup&gt;2&lt;/sup&gt;</td>
<td>50 mg/dL&lt;sup&gt;2&lt;/sup&gt;</td>
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<tr>
<td>PTH</td>
<td>200 pg/ml</td>
<td>200 pg/ml</td>
</tr>
<tr>
<td>HCO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>23 mEq/L</td>
<td>19 mEq/L</td>
</tr>
</tbody>
</table>

Green = K/DOQI™ treatment goal attained

CARE – Projected Daily & Annual Per Patient Costs of Phosphate Binder Therapy

The Role of Calcium-based Phosphate Binders for Attainment of K/DOQI™ Bone Guidelines

Treatment of Sevelamer-Induced Metabolic Acidosis

- Increase dialysate bicarbonate
- Alkali supplements
  - Citrated compounds contraindicated
  - NaHCO₃ may compete with phosphorus for binding to sevelamer
- Reformulation of Renagel® so that it contains less chloride and more carbonate or acetate anion

Conclusions Based on Comparative Trials of Phosphate Binders

- Efficacy and cost considerations indicate that calcium acetate should remain first-line phosphate binder therapy.
- Epidemiologic studies indicate that adequate control of serum phosphorus is fundamental. Given the high prevalence and attributable mortality risk of hyperphosphatemia our treatment goal should continue to focus on maintaining serum phosphorus within K/DOQI™ guidelines.
- Achieving only the K/DOQI™ goal for Ca x P product as the result of a low serum calcium despite a persistently elevated serum phosphorus is not an appropriate therapeutic goal of phosphate binder therapy.
- Well-designed clinical studies must document the postulated advantages of newer, more expensive phosphate binder therapies before widespread implementation of an exorbitantly expensive Medicare program to fund the cost of phosphate binder therapy.
Posttest Questions

1. Unique challenges dietitians face with serum calcium control include (choose all that apply):
   a. The use of more dairy products to keep bones strong.
   b. The use of calcium antacids for upset stomach.
   c. Mistiming of calcium based binders.
   d. Calcium fortified beverages and breakfast items.

2. When reviewing protein needs with a patient, it is important to encourage high biological value protein, low phosphorus sources.
   True or False.

3. Sources of very low to average milligram phosphorus to grams of protein ratio include (choose all the apply):
   a. Watermelon
   b. Cottage cheese
   c. Shrimp
   d. Ground beef
   e. Navy beans
   f. Peanut butter

4. Phosphate additives are more absorbable than the phosphate found naturally in food.
   True or False.

5. Way to be successful in meeting the K/DOQI™ guidelines include:
   a. Continual, on-going education regarding binder needs and hidden dietary sources of calcium and phosphorus.
   b. Encouraging patients to read labels looking for phosphate additives.
   c. Working with the nephrologist to balance phosphate binder needs with dietary phosphorus intake.
   d. All of the above.

6. Which of the following statements is least accurate?
   a. Gastrointestinal phosphate absorption is a linear function of intake such that roughly 60-70% of the phosphorous contained in the diet is absorbed.
   b. Unlike calcium absorption, phosphorus absorption is tightly regulated at the gut level and does not increase further with increases in dietary phosphorus intake.
   c. Renal excretion of phosphate is the principle factor responsible for maintenance of external phosphorus balance.
   d. Abnormal phosphorous metabolism is present in patients with chronic kidney disease even before the onset of end-stage renal disease.
   e. Dietary restriction of phosphorus remains the cornerstone of therapy with regard to attainment of NKF-K/DOQI™ guidelines for serum phosphorus.

7. Which of the following statements is correct regarding phosphorus metabolism in dialysis patients?
   a. Each three time per week standard dialysis treatment removes approximately 1,000 mg phosphorus.
   b. Phosphorus removal during a hemodialysis session is most efficient during the first 2–3 hours.
   c. Short daily dialysis or long nocturnal dialysis is more effective for phosphate clearance than standard thrice weekly dialysis.
   d. Despite dietary phosphorus restriction and three-times per week intermittent hemodialysis, most patients require dietary phosphate binders to achieve NKF-K/DOQI™ guidelines for serum phosphorus control to less than 5.5 mg/dL.
   e. All of the above.

8. Which of the following factors regulate PTH secretion by the parathyroid gland?
   a. Hyperphosphatemia is somehow directly sensed by the parathyroid gland and leads to increased PTH production by stabilizing mRNA for PTH.
   b. 1,25 (OH)₂ vitamin D binds its intracellular vitamin D receptor and the complex binds to the PTH promoter segment thereby inhibiting transcription of mRNA for PTH.
   c. Serum calcium is the most important regulator of moment-to-moment PTH secretion.
   d. Calcimimetics like cinacalcet sensitize the calcium sensing receptor leading to more effective suppression of PTH secretion for any given level of serum ionized calcium.
   e. All of the above.

9. Which of the following is not a consequence of abnormal phosphorus metabolism in patients with end-stage renal disease on maintenance hemodialysis?
b. Amorphous calcium-phosphate deposition in tissues such as the heart and lung.
c. Increased risk of all-cause and cardiovascular mortality.
d. Increased risk of breast and uterine cancer.
e. Hydroxyapatite deposition in the walls of blood vessels.

10. Which of the following is the most accurate statement?
   a. Aluminum containing phosphate binders were abandoned for long-term use in dialysis patients because of lack of efficacy and high cost.
   b. Calcium citrate is not a suitable phosphate binder for dialysis patients since it can lead to enhanced absorption of aluminum from the diet and dramatically increase risk of aluminum encephalopathy and aluminum-induced osteomalacia.
   c. Calcium acetate, like calcium citrate, also enhances gastrointestinal aluminum absorption.
   d. Calcium carbonate has been shown to be a more effective phosphate binder than calcium acetate.
   e. The CARE study found that sevelamer is equally efficacious to calcium acetate with regard to control of serum phosphorus.

11. Which of the following statements is true?
   a. Sevelamer is a quaternary amine anion exchange resin which binds phosphorus in exchange for release of the leaving anion chloride.
   b. Sevelamer treatment results in reduction of total and LDL cholesterol by functioning as a bile acid sequestrant akin to cholestyramine.
   c. Sevelamer hydrochloride use may cause metabolic acidosis by release of HCl acid in exchange for binding of phosphate, bicarbonate, or bile acids.
   d. Both short-term and long-term studies reveal lower serum bicarbonate levels in dialysis patients treated with sevelamer hydrochloride compared to patients treated with calcium-containing phosphate binders.
   e. All of the above.

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Post Program Self Assessment

Renal Dietitians on the Front Line: The Role of Calcium-based Phosphate Binders for Attainment of K/DOQI™ Bone Guidelines

Part 1 (05-AM-63-C-M-001)

Answer Sheet

1. A B C D
2. T F
3. A B C D E F
4. T F
5. A B C D
6. A B C D E
7. A B C D E
8. A B C D E
9. A B C D E
10. A B C D E
11. A B C D E

To aid us in evaluating the effectiveness of this activity, please complete and return this questionnaire at the end of the activity. If you wish to receive CE credits, you must return this completed form.

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Please check your professional title:
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☑ Nurse/Nurse Practitioner
☑ Pharmacist/PharmD
☑ Other: ________________________

Please evaluate or answer the following:

Did the program meet your expectations?
☑ yes ☐ no

Were the course materials effective?
☑ yes ☐ no

Please complete other side ☜
Were the presentations free of commercial bias?

- [ ] yes  - [ ] no

If no, why not:

__________________________________________________________________________________________

Objectives:—Upon completion of this activity were you able to:

Describe patient types that are appropriate for therapy with calcium-based phosphate binders.

- [ ] yes  - [ ] no

Correlate the role of dietary restriction of phosphorus in the treatment of patients with ESRD and the balance between diet and drug therapy.

- [ ] yes  - [ ] no

Describe the risk factors for cardiac calcification in patients with ESRD and discuss the issues surrounding the use of calcium based phosphate binders in this patient population.

- [ ] yes  - [ ] no

Review and discuss current studies of calcium acetate and sevelamer hydrochloride and their impact on patient care.

- [ ] yes  - [ ] no

Review current K/DOQI™ bone guidelines and describe the clinical role of the renal dietitian in attaining these guidelines.

- [ ] yes  - [ ] no

Using the following scale, please rate each presenter by checking the appropriate box. (1=Poor  2=Fair  3=Satisfactory  4=Good  5=Excellent)

Dana Sturtevant, MS, RD
Value of topic
- [ ] 1  - [ ] 2  - [ ] 3  - [ ] 4  - [ ] 5
Quality of Presentation
- [ ] 1  - [ ] 2  - [ ] 3  - [ ] 4  - [ ] 5

Lisa Murphy-Gutekunst, MsEd, RD, CSR, CDN
Value of topic
- [ ] 1  - [ ] 2  - [ ] 3  - [ ] 4  - [ ] 5
Quality of Presentation
- [ ] 1  - [ ] 2  - [ ] 3  - [ ] 4  - [ ] 5

Charles R. Nolan, MD
Value of topic
- [ ] 1  - [ ] 2  - [ ] 3  - [ ] 4  - [ ] 5
Quality of Presentation
- [ ] 1  - [ ] 2  - [ ] 3  - [ ] 4  - [ ] 5

Rate the overall clinical relevance of today’s program to your practice needs:

- [ ] 1  - [ ] 2  - [ ] 3  - [ ] 4  - [ ] 5

What one new thing did you learn from this program?

__________________________________________________________________________________________

How will you modify your practice performance as a result of completing this program?

__________________________________________________________________________________________

What recommendations do you suggest to improve this program?

__________________________________________________________________________________________

What topics would you like to see in future presentations?

__________________________________________________________________________________________

Please indicate how often you utilize the following formats to receive continuing professional education:

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<th>Format</th>
<th>Frequently</th>
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<th>Seldom</th>
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- [ ] yes  - [ ] no

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Address: ________________________________________________________________

City: __________________________ State: ______ Zip: ________________________

E-mail: __________________________ Last 4 digits of Social Security number ______________________

Signature: ________________________________________________________________

Thank you.
Additional Reading