Urol Res (1987) 15:63–65

Urological Research

Originals

Chemical Factors Governing the State of Saturation Towards Brushite and Whewellite in Urine of Calcium Stone Formers

D. Ackermann[1] and J. M. Baumann[2]

[1] Department of Urology, University of Berne, Berne, Switzerland
[2] Department of Urology and Stone Research Laboratory, Regionalspital, Biel, Switzerland

Accepted: February 9, 1987

Summary. Variations of urinary pH and concentrations of calcium, phosphate, oxalate, magnesium and citrate have been produced by 4 different diets given to 19 idiopathic calcium stone formers. The state of saturation towards whewellite and brushite was directly measured in the 76 urine samples by equilibration with the corresponding salts and was compared to chemical constituents by regression analyses. The state of saturation towards calcium oxalate monohydrate was significantly governed only by the urinary oxalate concentration, and a soluble oxalate fraction not contributing to calcium oxalate chelation was demonstrated. The state of saturation towards brushite was exclusively determined by urinary calcium and pH, the latter below 5.5 showing a high influence on brushite solubility.

Key words: Calcium stones, Urinary supersaturation, Calcium oxalate, Brushite.

Urinary supersaturation is the driving force of crystallization processes involved in stone formation. The state of saturation can be expressed by an activity product ratio (APR), a concentration product ratio (CPR) or relative saturation [7]. APR and CPR are the ratios of the activity products or concentration products respectively, before and after equilibration of urine with stone forming salts, the main problem being to reach true equilibria. Relative saturation is defined as ratio of the activity product of urine with respect to a stone forming salt and the thermodynamic solubility product of the salt. Activity products are obtained by the chemical analysis of at least 9 urine constituents and by calculation of their 22 [8] or 31 [5] complexes by computer programmes, the main problem being uncertainties on the number of these complexes and on some of their stability constants. Most information about the factors governing the state of urinary saturation towards stone salts have been obtained by the examination of urine in different groups of stone formers and in healthy controls [5, 8]. In this study variations of urinary composition were produced by 4 different diets given to 19 calcium stone formers, and the effect of these chemical variations on the state of urinary saturation was studied by regression analysis.

Material and Methods

76 urine portions were collected from 19 recurrent and idiopathic (normal renal function, normal values of calcium and uric acid in serum and lack of urinary infection) calcium stone formers under the 4 different diets listed in Table 1.

Urinary calcium was measured with a Corning Calcium Analyzer, model 940, magnesium by atomic absorption UNICAM Sp 1900, citrate enzymatically (Boehringer kit Nr. 139,076), pH with a pH-meter Methrom, Herisau, model E603, phosphorus by the method of Bisaz et al. [2] and oxalic acid by the method of Drawert et al. [4], which we adapted for urine by preparing the urine samples with EDTA to dissolve calcium oxalate precipitates.

The state of urinary saturation with respect to calcium phosphate was determined by the equilibration of urine with 10 mg/ml brushite and with respect to calcium oxalate by the equilibration with 10 mg/ml whewellite according to the methods previously described [1]. The state of saturation was expressed as ratio of the concentration products of (calcium) x (oxalate) or (calcium) x (phosphate) in the native urine and the concentration products of (calcium) x (oxalate) or (calcium) x (phosphate) after equilibration. The results of chemical and physico-chemical analyses were plotted and examined for correlations by a computer programme calculating the linear correlation coefficients and the *t*-test for correlation coefficients. Correlations were defined as signficant when the correlation coefficient r was > 0.5 and $p < 0.001$.

Table 1. Composition of the 4 different diets given to 19 idiopathic calcium stone formers

	diet A	diet B	diet C	diet D
calcium (mg)	250	500	500	1,200
oxalate (mg)	900	900	20	20
phosphate (mg)	400	400	800	800
magnesium (mg)	100	180	100	180

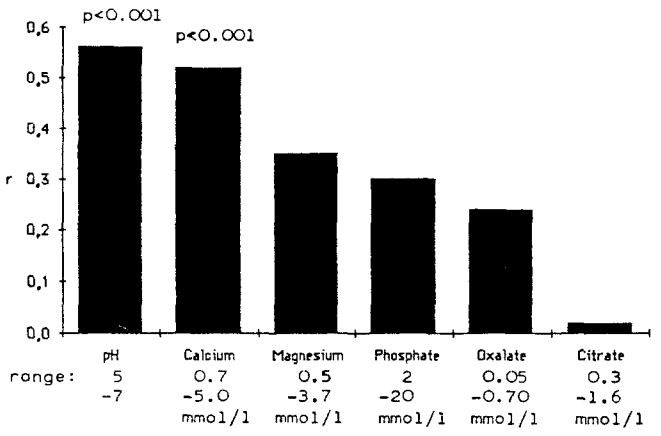

Fig. 1. Correlations of chemical parameters to the state of saturation towards brushite

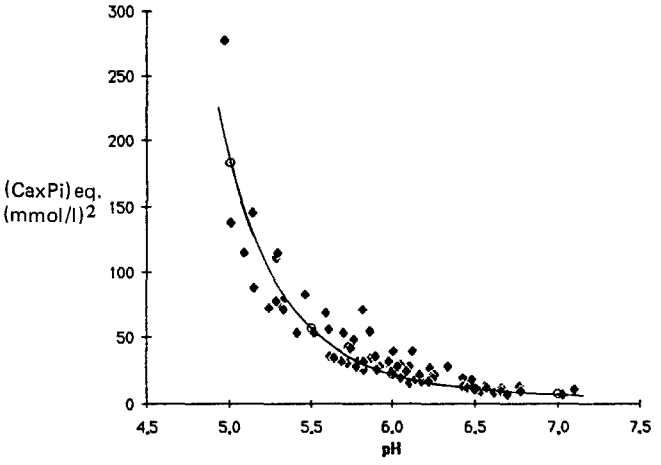

Fig. 2. Influence of pH on the concentration product Cax Pi after equilibration of urine (♦) and of 0.15 molar NaCl (–o–) with 10 mg/ml brushite

Results

Under the 4 diets the concentrations of the chemical parameters varied by factors 5x to 14x (Fig. 1). The state of the urinary saturation towards brushite showed significant correlations to the calcium concentration and to pH. pH influenced the concentration product of brushite solubility as shown in Fig. 2. The solubility of brushite was almost identical in the urine and in a 0.15 molar saline solution. The influence of pH on the state of saturation towards brushite in the individual urine is shown in Fig. 3.

The state of the urinary saturation towards whewellite was significantly influenced by the oxalate concentration (Fig. 4). Plotting urinary oxalate versus calcium concentration after equilibration with whewellite showed that at the observed calcium range (0.7 to 5.0 mmol/l) the oxalate concentration in saturated urine was almost independent of the calcium concentration, and even at high calcium concentration the oxalate did never fall below a minimal value (Fig. 5). However, after an artificial decrease of calcium by the addition of sodium oxalate and the precipitation of calcium oxalate, a hyperbola-like curve was obtained which fitted best to the formula given in Fig. 5. A comparison of the influence of the 4 different diets on urinary calcium and oxalate concentrations showed that the influence of diets A and D differed significantly from diets B and C. Urinary oxalate dropped with increasing calcium concentration.

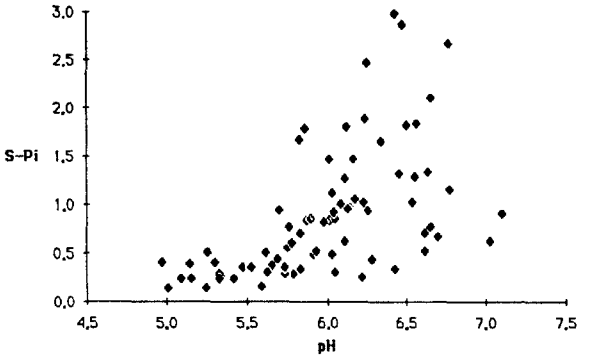

Fig. 3. Influence of pH on the state of saturation towards brushite (*S-Pi*) in the individual urines. $r = 0.56$, $n = 76$, $p < 0.001$

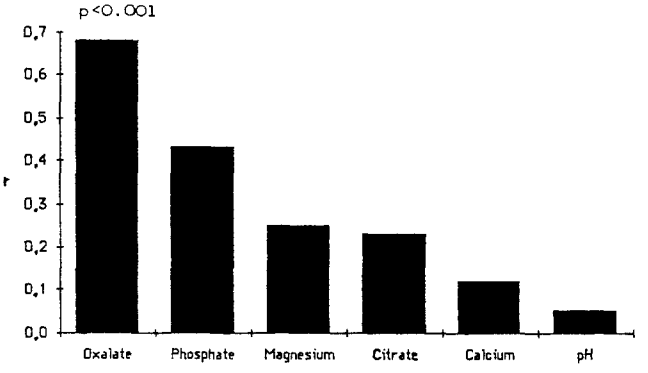

Fig. 4. Correlations of chemical parameters to the state of saturation towards whewellite

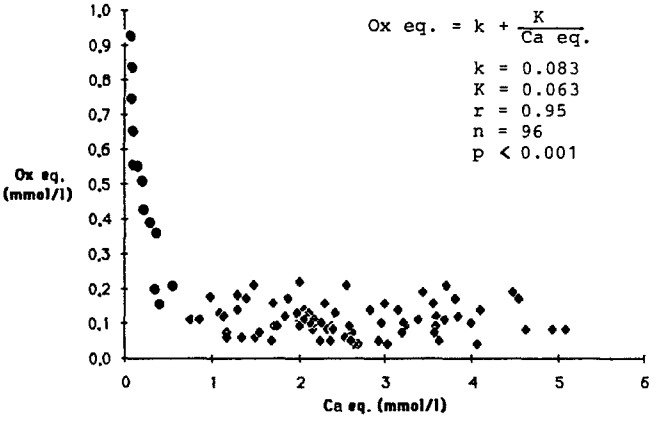

Fig. 5. Oxalate versus calcium concentrations after equilibration with 10 mg/ml whewellite in native urine (♦) and in urines after precipitation of calcium oxalate by the addition of sodium oxalate (•)

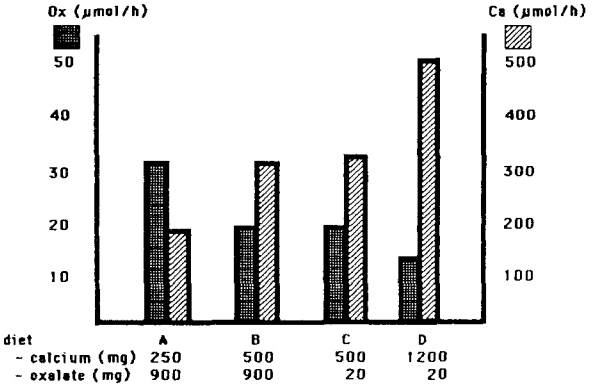

Fig. 6. Dietary influence on oxalate and calcium excretions

Discussion

Although a high variability in the urinary concentrations of measured parameters was observed under the 4 different diets of this study, the state of urinary saturation towards whewellite and brushite was only governed by one or two factors respectively. Urine volume, which is also important, drops out of consideration in our study for reasons of a fixed fluid intake. In agreement with the findings of others [6], urinary saturation towards brushite was dominated by the calcium concentration and by pH. For stone metaphylaxis it seems important to note that at a pH below 5.5 brushite solubility is extremely increased and that in this range urine was always found to be undersaturated towards brushite (Fig. 3).

The plot of urinary oxalate versus calcium concentration after equilibration with whewellite (Fig. 5) is the key to the comprehension of our findings in the calcium oxalate system. At high oxalate concentrations calcium tends to reach zero, whereas at high calcium concentrations the average oxalate was always above the minimal value k given in the formula of Fig. 5. It can therefore be concluded that k represents a soluble oxalate fraction not contributing to calcium oxalate chelation and probably bound to urinary macromolecules, as already suggested by others [10]. k, which can be calculated by the formula $k = \text{Ox eq.} - (\text{K} \times \text{Ca eq.}^{-1})$, should therefore be subtracted from the oxalate concentration before forming concentration products. (Ox eq. and Ca eq. denote oxalate and calcium concentrations in urine saturated with respect to whewellite.) K in the formula given in Fig. 5, is such a corrected product for whewellite solubility. Multiplication of K (0.063) by the free fraction of Ca (0.55) and of oxalate (0.8) and the square of the activity coefficient for divalent ions (0.33^2) according to the procedure of Marshall and Robertson [6] gives a value of 0.003 which equals the thermodynamic solubility product of calcium oxalate, reported from 0.0022 to 0.0036 mmol/l^2 [3].

The state of saturation towards whewellite can therefore be calculated by the formula $\text{Ca} \times (\text{Ox} - k) \times K^{-1}$.

Higher values are obtained by using this procedure than by the calculation of the corresponding concentration product ratios. The same observation was made comparing CPR and APR with relative saturation towards calcium oxalate [7]. Subtracting k from urinary oxalate concentration produces a corrected oxalate range from 0.01 to 0.53 with a factor of variation of 53 benign 4 times the one of the non-corrected oxalate. In our study oxalate was the only factor which significantly governed urinary supersaturation towards whewellite. A predominant effect of oxalate on the state of urinary supersaturation towards calcium oxalate has also been found by others [9]. In our study, the effect of urinary calcium on the saturation towards whewellite was probably cancelled by a decrease of oxalate with increasing calcium as shown in Fig. 6. Also magnesium, citrate and phosphate often used for therapeutic purposes had, under the conditions of this study, neither significant influence on the state of saturation towards whewellite nor towards brushite. It is therefore concluded that urinary supersaturation in stone formers is mainly governed by factors with a high influence on solubility (e.g. pH) or showing big variations in their urinary concentrations (e.g. oxalate). Interferences between some constituents may also be important. Such phenomena can only be detected by computer calculations or by direct measurement of solubilities in urine. The latter method was able to determine a soluble oxalate fraction not contributing to calcium oxalate chelation.

References

1. Baumann JM, Lauber K, Lustenberger FX, Wacker M, Zingg EJ (1985) Crystallization conditions in urine of patients with idiopathic recurrent calcium nephrolithiasis and with hyperparathyroidism. Urol Res 13:169–174
2. Bisaz S, Russell RGG, Fleisch H (1968) Isolation of inorganic pyrophosphate from bovine and human teeth. Arch Oral Biol 13:683–696
3. Blomen LJMH, Bijvoet OLM, van der Linden H (1982) Die Löslichkeit von Calciumoxalat Monohydrat. In: Vahlensieck W, Gasser E (eds) Fortschritte der Urologie und Nephrologie. Steinkopff, Darmstadt, 17:159–166
4. Drawert F, Paul H, Hagen W (1981) Enzymatische Bestimmung von Oxalsäure und Ameisensäure im Bier. Brauwissenschaft 3:57–61
5. Marangella M, Daniele PG, Ronzani M, Sonego S, Linari F (1985) Urine saturation with calcium salts in normal subjects and idiopathic calcium stone formers estimated by an improved computer model system. Urol Res 13:189–193
6. Marshall RW, Robertson WG (1976) Nomograms for the estimation of the saturation of urine with calcium oxalate, calcium phosphate, magnesium ammonium phosphate, uric acid, sodium acid urate, ammonium acid urate and cystine. Clin Chim Acta 72:253–260
7. Pak CYC, Hayashi Y, Finlayson B, Chu S (1977) Estimation of the state of saturation of brushite and calcium oxalate in urine: A comparison of three methods. J Lab Clin Med 89: 891–901
8. Robertson WG, Peacock M, Nordin BEC (1968) Activity products in stone-forming and non-stone-forming urine. Clin Sci 34:579–594
9. Robertson WG, Peacock M (1980) The cause of idiopathic calcium stone disease: Hypercalciuria or hyperoxaluria? Nephron 26:105–110
10. Sheinfeld J, Finlayson B, Reid F (1978) Ultrafiltration evidence of ion binding by macromolecules in urine. Invest Urol 15. 462–464

Dr. D. Ackermann
Department of Urology
University of Berne
Inselspital
CH-3010 Bern