Nephrolithiasis(kidney stone disease) is a prevalent and excruciatingly painful cause of morbidity and a rare cause of mortality, yet it is usually somewhat preventable. Approximately 12% of the U.S. population will form at least one renal stone at some point, but only about 10% of all cases can be attributed to metabolic disorders, such as hyperparathyroidism and intestinal or pancreatic diseases (1 ,2). In any event, kidney stones may develop when the concentration of urinary constituents in the lumen of renal tubules exceeds their solubility. Although crystalluria itself does not inevitably lead to stone formation, crystals might attach to renal epithelium and grow into stones, resulting in pain and possible renal damage (3). About 80% of all kidney stones are composed of calcium oxalate, alone or surrounding a calcium phosphate core (4). Thus, attempts to prevent calcium stones have focused on reducing calcium and oxalate urinary concentrations by reducing the rate of urinary excretion of both calcium and oxalate as well as by increasing urine volume.

In fact, dietary calcium has long been suspected of increasing the risk of kidney stone formation. In the past, calcium intake was considered to play a major role simply because calcium is the primary component of kidney stones. Furthermore, 20 to 40% of patients with recurrent stones have hypercalciuria (5). Physicians have consequently advised patients, even those who do not suffer from hypercalciuria, to restrict calcium intake in order to prevent kidney stone recurrence. However, there exist no data demonstrating that such dietary restrictions decrease the rate of stone formation (3). In actuality, among healthy subjects, urinary calcium increases represent only about 8% of the amount by which dietary calcium intake is increased (6). Furthermore, calcium is a weak promoter of crystallization (2).

The observation that patients suffering from recurrent kidney stones actually fare worse when placed on a restricted calcium diet was first reported in 1976, by Ettinger (7). A physiological explanation was not proposed, though, until Bataille et al. found that calcium restriction leads to increased intestinal absorption of oxalate, which has only recently been proposed to be the limiting factor in calcium oxalate stone formation (8). Indeed, it has been demonstrated that calcium oxalate saturation of urine rises rapidly with small increases in oxalate concentration (4). Curhan et al. later hypothesized that calcium binds with oxalate in the intestinal lumen, leading to its excretion in the stool and thereby abating oxalate absorption (10).

Unfortunately, such a mechanism has not been proven, and it is even difficult to demonstrate through statistical studies that calcium may have a protective effect. One major problem is that the interpretation of much research is limited by study design. For instance, retrospective dietary studies of the relationship between diet and kidney stone recurrence can be limited by dietary recall bias or by modifications of dietary habits because of the disease. In addition, many prospective studies have only examined changes in urine composition instead of actual changes in kidney stone formation rates (3). Moreover, although several case-control studies of diet and kidney stone formation have not shown a correlation between calcium intake and kidney stone formation, the interpretation of these studies is complicated by the lack of control for other dietary risk factors associated with stone formation (3).

Curhan et al. conducted quite an impressive prospective epidemiological study of kidney stone occurrence among 45,619 men between the ages of 40 and 75 who were followed for four years after a standardized dietary history was obtained (10). In 1986, these men, none of whom had a history of kidney stones, completed a questionnaire on diet, medical history, and medications. Followup questionnaires were completed in 1988 and 1990 with a response rate of greater than 90%. Weighing all foods and beverages consumed by 127 of the men during two-week periods six to eight months apart demonstrated the validity of the questionnaire (Measured and calculated dietary calcium intakes varied by only 1%). 505 stones were reported, and examination of the medical records of 60 men strongly validated the methodology used. The results showed that the incidence of symptomatic kidney stones was lower by almost 50% among the subjects with the highest energy-adjusted calcium intake (a mean of 1326mg per day) than among those whose intake was the lowest (a mean of 516 mg per day). Men who drank two or more 8-ounce glasses of skim milk per day had a relative risk of kidney stones of 0.58 compared to those who drank less than one glass per month. Inverse relationships were also found for cottage cheese, ricotta cheese, yogurt, and sherbet. Interestingly, no significant association, either protective or deleterious, was found between dietary calcium supplements and kidney stones. A family history of kidney stones was reported in about a fourth of the subjects, but the effects of dietary calcium content were also maintained in this group.

Although the Curhan study suggests that calcium restriction actually increases the risk of kidney stone formation and was well-received by authorities on the subject, it has several limitations (11,12). For instance, the population to which they intend their results to be generalized is the middle-aged and older male population of America who do not suffer recurrent kidney stones. Thus, an obvious question which remains is whether or not the effect of increasing dietary calcium intake is similar among women or younger men or those people who have recurrent kidney stones. Although one might be tempted to assume that all human kidneys function alike and therefore the findings of the Curhan study might be extended to women, younger men, and even recurrent kidney stone sufferers, this issue has not been specifically addressed. Also, the role of calcium supplements as opposed to dietary calcium requires further study before extrapolating the results found with dietary calcium. A deeper understanding of the physiological mechanisms at play could explain the findings of extensive epidemiological studies such as that of Curhan. For example, if the Curhan model of calcium causing oxalate precipitation in the intestine and therefore decreased oxalate absorption was proven correct, one can rationalize why calcium supplement use exhibited no protective effect. This is because supplements in the study were typically taken without oxalate-rich foods (such as chocolate, nuts, tea, and spinach). Thus, one might argue that in order to lower one's risk of forming a kidney stone, one can take calcium supplements with oxalate-rich foods or limit one's intake of oxalate, although neither hypothesis has been extensively studied. One major problem is that only limited data are available on the oxalate contents of food sources and the bioavailability of oxalate (13). A comprehensive nutrient database including oxalate would therefore need to be established before physicians could even advise their patients on which foods to either avoid or take with calcium supplements.

There exist several other dietary factors which influence kidney stone formation about which physicians might counsel their patients. Indeed, a nutritional approach to kidney stone disease prevention is of paramount importance for it not only might save patients from unnecessary pain but would prove to be cost-effective as well. For example, in 1986, more than $2 billion was spent on the removal and fragmentation of kidney stones, even before the widespread use of extracorporeal shockwave lithotripsy (14). It is generally accepted that a high fluid intake (enough to produce at least two liters of urine per day) helps prevent kidney stone disease, although one should stress that the impact of such advice requires skill and enthusiasm on the part of the advising physician (10). Other dietary factors found to correlate with kidney stone formation include animal protein intake, which associates directly with the risk of kidney stone formation (10,15). Not surprising, then, is the fact that vegetarians are less prone to kidney stone disease (11). In addition, excessive sodium intake associates directly while potassium intake associates inversely with kidney stone formation (3). The reason for the effect of sodium intake is thought to be that a diet high in sodium results in increased sodium and calcium excretion due to inhibition of sodium and calcium reabsorption in the proximal tubule and along the loop of Henle (16). One reason for the effect of potassium lies in its reduction of urinary calcium excretion (17). Some studies have suggested that sucrose intake, oxalate intake, and very high doses of Vitamin C (which breaks down to oxalate) associate directly with kidney stone formation, but the findings of these studies remain controversial (3).

To recapitulate, studies have implicated a number of dietary factors in the risk of kidney stone formation, although the findings of some studies remain more controversial than others. The general policy of calcium restriction was not challenged until very recently, and the role of calcium in kidney stone formation is yet to be thoroughly reexamined. Perhaps it might be reasonable to advise patients with hypercalciuria and recurrent kidney stones to limit calcium intake, but there exists no legitimate reason to offer the same advice to other patients, except in the rare instances of excessive intake of greater than three grams per day. After all, calcium is obviously involved in many biological processes other than kidney stone formation. The recommended daily allowance of calcium for adults is 800 mg per day to prevent a negative calcium imbalance, bone mineral loss, and increased intestinal absorption of oxalate. Thus, it would be ridiculous for any physician to advise a postmenopausal woman with no history of kidney stone disease to restrict her calcium intake. In any case, a physician must carefully evaluate the benefits of calcium intake and the possible risk of kidney stone formation individually for each patient before advising restricted calcium intake, and more research must be conducted before physicians can assure their patients that calcium actually has a protective effect against kidney stone formation.

REFERENCES

1. Sierkowski R, Finlayson B, Landes RR, Finlayson CD, Sierkowski N. The frequency of urolithiasis in hospital discharge diagnoses in the United States. Invest Urol 1978; 15: 438-441.

2. 2. Jaeger P. Prevention of recurrent calcium stones: Diet versus Drugs. Miner Electrolyte Metab 1994; 20: 410-413.

3. 3. Curhan GC, Curhan SG. Dietary factors and kidney stone formation. Comprehensive Therapy 1994; 20: 485-489.

4. Coe FL, Parks JH, Asplin JR. The pathogenesis and treatment of kidney stones. N Engl J Med 1992; 327: 1141-1152.

5. Pak CYC. Medical management of nephrolithiasis in Dallas: update 1987. J Urol 1988; 140: 461- 467.

6. Lemann J Jr. Pathogenesis of idiopathic hypercalciuria and nephrolithiasis. In: Coe, FL, Favus, MJ, eds. Disorders of bone and mineral metabolism. New York: Raven Press, 1992: 685-706.

7.Ettinger B. Recurrent nephrolithiasis: natural history and effect of phosphate therapy. A double- blind controlled study. Am J Med 1976; 61: 200-206.

8. Bataille P, Charransol G, Gregoire I, Daigre JL, Coevoet B, Makdassi R, Pruna A, Locquet P, Sueur JP, Fournier, A. Effect of calcium restriction on renal excretion of oxalate and the probability of stones in the various pathophysiological groups with calcium stones. J Urol 1983; 130: 218-223.

9. Borsatti A. Calcium oxalate nephrolithiasis: defective oxalate transport. Kidney Int 1991; 39: 1283-1298.

10. Curhan GC, Willett WC, Rimm EB, Stampfer MJ. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. N Engl J Med 1993; 328: 833-838.

11. Lemann J Jr. Composition of the diet and calcium kidney stones. N Engl J Med 1993; 328: 880- 882.

12.Menon M. Renal Calculi: A Prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. J Urology 1993; 150: 563-564.

13.Massey LK, Roman-Smith H, Sutton RL. Effect of dietary oxalate and calcium on urinary oxalate and risk of formation of calcium oxalate kidney stones. J Am Diet Assoc 1993; 93: 901-906.

14.Lingeman JE, Smith LH, Woods JR, Newman DM. Urinary calculi: ESWL, endourology and medical therapy. Philadelphia: Lea & Febiger, 1989.

15.Breslau NA, Brinkley L, Hill KD. Relationship of animal protein-rich diet to kidney stone formation and calcium metabolism. J Clin Endo Metab 1988; 66: 140-146.

16.Kleeman CR, Bohannan J, Bernstein D. Effect of variation in sodium intake on calcium excretion in normal humans. Proc Soc Exp Biol Med 1964; 115: 29-32.

17.Lemann J Jr, Pleuss JA, Gray RW. Potassium administration increases and potassium deprivation reduces urinary calcium excretion in healthy adults. Kidney Int 1991; 39: 973-983.