Urol Res (2006) 34: 1–7
DOI 10.1007/s00240-005-0001-9

ORIGINAL PAPER

Alberto Trinchieri · Renata Lizzano
Federica Marchesotti · Giampaolo Zanetti

Effect of potential renal acid load of foods on urinary citrate excretion in calcium renal stone formers

Received: 25 June 2005 / Accepted: 23 August 2005 / Published online: 20 January 2006

Abstract The aim of this study was to investigate the influence of the potential renal acid load (PRAL) of the diet on the urinary risk factors for renal stone formation. The present series comprises 187 consecutive renal calcium stone patients (114 males, 73 females) who were studied in our stone clinic. Each patient was subjected to an investigation including a 24-h dietary record and 24-h urine sample taken over the same period. Nutrients and calories were calculated by means of food composition tables using a computerized procedure. Daily PRAL was calculated considering the mineral and protein composition of foods, the mean intestinal absorption rate for each nutrient and the metabolism of sulfur-containing amino acids. Sodium, potassium, calcium, magnesium, phosphate, oxalate, urate, citrate, and creatinine levels were measured in the urine. The mean daily PRAL was higher in male than in female patients (24.1 ± 24.0 vs 16.1 ± 20.1 mEq/day, $P = 0.000$). A significantly ($P = 0.01$) negative correlation ($R = -0.18$) was found between daily PRAL and daily urinary citrate, but no correlation between PRAL and urinary calcium, oxalate, and urate was shown. Daily urinary calcium ($R = 0.186$, $P = 0.011$) and uric acid ($R = 0.157$, $P = 0.033$) were significantly related to the dietary intake of protein. Daily urinary citrate was significantly related to the intakes of copper ($R = 0.178$, $P = 0.015$), riboflavin ($R = 0.20$, $P = 0.006$), piridoxine ($R = 0.169$, $P = 0.021$) and biotin ($R = 0.196$, $P = 0.007$). The regression analysis by stepwise selection confirmed the significant negative correlation between PRAL and urinary citrate ($P = 0.002$) and the significant positive correlation between riboflavin and urinary citrate ($P = 0.000$). Urinary citrate excretion of renal stone formers (RSFs) is highly dependant from dietary acid load. The computation of the renal acid load is advisable to investigate the role of diet in the pathogenesis of calcium stone disease and it is also a useful tool to evaluate the lithogenic potential of the diet of the individual patient.

Keywords Renal acid load · Urinary citrate excretion · Renal stone

A. Trinchieri (✉)
Urology Unit, Lecco Hospital, Lecco, Italy
E-mail: a.trinchieri@ospedale.lecco.it
Tel.: +39-341-489118
Fax: +39-341-489328

A. Trinchieri · R. Lizzano · F. Marchesotti · G. Zanetti
Department of Nephrourology, IRCCS Ospedale Maggiore di Milano, Milan, Italy

A. Trinchieri
Via dell'Eremo 9/11, 23900 Lecco, Italy

Introduction

It is well known that both an increase in lithogenic salts or a decrease in inhibitors of calcium crystallization in urine increases the risk of calcium stone formation.

A number of substances are known to inhibit calcification in normal urine [1] and among these citrate is known to be a powerful inhibitor of crystal formation and aggregation.

Citrate forms soluble complexes with calcium [2], thus reducing relative supersaturation of calcium-containing crystals. In addition, citrate inhibits the growth of hydroxyapatite and calcium oxalate crystals [3–5] and the agglomeration of calcium oxalate monohydrate crystals [6].

A number of factors may explain hypocitraturia including postrenal bacterial consumption, impaired renal function, hyperparathyroidism and hypokaliemia [7–12].

Overt hypocitraturia is present in patients with calcium stones secondary to renal tubular acidosis or to gastrointestinal malabsorption, but a mild reduction in daily citrate excretion of idiopathic calcium stone formers has also been reported [10, 12–14].

Because of the presence of normal or high serum citrate levels Rudman et al. [15] have suggested that the hypocitraturia found in idiopathic calcium stone patients could be genetically determined by an excessive

net tubular reabsorption of a normal filtered load of citrate reflecting a rapid transport into tubular cells or a rapid oxidation within these cells.

On the other hand, urinary citrate excretion is reported as influenced by dietary factors, such as the caloric, carbohydrate, sodium chloride, and citrate content of the diet [16, 17]). Less than 1% of the citrate in urine is directly derived from dietary citrate, the major part being formed as a metabolic consequence of the dietary intake of other nutrients. Particularly the metabolic acid load generated by the diet may enhance the renal reabsorption of citrate and reduce its excretion [18–20]. Furthermore, an even modest deficiency of potassium may induce intracellular acidosis enhancing the luminal transport of citrate and its mitochondrial metabolism.

The aim of this study was to investigate the influence of the potential renal acid load (PRAL) of foods on the urinary risk factors for stone formation and particularly on the urinary excretion of citrate.

Materials and methods

We evaluated 187 consecutive patients with idiopathic calcium stone disease (114 males and 73 females, age range 13–82 years) with normal renal function and uninfected urine.

All patients had previously been investigated according to a strict protocol to exclude those with hyperparathyroidism, renal tubular acidosis, and other specific diseases, and were thus classified as "idiopathic stone formers". The stone formers were judged to be metabolically active at the time of clinical assessment if they had spontaneously passed a urinary stone or if they had undergone a treatment for a renal or ureteral stone during the previous 12 months.

The patients were investigated when receiving no treatment and while they followed their normal activities and ate their usual diet.

Each participant was subjected to an investigation including a 24-h dietary record and 24-h urine sample taken over the same period. Nutrients and calories were calculated by means of food composition tables using a computerized procedure (Terapia Alimentare Windows Release 5.00.00—Dietosystem). Daily PRAL was calculated for considering the mineral and protein composition of foods, the mean intestinal absorption rate for each nutrient and the metabolism of sulfur-containing amino acids.

To calculate the PRAL value we applied the original calculation model described by Remer and Manz [21]. The food-induced excretions of the more important mineral cations (sodium, potassium, calcium, and magnesium) and anions (chloride, phosphate, and sulfate) were estimated on the basis of their dietary intakes or the intakes of their metabolic precursors. The intakes of nutrients were preliminary corrected by factors expressing the average net intestinal absorption rate in adults for each mineral ion and for total protein. The intakes in milligrams of sodium, potassium, calcium, and magnesium were divided by the corresponding atomic weights in order to calculate the urinary excretion of cations and anions in mmoles. For the divalent cations, calcium and magnesium, the ionic valence (×2) and for phosphorus the grade of dissociation at pH 7.4 (×1.8) were also considered. Sulfate excretion was estimated as the result of the metabolism of sulfur-containing amino acids, methionine and cysteine, on the basis of their atomic weights and assuming an average content in total protein intake of 2.4 and 2.0%, respectively, for methionine and cysteine. The so calculated values of food-induced potential urinary excretion of each ion were used to indirectly determinate the food-related potential acid urinary excretion as the difference of the sum of the non-carbonate anions minus the sum of mineral cations.

Twenty-four hour specimens of urine were collected in which urinary concentrations of potassium, sodium, calcium, phosphate, oxalate, urate, citrate, magnesium, and creatinine were measured, together with urinary volumes.

Sodium and potassium concentrations were measured by flame photometry; calcium, magnesium, phosphate, urate, and creatinine by conventional colorimetric methods; oxalate and citrate by enzymatic analysis, respectively, with oxalate oxidase and citrate lyase. Urinary pH was measured on a fresh morning, urinary sample by a Corning pHmeter.

The mean values were calculated and compared by Student's unpaired *t* test with the Statistical Package for the Social Sciences (SPSS). Additional SPSS programs for linear correlation and stepwise regression analysis were used.

Results

The mean (±SD) daily intakes of nutrients and the mean values of urinary risk factors for stone formation in male and female patients are shown in Tables 1 and 2.

Table 1 Body mass index (BMI), weight, height and daily intakes of nutrients in male and female renal stone formers (RSFs)

	Males	Females	*P* value
BMI (kg/m^2)	24.6 ± 4.1	22.5 ± 4.1	0.000
Weight (kg)	74 ± 12	58 ± 11	0.000
Height (cm)	173 ± 7	161 ± 6	0.000
PRAL (mEq)	24.1 ± 24.0	16.1 ± 20.1	0.000
Energy (kcal)	2181 ± 627	1731 ± 524	0.020
Proteins (g)	89 ± 26	70 ± 25	0.000
Carbohydrates (g)	325 ± 102	246 ± 75	0.000
Lipids (g)	66 ± 28	58 ± 29	0.057
Calcium (mg)	724 ± 394	580 ± 402	0.017
Phosphorus (mg)	1261 ± 420	1033 ± 453	0.000
Potassium (mg)	2553 ± 964	2186 ± 953	0.012
Sodium (mg)	2994 ± 4051	2388 ± 3689	0.305
Magnesium (mg)	183 ± 68	139 ± 60	0.000

Table 2 Urinary risk factors for stone formation in male and female renal stone formers (RSFs)

	Males	Females	*P* value
Ur pH	5.75 ± 0.45	5.78 ± 0.46	0.652
Volume (ml)	1842 ± 703	1834 ± 743	0.940
Ca (mg)	238 ± 128	176 ± 114	0.001
UA (mg)	549 ± 211	480 ± 162	0.019
Ox (mg)	23.7 ± 11.6	23.0 ± 10.6	0.661
Cit (mg)	428 ± 234	484 ± 224	0.106
K (mEq)	63 ± 20	54 ± 18	0.002
Na (mEq)	192 ± 77	149 ± 51	0.000
Mg (mg)	89 ± 31	74 ± 30	0.001

The mean daily PRAL was higher in male than in female renal stone formers (RSFs) (24.1 ± 24.0 vs 16.1 mEq/day, $P = 0.000$).

Furthermore, the daily dietary intake of energy, proteins, carbohydrates, calcium, phosphate, potassium, and magnesium were higher in men than in women. On the contrary, no significant difference in the intakes of lipids and sodium between men and women was observed.

The daily urinary excretion of calcium, magnesium, sodium, potassium, and uric acid were higher in men compared to women, whereas, no difference between men and women was observed for daily urinary citrate and oxalate, urinary pH and urinary volume.

Table 3 shows the correlations of daily intakes of nutrient and the urinary excretion of calcium, citrate, oxalate, and urate.

A negative correlation (−0.18) was found between daily PRAL and daily urinary citrate ($P < 0.01$), whereas, the PRAL was not significantly related to the daily urinary excretion of calcium, oxalate, and urate. Daily urinary calcium ($R = 0.186$, $P = 0.011$) and uric acid ($R = 0.157$, $P = 0.033$) were significantly related to the dietary intake of protein.

Furthermore, PRAL was inversely related to urinary potassium ($R = -0.21$, $P = 0.004$) and to urinary pH ($R = -0.12$, $P = 0.094$) and dietary sodium was directly related to urinary sodium ($R = 0.55$, $P = 0.000$) (data not shown in Tables).

The weight was significantly correlated to urinary calcium ($P = 0.000$), urate (0.003), and citrate (0.019); height to calcium (0.025), citrate (0.000), and oxalate (0.036); body mass index (BMI) to calcium (0.000), urate (0.005), and citrate (0.016).

In Table 4 the correlations of daily intakes of micronutrients and the urinary excretion of calcium, citrate, oxalate, and urate are shown.

Daily urinary citrate was significantly related to the intakes of copper ($R = 0.178$, $P = 0.015$), riboflavin ($R = 0.20$, $P = 0.006$), piridoxine ($R = 0.169$, $P = 0.021$), and biotin ($R = 0.196$, $P = 0.007$). Daily urinary calcium was significantly related to the intake of calciferol ($R = 0.155$, $P = 0.035$) and daily intake of urate to the intake of niacin ($R = 0.214$, $P = 0.003$).

The regression analysis by stepwise selection confirmed the significant negative correlation between PRAL and urinary citrate ($P = 0.008$) and the significant positive correlation between weight and riboflavin with urinary citrate ($P = 0.001$).

Discussion

Robertson [22] was the first to popularize the lithogenic role of a protein-rich diet and after him case-control studies confirmed a greater dietary intake of proteins, animal proteins in particular, in renal stone patients compared with healthy subjects [23–25].

Finally, a large scale, population-based, prospective study [26] of incident stone formation demonstrated that high dietary calcium intake and high dietary potassium intake were both associated with a lower risk of incident stone formation while animal protein intake was associated with a higher risk of stone formation.

Diets rich in animal protein are acidogenic because amino acids are metabolized to non-volatile acid as pointed out by the pioneering studies of Lemann [27, 28] who have clearly shown that the major endogenous acids are sulfuric acid and organic acids.

The acid load related to protein metabolism titrates the plasma bicarbonate concentration to a value slightly lower than normal stimulating bone resorption and inhibiting bone formation [29]. The buffering of the acid generated from diet chronically mobilizes calcium from bone increasing urinary calcium excretion.

On the other hand, even small reductions in the plasma bicarbonate concentrations can enhance the renal reabsorption of citrate and reduce its excretion in the urine [30]. In fact a high consumption of proteins has been associated with a reduced urinary excretion of citrates subsequent to mild acidosis [16, 17, 31].

If the effect of high-meat diets is well known and its role in the pathogenesis of calcium renal stones has been well emphasized, on the contrary the potential effect of dietary alkali has been often disregarded.

In fact foods contain a substantial amount of potential alkali that should be also considered in estimating their ''net'' effective acid production [32, 33].

The above reported data from Curhan et al. [26] have clearly shown that the reduced intake of potassium is the more important feature characterizing the diet of stone forming subjects (more relevant than the so often emphasized role of the reduced calcium intake and also of the increased meat consumption!) and it has to be pointed out that potassium derived mainly from foods also rich in organates which are converted in vivo to bicarbonate. The ''natural'' diet of human beings, over millions of years, contained large amounts of potassium and bicarbonate-yielding precursors (such as citrate), derived from fruits and vegetables and little of the scarce sodium chloride, whereas, in modern times the intake of meat and animal derivatives together with the now easily

Table 3 Correlations between daily excretion of citrate, calcium and body mass index (BMI), weight, height and intakes of nutrients

	Calcium	Citrate	Oxalate	Urate
BMI (kg/m^2)				
R	0.279	0.177	0.031	0.205
Sig	(0.000)	(0.016)	(0.671)	(0.005)
Weight (kg)				
R	0.305	0.172	0.110	0.220
Sig	(0.000)	(0.019)	(0.135)	(0.003)
Height (cm)				
R	0.164	0.610	0.154	0.108
Sig	(0.025)	(0.000)	(0.036)	(0.141)
Energy (kcal)				
R	0.141	−0.106	0.023	0.100
Sig	(0.054)	(0.152)	(0.757)	(0.173)
Protein (g) (total)				
R	0.186	−0.077	0.044	0.157
Sig	(0.011)	(0.293)	(0.555)	(0.033)
Animal				
R	0.178	−0.105	0.093	0.132
Sig	(0.015)	(0.153)	(0.207)	(0.071)
Vegetable				
R	0.092	0.117	−0.077	0.103
Sig	(0.213)	(0.111)	(0.298)	(0.161)
Carbohydrate (g) (total)				
R	0.106	−0.101	−0.003	0.098
Sig	(0.150)	(0.169)	(0.964)	(0.182)
Refined				
R	0.026	−0.044	0.055	0.090
Sig	(0.727)	(0.550)	(0.456)	(0.221)
Complex				
R	0.149	−0.086	−0.033	0.086
Sig	(0.042)	(0.246)	(0.656)	(0.241)
Fats (total)				
R	0.106	−0.074	0.040	0.033
Sig	(0.149)	(0.317)	(0.584)	(0.651)
Saturated				
R	0.044	−0.074	0.115	−0.053
Sig	(0.548)	(0.315)	(0.117)	(0.471)
Monounsaturated				
R	0.092	−0.068	0.058	0.065
Sig	(0.211)	(0.358)	(0.432)	(0.381)
Polyunsaturated				
R	−0.020	0.015	−0.033	0.052
Sig	(0.789)	(0.838)	(0.655)	(0.484)
Cholesterol				
R	0.201	−0.081	−0.040	0.063
Sig	(0.006)	(0.275)	(0.588)	(0.394)
Calcium				
R	0.050	0.051	0.101	−0.006
Sig	(0.501)	(0.492)	(0.171)	(0.939)
Phosphate				
R	0.142	−0.068	0.007	0.068
Sig	(0.052)	(0.360)	(0.924)	(0.357)
Potassium				
R	0.104	0.085	−0.044	0.155
Sig	(0.157)	(0.251)	(0.552)	(0.034)
Sodium				
R	−0.043	−0.032	−0.010	−0.036
Sig	(0.559)	(0.666)	(0.893)	(0.623)
Magnesium				
R	0.224	0.012	0.044	0.141
Sig	(0.002)	(0.870)	(0.549)	(0.054)
Chloride				
R	0.093	−0.039	0.064	0.082
Sig	(0.208)	(0.594)	(0.385)	(0.266)
PRAL				
R	0.092	−0.180	0.043	−0.004
Sig	(0.211)	(0.014)	(0.557)	(0.955)

Table 4 Pearson's correlations between daily excretion of citrate, calcium, oxalate and urate and vitamins and oligoelements

	Calcium	Citrate	Oxalate	Urate
Calciferol				
R	0.155	−0.046	0.029	0.102
Sig	(0.035)	(0.535)	(0.694)	(0.165)
Riboflavin				
R	0.040	0.200	0.065	0.096
Sig	(0.584)	(0.006)	(0.380)	(0.191)
Niacin				
R	0.105	−0.102	0.019	0.214
Sig	(0.154)	(0.166)	(0.799)	(0.003)
Pyridoxine				
R	0.019	0.169	0.061	0.102
Sig	(0.802)	(0.021)	(0.406)	(0.164)
Ascorbic acid				
R	0.029	0.080	0.046	0.144
Sig	(0.692)	(0.280)	(0.535)	(0.049)
Biotin				
R	0.076	0.196	0.040	0.093
Sig	(0.305)	(0.007)	(0.586)	(0.206)
Copper				
R	−0.015	0.178	0.037	0.035
Sig	(0.844)	(0.015)	(0.614)	(0.632)
Zinc				
R	0.186	−0.100	0.031	0.237
Sig	(0.011)	(0.172)	(0.671)	(0.001)

available sodium chloride has dramatically increased and the fruit and vegetables intake has reduced [34].

A low-potassium diet can cause low-grade deficiencies of both potassium and bicarbonate that are generally unrecognized because they are not usually severe enough to cause well-characterized hypokaliemia or metabolic acidosis. A chronic dietary depletion of potassium induces increased urinary excretion of calcium and decreased urinary excretion of citrate as supplemental potassium bicarbonate (but not potassium chloride) induces not only a reduction in the urinary excretion of calcium but also an increase in urinary citrate [35, 36].

The evaluation of the PRAL of foods is a powerful tool to estimate the cumulative effect of both the acid load of protein and the alkali content of diet. Net alkali content in food can be estimated as the sum of non-combustible cations (Na + K + Ca + Mg) minus the sum of non-combustible anions (Cl + 1.8 P) although not all of the alkali content of food is absorbed.

Remer and Manz [21] developed a physiologically based calculation model taking into account the mineral composition of foods and their average intestinal absorption rates that proved to be appropriate for the prediction of renal net acid excretion from nutrient intake data.

The results of this calculation could be biased by the relative inefficacy of dietary recall to estimate the correct intake of some nutrients. In particular the estimate of dietary sodium intake by dietary recall could be less reliable considering the high standard deviations from the mean that characterize our estimates of dietary sodium intake. As a consequence, although the mean values of sodium intake in male and female patients were strikingly different, we were not able to show a significant difference between them, whereas, urinary excretion of sodium was significantly higher in men than in women. However, dietary sodium was very well correlated to sodium excretion and we have also to consider that in the great majority of foods sodium content is strictly combined to an equivalent chloride amount, counterbalancing at a great extent the potential bias of an incorrect estimate of dietary sodium: in fact in the computation of PRAL sodium and chloride act with an opposite sign. Particularly sodium and chloride are equally represented in grain products, dairies and meats that are the major sources of sodium intake from the diet. On the contrary, sodium and chloride are contained in low quantities in fruit and vegetables with some relatively rare exceptions as bananas and kiwi fruits which have a relatively high chloride content, exceeding the sodium content or on the contrary spinach which have a relatively high content of sodium in comparison to chloride. Finally, a previous study demonstrated that the estimate of other nutrients by the method of dietary recall were sufficiently reliable to be used for the purpose of epidemiological studies [25].

Using the model developed by Remer and Manz, we were able to show that the cumulative PRAL of diet was significantly and negatively correlated to the urinary excretion of citrate in RSFs, whereas, no significant correlation was demonstrable between the urinary output of citrate and the intake of other single nutrients (with the exception of some vitamins of the B complex).

Urinary citrate was also dependent by weight that is known to be the major determinant of the excretion of organic acids representing the endogenous contribution to the total renal net acid excretion in the urine.

In fact daily excretion of organic acid could be estimated, expressed in mEq/day, as body surface area (m^2) × 41 (mEq/day/1.73 m^2) divided by 1.73 m^2 or as body weight × 0.66 [21].

On the other hand, BMI has been previously demonstrated to be negatively correlated with urinary pH [37].

Some dietary factors which were previously identified as potential determinants of urinary citrate excretion, such as protein and potassium intake, were not significantly correlated to urinary citrate excretion in our study. In fact dietary animal protein intake and potassium

Table 5 Results of regression analysis by stepwise method assuming urinary citrate excretion as dependant variable

Determinants	Beta standardized coefficient	*t*	*P* value
Weight	0.280	3.364	0.001
Riboflavin	0.300	3.561	0.001
PRAL	−0.222	−2.691	0.008
Niacin	−0.191	−2.299	0.023

Table 6 Calculated potential renal acid load (PRAL) of more frequently consumed foods (related to 100 g of edible portion)

> +20	Hard cheeses (cheddar, parmesan, etc)
+20 to +10	Fishes (trout) and meats (corned canned beef, liver sausage, salami)
	Cheeses (camambert, cottage)
	Oat flakes, brown rice
+10 to 0	Fishes (cod, herring) and meats (beef, chicken, turkey, lean pork)
	Fresh cheeses, creams, ice creams, butter, milk, yogurt
	Eggs
	Walnuts, peanuts
	Chocolate
	Lentils, peas
	Grain products (bread, cornflakes, noodles, white rice, spaghetti)
0 to −5	Vegetables
	Fruits and fruit juices
	Beer and wines
< −5	Apricots, bananas

intake tend to be, respectively, in negative and positive, to urinary citrate excretion, but the correlation did not reach the statistical significance. On the contrary, the cumulative effect of all these dietary factors, expressed by PRAL of diet, was strong enough to produce a very significant correlation between dietary PRAL and urinary citrate.

This observation confirms that the effect of foods on metabolism are the result of the complex interaction of the effect of every single nutrient, as a consequence trying to evaluate the effect of a single nutrient without taking into account the potential interactions of other nutrients that could counterbalance or enhance its effect could produce unreliable conclusions.

We were also not able to show any significant correlation between urinary calcium excretion and PRAL, although the direct relation of protein intake and urinary calcium excretion was confirmed.

The effect of protein intake on urinary excretion of calcium probably involves a more complex mechanism than the simple acidogenic effect while the citrate excretion seems to be more dependent on the modification of the intracellular pH.

In fact the good correlation between total protein, in particular animal protein, and urinary calcium excretion can be explained by the endogenous acid load constituted by the oxidation of sulfated proteins (methionine, cysteine) involving both a reduction in tubular calcium reabsorption and a state of chronic acidosis, with consequent mobilization of calcium from the bone, but also by other metabolic effects of ingested proteins such as the enhanced intestinal absorption of calcium induced by the dietary load of methionine and lysine [38]. On the contrary, the potential acid load of diet by itself could exert only a subtle effect on urinary calcium that could not be enough strong to imply a significant correlation between PRAL of diet and urinary calcium excretion.

Data on micronutrients suggest that vitamins and oligoelements could play a role in the metabolism of some urinary risk factors for stone formation, although this topic deserves further study and deeper knowledge. In particular, the relation between the dietary intake of some B-group vitamins and urinary citrate is not easily explainable, these micronutrients being involved in many aspects of metabolism (including oxidative and fatty acids metabolism).

On the other hand, the highest amounts of riboflavin, piridoxine and biotin are in meat, liver, milk, and dairy products, eggs and enriched cereals which are not to be considered alkali-producing foods, so excluding the hypothesis of a common dietary source of such vitamins and citrate.

In conclusion the results of the present study suggest that a diet with a very low potential acid load should be encouraged in renal stone patients for the prevention of recurrent stones. This result can be obtained by the restriction of animal proteins but also by abundant supplementation with vegetables and fruits. The fruits, fruit juices, vegetables and alkali-rich low-phosphorus beverages have the lowest (negative) PRAL values and neutralize the dietary acid load of fish, meats, and cheeses that have the highest (positive) PRAL values. This dietary advice represents an alternative to the neutralization of the dietary acid load by the pharmacological administration of potassium bicarbonate or citrate [39].

We suggest the use of this model of computing the PRAL to further investigate the role of diet in the pathogenesis of calcium stone disease and as useful tool to evaluate the lithogenic potential of the diet of the individual patient (Tables 5, 6).

References

1. Fleisch H (1978) Inhibitors and promoters of stone formation. Kidney Int 13:361–371
2. Hastings BA, McLean FC, Eichelberger L, Hall JL, Da Costa E (1934) The ionization of calcium, magnesium and strontium citrates. J Biol Chem 107:351–370
3. Bisaz S, Felix R, Neuman WF, Fleisch H (1978) Quantitative determination of inhibitors of calcium phosphate precipitation in whole urine. Miner Electrolyte Metab 1:74–83
4. Meyer JL, Smith LH (1975) Growth of calcium oxalate crystals: II. Inhibition by natural urinary crystal growth inhibitors. Invest Urol 13:31–35
5. Sutor DJ, Percival JM, Doonan S (1978) Isolation and identification of some urinary inhibitors of calcium phosphate formations. Clin Chim Acta 89:273–278
6. Kok DJ, Papapoulos SE, Bijovoet OLM (1986) Excessive crystal agglomeration with low citrate excretion in recurrent stone-formers. Lancet 1:1056–1058
7. Conway NS, Maitland AIL, Rennie J (1949) The urinary citrate excretion in patients with renal calculi. Br J Urol 21:30–38
8. Hodgkinson A (1962) Citric acid excretion in normal adults and in patients with renal calculus. Clin Sci 23:203–212
9. Hodgkinson A (1963) The relation between citric acid and calcium metabolism with particular reference to primary hyperparathyroidism and idiopathic hypercalciuria. Clin Sci 24:167–178

10. Menon M, Mahle CJ (1983) Urinary citrate excretion in patients with renal calculi. J Urol 129:1158–1160
11. Schwille PO, Scholz D, Schwille K, Leutschaft R, Goldberg I, Sigel A (1982) Citrate in urine and serum and associated variables in subgroups of urolithiasis. Results from an outpatient stone clinic. Nephron 31:194–202
12. Welshman SG, McGeown MG (1976) Urinary citrate excretion in stone-formers and normal controls. Br J Urol 48:7–11
13. Parks JH, Coe FL (1986) A urinary calcium-citrate index for the evaluation of nephrolithiasis. Kidney Int 30:85–90
14. Trinchieri A, Mandressi A, Luongo P, Rovera F, Longo G (1992) Urinary excretion of citrate, glycosaminoglycans, magnesium and zinc in relation to age and sex in normal subjects and in patients who form calcium stones. Scand J Urol Nephrol 26:379–386
15. Rudman D, Kutner MH, Redd SC II, Waters WC IV, Gerron GG, Bleier J (1982) Hypocitraturia in calcium nephrolithiasis. J Clin Endocrinol Metab 55:1052–1057
16. Goldfarb S (1988) Dietary factors in the pathogenesis andprophylaxis of calciu nephrolithiasis. Kidney Int 34:544
17. Kok DJ, Iestra JA, Doorenbos CJ, Papapoulos SE (1990) The effects of dietary excess in animal protein and in sodium on the composition and the crystallization kinetics of calcium oxalate monohydrate in urines of healthy men. J Clin Endocrinol Metab 71:861
18. Hamm LI (1990) Renal handling of citrate. Kidney Int 38:728–735
19. Adam WR, Koretsky AP, Weiner MW (1986) 31P-NMR in vivo measurement of renal intracellular pH: effect of acidosis and K + depletion in rats. Am J Physiol 251:F904–F910
20. Wright SH, Kippen I, Wright EM (1982) Effect of pH on the transport of Krebs cycle intermediates in renal brush border membranes. Biochem Biophys Res Commun 684:287–290
21. Remer T, Manz F (1995) Potential renal acid load of foods and its influence on urine pH. J Am Diet Assoc 95:791–797
22. Robertson WG, Peacock M, Hodgkinson A (1979) The effect of dietary changes on the incidence of urinary tract in the UK between 1958 and 1976. J Chronic Dis 32:469–476
23. Coe FL, Moran E, Kavalich AG (1976) The contribution of dietary purine over-consumption to hyperuricosuria in calcium oxalate stone formers. J Chronic Dis 29:793–800
24. Robertson WG, Peacock M, Heyburn PJ, Hanes F, Rutherford A, Clementson E, Swaminathan R, Clark PB (1979) Should recurrent calcium-containing stone-formers become vegetarians? Br J Urol 51:427–431
25. Trinchieri A, Mandressi A, Luongo P, Longo G, Pisani E (1991) The influence of diet on urinary risk factors for stones in healthy subjects and idiopathic renal calcium stone formers. Br J Urol 67:230–236
26. Curhan GC, Willett WC, Rimm EB et al (1993) A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. N Engl J Med 328:833–838
27. Lemann J Jr, Relman AS (1959) The relation of sulfur metabolism in acid-base balance and electrolyte excretion: the effects of DL-methionine in normal man. J Clin Invest 38:2215–2223
28. Lemann J Jr, Lennon EJ, Goodman AD, Litzow JR, Relman AS (1965) The net balance of acid in subjects given large loads of acid or alkali. J Clin Invest 44:507–517
29. Bushinsky DA, Wolbach W, Sessler NE et al (1993) Physicochemical effect of acidosis on bone calcium flux and surface ion composition. J Bone Miner Res 8:93–102
30. Simpson DP (1983) Citrate excretion: a window on renal metabolism. Am J Physiol 244:F223–F234
31. Breslau NA, Brinkley L, Hill KD, Pak CYC (1988) Relationship of animal protein-rich diet to kidney stone formation and calcium metabolism. J Clin Endocrinol Metab 6:140
32. Oh MS (1989) A new method for estimating G-I absorption of alkali. Kidney Int 36:915–917
33. Sakhaee K, Williams RH, Oh MS, Padalino P, Adams-Huet B, Whitson P, Pak CY (1993) Alkali absorption and citrate excretion in calcium nephrolithiasis. J Bone Miner Res 8:789–794
34. Morris RC, Schmidlin O, Tanaka M, Foreman A, Frassetto L, Sebastian A (1999) Differing effects of supplemental KCl and KHCO3: pathophysiological and clinical implications. Semin Nephrol 19:487–493
35. Lemann J Jr, Pleuss JA, Gray RW et al (1991) Potassium administration reduces and potassium deprivation increases urinary calcium excretion in healthy adults. Kidney Int 39:973–983
36. Sakhaee K, Alpern R, Jacobson HR et al (1991) Contrasting effects of various potassium salts on renal citrate excretion. J Clin Endocrinol Metab 72:396–400
37. Maalouf NM, Sakhaee K, Parks JH, Coe FL, Adams-Huet B, Pak CY (2004) Association of urinary pH with body weight in nephrolithiasis. Kidney Int 65:1422
38. Licata AA, Bau E, Bartter FC, Cox G (1979) Effects of dietary protein on urinary calcium in normal patients and in patients with nephrolithiasis. Metabolism 28:895–900
39. Maurer M, Riesen W, Muser J, Hulter HN, Krapf R (2003) Neutralization of Western diet inhibits bone resorption independently of K intake and reduces cortisol secretion in humans. Am J Physiol Renal Physiol 284:F32–F40