Supplemental Information

Supplemental Methods

Recruitment, Inclusion/Exclusion Criteria, and Enrollment Dates

For the parent study, patients were recruited from nephrology clinics. Inclusion criteria included 1) men or women 35 years of age or older of any race/ethnicity, 2) GFR ≤ 45 mL/min, 3) intact serum PTH ≥ 37 pg/mL (above the mean of the normal range), 4) ability to perform two 3-week balance studies, 5) on stable doses of diuretics for at least two months, and 6) women were required to be post-menopausal (21). Exclusion criteria included 1) uncontrolled underlying disease (e.g. diabetes, lupus, hypertension), 2) taking drugs that alter calcium and phosphorus homeostasis including cholecalciferol (besides that given as part of the study protocol), ergocalciferol, active vitamin D metabolites, calcimimetics, or PTH analogues in the prior 30 days, 3) plans to initiate dialysis within 6 months, 4) serum calcium > 10.5 mg/dL, 5) serum phosphate > 5.5 mg/dL, 6) intestinal disease that alters mineral absorption (e.g. celiac disease, small bowel resection, bariatric surgery). As previously reported (21), one patient inadvertently remained on 2 mcg/d paricalcitol during the study, but, despite this, had the lowest calcium and phosphorus absorption values. Rolling enrollment began in May 2010 and continued through August 2011, with the final subject completing the study in November 2011.

Adherence Assurance Measures

Adherence assurance measures were taken during the balance studies. Pill counts, diet checklists, encouragement at each meal to consume all food and beverages, and leftover weigh-back recording and analysis of leftovers for mineral content were used for adherence with diet and supplements. A non-absorbable fecal marker (polyethylene glycol, PEG m.w.3500) was given 3/g day to assess fecal collection adherence, and urine Cr was measured for each day to account for urine collection adherence. Research center staff were trained to appropriately time, collect, record, and measure urine volume from collections. Steps were taken to minimize error in urine collection timing and pooling: the start and end

time of each collection was written on the urine collection bottle kept in the patient room; urine collection end times were designated on the study visit flowsheets and overseen by research center staff; at the end time of the collection, the completed urine collection bottle was removed from the patient room; and a set of dedicated graduated cylinders were used to measure urine volumes of collections to the nearest 1 mL. As previously reported(21), dietary adherence was high (>90% of prescribed dietary calcium and phosphorus consumed), which was assessed by weighing back any uneaten portions of food items and analyzing for phosphorus content, and subtracting from the full cycle menu day meal values. Creatinine-corrected 24-hour urine P values differed minimally from uncorrected values (0.0-27 mg/d); adherence for calcium carbonate and placebo was 100% by pill count; and mean percent fecal PEG recovery was >80%.

Statistical Methods: Standard Deviation, %CV, and Reliability Calculations

Within-Subject Variation. Within-subject standard deviations (s_i where i = subject 1 to 8) were calculated from the individual 13 collections ($x_{i,j}$ where j = collection 1 to 13) and the mean of the 13 collections within that subject ($\bar{x}_i$): $s_i = \sqrt{\frac{\sum(x_{i,j}-\bar{x}_i)^2}{13-1}}$. Within-subject %CV ($\%CV_i$) was calculated from these within-subject standard deviations (s_i) and the within-subject mean of 13 collections ($\bar{x}_i$): $\%CV_i = \frac{s_i}{\bar{x}_i} \cdot 100$.

Among-Subject Variation. Among-subject standard deviations (S) were calculated from each subject's 13-day average ($\bar{x}_i$), and the mean of all eight subjects' 13-day averages ($\bar{X}$): $S = \sqrt{\frac{\sum(\bar{x}_i-\bar{X})^2}{8-1}}$. Among-subject %CV was calculated from this among-subject standard deviation and the among-subject mean of 13-day averages: $\%CV = \frac{S}{\bar{X}} \cdot 100$.

Reliability (Spearman-Brown Prediction Formula). The Spearman-Brown Prediction Formation is $r^* = n^*rho/(1+(n-1)rho)$, where *rho* is the reliability of the reliability of a single measure (intraclass correlation coefficient), and r^* is the reliability of the measure with *n* number of replicates(26).

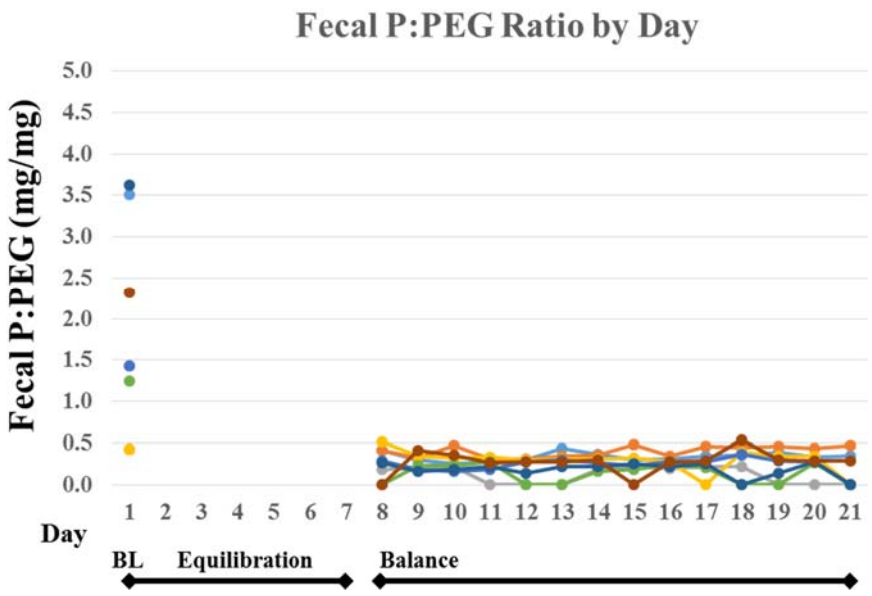
Supplemental Results

Variation and Reliability of Fecal P, Ca, and P:PEG and Ca:PEG Ratios

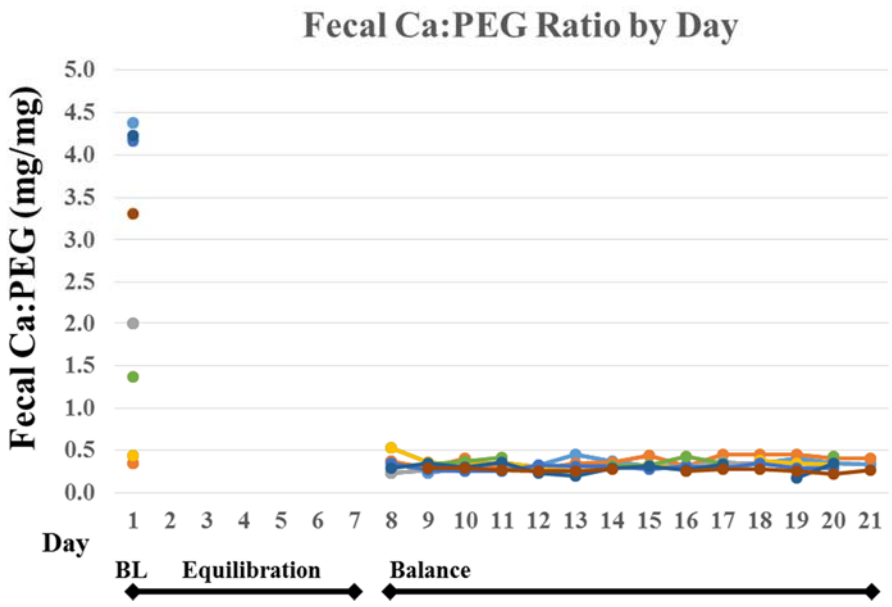
As expected, very wide within and among subject variation in absolute values (mg) of daily fecal P and Ca excretion were observed. For fecal P, standard deviations within subjects averaged 449 mg/d and ranged from 301 to 687 mg/d (%CV=54, range 45-62%) and among subjects standard deviation was 193 mg/d (%CV = 24%). For fecal Ca, standard deviations within subjects averaged 533 mg/d and ranged from 301 to 1054 mg/d (%CV=53, range 46-62%) and among subjects standard deviation was 400 mg/d (%CV = 40%). Adjustment for fecal PEG excretion by expressing fecal P and Ca as P:PEG and Ca:PEG (mg:mg) ratios greatly reduced within subject variation: for fecal P, within subject standard deviations averaged 0.053 and ranged from 0.015 to 0.083 mg:mg (%CV = 18, range 8-26%), and for fecal Ca:PEG, within subject standard deviations averaged 0.048 and ranged from 0.021 to 0.067 mg:mg (%CV=15, range 8-21%). Among subjects, fecal P:PEG standard deviation was 0.072 mg:mg (%CV=25%) and fecal Ca:PEG standard deviation was 0.040 mg:mg (%CV=12%). The intraclass correlation coefficient for fecal P (unadjusted mg) was rho = 0.08 (95%CI: 0, 0.38), for fecal Ca (unadjusted mg) was rho= 0.19 (95%CI: 0.05, 0.55), for fecal P:PEG ratio was rho = 0.60 (95%CI: 0.37, 0.87), and for fecal Ca:PEG ratio was rho= 0.36 (95%CI: 0.16 , 0.72). From these values, the number of replicates needed to achieve ≥75% reliability for fecal P is 33 (95%CI: 6, unable to define upper-bound), for fecal Ca is 14 (95%CI: 3, 56), for fecal P:PEG ratio is 2 (95%CI: 1, 6), and for fecal Ca:PEG ratio is 6 (95%CI: 2, 16).

Supplemental Figure S1.

A)



B)



Supplemental Figure S1. Daily variation in **A**) Fecal P:PEG ratios and **B**) Fecal Ca:PEG ratios during the balance studies. Day 1-7 is the diet equilibration period, and Day 8-21 is the balance period. BL = baseline, which represents a fecal collection before the controlled diet began and before the 3 g/d of PEG were given.