

CRYSTALLURIA AND ITS POSSIBLE SIGNIFICANCE

A Patient–control Study

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Abstract. The significance of crystalluria in the diagnosis and prognosis of urolithiasis remains a controversial subject in the current urological literature. In this study, in addition to the standard urolithiasis clinical and biochemical work-up, routine urine microscopy was performed to study crystals in 1 fresh and 2 stored morning urine samples from 140 urinary stone patients and 42 controls. Crystalluria was more frequently detected in patients (9.3% of the fresh samples) than in controls (2%). Storing the samples for 6 hours did not increase the frequency percent of detected crystalluria either in patients or controls. However, in the samples stored for 24 hours, the frequency of crystalluria increased to 27.1% in patients and only to 12% in controls, though the pH did not change from that of the fresh sample. In addition, while calcium oxalate crystals in patients formed aggregates whether in fresh or 24 hour samples, those of controls did not. This denotes a characteristic change in the physico-chemical properties of the urine of stone formers from that of controls. Accordingly, the study of crystalluria in patients with urolithiasis seems to help in the proper evaluation and, maybe, treatment of the disease.

Key words: urolithiasis, clinical investigations, urine sampling, urine microscopy, calcium oxalate crystals, uric acid crystals, crystal aggregates, in vitro crystal formation, mechanisms of stone formation, urinary pH, hyperuricosuria.

The significance of crystalluria in the diagnosis and prognosis of urolithiasis remains a controversial subject in the current urological literature (Winkens et al., 1987; Robertson et al., 1971; Werness et al., 1981; Rose, 1982; Rodgers & Spector, 1987). In this series, routine urine microscopy was utilized to study crystalluria in 140 urinary stone formers and 42 normal persons.

METHODS

In addition to the routine clinical and biochemical work-up, one morning urine sample was taken from

each of the 140 urinary stone formers and the 42 controls. Part of the sample was centrifuged as soon as passed by the patient or normal person, in the laboratory thus ensuring conducting the study on a fresh sample almost at body temperature. After pouring off the supernatant fluid, the urine sediment was shaken and a drop was tapped on a microscopic glass slide and covered with a coverglass. Dry high power ($\times 400$) microscopic examination was, then, immediately proceeded with. The type of the crystals present, their number per high power field, their size and the presence or absence of aggregates was reported. The remaining part of the sample, stored at airconditioned room temperature, was similarly processed and examined 6 hours and 24 hours later. All of the study was performed by one and the same urine microscopist uninformed about the patient or control status of the samples.

In statistical analysis of the data, Kendall's tau-c test (crosstabulation statistics 7 procedure of the SPSS PC+ software) was applied to the comparison between the two groups.

RESULTS

Patients

In the 140 urinary stone patients studied, calcium oxalate crystals were microscopically detected in the fresh urine sample only in 9.3% of the cases (Tables I and II). When the samples were left at room temperature for 6 hours, there was no increase in the number of cases with detected crystalluria. However, in the samples left for 24 hours, the percentage of samples with microscopically detected crystalluria almost trebled (27.1%, Table II), though the pH of all these 140 samples left at room temperature for 24 hours did not change from that of the fresh sample. Tables I and II show the number and size of calcium oxalate crystals of these patients in the fresh, 6 hour-stored and 24 hour-stored samples. Large crystals, detected only in one fresh and one 6 hours-stored samples (0.7% of

Table I. Percentage distribution of 140 urinary stone patients (Pts) and 42 controls (Cts) by oxalate crystal size in a fresh urine sample (sample 1), samples stored for 6 hours (sample 2) and 24 hours (sample 3)

Crystal size	Sample 1		Sample 2		Sample 3	
	Pts	Cts	Pts	Cts	Pts	Cts
No crystals	90.7	98	92.1	98	74.3	88
Small crystals	5.0	0	3.6	0	10.0	5
Medium crystals	3.6	2	3.6	2	12.1	5
Large crystals	0.7	0	0.7	0	3.6	2

Table II. Percentage distribution of 140 urinary stone patients (Pts) and 42 controls (Cts) by number of oxalate crystals in a fresh urine sample (sample 1), samples stored for 6 hours (sample 2) and 24 hours (sample 3)

No. of crystals per high power field	Sample 1		Sample 2		Sample 3	
	Pts	Cts	Pts	Cts	Pts	Cts
0	90.0	98	90.7	98	72.9	88
1-9	2.9	0	3.6	0	11.4	5
10-19	5.0	0	4.3	0	8.6	5
20-29	0.7	0	0	0	2.9	0
30-39	0.7	0	0.7	0	2.1	0
50+	0.7	2	0.7	2	2.1	2

Table III. Percentage distribution of 140 urinary stone patients (Pts) and 42 controls (Cts) by the presence of oxalate crystal aggregates in a fresh urine sample (sample 1), samples stored for 6 hours (sample 2) and 24 hours (sample 3)

Aggregates	Sample 1		Sample 2		Sample 3	
	Pts	Cts	Pts	Cts	Pts	Cts
Absent	98.6	100	99.3	100	96.4	100
Present	1.4	0	0.7	0	3.6	0

each group), were detected in five (3.6%) of the samples stored for 24 hours and were not associated with crystal aggregates in any of the seven samples.

In the fresh samples, only two patients (1.4%) had calcium oxalate crystal aggregates, while in the samples stored for 24 hours, aggregates were found in 5 patients (3.6%, Table III).

No uric acid crystal aggregates were seen in this study and only 5 patients (3.6%) had uric acid crystals in their fresh samples.

Controls

In the 42 controls, calcium oxalate crystals were microscopically detected in the fresh urine sample of only one person (2%).

When the samples were left at room temperature for six hours, there was no increase in the number of persons with detected crystalluria. However, in the samples left for 24 hours, calcium oxalate crystalluria was detected in 5 samples (12%), though the pH did not change from the pH of the fresh sample. Tables I and II show

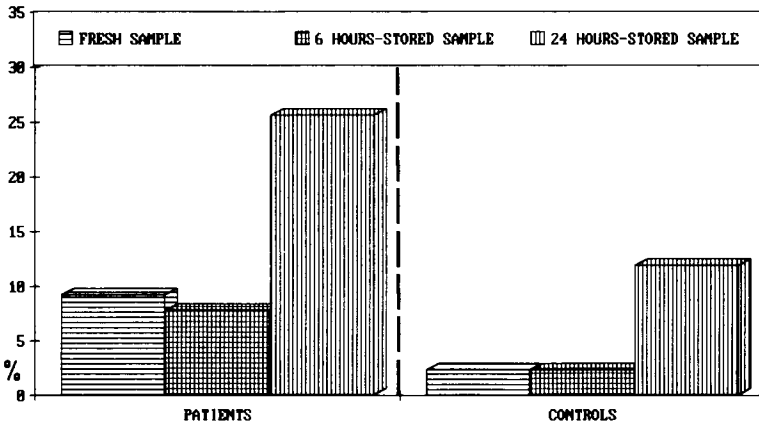


Fig. 1. Frequency percent of crystalluria in 140 patients and 42 controls in the fresh, 6 hour-stored and 24 hour-stored urine samples.

the number and size of calcium oxalate crystals of the 42 controls in the fresh, six hour-stored and 24 hour-stored samples. Large crystals were only detected in one of the last-mentioned samples.

In the fresh samples, none of the controls had microscopically detectable calcium oxalate aggregates. Furthermore, storing the samples for six hours and for 24 hours, did not lead to the appearance of aggregates in the samples from any of the 42 controls (Table III). Also, none of the controls had uric acid crystals or crystal aggregates.

The differences detected, in this study, between patients and controls are plotted in Figs. 1, 2 and 3. The difference between the two groups in the frequency of crystalluria was statistically significant ($p=0.02$) in the samples

stored for 24 hours, almost significant ($p=0.05$) in the fresh samples and non significant in the 6 hour-stored samples ($p=0.07$). Furthermore, statistically significant difference ($p=0.03$) was shown in the distribution of the two groups by crystal size in the 24 hour-stored sample.

DISCUSSION

In this series, crystalluria of a relative frequency percent of 9.3 in fresh urine samples is lower than that reported by Winken et al. (1987) and Fazil Marrikar et al. (1989).

Meanwhile, a 2% frequency of crystalluria in the controls of this series denotes that crystalluria can be found in both stone formers and controls (Azoury et al., 1987), though its inci-

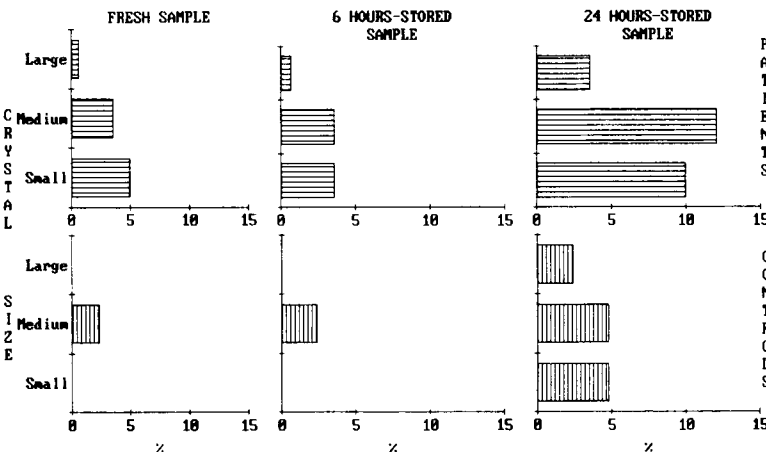


Fig. 2. Percentage distribution of crystalluria by crystal size in 140 patients (top row) and 42 controls (bottom row) in the fresh, 6 hour-stored and 24 hour-stored urine samples.

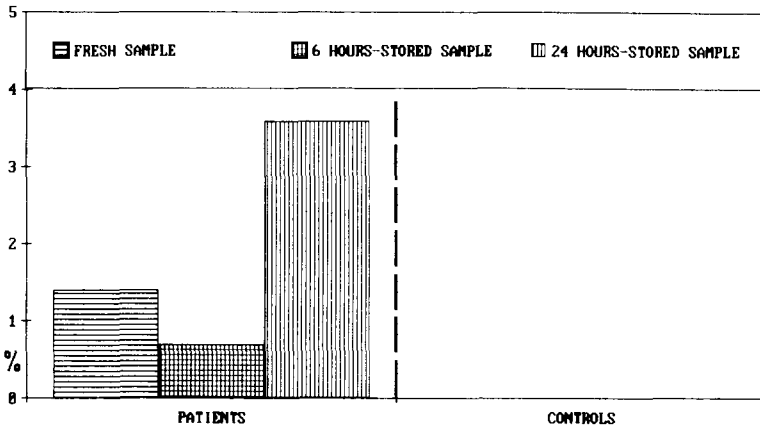


Fig. 3. Frequency percent of crystal aggregates in 140 patients and 42 controls in the fresh, 6 hour-stored and 24 hour-stored urine samples.

dence in the latter is much more less. In addition, while calcium oxalate crystals in patients tend to form aggregates whether in fresh urine samples or 24 hour-stored samples, those of controls do not.

Accordingly, this denotes a characteristic change in the physico-chemical properties of the urine of stone formers from that of controls.

In confirmation with this is the previously found higher incidence of crystalluria (33.3%) in stone formers with a 24-hour urinary pH value < 5.5 than in those with a 24-hour urinary pH > 5.4 (18.2%) (unpublished results). It is known that the former urinary pH value denotes a urinary state of super-saturation with uric acid and in some may exceed its formation product (Tiselius & Larsson, 1983) in addition of being below the increase of the inhibition index of calcium oxalate crystal growth (Tiselius, 1981).

Furthermore, while crystalluria and aggregates were present in the fresh urine samples of 20% of hyperuricosurics, none of the patients with urinary disturbances other than hyperuricosuria had aggregates in their fresh urine sample (unpublished results). Therefore, it seems that uric acid saturation is not only correlated with the volume of calcium oxalate crystals (Robertson et al., 1971) but may also be correlated with the process of its aggregation.

Accordingly, unlike Winkens et al. (1987) though in agreement with Robertson et al. (1971), Werness et al. (1981), Rose (1982) and Rodgers & Spector (1987), the study of crystals

in the patients with urolithiasis seems to help in the proper evaluation and, maybe, treatment of the urolithiasis disease.

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REFERENCES

- Azoury R, Robertson WG, Garside J. Observations on in vitro and in vivo calcium oxalate crystalluria in primary calcium stone formers and normal subjects, *Br J Urol* 1987; 59: 105-110.
- Fazil Marickar YM, Sachidev K, Joseph T, Sindhu S, Vathsala R. The relative merits of early morning vs. random urine samples for studying crystalluria. In: Walker VR, Sutton RAL, Bert Cameron EC, Pak CYC, Robertson WG, eds. *Urolithiasis*. New York and London: Plenum Press, 1989: 411-422.
- Robertson WG, Peacock M, Nordin BEC. Calcium oxalate crystalluria and urine saturation in recurrent renal stone-formers. *Clin Sci* 1971; 40: 365-374.
- Rodgers AL, Spector M. Crystalluria. In: Rous SN, ed. *Stone disease: diagnosis and management*. New York and London: Grune and Stratton, 1987: 47-55.
- Rose GA. Laboratory investigations. In: Rose GA, ed. *Urinary stones: clinical and laboratory aspects*. Lancaster: MTP Press Ltd. 1982: 153-155.
- Tiselius HG. Urinary excretion of citrate in normal subjects and patients with urolithiasis. In: Smith LH, Robertson WG, Finlayson B, eds. *Urolithiasis: clinical and basic research* New York: Plenum Press, 1981: 39-44.

Tiselius HG, Larsson L. Urinary excretion of urate in patients with calcium oxalate stone disease. *Urol Res* 1983; 11: 279–283.

Werness PG, Bergert JH, Smith LH. Crystalluria. In: Smith LH, Robertson WG, Finlayson B, eds. *Uro-*

lithiasis: clinical and basic research. New York and London: Plenum Press, 1981: 17–20.

Winkens RAG, Wielders JPM, Degenaar CP, van Hooff JP. Is crystalluria of diagnostic importance? *Tijdschr NVKC* 1987; 12: 135–136.