Renal Dietitians on the Front Line:
The Role of Calcium-Based Phosphate
Binders for Attainment of K/DOQI™
Bone Guidelines Part 2

Table of Contents

Introduction and Overview ........................................ 3
Bone and Mineral Metabolism: Fighting the Battle,
Winning the War .................................................... 5
Cardiovascular Calcification in Dialysis Patients and
Potential Risks of Treatment With Calcium-Containing
Phosphate Binders .................................................. 13
Posttest Questions .................................................. 22
Post Program Self-Assessment ................................. 23
Additional Reading ................................................... Inside back cover

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 dis-
case. This condition is not only a major factor in the
development of secondary hyperparathyroidism and
renal osteodystrophy, but is also independently associ-
ated with an increased risk of death. The mechanism
whereby hyperphosphatemia increases mortality risk
is unknown, but it may promote cardiovascular calci-
fication. 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 phos-
phate binders is often unavoidable. The most com-
monly 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 2 part accredited CD series is
to critically examine these issues and provide rational
guidelines for the use of calcium-based phosphate bind-
ers in patients with end-stage renal disease in the con-
text 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 should 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 calcifica-
   tion 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 cal-
   cium 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
Cathi J. Martin, RD, CSR, LDN
Regional Renal Dietitian,
Renal Care Group of Springfield, Nashville, TN

Bone and Mineral Metabolism:
Fighting the Battle, Winning the War
Jennifer Kurzawa, RD
Renal Osteodystrophy Manager,
Gambro Healthcare, Old Bridge, NJ

Cardiovascular Calcification
in Dialysis Patients and Potential Risks
of Treatment With Calcium-Containing
Phosphate Binders
Charles R. Nolan, MD
Professor of Medicine and Surgery
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 Board for Nabi Biopharmaceuticals.
Dr. Nolan does not intend to discuss any non-FDA-approved or investigational use of any product/device.

Ms. Kurzawa does not have any relevant financial relationships with any commercial interests.
Ms. Kurzawa does not intend to discuss any non-FDA-approved or investigational use of any product/device.

Ms. Martin has received financial support and has participated in a Consultant/Advisor Board for Shire Pharmaceuticals, Amgen, and Abbott Laboratories.
Ms. Martin does not intend to discuss any non-FDA-approved or investigational use of any product/device.
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.
The Academy designated this educational activity for 1.3 contact hours. Participants must register, listen to the lecture, and complete and submit the program evaluation form in order to receive credit. A CE certificate will be issued within 6 to 8 weeks following receipt of your materials.
It is the policy of the American Academy of CME, Inc. to ensure balance, independence, objectivity, and scientific rigor in all sponsored educational activities. Any and all financial relationships between faculty and the commercial supporters of the CME activity and products being discussed are to be disclosed by the faculty to the attendees at the time of the activity. Discussion of any non-FDA-approved product or device shall also be made known to the audience.

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
Introduction and Overview


Used with permission.
Dietitians on the Front Line

The Battle...

- Most patients
- All clinics!

The War... in the Chronic Kidney Disease Population

- Achieving K/DOQI™ Guidelines

Choose Your Allies

- Patients
- Physicians
- Nurses
- Patient care technicians
- Unit secretaries
- Social workers
- Pharmacists
- Dietitians
- Published studies and guidelines

The Clinical Divide:
Dietitian and Physician

Build a bridge

- Maintain a strong database
- Identify your expertise
- Be assertive
- Communicate
- Be proactive
- Develop a relationship
Identify Your Enemies
- Hyperphosphatemia
- Hypercalcemia
- Elevated Ca x P
- Bone disease
- Calcifications
- Calciphylaxis
- Secondary hyperparathyroidism

Fight the Battle
- Monitor trends in lab results and patient status
- Individualize therapy & education
- Be creative and think outside the box
- Design patient approaches geared for success
- Analyze all factors affecting outcomes
  - Patient barriers
  - Dietary aspects
  - Phosphate binders
  - Dialysate
  - SHPT and vitamin D therapy
  - Other medications: prescribed and OTC

Patient Barriers
- Comprehension
- Compliance
- Motivation
- Time
- Kinetics
- Vascular access
- Finances
- Domestic situation
- Overall health

Ammunition
- Teamwork
- Education
- Relationships
- Interaction
- Motivation
- Communication
- Empathy
A Key to Success: Time Spent With the Patient

Win the War: Educate Patients That These Are *Their* Goals!

**K/DOQI Guidelines**
- Serum calcium: 8.4-9.5mg/dl
- Serum phosphorus: 3.5-5.5mg/dl
- Ca x P: <55mg²/dl²
- Intact PTH: 150-300pg/ml

---

**Case Study: New Patient**

- 60 y/o male with progressive CKD for past 5 years
- Admission labs
  - Albumin – 3.8mg/dl
  - Calcium – 9.7mg/dl
  - Phosphorus – 7.2mg/dl
  - bicPTH – 327pg/ml
  - Potassium – 3.8mg/dl
  - K/vD = 1.23
- Dialysis prescription
  - Medium-sized dialyzer: 3 hours TW
  - 3.0K+ - 2.5Ca++
- No med list: takes 3 phosphorus pills per MD; no prescription plan

---

**Take a Closer Look: Information Gathering**

- Poor catheter access
- 260 blood flow
- Per patient
  - Drinks orange juice daily for extra K+ calcium fortified
  - Not told to take blue and white phosphorus pills *with* meals—to bring med list
  - No previous contact with a registered dietitian
The Role of Calcium-Based Phosphate Binders for Attainment of K/DOQI™ Bone Guidelines

Initial Interventions:
The Front Line

- Nutrition and diet education
  - Review labs
  - Implement nutrient and binder education
  - Address bone disease, adequacy, calcifications, etc
  - Educate patient to avoid calcium-fortified foods

- Review medication list (listed calcium acetate 667mg TID)
  - Change order to “with meals”
  - Educate patients on proper binder administration

Initial Interventions:
The Front Line (cont)

- Secondary hyperparathyroidism
  - Initiate IV vitamin D sterol

- Poor adequacy and blood flow
  - Per MD
    - Changed to larger dialyzer
    - Increased time to 3-1/2 hours
    - AVF maturing

Follow-up
Three Weeks After Initial Intervention

- Labs
  - Phosphorus: 6.7mg/dl
  - Calcium: 10.7mg/dl
  - hsPTH: 60pg/ml
  - Potassium: 5.2mg/dl
  - Kt/v: 1.27

- Additional information
  - Per patient
    - Started bone health pill recommended by blond after discussion about bone disease
    - Forget to take binder 3-4 times per week

  - Per physician
    - Plan to change phosphate binder to a non-Ca²⁺-based binder
    - Plan to begin using AVF in next 2 weeks

  - Per dialysis staff
    - Patient often brings peanut butter sandwiches with him
Identify the Problems

<table>
<thead>
<tr>
<th>Hypercalcemia</th>
<th>Binder non-adherence</th>
<th>Lack of prescription plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperphosphatemia</td>
<td>Dietary non-compliance</td>
<td>Inadequate clearance</td>
</tr>
<tr>
<td>Bone health pill</td>
<td>Low biPTH</td>
<td>Vitamin D</td>
</tr>
</tbody>
</table>

Continued Efforts

- Decrease vitamin D as per K/DOQI™ guideline 6.7
- Monitor serum calcium
- Reinforce diet and binders
- Investigate bone health supplement—reveals calcium carbonate
- Compare price of binders—reveals non-calcium-based binder may cost 4 to 7 times more, depending on dosage and retailer
- Consider combination of phosphate binders based on finances and K/DOQI™ guideline 6.3a

Patient Scenarios

Patient A
- 3 months of calcium/phosphorus/CaP/biPTH within target ranges
- Biweekly labs: increased phosphorus
  - No changes per patient
- Monthly labs: increased phosphorus, biPTH
  - Patient now reveals he ran out of phosphate binders
- Follow-up labs: improved phosphorus and biPTH; increased calcium
  - Restated calcium acetate
  - Increased vitamin D

Analysis
- Why did the patient run out of binders?
- Did the increased phosphorus stimulate increased biPTH release?
- Did increased dose of vitamin D stool lead to increased serum calcium?
- Is the phosphate binder appropriate?
Patient Scenarios (cont)

- **Patient B**
  - BiPb, calcium elevated for past 3 months
  - Intermittent vitamin D therapy
  - Non-calcium-based binder
  - 2.5mEq/L calcium dialysate
  - Biweekly labs: increased phosphorus
  - Monthly labs: further increase in bioPTP, calcium, phosphorus

- **Analysis**
  - Would a calcimimetic drug be indicated?
  - Could a lower calcium dialysate be used?
  - What degree of diet and binder adherence has the patient achieved?
  - Has the secondary hyperparathyroidism progressed, leading to bone release of calcium and phosphorus?
  - Would additional day of dialysis improve serum phosphorus levels?

What Next?

- Refer to "K/DOQI™ Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease" for in-depth discussions and recommendations
- Develop an interdisciplinary plan to address interventions for renal osteodystrophy management based on current guidelines and individualized for the patient

There Is Not Always Just One Answer

- Consider the different approaches and combinations of therapies to reach target ranges
- Integrate clinical practice guidelines, monitor laboratory results, and communicate with the patient and healthcare team to develop the best plan for each patient

Selecting a Phosphate Binder

- **K/DOQI™ recommends**
  - Guideline 3.3
    - Both calcium-based phosphate binders and other non-calcium, nonaluminum, nonmagnesium-containing phosphate-binding agents (such as Sevelamer HCl) are effective in lowering serum phosphorus levels (EVIDENCE), and either may be used as the primary therapy (OPINION).
  - Guideline 5.4
    - In dialysis, patients who remain hyperphosphatemic (serum phosphorus >5.5mg/dl [1.78mmol/L]) despite the use of either calcium-based phosphate binders or other non-calcium, nonaluminum, nonmagnesium-containing phosphate-binding agents, a combination of both should be used.
Selecting a Phosphate Binder (cont)

- **Guideline 5.5**
  The total dose of elemental calcium provided by the calcium-based phosphate binders should not exceed 1500mg/day (OPINION), and the total intake of elemental calcium (including dietary calcium) should not exceed 2000mg/day (OPINION).

- **Guideline 5.6**
  Calcium-based phosphate binders should not be used in dialysis patients who are hypercalcemic (corrected serum calcium of >10.2mg/dl [2.54mmol/L], or whose plasma PTH levels are <150mg/dl [16.5pmol/L] on 2 consecutive measures (EVIDENCE).

Selecting a Phosphate Binder (cont)

- **Guideline 5.7**
  Non-calcium-containing phosphate binders are preferred in dialysis patients with severe vascular and/or other soft tissue calcifications (OPINION).

- **Guideline 5.8**
  In patients with serum phosphate levels >7.0mg/dl (2.26mmol/L), aluminum-based phosphate binders may be used as short-term therapy (4 weeks), and for 1 course only, to be replaced by other phosphate binders (OPINION). In such patients, more frequent dialysis should also be considered (EVIDENCE).

Bone and Mineral Metabolism: Current Pharmaceutical Approaches

- **Phosphate binders**
  - Calcium acetate
  - Calcium carbonate
  - Sevelamer hydrochloride
  - Lanthanum carbonate
  - Aluminum-based: short-term only

- **Vitamin D sterols**

- **Calcimimetic**
  - Cacalcet HCL
Cardiovascular Calcification in Dialysis Patients and Potential Risks of Treatment With Calcium-Containing Phosphate Binders

Remember…

- Bone and mineral metabolism in chronic kidney disease is like a puzzle: each element is one piece in that puzzle.
- Bone disease and calcification risk are a function of many factors, not just one. Studies continue in order to gain more insight into this derangement and risk factors.

A Final Note…

“Obviously, the best phosphate binders are those that the patient will take consistently and as prescribed while limiting total calcium intake… the ability to adequately control serum phosphorus rests on appropriate education, patient compliance, and use of tolerable phosphate binders. The latter needs to be individualized for patients and thus will require continuous monitoring with renal dietitians.”


Role of Abnormal Mineral Metabolism in Cardiovascular Calcification in CKD

Hyperphosphatemia
Hypercalcemia

Calcium-phosphate deposition
Phenotypic change: VSMC develop osteoblast features

Vascular calcification

The “Calcium Load” Hypothesis

- Treatment with calcium-based phosphate binders is associated with excess gastrointestinal calcium absorption
- This excess “calcium load” results in cardiovascular calcification
- Excess cardiovascular calcification is the principal cause of the high cardiovascular mortality in patients with ESRD on dialysis
- Therefore, avoidance of CBP, and preferential use of non-calcium-containing phosphate binders, such as Sevelamer, would reduce the risk of cardiovascular calcification and cardiovascular mortality in ESRD

Ideal Study Design for Testing the “Calcium Load” Hypothesis

<table>
<thead>
<tr>
<th>Study Design Element</th>
<th>Adequate Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Groups: Calcium acetate vs Sevelamer</td>
<td>X</td>
</tr>
<tr>
<td>Randomized</td>
<td>X</td>
</tr>
<tr>
<td>Double-blind</td>
<td>X</td>
</tr>
<tr>
<td>Control of serum P and Ca × P comparable between groups</td>
<td>X</td>
</tr>
<tr>
<td>Dietary calcium intake comparable between groups</td>
<td>X</td>
</tr>
<tr>
<td>Calcium supplements prohibited in Sevelamer group</td>
<td>X</td>
</tr>
<tr>
<td>Dialysate [Ca] constant and comparable</td>
<td>X</td>
</tr>
<tr>
<td>Vitamin D use comparable between groups</td>
<td>X</td>
</tr>
<tr>
<td>Traditional cardiovascular risk factors comparable</td>
<td>X</td>
</tr>
<tr>
<td>Total and LDL cholesterol comparable</td>
<td>X</td>
</tr>
<tr>
<td>Mortality endpoint rather than surrogate endpoint</td>
<td>X</td>
</tr>
</tbody>
</table>
Sevelamer Slows Progression of CV Calcification


Used with permission.


Prudent Use of Medicare Money to Prevent CV Mortality in ESRD

Phosphate-binder therapy with Sevelamer HCl
- Efficacy vs alternative therapy (Ca acetate): Less
- Reduced cardiovascular calcification: Yes
- Reduced risk of cardiovascular mortality: Unknown
- Cost compared to alternative: Exorbitant
  (Calcium acetate + statin therapy)

Prudent Use of Medicare Money to Prevent CV Mortality in ESRD (cont)

Lifelong coverage for immunosuppression
- Quality of life advantage vs alternative: Yes
- Reduction in all-cause mortality: Definite
- Reduced cardiovascular calcification: Unknown
- Reduce CV mortality vs dialysis: Definite
- Cost compared to available alternative: Less

Prudent Use of Medicare Money to Prevent CV Mortality in ESRD (cont)

- Investment of 2-3 billion annually for non-CBPB therapy (Sevelamer) in the absence of outcome data documenting a significant mortality benefit is illogical (What about the number needed to treat?)
- Immunosuppressive therapy to maintain functioning renal allografts has been proven to reduce cardiovascular mortality in ESRD patients
- Medicare expenditure of 2-3 billion per year for lifelong immunosuppressive drug coverage would be a more cost effective and logical alternative for prevention of cardiovascular mortality (EVIDENCE)
Posttest Questions

1. Renal dietitians are the only members of the healthcare team who should be involved in bone and mineral metabolism management.
   a. True
   b. False

2. Common patient barriers to management of bone and mineral metabolism include:
   a. Comprehension.
   b. Compliance.
   c. Finances.
   d. Overall health.
   e. All of the above.

3. What is the K/DOQI target for calcium x phosphorus product?
   a. < 35 mg²/dl²
   b. < 45mg²/dl²
   c. < 55mg²/dl²
   d. < 65mg²/dl²
   e. < 75mg²/dl²

4. What factors affect serum calcium levels?
   a. Dialysate calcium concentration
   b. Dietary sources of calcium
   c. Vitamin D sterols
   d. Use of calcium-based phosphate binder
   e. All of the above

5. The most important consideration in choosing a phosphate binder regimen is what the patient is most likely to follow.
   a. True
   b. False

6. Which of the following statement(s) regarding the pathogenesis of cardiovascular disease in chronic kidney disease is correct?
   a. In the setting of uremia, formation of bone with deposition of hydroxyapatite may take place in arterial walls.
   b. Although cause and effect has not been established, observational studies have shown that the administered dose of calcium-containing phosphate binders correlates with the extent of calcification in coronary arteries and peripheral arteries.
   c. Although the exact mechanism is unknown, treatment with Sevelamer leads to less cardiovascular calcification compared to treatment with calcium-based phosphate binders.
   d. Numerous traditional and nontraditional (dialysis-related) risk factors may be involved in the pathogenesis of cardiovascular disease in patients with chronic kidney disease.
   e. All of the above.

7. Which of the following statements is most accurate?
   a. Treatment with HMG-CoA reductase inhibitors (statins) such as atorvastatin has been shown to reduce all-cause and cardiovascular mortality in dialysis patients.
   b. Treatment with Sevelamer and avoidance of calcium-containing phosphate binders has been shown to significantly reduce mortality in all patients with end-stage renal disease on maintenance hemodialysis.
   c. Cardiovascular mortality in dialysis patients is no higher than in the general population.
   d. Successful renal transplantation is the only therapy for end-stage renal disease, and, has been proven to significantly reduce all-cause and cardiovascular mortality.
Post Program Self-Assessment

Renal Dietitians on the Front Line: The Role of Calcium-based Phosphate Binders for Attainment of K/DOQI™ Bone Guidelines Module 2 (05-AM-63-C-M-001-2)

Answer Sheet

1. A B
2. A B C D E
3. A B C D E
4. A B C D E
5. A B
6. A B C D E
7. A B C D

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.

Send completed forms to:
American Academy of CME, Inc.
186 Tamarack Circle
Skillman, NJ 08558
or fax to (609) 921-6428

Please check your professional title:

- Dietitian
- Physician
- 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

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)

Cathi J. Martin, RD, CSR, LDN
Value of topic

Quality of presentation

Jennifer Kurzawa, RD
Value of topic

Quality of presentation

Charles R. Nolan, MD
Value of topic

Quality of presentation

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

1 2 3 4 5

Please complete other side ☛
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:

- Live symposia/conferences
  - [] Frequently
  - [] Occasionally
  - [] Seldom
  - [] Never

- Print materials/home study courses
  - [] Frequently
  - [] Occasionally
  - [] Seldom
  - [] Never

- Web-based CME
  - [] Frequently
  - [] Occasionally
  - [] Seldom
  - [] Never

- CD-ROM
  - [] Frequently
  - [] Occasionally
  - [] Seldom
  - [] Never

- Other: __________________________
  - [] Frequently
  - [] Occasionally
  - [] Seldom
  - [] Never

Occasionally, AACME will be seeking information regarding future needs and outcomes measurements.
May we contact you via e-mail for this purpose?  [ ] yes  [ ] no
If yes, please include your e-mail address here: _______________________________________________

In order to receive your CME/CE certificate, you must complete this portion and sign.

Time spent on this activity: Hours_______ (Max: 1 hr RD/1.3 Nurse)

**Print**

Name: _______________________________________________________________________________

Address: _____________________________________________________________________________

City: ___________________________  State: _____  Zip: ________________________________

E-mail: _________________________  Last 4 digits of Social Security number _____________________

Signature: __________________________________________________________________________

Thank you.
**Additional Reading**


