BONE AND MINERAL METABOLISM in the PD PATIENT

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Chief Medical Officer
Health Systems Management

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Clinical Associate Professor of Medicine
NYU School of Medicine
Spectrum of Bone Diseases in CKD

- Osteitis fibrosa cystica
  - Increase in bone turnover secondary to increased PTH
- Adynamic bone disease:
  - Decrease in bone turnover
  - Prevalent in the advanced stages of CKD
- Mixed uremic osteodystrophy
- Osteoporosis

Spectrum of Bone Diseases in CKD

LESS COMMONLY SEEN

- Osteomalacia
- Aluminum accumulation
- Amyloid bone disease
- Phosphate depletion
  - Affects a minority of patients with CKD or ESRD

CKD-BMD MORE THAN A BONE PROBLEM

- You also see:
  - Elevated PO4 levels
  - Elevations of PTH
  - Abnormalities in Ca levels
  - Decrease in 1,25 Vitamin D and any of its non PTH related effects
Hormonal Changes in CKD

Linear decline in 1,25 D ~ eGFR 60; precedes rise in PTH

N = 1814

*p < 0.001

Hormonal Response to Hyperphosphatemia

Phosphorus

PTH

1α-hydroxylase activity

Increased PTH

FGF-23

Increased 1,25(OH)2D3

Increased FGF-23

Increased 1,25(OH)2D3

Increased renal phosphorus excretion

FGF-23 = fibroblast growth factor-23. Phosphatonin, made by osteoblasts, (Fukagawa and Kazama NDT 20:1295, 2005)
CKD-BMM Biochemical Markers Associated with Greatest Mortality Risk

PO₄ biggest player? Is it the real deal or just a surrogate?

Multivariable-adjusted relative risk

Adapted from Block GA, et al. JASN 2004
META-ANALYSIS OF BMM LAB TESTS AS PREDICTOR OF DEATH RISK

Serum Levels of Phosphorus, Parathyroid Hormone, and Calcium and Risks of Death and Cardiovascular Disease in Individuals With Chronic Kidney Disease
A Systematic Review and Meta-analysis

META-ANALYSIS OF BMM LAB TESTS AS PREDICTOR OF DEATH RISK

Figure 3. Summary Estimates for Risks of All-Cause Mortality and Cardiovascular Mortality Associated With Levels of Serum Phosphorus, Parathyroid Hormone, and Calcium

<table>
<thead>
<tr>
<th>Phosphorus</th>
<th>No. of Cohorts</th>
<th>No. of Participants</th>
<th>Relative Risk (95% CI) Per Unit Increase</th>
<th>Increased Serum Phosphorus Better</th>
<th>Decreased Serum Phosphorus Better</th>
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</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Adequate adjustment</td>
<td>3</td>
<td>4651</td>
<td>1.35 (1.16-1.57)</td>
<td></td>
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<tr>
<td>Partial adjustment</td>
<td>10</td>
<td>87694</td>
<td>1.16 (1.09-1.23)</td>
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<tr>
<td>All studies combined</td>
<td>13</td>
<td>92345</td>
<td>1.18 (1.12-1.25)</td>
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<tr>
<td>Cardiovascular mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Adequate adjustment</td>
<td>1</td>
<td>17326</td>
<td>Not estimable</td>
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<tr>
<td>Partial adjustment</td>
<td>2</td>
<td>5881</td>
<td>1.14 (1.05-1.24)</td>
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<tr>
<td>All studies combined</td>
<td>3</td>
<td>23207</td>
<td>1.10 (1.06-1.13)</td>
<td></td>
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</tr>
</tbody>
</table>

### Meta-analysis of BMM Lab Tests as Predictor of Death Risk

**Figure 3. Summary Estimates for Risks of All-Cause Mortality and Cardiovascular Mortality Associated With Levels of Serum Phosphorus, Parathyroid Hormone, and Calcium**

<table>
<thead>
<tr>
<th></th>
<th>Increased Serum</th>
<th>Decreased Serum</th>
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<tbody>
<tr>
<td><strong>Phosphorus</strong></td>
<td></td>
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<tr>
<td>All-cause mortality</td>
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<tr>
<td>Adequate adjustment</td>
<td>1.85 (1.16-1.57)</td>
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<tr>
<td>Partial adjustment</td>
<td>1.16 (1.00-1.25)</td>
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</tr>
<tr>
<td>All studies combined</td>
<td>1.16 (1.00-1.26)</td>
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<tr>
<td>Cardiovascular mortality</td>
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<tr>
<td>Adequate adjustment</td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
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<tr>
<td>All studies combined</td>
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<table>
<thead>
<tr>
<th></th>
<th>Increased Serum</th>
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<tr>
<td><strong>Parathyroid hormone</strong></td>
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<td>All-cause mortality</td>
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<tr>
<td>Adequate adjustment</td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
<td>Partial adjustment</td>
<td>1.01 (0.96-1.06)</td>
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<tr>
<td>All studies combined</td>
<td>1.01 (1.00-1.02)</td>
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<tr>
<td>Cardiovascular mortality</td>
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<td></td>
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<tr>
<td>Adequate adjustment</td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
<td>Partial adjustment</td>
<td>Not estimable</td>
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<tr>
<td>All studies combined</td>
<td>1.05 (0.99-1.11)</td>
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<table>
<thead>
<tr>
<th></th>
<th>Increased Serum</th>
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<tr>
<td><strong>Calcium</strong></td>
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<tr>
<td>All-cause mortality</td>
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<tr>
<td>Adequate adjustment</td>
<td>1.07 (0.91-1.24)</td>
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<td>Partial adjustment</td>
<td>1.09 (0.96-1.20)</td>
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<td>All studies combined</td>
<td>1.08 (1.00-1.16)</td>
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<tr>
<td>Cardiovascular mortality</td>
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<tr>
<td>Partial adjustment</td>
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</tr>
<tr>
<td>All studies combined</td>
<td>1.15 (1.08-1.29)</td>
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</table>

*Palmer et al. JAMA V305:11:1119-1127, 2011*
BOTTOM LINE CKD-MBD

- Not just a Bone Disease
  - Fractures
  - Pain
- A systemic mineral metabolism disease
  - Extra-osseous calcification
  - Vascular “ossification” / calcification
- Is any of our increased CV risk profile related to poorly managed CKD-BMD?
Phosphate Facts - I

- Total Body Phosphate = about 700 g
  - 85% in bone and teeth as hydroxyapatite
  - 14% intracellular fluids mainly as organic phosphate
  - < 1% in extracellular fluid as inorganic phosphate
    - This is component easiest to get at with dialysis

- Main source of Phosphorous:
  - Dietary
  - Bone efflux (Increased PTH)

- Phosphate removal
  - Renal
  - Dialysis
  - Saliva and GI (prevent absorption with binders)

Badve PDI 28:S2, 2008
Hsu, AJKD Dis 1997
Weisinger Lancet 352:391-, 1998
Phosphate Facts - II

- **Dietary intake (about 1000 mg/day)**
  - Typical western diet 800-2000 mg (26-67 mmol)
  - Most Dialysis patients prescribed a dietary phosphate content of 550 to 1100 mg (18-36 mmol)
  - Phosphate content /gram protein – 14-15 mg/g

- **Typical fractional absorption from gut (60-86%)**
  - Reported absorption in patients ON binders 44 to 80%
  - Reported total PO$_4$ absorbed
    - No Binders or restriction (3,360-13,040 mg/wk)
    - Restricted diet and on binders (1,500-6,160 mg/wk)

*Badve and McCormick PDI 28:S2, 2008
Hsu, Am J Kidney Dis 1997
Mucci KI 53:1399-1404, 1998*
PHOSPHOROUS FACTS – III

Removal by dialysis

Phosphorous Statistics:
- Molecular weight - 96 Daltons
- Radius - 2.8 Angstroms
  - (urea 1.8A; Creat 3.0A)
- Hydrophobic (surrounded by water)
  - Radius functionally larger than 2.8A
- Slow to move from ICF to ECF
  - Unlike urea which readily does move
  - Remember most PO₄ in bone, teeth or ICF
- About 50% of circulating PO₄ is a Na, Ca or Mag salt
- Negatively charged
  - Not freely diffusible across all membranes
  - Living membrane vs. synthetic membrane

Kuhlman Blood Purif 2010; 29:137-144
PO$_4$ REMOVAL BY DIALYSIS

**Bottom line:**

- Acts more like a middle molecule than like Urea, Creatinine, Na.
- Kinetics vary markedly between PD and HD
- For PD: PO$_4$ removal correlates with Creatinine removal
- Residual renal function contributes in large part to phosphate excretion and subsequent phosphate balance
PO₄ REMOVAL BY DIALYSIS (cont’d)

- Peritoneal PO₄ removal/week is on the same magnitude of conventional 3/week HD.
- Peritoneal PO₄ clearance is from both diffusive and convective properties.
- Membrane transport characteristics DO play a role in phosphate clearance.
Treatment of Hyperphosphatemia

Diet P Restriction: <1000 mg/day

Renal and Dialysis P Removal

Phosphate Binders

Reducing P Flux From Bone by Controlling Secondary HPT

Maintain Serum P in “Healthy” Range

CONTROLLING PHOSPHOROUS

- Must limit PO intake
  - Diet
DIETS AND PHOSPHOROUS

- Unfortunately $\text{PO}_4$ in everything and if not there naturally we are adding it to everything. (Processed foods etc)
- However can reduce $\text{PO}_4$ in diet
  - Restrict Protein / $\text{PO}_4$ content
  - IF possible, use
    - Whey proteins
    - Boiled meats
PO$_4$ and PD

- If one encourages increased protein intake i.e. in patients with:
  - Malnutrition
  - Low serum albumin
  - Protein losses in dialysate

- As you recommend protein intake you also receive obligate PO$_4$ ingestion.
As you increase dietary Protein intake you are likely to increase PO$_4$ intake

PO$_4$ (mg) = 128 + 14 x protein (gms)
104 CRF pts, semiquantatative food frequency questionnaire, Nutr III software

CONTROLLING PHOSPHOROUS

- Must limit PO intake
  - Diet
- Must limit absorption from gut
PILL BURDEN IN ESRD

P-Binders: Major Source of Pill Burden

47% P-Binders
53% Others

Chiu et al, 2009
Selection Of P-Binders

- **Efficacy:**
  - Published clinical data indicates similar efficacy of available P-binders

- **Adherence considerations:**
  - Be mindful of pill burden
  - Lower frequency of administration not effective in recent RCTs

- **Limit Toxicity:**
  - GI tolerance greatest limitation for most P-binders
  - Limit/avoid calcium-based binders in most patients
  - Watch for metabolic acidosis with sevelamer hydrochloride
  - Watch LFTs with lanthanum carbonate (no reported evidence of abnormalities in humans)
CONTROLLING PHOSPHOROUS

- Must limit PO intake
  - Diet

- Must limit absorption from gut
  - Binders – Do work; will likely be needed
  - Minimize active Vitamin D (1,25 D) levels or analogues to minimize uptake from food
CONTROLLING PHOSPHOROUS

- Must limit PO intake
  - Diet

- Must limit absorption from gut
  - Binders
    - Minimize active Vit D (1,25 vit D) levels or analogues

- Minimize $PO_4$ efflux from bones
MINIMIZE PO4 EFFLUX FROM BONES

Decrease PTH activity
- Calcimemetics
- VDRAs
  - VDRAs have increased PO4 absorption as side effect
- Activity
CONTROLLING PHOSPHOROUS

- Must limit PO intake
- Minimize absorption from gut
- Minimize PO$_4$ efflux from bones
- Maximize PO$_4$ removal with:
  - Maintain Renal function
CLEARANCE OF VARIOUS SOLUTES
NATIVE KIDNEY FUNCTION vs PD

Contribution of RRF to Clearance of Small vs Large Solutes

Bammens et al, 2003
CREATININE CLEARANCE in PD
Importance of RKF

Fig 3. Time course of renal (gray bars), peritoneal (white bars), and total clearances (♦; liters per week per 1.73 m²) of creatinine from visits 1 to 5 (N = 24). For display purposes, data were grouped per visit. Median values are shown.

Bammens et al, AJKD 46,#3;2005:512-519
PHOSPHATE CLEARANCE IN PD
Importance of RKF

Fig 4. Time course of renal (gray bars), peritoneal (white bars), and total clearances (*, liters per week per 1.73 m²) of phosphate from visits 1 to 5 (N = 24). For display purposes, data were grouped per visit. Median values are shown.

Bammens et al, AJKD 46,#3;2005:512-519
# P Clearance and RRF

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Serum P</th>
<th>Total P clearance* (ml/min/1.73 m²)</th>
<th>Daily P excretion (mg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With RRF</td>
<td>18</td>
<td>5.13 ± 1.41</td>
<td>6.74 ± 2.95</td>
<td>471.6 ± 216.3</td>
</tr>
<tr>
<td>Anuric</td>
<td>38</td>
<td>5.27 ± 1.54</td>
<td>5.25 ± 1.14</td>
<td>399.9 ± 141.8</td>
</tr>
</tbody>
</table>

* P < 0.05

Study in PD patients; unaware of studies in HD patients

*Sedlacek et al, Am J Kidney Dis, 2000; 36: 1020-1024*
RESIDUAL KIDNEY FUNCTION AND PO4 REMOVAL

Native Kidney function plays a major role in PO4 homeostasis

- Contribution of total PO4 removal by native kidneys in PD:*
  - 63% of total PO4 removal at baseline
  - 49% at 7 months.

- In a cross section study of 252 PD patients**
  - Of those with RKF: 29% PO4 > 5.5
  - In anuric patients: 44% PO4 > 5.5

*Bammens et al AJKD 46:512-519, 2005
**Wang et al AJKD 43:712-720, 2004
CONTROLLING PHOSPHOROUS

- Must limit PO intake
- Minimize absorption from gut
- Minimize PO$_4$ efflux from bones
- Maximize PO$_4$ removal with:
  - Renal function
  - Dialysis
Phosphate Balance in Dialysis

HD remove about 1000 mg per treatment x 3 = 3000 mg/wk
PD remove about 400 mg per day x 7 = 2800 mg/week
DIALYTIC REMOVAL OF VARIOUS SOLUTES

Table 4 | Total mass removal (mg/week) in HD (n=20), APD (n=34), and CAPD (n=16) patients

<table>
<thead>
<tr>
<th></th>
<th>HD</th>
<th>APD</th>
<th>CAPD</th>
<th>Overall ANOVA</th>
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<tbody>
<tr>
<td>UN</td>
<td>89349 ± 34770</td>
<td>92025 ± 27429</td>
<td>11 1649 ± 40506</td>
<td>0.2</td>
</tr>
<tr>
<td>Cr</td>
<td>4746 ± 2009(^x)</td>
<td>6522 ± 1952(^x)</td>
<td>6918 ± 2572(^y)</td>
<td>0.008</td>
</tr>
<tr>
<td>P</td>
<td>2356 ± 864</td>
<td>2739 ± 1042</td>
<td>2790 ± 1022</td>
<td>0.4</td>
</tr>
<tr>
<td>p-Cresol</td>
<td>351 ± 232(^x)</td>
<td>175 ± 108(^x)</td>
<td>214 ± 147</td>
<td>0.003</td>
</tr>
</tbody>
</table>

ANOVA, analysis of variance; APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; HD, hemodialysis.

\(^x\)\(^y\)Parameters with same suffix differ significantly.
Phosphate Facts - IV

- Dietary intake (1000 mg/day)
  - Most Dialysis patients prescribed a diet phosphate content of 550 to 1100 mg / day (18-36 mmol)
  - Reported absorption in patients ON binders 44 to 80%
  - Total absorbed: (1,500-6,160 mg/wk)

- Conventional hemodialysis removal:
  - 800 to 1000 mg/Rx times 3 = 2400-3000 mg/wk

- Typical reported PD clearance:
  - 55-66 L/1.73m2/wk
  - Removal related to serum PO$_4$
  - If serum PO$_4$ is 5.5 mg/dL removal is 55mg/L x 60L=3300 mg/week

Badve and McCormick PDI 28:S2, 2008
Hsu, Am J Kidney Dis 1997
D/P for Creatinine and $\text{PO}_4$ are similar
RATES OF DIFFUSION FOR CREATININE AND PO₄ ARE SIMILAR

INFLUENCE OF MOLECULAR WEIGHT ON DIFFUSION RATE

Note D/P values for PO₄, Creatinine and Urea – Molecular weight influences rates of diffusion
Among patients with similar Kt/V, those with wCrCl < 60 had lower P clearance (4.3 ml/min) than those with wCrCl > 60 (7.0 ml/min).

Former had higher serum P (5.9 mg/dl) than latter (4.8 mg/dl)

Phosphate Removal on PD MAY NOT be related to Kt/V (N=13 patients)

Guzwiller et al, Clin Nephrol 2003
**PO$_4$ REMOVAL CORRELATES WITH CREATININE REMOVAL**

**Table 2a. Fluid and solute clearances, comparison across PD modality**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>CAPD</th>
<th>CCPD</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysate volume (L/day)</td>
<td>11.4 ± 4.2</td>
<td>8.2 ± 1.6</td>
<td>14.4 ± 3.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Ultrafiltration on PD (L/day)$^a$</td>
<td>1.04 (0.67–1.43)</td>
<td>1.16 (0.63–1.45)</td>
<td>0.99 (0.67–1.36)</td>
<td>0.478</td>
</tr>
<tr>
<td>Peritoneal Kt/V</td>
<td>1.74 ± 0.4</td>
<td>1.62 ± 0.3</td>
<td>1.86 ± 0.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Peritoneal creatinine clearance (L/wk/1.73 m$^2$ BSA)</td>
<td>45.6 ± 10.8</td>
<td>44 ± 8.1</td>
<td>47 ± 12.8</td>
<td>0.11</td>
</tr>
<tr>
<td>Peritoneal P/phosphate clearance (L/wk/1.73 m$^2$ BSA)</td>
<td>39.5 ± 11.3</td>
<td>40.9 ± 10.4</td>
<td>38.3 ± 12</td>
<td>0.199</td>
</tr>
</tbody>
</table>

$^a$Median (interquartile range). $P$ value by ANOVA if parametric variable, and by Kruskal-Wallis test if nonparametric. BSA, body surface area.

*Badve et al, CJASN Vol3:1711-1717, 2008*
PO₄ REMOVAL IS RELATED TO TRANSPORT TYPE (and Rx)

PO₄ REMOVAL IS RELATED TO TRANSPORT TYPE (and Rx)

PO₄ REMOVAL ON PD CORRELATES WITH:

Dialysis Modality, Independent of Peritoneal Transport Characteristics

Sunil V. Badve,*† Deborah L. Zimmerman,*† Greg A. Knoll, *†‡ Kevin D. Burns,*† and Brendan B. McCormick*†

*Division of Nephrology, Department of Medicine, University of Ottawa and The Ottawa Hospital Ottawa, Canada,
†Kidney Research Centre and ‡The Clinical Epidemiology Program, Ottawa Health Research Institute, Ottawa, Canada

Background and objectives: Hyperphosphatemia is an independent risk factor for mortality in ESRD, but factors regulating phosphate clearance on peritoneal dialysis (PD) are incompletely understood. The objective of this study was to test the hypothesis that peritoneal phosphate clearance is better with continuous ambulatory PD (CAPD) as compared with continuous cyclic PD (CCPD) after adjusting for membrane transport status.

Design, setting, participants, & measurements: In this cross-sectional and retrospective study, measurements of peritoneal phosphate clearance of 129 prevalent PD patients were reviewed. Patients were divided according to membrane transport status (high, high average, low average-low categories) and PD modality (CAPD or CCPD).

Results: Among high transporters, peritoneal phosphate clearances were comparable in both modalities. However, treatment with CAPD was associated with increased peritoneal phosphate clearance compared with CCPD among high-average transporters (42.4 ± 11.4 versus 36.4 ± 8.3 L/wk/1.73 m², P = 0.01), and low-average-low transporters (35.0 ± 5.9 versus 28.9 ± 11 L/wk/1.73 m², P = 0.034). On multivariate linear regression, PD modality, membrane transport category, and peritoneal creatinine clearance, but not Kt/V urea, were independently associated with peritoneal phosphate clearance.

Conclusions: Peritoneal phosphate clearance is determined by PD modality and membrane transport category, suggesting that PD regimes with longer dwell times may help control hyperphosphatemia in lower transporters.

PERITONEAL PO₄ REMOVAL IS MORE RELATED TO CREATININE REMOVAL THAN Kt/V

Table 2b. Fluid and solute clearances, comparison across peritoneal membrane transport status

<table>
<thead>
<tr>
<th>Variable</th>
<th>High</th>
<th>High-Average</th>
<th>Low-Average and Low</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysate volume (L/day)</td>
<td>12.7 ± 4</td>
<td>11.4 ± 4.5</td>
<td>10.6 ± 3.5</td>
<td>0.213</td>
</tr>
<tr>
<td>Ultrafiltration on PD (L/day) a</td>
<td>1.07 (0.69–1.5)</td>
<td>1.03 (0.62–1.40)</td>
<td>1.23 (0.86–1.45)</td>
<td>0.468</td>
</tr>
<tr>
<td>Peritoneal Kt/V</td>
<td>1.94 ± 0.5</td>
<td>1.71 ± 0.4</td>
<td>1.68 ± 0.3</td>
<td>0.035</td>
</tr>
<tr>
<td>Peritoneal creatinine clearance (L/wk/1.73 m² BSA)</td>
<td>53.9 ± 14.2</td>
<td>45.8 ± 8.8</td>
<td>39.2 ± 8.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Peritoneal phosphate clearance (L/wk/1.73 m² BSA)</td>
<td>49.6 ± 11.4</td>
<td>39.2 ± 10.3</td>
<td>33.2 ± 8.5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

aMedian (interquartile range). P value by ANOVA if parametric variable, and by Kruskal-Wallis test if nonparametric.

PO₄ REMOVAL BY PD
Correlation with Modality and Membrane Transport Characteristics

Methods:
- Reviewed data on 264 patients (61% CAPD)
- PET testing with 4.25% D & 24 hour urine for PO₄ clearance

Results:
- PO₄ Clₚ correlated best with Cr Clₚ than Urea Clₚ
- Hyperphosphatemia at 1 year (PO₄ > 5.5 mg/dl) found in 30% patients
- PO₄ levels negatively correlated with RKF and PO₄ Clₓ

Bernardo et al. CJASN 6:591-597, 2011
# PO₄ Removal by PD

**Correlation with Modality and Membrane Transport Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>CAPD</th>
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<tbody>
<tr>
<td><strong>Peritoneal Kt/V</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>1.47 ± 0.3</td>
<td>1.99 ± 0.4</td>
</tr>
<tr>
<td>High Average</td>
<td>1.74 ± 0.51</td>
<td>1.56 ± 0.5</td>
</tr>
<tr>
<td>Low Average</td>
<td>1.66 ± 0.2</td>
<td>1.46 ± 0.4</td>
</tr>
<tr>
<td>Low</td>
<td>1.58 ± 0.3</td>
<td>1.44 ± 0.3</td>
</tr>
<tr>
<td><strong>Peritoneal PO₄ Cl</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>46.9 ± 12.6</td>
<td>48.1 ± 13.0</td>
</tr>
<tr>
<td>High Average</td>
<td>39.3 ± 10.4</td>
<td>39.6 ± 9.3</td>
</tr>
<tr>
<td>Low Average</td>
<td>35.9 ± 7.8</td>
<td>31.6 ± 6.6</td>
</tr>
<tr>
<td>Low</td>
<td>33.9 ± 15.2</td>
<td>24.5 ± 9.0</td>
</tr>
</tbody>
</table>

*Bernardo et al. CJASN 6:591-597, 2011*
### PO₄ REMOVAL BY PD
*Correlation with Modality and Membrane Transport Characteristics*

<table>
<thead>
<tr>
<th>Variable</th>
<th>High</th>
<th>H Average</th>
<th>L Average</th>
<th>Low</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritoneal Kt/V</td>
<td>1.87 ± 0.5</td>
<td>1.63 ± 0.5</td>
<td>1.58 ± 0.4</td>
<td>1.51 ± 0.4</td>
<td>0.016</td>
</tr>
<tr>
<td>Peritoneal Cr Cl (L/W/1.73m²)</td>
<td>49.3 ± 12.2</td>
<td>41.8 ± 13.9</td>
<td>37.1 ± 8.8</td>
<td>34.3 ± 12.2</td>
<td>0.005</td>
</tr>
<tr>
<td>Peritoneal PO₄ Cl (L/W/1.73m²)</td>
<td>47.4 ± 12.6</td>
<td>39.4 ± 9.9</td>
<td>34.0 ± 7.6</td>
<td>31.4 ± 14.3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Bernardo et al. CJASN 6:591-597, 2011*
PO₄ REMOVAL IN PD IS RELATED TO TRANSPORT TYPE

Phosphate clearance is…

… about 90% of creatinine clearance (i.e. 4 hour PO₄ D/P = 0.53 v 0.59)

… reduced by 25% in lower v higher transporters

<table>
<thead>
<tr>
<th>N</th>
<th>RRF</th>
<th>Kt/V</th>
<th>D/P₃</th>
<th>CrC</th>
<th>PO₄ C</th>
<th>Serum PO₄</th>
<th>PO₄ excr</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>0</td>
<td>2.46</td>
<td>0.49</td>
<td>51.6 L</td>
<td>4.2 ml/min</td>
<td>6.0 mg/dl</td>
<td>331 mg</td>
</tr>
<tr>
<td>13</td>
<td>0</td>
<td>2.46</td>
<td>0.68</td>
<td>72.2 L</td>
<td>6.2 ml/min</td>
<td>4.7 mg/dl</td>
<td>422 mg</td>
</tr>
</tbody>
</table>

PET results distributed equally

PO4 CLEARANCE BY PD MODALITY

CAPD vs NIPD  
*Twardowski ASAIO Trans 36:M584-8, 1990*

- CAPD 8 L vs NIPD 26 cycles with 31 L
- Compared to CAPD – NIPD PO4 clearance were 17% lower while NIPD urea clearance was 31% higher

CAPD vs CCPD  

- Studies tend to show no significant difference with CAPD vs CCPD
- Unless you do a mid day exchange
  - CCPD+MDE> CCPD > CAPD (61 vs 45 vs 41 L/week)
BOTTOM LINE PO$_4$ and PD

- At times Kt/V will be OK but PO$_4$ elevated
- In this case – YES restrict PO$_4$ in Diet, use binders, but remember you may be able to adjust PD dialysis Rx also!!
- If on PD, consider a wet day, consider length of dwell time, consider an increase in instilled volume, review UF volume.
- Although KDOQI no longer recommends tracking Creatinine Clearance – remember PO$_4$ removal correlates well with it.
Priorities

- **Fix Phos**
  - Limit intake
  - Block absorption
  - Remove effectively by dialysis

- **Allow Ca$$^+$$ flexibility**
  - Low Ca$$^+$$ may contribute to PTH stimulation, low BP, cramps, arrhythmia
  - High Ca$$^+$$ may contribute to vascular calcification, BP stability, less cramps

- **PTH**
  - Fix Phos aggressively and Ca$$^+$$ within reason
  - Want at least small amount of Vit D around for its other effects
  - Calcimimetics after low dose Vit D
PD and Phosphorus Removal

- Removal of the same magnitude as with conventional HD
- Maximize daily P removal:
  - Maintain residual renal function
  - All measures that maximize creatinine clearances will maximize P removal:
    - Increase fill volume
    - Continuously wet abdomen in anuric subjects
    - Mid-day exchange for the long dwell in APD patients
- Consider increasing UF and remember pathway for water removal ( pores) is important.
CONCLUSIONS

- Phosphorus needs to be controlled
- $\text{PO}_4$ probably acts more like a middle molecule than a small solute
- Serum $\text{PO}_4$ hard to normalize with conventional dialytic therapies.
  - Remember: Diet, Binders, VDRA’s,
- When rounding in a PD unit:
  - Remember relationship to dwell time and PO4 diffusion rates, in general longer dwells and 24 hours worth of PD dwell help
- When rounding in an HD unit consider:
  - More frequent Therapies
    - (PD and SDHD, Daily Nocturnal HD)