Urol Res (1990) 18 [Suppl 1]:S37–S40

Urological Research

Prophylaxis in idiopathic calcium urolithiasis

D. Ackermann

Department of Urology, University Hospital, Berne, Switzerland

Summary. The most important measure in the prophylaxis of idiopathic calcium urolithiasis is dietary advice. Patients should be kept to a high-fluid intake, increasing their diuresis by at least 0.5 l. The mineral content of drinking water seems to be of minor importance, but the liquid should be low in carbohydrates and oxalate. The intake of animal proteins should be reduced to no more than five meals with meat, fish or poultry per week. Excesses of oxalate-rich food must be avoided. The daily intake of calcium in dairy products should be in the range of 800–1200 mg. Sodium and refined carbohydrates should be moderately restricted. Medical treatment is indicated only in cases of recurrence under the appropriate diet. Selective treatment according to urinary chemical composition is favoured; alkali citrate, thiazides, allopurinol, and pyridoxine are of major interest.

Key words: Calcium urolithiasis – Diet – Medical treatment

Calcium urolithiasis is a frequent disease in the Western world that has a high recurrence rate. The lifetime risk seems to be on the order of 5%–10% [20], and the recurrence rate in the absence of prophylactic measures lies in the range of 0.7 stone episodes per year [35]. In view of that, a prophylactic regimen is needed, despite the modern, less invasive therapies for stones such as extracorporeal shock-wave lithotripsy or endourologic stone removal. This review focuses on the prophylaxis of idiopathic calcium urolithiasis. Urolithiasis due to primary hyperparathyroidism or urinary obstruction are not discussed. The two mainstays in the prophylaxis of calcium urolithiasis are dietary advice and medical treatment; the latter is indicated only after failure of the appropriate diet to prevent stone formation.

Dietary factors

The dietary factors play a crucial role in the pathogenesis of calcium stone disease. Their importance is mainly derived from epidemiological data and physicochemical considerations. There are no data from randomized clinical trials.

Fluid intake

A high-fluid intake is recommended to increase urinary volume and decrease urinary supersaturation. Stone prevalence is higher in populations with a low urinary volume [28, 34]. In the study of Hosking et al. [15] on the stone clinic effect, patients with metabolically active stone disease did not increase their urinary volumes, whereas 60% of the patients who remained without recurrence for about 5 years increased their diuresis by an average of 500 ml. Strauss et al. [40] observed a marked impact of the urinary volume on stone risk. Stone risk was diminished by 25% when urinary volume was increased by 1 l/day. The importance of high urinary output to stone recurrence was questioned by Ljunghall et al. [21]; however, their analysis should be considered with reservations. The patients increased their urinary volumes only moderately over the years, and the recurrence rate was compared with the average urinary volumes. It would have been more relevant to look at the intraindividual changes in urinary volume. Therefore, the data from that study do not justify negation of the importance of high urinary volume to stone recurrence.

The mineral content of the drinking water is of minor interest. Water hardness does not seem to be strongly associated with calcium stone disease [37]. A high calcium content in the drinking water has no harmful effect on the crystallization conditions in urine; in fact, in cases of excessive oxalate intake, it acts beneficially by lowering urinary oxalate [1, 16]. An important positive association exists between urinary stone disease and soda (sugared cola) consumption [38].

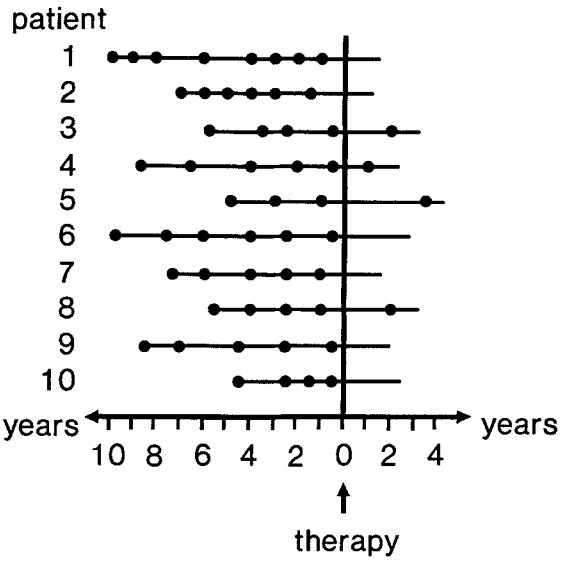

Fig. 1. Example of data presentation from a trial using one-group design (●, stone episode)

Animal protein and sodium

Stone prevalence parallels the consumption of animal protein [32]. A high intake of the latter leads to an increase in urinary calcium, oxalate and uric acid and a decrease in citrate and pH. Increased dietary sodium has a calciuric effect [14]. By restricting dietary protein from 96 to 60 g/day and sodium from 174 to 67 mEq/day, Wasserstein (cited in [14]) reduced levels of urinary calcium by 35%, sodium by 66%, urate by 25% and oxalate by 2% and achieved an increase in citrate of 35%. All of these urinary components were changed in favor of a diminished risk of stone formation.

Oxalate and calcium

Quite obviously, urinary oxalate is much more important than calcium to the risk of stone formation [31, 33]. A low-calcium diet might promote hyperoxaluria due to increased intestinal oxalate absorption [17, 25] and result in a negative calcium balance [14].

Refined carbohydrates

The intake of refined carbohydrates or glucose increases calcium excretion in the urine, which is even more pronounced in stone-formers, possibly because of an abnormal plasma insulin response [29]. There is some evidence that refined carbohydrates also lead to an increase in urinary oxalate and *N*-acetyl-β-glucosaminidase. The latter might be attributable to renal tubular cell damage [19].

Dietary fibers

Increased consumption of dietary fibers reduces urinary calcium. However, the benefit of this regimen remains a matter of debate since its impact on oxaluria remains unclear: two studies showed an increase in urinary oxalate [7, 9], one indicated no change [30] and one revealed a decrease [41]. Therefore, we do not yet have sufficient data to recommend a high intake of dietary fibers for the prophylaxis of idiopathic calcium urolithiasis.

Medical prophylaxis

Principally, medicaments are only recommended after the failure of dietary advice. A variety of medications are used in the prophylaxis of recurrent idiopathic urolithiasis, and there are many reports of their beneficial effects. Preceding the discussion of different medical treatments, a few comments on study design seem to be justified. Studies often use the one-group design, and the data are presented as in Fig. 1. According to Churchill [5] and Churchill and Taylor [6], these trials may be biased by several factors:

1. At the start of treatment, patients might have received not only the drug but also some dietary advice. An improvement could be the consequence of such co-interventions (stone clinic effect).
2. Was the stone activity measured in the same way during the retrospective phase and the prospective period?
3. The variability in natural history and the statistical regression to the mean might be attributable to the improvement.
4. Only patients willing to take the drug are included in the trial. These patients are also more compliant with regard to co-interventions.
5. Very often, the number and outcome of patients lost to follow-up are not reported. Considering these factors, the evaluation of medical treatments should rely mainly on randomized clinical trials.

Alkali citrate

Butz and Schwab [4] initiated a randomized trial comparing alkali citrate with diet. After 1 year, 4/10 patients in the diet group experienced a stone relapse as compared with 2/10 subjects in the drug-treated group. The number of cases and the follow-up period were too small to enable final conclusions to be drawn, but there is evidence for a beneficial clinical effect of alkali citrate. This is supported by one-group studies showing a decrease in stone activity after the addition of alkali citrate to an unsuccessful therapy [27].

Thiazides

Six randomized trials using thiazides were found in the literature [3, 12, 18, 24, 35, 36]; in none of these were patients selected according to urinary chemical composition. Four investigations showed a good clinical efficacy, but some reservations should be mentioned. Ettinger et al. [12] presented the strongest data for thiazide efficacy. There were 22.6% drop-outs due to side effects in the thiazide group as compared with 3% in the placebo

Table 1. Common-sense diet recommended as prophylaxis against idiopathic calcium urolithiasis

Fluid intake	Increases urinary output by >500 ml; mineral content of drinking water of minor importance; fluid should be low in carbohydrates and oxalate
Animal protein	$\leqslant 5\times$ meat, fish or poultry per week
Sodium	Moderately restricted
Oxalate	No excesses of oxalate-rich food
Calcium	Daily intake of 800–1,200 mg calcium in dairy products
Refined carbohydrates	Moderately restricted

Table 2. Selective medical treatment indicated after the failure of appropriate diet to control idiopathic stone disease

Therapy	Urinary Composition	Clinical Setting
Alkali citrate	Hypocitruria Hypercalciuria Hyperuricuria	Distal renal tubular acidosis, medullary sponge kidney
Thiazides	Hypercalciuria	Low bone density, medullary sponge kidney
Allopurinol	Normocalciuric Hyperuricuria	Gout
Pyridoxine	Hyperoxaluria	Mild metabolic hyperoxaluria

group. The drop-outs were not considered in the final analysis, which leads us to ask whether the results were not biased by a negative selection against the placebo group. In the study of Laerum and Larsen [18], 2/23 patients became worse under thiazides, indicating that patient selection might be important. In the other two trials showing a beneficial effect, co-interventions could not be ruled out, since the controls received no placebo tablets and patients in the drug-treated group could have changed their dietary habits, e.g. in terms of increased fluid intake due to the regular ingestion of tablets [24, 35]. Two studies failed to find a beneficial effect for thiazides [3, 36]; however, the follow-up period was <2 years and the statistical power [22] was insufficient in both. According to Churchill and Taylor [6], a benefit rate of 50% could not be excluded in both trials, as the number of patients was too small.

Allopurinol

Two randomized trials demonstrated the clinical efficacy of allopurinol [11, 39] and two did not [23, 35]. The two studies achieving positive results used selected patients with either hyperuricuria [11] or hyperuricemia [39]. In the other two studies using unselected patients, the statistical power was not calculated [23, 35].

Orthophosphate

Robertson et al. [35] observed a significant benefit of neutral phosphate in unselected patients. However, some influence by co-interventions cannot be excluded in this study. In the trial of Ettinger [10], stone activity did not diminish; the results were questioned since an acid phosphate was used at a low dose [42].

Magnesium

In another randomized study, Ettinger et al. [12] could not find a beneficial effect for treatment using magnesium hydroxide in unselected patients; however, statistical power was not calculated, indicating a lack of efficacy.

Cellulose phosphate, pyridoxine and glycosaminoglycans

No randomized clinical trials using these medicaments were found. A variety of studies using the statistically weak one-group design, with or without nonequivalent comparison groups [5], report improvement in stone activity [8, 13, 26]. The relatively high rate of side effects that occur during treatment with cellulose phosphate [2] or pentosan polysulphate [8] is worth mentioning.

Conclusions

From the above discussions, it is quite obvious that dietary advice should be the first step in the prophylactic treatment of idiopathic calcium urolithiasis. The recommended dietary regimen corresponds to a common-sense diet in the Western world and should not to be too strict (Table 1). Under these dietary measures, 60% of patients are expected to show no recurrence after 5 years, and the stone-episode rate should be reduced to at least 0.2 per patient per year. Medical treatment is indicated only after the failure of appropriate diet to control stone formation. Despite the lack of hard data from randomized clinical trials with respect to patient selection, a selective medical treatment is favoured that takes into account individual urinary composition and clinical setting (Table 2).

References

1. Ackermann D, Baumann JM, Futterlieb A, Zingg EJ (1988) Influence of calcium content in mineral water on chemistry and crystallization conditions in urine of calcium stone formers. Eur Urol 14:305
2. Backman U, Danielson BG, Johansson G, Ljunghall S, Wikström B (1980) Treatment of recurrent calcium stone formation with cellulose phosphate. J Urol 123:9
3. Brocks P, Dahl C, Wolf H, Transbol I (1981) Do thiazides prevent recurrent idiopathic calcium stones? Lancet II:124
4. Butz M, Schwab G (1990) Alkalicitrate versus diet: a randomized long-term trial in recurrent calcium stone formers. In: Vahlensieck W, Gasser G, Hesse A, Schoeneich G (eds) Proceedings of the 1st European Symposium on Urolithiasis. Excerpta Medica, Amsterdam Hong Kong Princeton Sydney Tokyo, p 184

5. Churchill DN (1987) Medical treatment to prevent recurrent calcium urolithiasis. Miner Electrolyte Metab 13:294
6. Churchill DN, Taylor DW (1985) Thiazides for patients with recurrent calcium stones: still an open question. J Urol 133:749
7. Classen A, Busch B, Gertz B, Weber A, Miersch WD, Hesse A (1989) Dietary fiber and urolithiasis: II. Effects of a high dietary fiber intake on the urine composition in man. In: Walker VR, Sutton RAL, Cameron ECB, Pak CJC, Robertson WG (eds) Urolithiasis. Plenum Press, New York London, p 869
8. Danielson BG, Fellström B, Wikström B (1989) Glycosaminoglycans as inhibitors of renal stone formation. In: Walker VR, Sutton RAL, Cameron ECB, Pak CYC, Robertson WG (eds) Urolithiasis. Plenum Press, New York London, p 101
9. Ebisuno S, Morimoto S, Yoshida T, Fukatani T, Yasukawa S, Ohkawa T (1986) Rice-bran treatment for calcium stone formers with idiopathic hypercalciuria. Br J Urol 58:592
10. Ettinger B (1976) Recurrent nephrolithiasis: natural history and effect of phosphate therapy. Am J Med 61:200
11. Ettinger B, Tang A, Citron JT, Livermore B, Williams T (1986) Randomized trial of allopurinol in the prevention of calcium oxalate calculi. N Engl J Med 315:1386
12. Ettinger B, Citron JT, Livermore B, Domant LI (1988) Chlorthalidone reduces calcium oxalate calculous recurrence but magnesium hydroxide does not. J Urol 139:679
13. Gill HS, Ros GA (1986) Mild metabolic hyperoxaluria and its response to pyridoxine. Urol Int 41:393
14. Goldfarb S (1988) Dietary factors in the pathogenesis and prophylaxis of calcium nephrolithiasis. Kidney Int 34:544
15. Hosking DH, Erickson SB, Berg CJ von den, Wilson DM, Smith LH (1983) The stone clinic effect in patients with idiopathic calcium urolithiasis. J Urol 130:1115
16. Jaeger P, Portmann L, Jacquet AF, Burckhardt P (1984) Drinking water for stone formers: is the calcium content relevant? Eur Urol 10:53
17. Jaeger P, Portmann L, Jacquet AF, Burckhardt P (1985) Influence of the calcium content of the diet on the incidence of mild hyperoxaluria in idiopathic renal stone formers. Am J Nephrol 5:40
18. Laerum E, Larsen S (1985) Thiazide prophylaxis of urolithiasis: a double blind study in general practice. In: Schwille PO, Smith LH, Robertson WG, Vahlensieck W (eds) Urolithiasis and related clinical research. Plenum Press, New York London, p 475
19. Li MK, Kavanagh JP, Prendiville V, Buxton A, Moss DG, Blacklock NJ (1986) Does sucrose damage kidneys? Br J Urol 58:353
20. Ljunghall S (1985) Incidence of renal stones in Western countries. In: Schwille PO, Smith LH, Robertson WG, Vahlensieck W (eds) Urolithiasis and related clinical research. Plenum Press, New York London, p 31
21. Ljunghall S, Fellström P, Johansson G (1988) Prevention of renal stones by a high fluid intake? Eur Urol 14:381
22. Marks RG (1982) Designing a research project. Van Nostrand Reinhold, New York, p 124
23. Miano L, Petta S, Paradiso Galatioto G, Goldoni S, Tubaro A (1985) A placebo controlled double-blind study of allopurinol in severe recurrent idiopathic renal lithiasis. Preliminary results. In: Schwille PO, Smith LH, Robertson WG, Vahlensieck W (eds) Urolithiasis and related clinical research. Plenum Press, New York London, p 521
24. Mortensen JT, Schultz A, Ostergaard AH (1986) Thiazides in the prophylactic treatment of recurrent idiopathic kidney stones. Int Urol Nephrol 18:265
25. Nakada T, Sasagawa I, Furuta H, Katayama T, Shimazaki J (1988) Effect of high-calcium diet on urinary oxalate excretion in urinary stone formers. Eur Urol 15:264
26. Pak CYC, Nicar MJ, Britton F (1983) Clinical experience with sodium cellulose phosphate. World J Urol 1:180
27. Pak CJC, Fuller C, Sakhaee K, Preminger GM, Britton F (1985) Long-term treatment of calcium nephrolithiasis with potassium citrate. J Urol 134:11
28. Pierce LW, Bloom B (1945) Observations on urolithiasis among American troops in a desert area. J Urol 54:466
29. Rao PN, Gordon C, Davis D, Blacklock NJ (1982) Are stone formers maladapted to refined carbohydrates? Br J Urol 54:575
30. Rao PN, Jenkins IL, Robertson WG, Peacock M, Blacklock NJ (1985) The effect of "high fibre biscuits" on urinary risk factors for stone formation. In: Schwille PO, Smith LH, Robertson WG, Vahlensieck W (eds) Urolithiasis and related clinical research. Plenum Press, New York London, p 425
31. Robertson WG, Peacock M (1980) The cause of idiopathic calcium stone disease: hypercalciuria or hyperoxaluria? Nephron 26:105
32. Robertson WG, Peacock M (1982) The pattern of urinary stone disease in Leeds and in the United Kingdom in relation to animal protein intake during the period 1960– 1980. Urol Int 37:394
33. Robertson WG, Peacock M, Heyburn PJ, Marshall DH, Clark PB (1978) Risk factors in calcium stone disease of the urinary tract. Br J Urol 50:449
34. Robertson WG, Peacock M, Heyburn PJ, Hanes FA (1980) Epidemiological risk factors in calcium stone disease. Scand J Urol Nephrol 53:15
35. Robertson WG, Peacock M, Selby PL, Williams RE, Clark P, Chisholm GD, Hargreaves TB, Rose MB, Wilkinson H (1985) A multicentre trial to evaluate three treatments for recurrent idiopathic calcium stone disease – a preliminary report. In: Schwille PO, Smith LH, Robertson WG, Vahlensieck W (eds) Urolithiasis and related clinical research. Plenum Press, New York London, p 545
36. Scholz D, Schwille PO, Sigel A (1982) Double-blind study with thiazide in recurrent calcium lithiasis. J Urol 128:903
37. Shuster J, Finlayson B, Schaeffer R, Sierakowski R, Zoltek J, Dzegede S (1982) Water hardness and urinary stone disease. J Urol 128:422
38. Shuster J, Finlayson B, Schaefer L, Sierakowski R, Zoltek J, Dzegede S (1985) Primary liquid intake and urinary stone disease. J Chronic Dis 38:907
39. Smith MJV (1977) Placebo versus allopurinol for renal calculi. J Urol 117:690
40. Strauss AL, Coe FL, Deutsch L, Parks JH (1982) Factors that predict relapse of calcium nephrolithiasis during treatment. Am J Med 72:17
41. Strohmaier WL, Kalchthaler M, Bichler KH (1989) Calcium metabolism in normal subjects and in hypercalciuric patients treated with Farnolith. In: Walker VR, Sutton RAL, Cameron ECB, Pak CJC, Robertson WG (eds) Urolithiasis. Plenum Press, New York London, p 873
42. Thomas WC (1978) Use of phosphates in patients with calcareous renal calculi. Kidney Int 13:390

Priv.-Doz. Dr. D. Ackermann
Urologische Universitätsklinik
Inselspital
CH-3010 Bern
Switzerland