به نام خداوند جان و خرد

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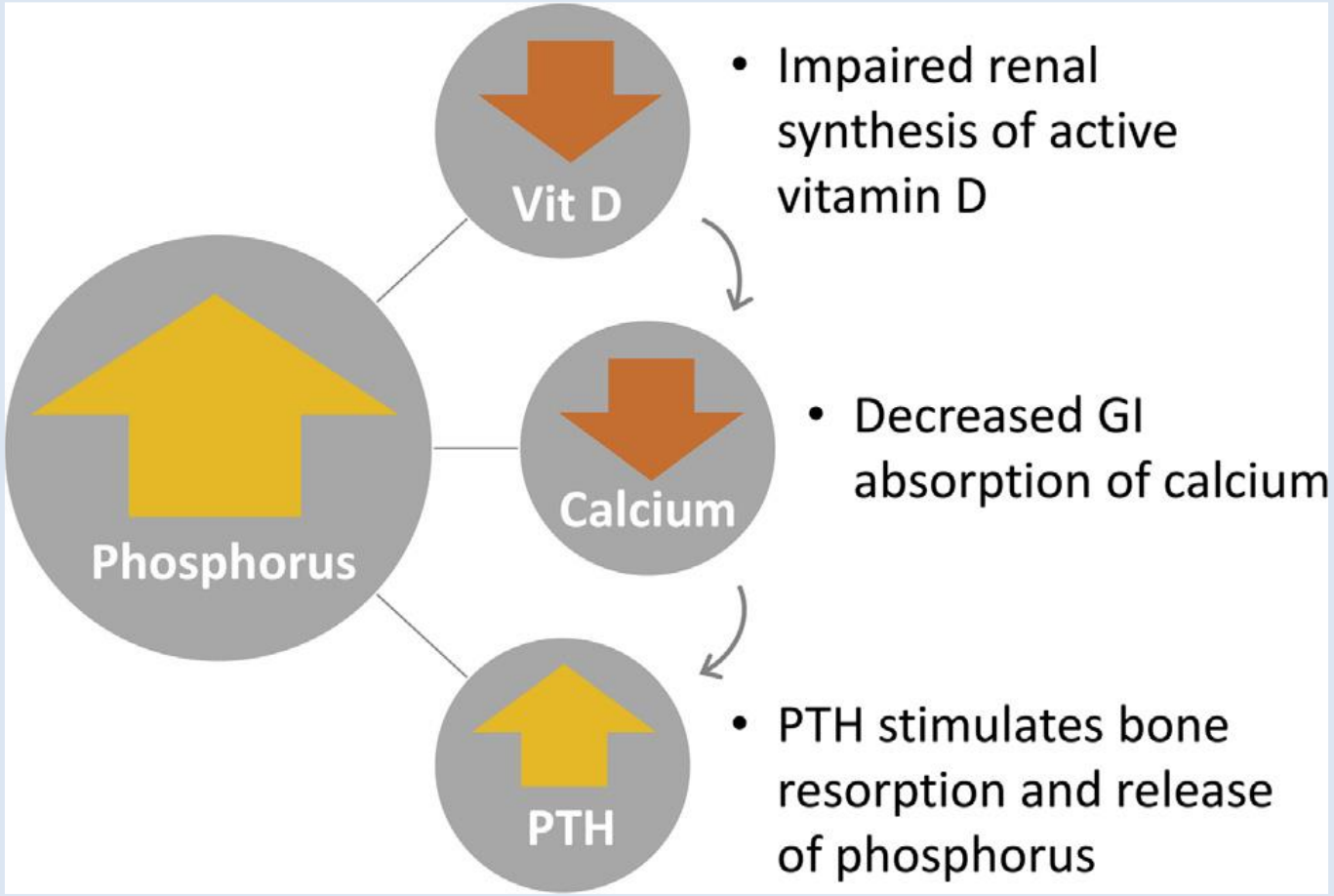
Management of Hyperphosphatemia in ESRD Disease

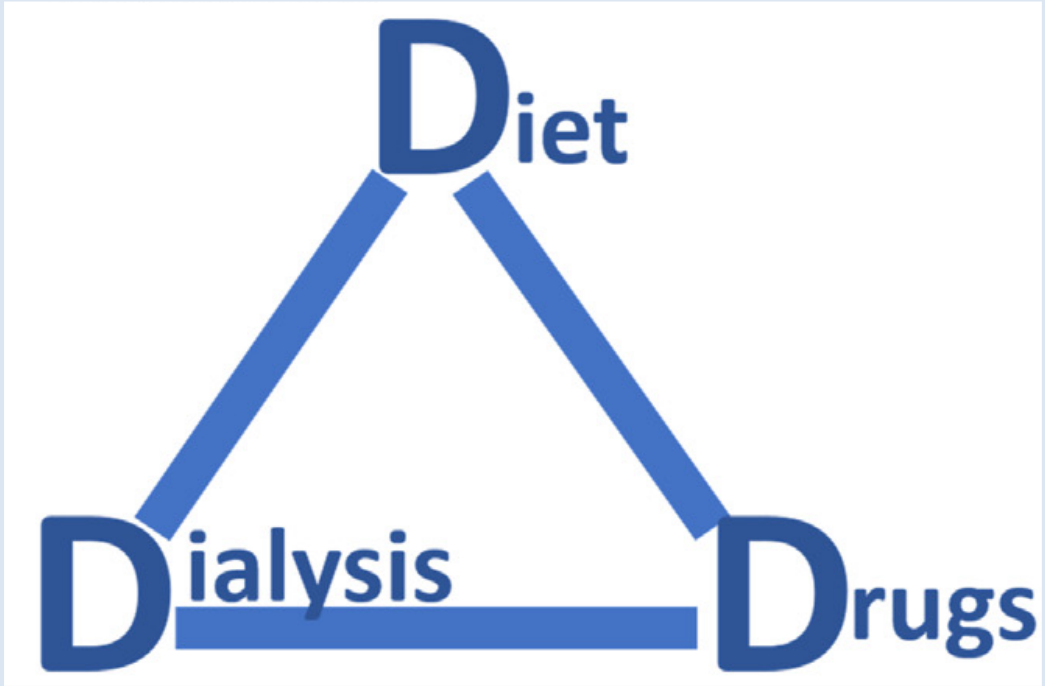
A simplified overview of disordered mineral metabolism in CKD–MBD



Organic phosphates form the structural components of cells and are distributed

- Skeleton (85%)
- Soft tissue (14%)
- Teeth(0.4%)
- Blood (0.3%)
- Extravascular fluid (0.3%)

3Ds of hyperphosphatemia management



Management of Hyperphosphatemia in End-Stage Renal Disease/Journal of Renal Nutrition/

Hidden sources of phosphorus

❖Food additives:

1. pH regulators
2. stabilizers
3. flavor/color enhancers

Dietary phosphorus in the form of food additives has roughly doubled from 1990 to 2005,

❖Poor labeling of phosphorus content

❖Phosphorus in medications.

Common medications high in phosphorus include:

- 1. Paroxetine (antidepressant)
- 2. Amlodipine (calcium channel blocker)
- 3. Lisinopril (antihypertensive)
- 4. Sitagliptin (antidiabetic)

- In the United States, the recommended daily allowance of phosphorus for adults is 900 mg/day
- **The highest concentrations of naturally occurring phosphorus:**

a) cereal grains (120–360 mg/100 g)

b) cheese (220–700 mg/100 g)

c) egg yolk (586 mg/100 g)

d) legumes (300–590 mg/100 g)

e) fish and meat (170–290 mg/100 g)

Source:	Plant	Animal	Inorganic Additives
Common Foods:	Grains Legumes Nuts	Meat Cheese Fish	Soda Prepared Foods Canned Foods
Bioavailability:	30-50%	60-90%	**90-100%**

- 30% of patients receiving dialysis take at least 1 medication containing phosphorus

- This source of phosphorus is clinically significant for patients with advanced CKD, given that more than 25% of these patients are prescribed 25 tablets per day for a range of conditions

- Patients should be encouraged to consume foods with the least amount of inorganic phosphate, low phosphorus-to-protein ratios, and adequate protein content

- with a recommended daily protein intake of 1–1.2 g/kg/day for patients receiving dialysis, it is extremely difficult to keep phosphorus levels below 900 mg/day

- meats and poultry without breading, marinades, or sauces
- seafood is an excellent source of low fat protein, with lower phosphorus content than red meat
- use of dairy Substitutes
- use of egg white in cooking and baking, as the yolk contains the majority of the phosphorus in eggs

Dialytic Removal of Phosphorus

- Conventional dialysis treatment removes only a fraction of absorbed Phosphorus
- A dietary phosphorus consumption of 1,000 mg/day with a 70% GI absorption rate provides an approximate weekly phosphorus burden of 5,000 mg
- Standard hemodialysis (4 hours) removes, on average, 700–900 mg of phosphorus, amounting to a weekly phosphorus removal of 2,100– 2,700 mg with a conventional thrice weekly hemodialysis regimen

- Alternative strategies targeting phosphorus kinetics to increase dialytic phosphorus removal, including frequency, duration, and timing of dialysis, have been investigated

Table 1. A Comparison of Phosphorus Removal Between Dialysis Modalities

Modality	Frequency	Phosphorus Removal (mg/wk)	Reference
Conventional HD	3 × 4 h	1,572 ± 366	104
Extended HD	3 × 5 h	3,400 ± 647	105
Short daily HD	6 × 3 h	2,452 ± 720	56
Nocturnal daily HD	6 × 6-8 h	8,000 ± 2,800	106
CAPD	24.0 h*	2,790 ± 1,022	107
APD, CCPD	18.5 ± 7.3 h*	2,739 ± 1,042	107

APD, automated PD; CAPD, continuous ambulatory PD; CCPD, continuous cycling PD; HD, hemodialysis; PD, peritoneal dialysis.
*Dwell time.

Drug Therapy

- Phosphate Binders
- Vitamin D
- Calcimimetics

Phosphate Binders

- Aluminum hydroxide
- Calcium-based binders
- Iron-based agents

1. sucroferric oxyhydroxide
2. ferric citrate

- Resin-based ion exchange binders
- Lanthanum carbonate

Table 2. Comparison of Common Phosphate Binding Oral Agents in Chronic Kidney Disease

Phosphate Binder	Pros	Cons
Calcium-based: calcium acetate calcium carbonate calcium citrate	• Increases calcium and can correct hypocalcemia • Low cost • Moderate pill burden	• Hypercalcemia and/or positive calcium balance • Cardiovascular calcification
Sevelamer-based: sevelamer carbonate sevelamer hydrochloride	• No systemic absorption • Potentially less vascular calcification (calcium-free) • Lowers LDL cholesterol • Improvement in metabolic acidosis with carbonate variant	• Adverse GI effects • High pill burden • High cost • Binds fat-soluble vitamins • Metabolic acidosis with the hydrochloride variant
Iron-based: sucroferric oxyhydroxide	• Lower pill burden • Minimal systemic absorption, no iron overload • Greater efficacy • Increased GI motility which might be beneficial in constipated and PD patients	• High cost
Iron-based: ferric citrate	• Noninferior to sevelamer, well tolerated, beneficial effect on renal anemia	• Systemic absorption with potential for iron overload
Lanthanum carbonate	• Twice as potent as calcium and sevelamer	• High cost • Systemic absorption and potential tissue deposition/toxicity • GI intolerance, nausea • Difficult to chew

GI, gastrointestinal; LDL, low-density lipoprotein; PD, peritoneal dialysis.

Vitamin D

- Nutritional vitamin D: must undergo hydroxylation in the liver and kidney to become active.
- Non-nutritional vitamin D: can be synthesized in the skin from exposure to sunlight
- Active vitamin D and vitamin D analogs :

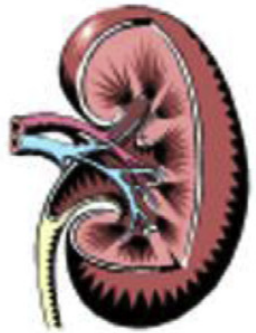
1. Calcitriol:
2. Paricalcitol
3. Doxercalciferol

Calcimimetics

- Calcimimetics activate the calcium-sensing receptor to inhibit calcium-regulated PTH secretion
- By reducing PTH, calcimimetics also decrease bone resorption and thus decrease the contribution of serum phosphorus from bone
- Potential limitations of calcimimetics include hypocalcemia and nausea/vomiting

Source of High Phosphorus

Treatments and Limitations



KIDNEY

Loss of kidney function and impaired renal excretion of phosphorus

Regular dialysis:
Dialyzer removes phosphorus from the blood

- Dialysis removal not sufficient to reach target range

GUT

Dietary phosphorus absorption

Dietary changes:
Reduce intake of phosphorus and phosphate additives

- Increased protein requirement necessitates dietary phosphorus

Phosphate binders:
Reduce phosphorus absorption

- High pill burden and adverse GI effects

BONE

Bone resorption releases stored phosphorus

Vitamin D:
Increases calcium and suppresses PTH

- Can increase phosphorus absorption from gut

Calcimimetics:
Suppress PTH-induced bone turnover and phosphorus release

- Possible hypocalcemia and GI symptoms

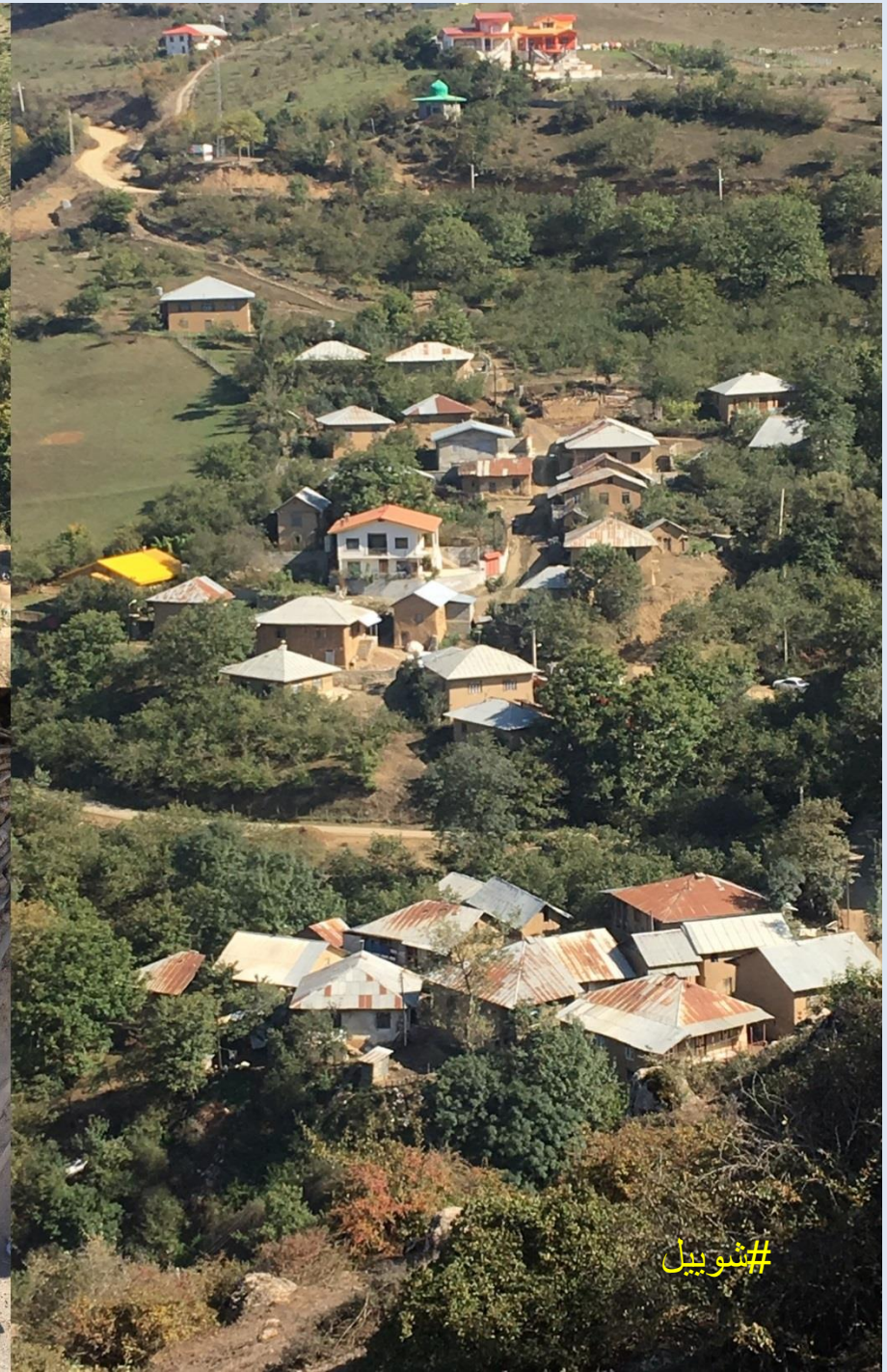
lanthanum carbonate (Fosrenol)

- Initial: 750-1500 mg/day PO in divided doses
- Titrate by 750 mg increments q2-3Weeks until acceptable serum phosphate level attained
- Doses up to 4500 mg were evaluated in clinical trials; most patients required a total daily dose between 1500-3000 mg to reduce plasma phosphate levels to <6.0 mg/dL
- **fosrenol price:** $1,138 for a supply of 90

sucroferric oxyhydroxide (Velphoro)

- Initial: 500 mg PO TID with each meal
- The highest daily dose studied in a Phase 3 clinical trial in patients with ESRD was 6 tablets (3,000 mg/day)
- **Velphoro Prices:** $1,517 for a supply of 90 tablets

Tenapanor (IBSRELA)



ممنون از توجه شما

من اینجا ریشه
در خاکم ...

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