Diet and fluid prescription in stone disease

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Dietary factors play an important role in kidney stone formation, and dietary modification can reduce the risk of stone recurrence. Because stone recurrence rates may be as high as 30–50% after 5 years, individualized dietary intervention to prevent stone recurrence should be offered to every patient willing to participate in a diagnostic work-up and to adhere to treatment recommendations. The necessity of prescribing medical therapy to select patients does not obviate the need for an effective dietary and/or fluid prescription. In this review, we summarize specific dietary and fluid recommendations, and emphasize several key concepts. First, risk factors for stone formation vary by age and sex. Second, recommendations should be tailored to the individual patient based on urinary profile and stone type. Third, it is essential that the patient perform follow-up measurements to evaluate the impact of dietary recommendations. Fourth, it is important to distinguish stone passage from new stone formation. If a patient implements dietary changes and then passes a pre-existing stone, this does not mean that the intervention was not effective. Finally, because of the relative paucity of randomized trials, observational studies provide the basis for many clinical recommendations. Adequate fluid intake and appropriate dietary modifications may substantially reduce the morbidity and costs associated with recurrent nephrolithiasis.

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Kidney stone disease is common and the prevalence is rising in the US[1] and other countries. Up to 12% of men and 6% of women in the US will develop a kidney stone at some point in their lives.[1] Lifestyle factors, including diet and obesity, are likely responsible for this increase.

Because stone recurrence rates may be as high as 30–50% after 5 years,[2] specific, individualized dietary interventions to prevent stone recurrence should be offered to every patient willing to participate in a diagnostic work-up and to adhere to treatment recommendations. The necessity of prescribing medication to select patients does not obviate the need for an effective dietary and/or fluid prescription. For example, the reduction in urinary calcium excretion obtained with a thiazide diuretic may be inadequate without concurrent dietary sodium restriction.

Because most data in the field of diet and stone disease are from observational and physiologic studies rather than randomized trials, consensus on the specifics of dietary modification is lacking. The following discussion is based on several key concepts. First, although short-term intervention studies examining changes in urine composition are of interest, clinical recommendations should be based on studies using actual stone formation as the outcome. Stone formation cannot be perfectly predicted by urinary composition, and it is likely that there are many factors that influence urinary supersaturation but are not accounted for by the formulas used to calculate supersaturation (e.g., phytate). Second, it is important to tailor recommendations based on stone type and urinary profile (two 24-h urine collections obtained at least 6 weeks after a stone episode are required as part of the initial evaluation). For example, we do not recommend dietary oxalate restriction to individuals with pure uric acid stones or to those with low urinary oxalate excretion. Third, dietary risk factors vary by age and sex. Fourth, it is essential that the patient perform follow-up measurements to evaluate the impact of dietary recommendations. If the urine composition does not change despite a dietary change, then alternative approaches should be tried. Finally, it is important to distinguish stone passage from new stone formation. If a patient implements dietary changes and then passes a pre-existing stone, this does not indicate treatment failure.

DIETARY RISK FACTORS FOR CALCIUM STONE DISEASE

Because approximately 80% of kidney stones contain calcium, and the majority of calcium stones consist primarily

of calcium oxalate,[3] most studies to date have focused on the prevention of calcium oxalate nephrolithiasis. Putative dietary promoters and inhibitors of calcium kidney stones are listed in Table 1. Specific dietary prescriptions based on urinary abnormalities are presented in Table 2.

Calcium

Until relatively recently, higher calcium intake was thought to increase the risk of stone formation. In normal individuals, approximately 20% of ingested calcium is absorbed; this proportion increases in individuals with idiopathic hypercalciuria.[4] However, there is substantial evidence demonstrating that a higher calcium diet is associated with a reduced risk of stone formation. One potential mechanism to explain this apparent paradox is that the higher calcium intake will bind dietary oxalate in the gut, thereby reducing oxalate absorption and urinary excretion. It is also possible that dairy products (the major source of dietary calcium) may contain other inhibitory factors.

Table 1 | Putative dietary promoters and inhibitors of calcium kidney stones[a]

Dietary factor	Proposed mechanism(s)
Promoters	
Oxalate	Increased urinary oxalate excretion
Sodium	Increased urinary calcium excretion
Animal protein	Increased urinary calcium and uric acid excretion; reduced urinary citrate excretion
Vitamin C	Increased oxalate generation and excretion
Carbohydrates	Increased urinary calcium excretion
Inhibitors	
Dietary calcium	Binding of dietary oxalate in gut
Potassium	Increased urinary citrate excretion; reduced urinary calcium excretion
Phytate	Inhibition of calcium oxalate crystal formation
Magnesium	Reduced dietary oxalate absorption; inhibition of calcium oxalate crystal formation
Vitamin B_6	Vitamin B_6 deficiency may increase oxalate production and oxaluria

[a]Phosphorus and n-3 fatty acids are discussed in the text.

Table 2 | Dietary prescription for calcium stone prevention according to urinary risk factor

Urinary abnormality	Dietary changes
High calcium	Adequate dietary calcium intake Reduce non-dairy animal protein intake (5–7 servings of meat, fish, or poultry/week) Reduce sodium intake <2.4 g/day Reduce sucrose intake
High uric acid	Reduce purine intake
High oxalate	Avoid high-oxalate foods Avoid vitamin C supplements Adequate dietary calcium intake
Low citrate	Increase fruit and vegetable intake Reduce non-dairy animal protein intake
Low volume	Increase total fluid intake to maintain urine volume >2 l/day

Recent data from several large prospective observational studies in men and women consistently support a reduced risk of stone formation with increasing dietary calcium intake. Compared to individuals in the lowest quintile of dietary calcium intake, those in the highest quintile had more than a 30% lower risk of forming a stone.[5–7] These results were adjusted for multiple factors, including age, body mass index, total fluid intake, the use of thiazide diuretics, and the intake of nutrients such as animal protein, magnesium, phosphorous, sodium, and potassium. As an example of how risk factors vary by age, there was no association between dietary calcium and stone formation in men aged 60 years or older.[8]

A 5-year randomized controlled clinical trial compared stone recurrence in patients with a history of calcium oxalate nephrolithiasis and idiopathic hypercalciuria assigned to a diet low in calcium (400 mg/day) or to a diet with normal calcium content (1200 mg/day) and low amounts of animal protein and salt.[9] At the end of the study, the risk of developing a recurrent stone on the normal calcium diet was 51% lower than for the low-calcium diet.[9] Because dietary sodium and animal protein may both contribute to the formation of calcium stones, this trial, although suggestive, did not directly address the independent role of dietary calcium in the pathogenesis of kidney stones.

Data also suggest that the impact of supplemental calcium is different from dietary calcium. In an observational study of older women, calcium supplement users were 20% more likely to form a stone than women who did not take supplements.[6] In younger women and men, there was no association between calcium supplement use and risk of stone formation.[5,7] The discrepancy between the risks from dietary calcium and calcium supplements may be due to the timing of calcium intake. In these studies, calcium supplements were often taken in between meals, which would diminish binding of dietary oxalate. The Women's Health Initiative clinical trial also demonstrated an increased risk of stones with calcium supplementation, but these results are difficult to interpret. The Women's Health Initiative participants were instructed to take their supplements with meals, but the supplements contained both calcium and vitamin D.

A patient with calcium urolithiasis who wishes to continue calcium supplementation should collect 24-h urine samples on and off the supplement. If the urinary supersaturation of the calcium salt in question increases during the period of supplement use, the supplement should be discontinued.

Oxalate

The role of dietary oxalate in the pathogenesis of calcium oxalate nephrolithiasis is unclear.[10] First, the proportion of urinary oxalate derived from dietary oxalate is controversial; estimates range from 10 to 50%.[10] A large amount of urinary oxalate is derived from the endogenous metabolism of glycine, glycolate, hydroxyproline, and dietary vitamin C. Second, much of the oxalate in food may not be readily absorbed due to low bioavailability. Finally, significant

variation can exist between individuals with respect to the alimentary absorption of oxalate. For instance, up to one-third of patients with calcium oxalate nephrolithiasis may experience increased absorption of dietary oxalate, and in some cases a deficiency of oxalate degradation by *Oxalobacter formigenes* in the gut could be the culprit.[10]

Because past measurements of the oxalate content in food may be unreliable, prospective studies of the relation between dietary oxalate and the risk of kidney stone formation have not been conducted. Recently, however, reliable assays for the direct determination of the oxalate content of food, including ion chromatography and capillary electrophoresis, have been developed, and large-scale studies of the relation between dietary oxalate and kidney stone formation are ongoing.

Calcium stone formers with hyperoxaluria should limit their intake of certain nuts (including almonds, peanuts, cashews, walnuts, and pecans), certain vegetables (including beets and spinach), wheat bran, rice bran, and chocolate.

Sodium

High sodium intake, and a subsequent decrease in proximal sodium reabsorption, reduces renal tubular calcium reabsorption. Randomized trial data confirm the powerful effect of concomitant dietary sodium and animal protein restriction on reducing urinary calcium excretion.[9] Observational studies found a positive, independent association between sodium consumption and new kidney stone formation in women but not men.[5,6]

Potassium

Dietary potassium restriction can increase urinary calcium excretion. Hypokalemia stimulates tubular citrate reabsorption, thereby decreasing the urinary excretion of citrate, an important inhibitor of calcium oxalate stone formation. Potassium in food also accompanies organic anions such as citrate that are metabolized to bicarbonate. Thus, the consumption of potassium-containing foods such as fruits and vegetables represents an alkali load that increases the urinary excretion of citrate. Higher potassium intake is inversely associated with incident kidney stones in men and older women,[5,6] but not younger women.[7]

Animal protein

The metabolism of sulfur-containing amino acids in animal flesh generates sulfuric acid. As such, dietary animal protein represents an acid load that increases urinary calcium excretion and reduces urinary citrate excretion. Dietary protein may also lead to an increase in calcitriol production (possibly induced by an increase in renal mass). A positive association between animal protein consumption and new kidney stone formation has been shown in men but not women.[5–7]

Phytate

Phytate (inositol hexaphosphate) has come under increasing scrutiny as a dietary factor that may play a role in the formation of calcium-containing stones. Phytate (found in many foods high in fiber, such as cereals, legumes, and vegetables) binds strongly to calcium and exhibits a strong inhibitory effect on urinary crystallization of calcium salts such as calcium oxalate and calcium phosphate. Urinary levels of phytate in some calcium oxalate stone formers are abnormally low, and dietary intake contributes significantly to urinary levels of phytate.[11]

Observational data from younger women showed that dietary phytate was inversely associated with incident kidney stone formation.[7] However, a recent study of men showed no relation between dietary phytate and the risk of kidney stone formation.[8]

Vitamin C

Vitamin C can be metabolized to oxalate; thus, higher vitamin C intake could increase the risk of calcium oxalate stone formation. A metabolic trial demonstrated that 1000 mg of supplemental vitamin C consumed twice daily increased urinary oxalate excretion by 22%.[12] A recent observational study in men found that those who consumed 1000 mg or more per day of vitamin C had a 40% higher risk of stone formation compared to men who consumed less than 90 mg/day (the recommended dietary allowance).[8] Because this relation was observed only after adjusting for dietary potassium intake, we do not recommend restricting dietary vitamin C (as foods high in vitamin C are also high in inhibitory factors such as potassium). However, a calcium stone former with hyperoxaluria should be instructed to discontinue vitamin C supplements.

Magnesium

Magnesium complexes with oxalate, potentially decreasing calcium oxalate supersaturation in the urine. Magnesium may also reduce oxalate absorption in the gastrointestinal tract. There have been a few randomized trials examining the impact of magnesium supplementation on stone recurrence. However, magnesium was given in combination with other compounds (e.g., thiazide diuretic or potassium citrate) and the dropout rates were high. It is uncertain whether magnesium supplementation has an independent beneficial effect. Higher dietary magnesium was associated with a 30% lower risk of stone formation in men,[8] but no association has been observed in women.[6,7]

Carbohydrates

Carbohydrate ingestion results in increased urinary calcium excretion, an effect that may be at least partially mediated by insulin. A positive association between sucrose intake and new kidney stone formation has been shown in women but not men.[5–7]

Vitamin B_6

Vitamin B_6 is a cofactor in oxalate metabolism, and vitamin B_6 deficiency increases oxalate production and oxaluria. Although vitamin B_6 has a therapeutic role in selected

patients with type 1 primary hyperoxaluria,[13] the use of vitamin B_6 in other settings remains unclear. Observational data failed to identify vitamin B_6 consumption as a risk factor for stone formation in men.[14] In women, large doses of vitamin B_6 may reduce the risk of kidney stone formation.[15]

Phosphorus

Phosphorus decreases intestinal absorption of dietary calcium. Neutral phosphate supplementation can decrease renal calcium excretion. Human data to support the role of dietary phosphorus as a risk factor for calcium stones are lacking.

n-3 fatty acids

It has been proposed that dietary fatty acids modulate the urinary excretion of calcium and oxalate, and that fish oil supplementation lowers urinary calcium and oxalate. However, a recent prospective study showed no association between the intake of n-3 fatty acids and the risk of kidney stone formation.[16]

Calories

Higher body mass index, higher weight, larger waist circumference, and weight gain are associated with an increased risk of kidney stone formation, independent of diet.[17] Although there are no data currently to support weight loss as treatment for stone disease, stone formers should exercise and modulate their intake of calories as needed to maintain a healthy weight.

BEVERAGES AND CALCIUM STONES

Total fluid

Nephrolithiasis is a disease of concentration. Modifying the concentration of the lithogenic factors is the focus of stone prevention. The concentration of calcium, for example, can be lowered by reducing urinary calcium or by increasing urine volume. Thus, fluid intake is a critical component of stone prevention. Observational studies[5–7] and a randomized controlled trial[18] have demonstrated that higher fluid intake reduces the risk of stone formation. However, patients need to be given specific advice on how much to drink to form at least 2 l of urine per day. In addition to fluid intake, other factors such as insensible loss and water contained in foods influence urine volume. Rather than broadly recommending eight glasses of water per day, the recommendation can be tailored to the individual patient by using the information on total volume from the 24 h urine collections. For example, if an individual produces 1.5 l of urine per day, consuming an additional two eight ounce (240 ml) glasses of water would raise their output to the target of 2 l.

Some clinicians believe that a patient should have urine that is very light in color and should wake up at least once per night. There are no data to support the use of color as a guide, and the desire to have constantly dilute urine needs to be balanced against the need for sleep.

Individual beverages

Patients often want to know what they should and should not drink. The role of specific beverages in kidney stone formation is delineated in Table 3. Despite previous beliefs to the contrary, alcoholic beverages, coffee, and tea do not increase the risk of stone formation. In fact, observational studies have found that coffee, tea, beer, and wine reduce the risk of stone formation.[19,20] Although citrus juices theoretically could reduce the risk of stone formation, there was no association with orange juice; grapefruit juice intake was associated with a 40% higher risk of stone formation.[19,20] Grapefruit juice is known to have a number of effects on intestinal enzymes, but the mechanism for the observed increased risk is unknown.

Previous studies suggested an increased risk for soda consumption. In the observational studies, unadjusted results also suggested an increased risk. However, after controlling for other dietary components, consumption of soda (with or without caffeine; diet or sugared) was not associated with the risk of stone formation.[19,20]

Milk intake likely reduces the risk of calcium kidney stone formation. In published observational data, skim and whole milk were not associated with risk.[19,20] However, the multivariate hazard ratios presented in these studies adjusted for the intake of dietary calcium.

PREVENTION OF STONE RECURRENCE – OTHER STONE TYPES

For the less common stone types, little data exist to support the role of specific dietary recommendations. Therefore, the following recommendations are based on pathophysiology.

Uric acid stones

The two driving forces for uric acid crystal formation are the uric acid concentration and urine pH (the solubility of uric acid increases substantially as the urine pH increases from 5.0 to 6.5). Decreasing the consumption of meat, chicken, and seafood will decrease purine intake and uric acid production, and also may increase urinary pH. Higher intake of fruits and vegetables may raise the urine pH and reduce the risk of uric acid crystal formation.

Table 3 | Beverage type and possible effects on calcium stone formation[a]

Beverage type	Putative risk	Proposed mechanism(s)
Coffee and tea	Decreased	Caffeine interferes with anti-diuretic hormone action, leading to decreased urinary concentration
Alcohol	Decreased	Alcohol inhibits secretion of anti-diuretic hormone, leading to decreased urinary concentration
Milk	Decreased	Binding of dietary oxalate in gut
Grapefruit juice	Increased	Unknown

[a]Orange juice and cola are discussed in the text.

Cystine stones

Cystine stone disease usually requires medication for prevention. However, restricting dietary sodium may reduce the urinary excretion of cystine. Because the solubility of cystine increases as urinary pH rises, fruit and vegetable consumption may be beneficial. Although there is little evidence to support the dietary restriction of proteins high in cystine, reducing animal protein intake may be beneficial by increasing urine pH.

Calcium phosphate stones

Information on dietary factors related to calcium phosphate stone formation is limited. Because patients with type 1 renal tubular acidosis and stone disease may benefit from alkali supplementation, generally in the form of potassium citrate, they may also benefit from a diet high in fruits and vegetables. It should be noted, however, that an increase in urinary pH can increase the risk of calcium phosphate crystal formation. Dietary maneuvers directed at decreasing urinary calcium excretion (see Table 2) would also be expected to decrease calcium phosphate stone recurrence.

CONCLUSION

Dietary factors play an important role in kidney stone formation, and dietary modification can reduce the risk of stone recurrence. Unfortunately, randomized trial data are lacking for most dietary interventions. Given the complexity of stone disease, clinical recommendations should be based on studies examining actual kidney stone formation rather than changes in urine composition. Most stone formers will need to increase fluid intake to produce at least 2 l of urine per day, and the calcium oxalate stone former with hypercalciuria should be encouraged to eat a diet with adequate calcium and low in animal protein and sodium. Dietary interventions, and subsequent evaluations of therapeutic efficacy, should be based on the results of multiple 24-h urine collections.

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