HOW TO ASSESS THE EFFICACY OF PHOSPHATE BINDERS

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Introduction and Aims

◆ Clinical assessment of the efficacy of a phosphate binder (PB) is difficult. Testing exclusively the changes of serum or urinary phosphate levels after PBs prescription could be misleading. Decreased dietary phosphate intake due to gastrointestinal irritiation due to PB, non-compliance with the medication, or incomplete 24 h urine collection, are some examples of potential confounders.

◆There is a strong correlation between dietary nitrogen and phosphate intake. Thus, the ratio between urine phosphate excretion and protein catabolic rate estimated by urine urea nitrogen excretion may reflect the intestinal phosphate absortion.

◆Aims: This study analyzes the changes in serum phosphate and urinary phosphate excretion after the prescription of PBs in patients with CKD stage 4-5 pre-dialysis, and the usefulness of the ratio between urine phosphate excretion and protein catabolic rate (Pu/PCR). In other words, how much phosphate is collected in urine by each gram of estimated dietary protein intake.

Patients and Methods

◆ Retrospective observational cohort study which included 339 adult patients (mean age 67 ± 14 years, 141 women) with eGFR < 30 ml/min/1.73 m^2, referred for outpatient follow-up from Feb. 2008 to Dec. 2015. Exclusion criteria were: clinical instability including poor nutritional status, recent AKI, and patients on corticosteroids or any therapy with potential influence on bone-mineral metabolism (vitamin D, bisphosphonates, denosumab, etc.).

◆After a baseline biochemical study (see table 1), patients were divided into 2 subgroups according to they were treated ("cases") or not ("controls") with PBs. Dietary phosphate restriction was prescribed to both subgroups. After 45-60 days on treatment (PBs + diet or only diet), the same biochemical parameters were analyzed again.

◆PBs prescriptions included the most common commercial preparations at conventional doses (aluminum salts, calcium acetate or carbonate, magnesium hydroxide, sevelamer, and lanthanum carbonate). Each treatment was normalized using the "relative phosphate-binding coefficient" described by Daugirdas et al (Semin Dial. 2011;24:41–9).

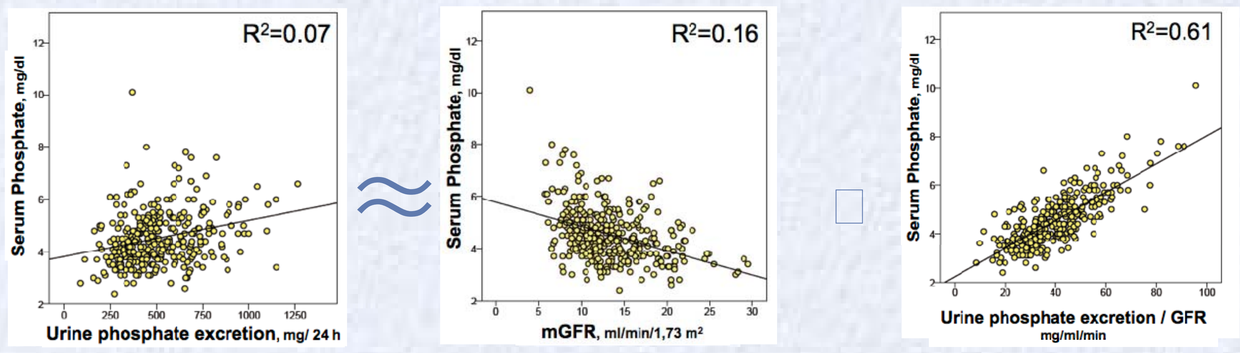
◆ Renal function was assessed by eGFR (MDRD-4) and mGFR (combined urea and creatinine clearances). Protein catabolic rate (PCR) was estimated from 24 hours urinary urea nitrogen excretion according to Maroni´s formula. The proposed parameter for assessing PBs efficacy was calculated: Total urine phosphate excretion (Pu) / PCR (g/24 h) (Pu/PCR), expressed as mg/g

Results

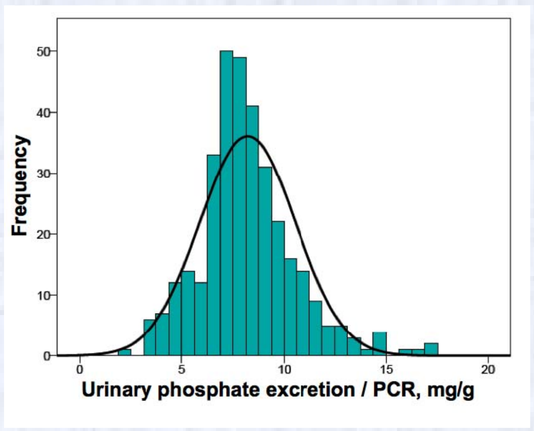
Clinical and biochemical characteristics

Variable	Phosphate Binders Subgroup	Control Subgroup	p
N	260	79	
Age, years	65 ±14	72 ±11	<0.0001
Sex, male / female	148 / 112	50 / 29	0.315
eGFR, ml/min/1.73 m^2	14.4 ±3.8	17.9 ±4.7	<0.0001
mGFR, ml/min/1.73 m^2	13.1 ±4.2	14.5 ±5.2	0.018
Protein Catabolic Rate (PCR), g/Kg/day	0.83 ±0.26	0.81 ±0.26	0.625
Serum Albumin, g/dl	4.02 ±0.39	3.97 ±0.42	0.272
Serum total calcium, mg/dl	9.1 ±0.7	9.2 ±0.6	0.248
Serum ionic calcium, mmol/l	1.22 ±0.11	1.24 ±0.08	0.238
Serum phosphate, mg/dl	4.7 ±1.0	3.8 ±0.8	<0.0001
Serum magnesium, mg/dl	2.05 ±0.35	2.04 ±0.29	0.944
Serum bicarbonate, mmol/l	21.5 ±3.7	22.3 ±3.4	0.092
PTH, pg/ml	281 ±220	199 ±156	0.004
Urine calcium, mg/24 h	37 ±31	39 ±29	0.236
Urine phoshate (Pu), mg/24 h	539 ±199	421 ±181	<0.0001
Fractional phosphate excretion, %	41.5 ±8.5	36.9 ±9.7	<0.0001
Urine phosphate (Pu) / mGFR, mg/ml/min	42.6 ±13.5	29.7 ±8.9	<0.0001
Urine phosphate (Pu) / PCR, mg P / g protein	8.59 ±2.32	7.00 ±1.98	<0.0001

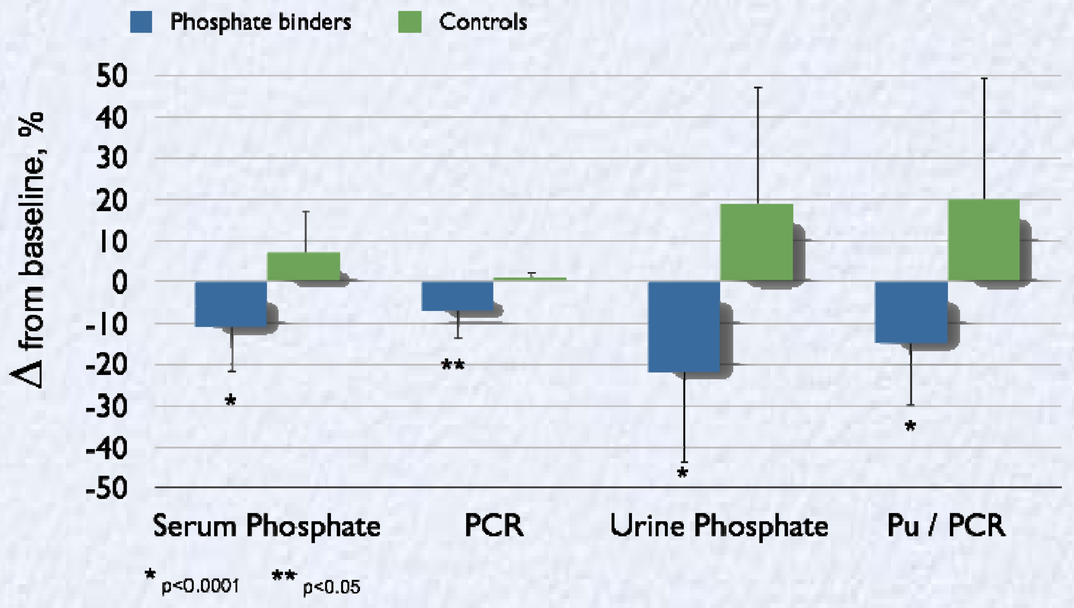
Relationships among GFR, urine phosphate, and serum phosphate



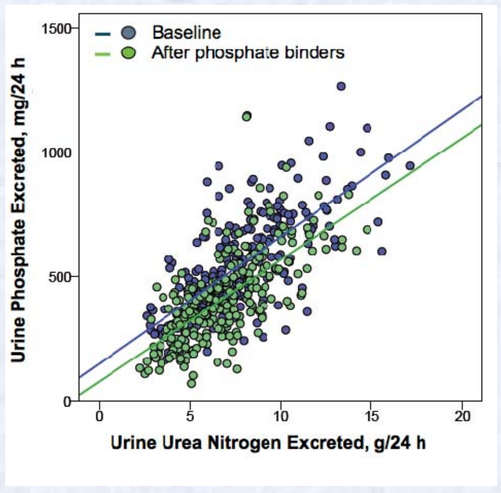
Frequency distribution of Pu / PCR in the whole study group

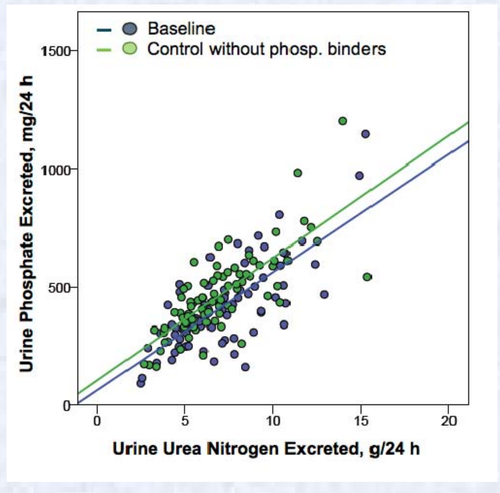


Changes in parameters of interest after PBs + diet (cases) or only diet (controls)

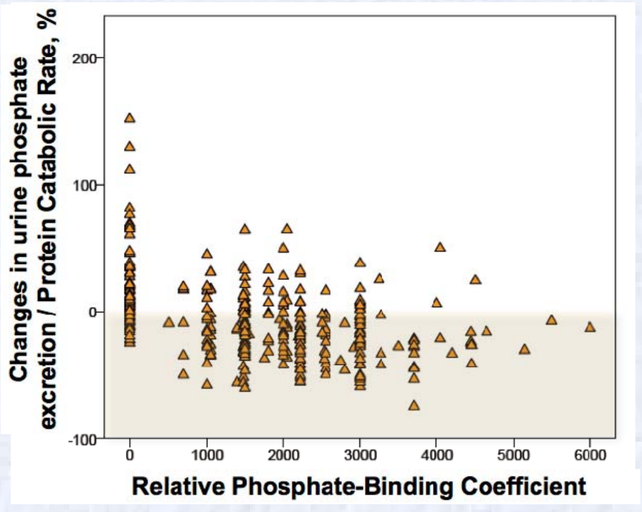


Linear regression lines before and after PBs prescrption (cases) or dietary phosphate restriction (controls)





Changes in Pu / PCR according to relative PB coefficient



Conclusions

✓ The proposed parameter Pu / PCR (urine phosphate relative to protein intake) may reflect the intestinal absorption of phosphate, and therefore, its variation after the prescription of phosphate binders (PBs) may be a useful tool for estimating the pharmacological efficacy of these drugs

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