Biosciences, Biotech. Research Asia Vol. **2,** No.(**2**) 73-78 (2004)

CRYSTALLURIA : A MEANS TO AVOID A HIGH-RISK EXTRA CORPOREAL LITHOTRIPSY ?

A. Driouch[1], Z. Kaid-Omar[1], D.H. Taleb-bendiab[2] , M. Daudon[3], A. Semmoud[4] and A. Addou[1*]

[1]Laboratoire STEVA, Faculté des Sciences, University of Mostaganem (Algeria)
[2]Service d'Urologie, Centre Hospitalier Universitaire, Oran, (Algérie)
[3]Laboratoire de Biochimie A, Hôpital Necker, Paris, (France)
[4]Laboratoire de Spectroscopie Infrarouge et Raman,
Université des Sciences et Technologies, Villeneuve d'Ascq, (France)

(Received November 18, 2004; Accepted December 19, 2004)

ABSTRACT

For about ten years, several research teams have been seeking means to predict the impact resistance of the *in situ* stones basing their argument on the radiological aspect, composition of previously collected stones from patients as well as biological anomalies characterised in urine.

In the present study, the workers compared the nature of the urinary crystals of the first morning urine after storing at +4°C, to the composition of the stones surgically removed or spontaneously evacuated or after treatment by E.C. L. The results have shown that the frequency of crystalluria was very high (92.6%). The crystalline species that was the most frequent was weddellite (46.7%) followed by amorphous complex urates (20.3%), calcic phosphates (12.5%), dihydrated uric acid (7.1%) and struvite (6.8%). The comparison between crystalluria and stone composition has shown that the dominant or pure weddellite crystalluria was associated with stones where weddellite was the major or pure constituent in 49% of the cases. Crystalluria cases where whewellite was found whether pure or major, were associated with stones where whewellite was the major constituent in 83.6% of the cases. On the other hand, crystalluria of complex amorphous urates was rarely associated with uric acid stones (5.7%) and that of dihydrated uric acid was in 38.1% of the cases. Struvite crystalluria was observed in the urine of patients that presented an infection lithiasis mainly composed of struvite in 62.9% of the cases.

Key words: Crystalluria, Urinary Stones, Whewellite; Weddellite, Extra-Corporeal Lithotripsy.

INTRODUCTION

It is well known today that among the calcium oxalate stones, which are by far the most frequent, the dihydrated forms (weddellite) are relatively friable and in principle accessible to extra-corporeal lithotripsy. On the other hand, the monohydrated forms are much harder and can sometimes resist entirely to fragmentation or break up into large fragments of which some cannot be expelled while others will migrate in the ureter by causing renal colic requiring complementary action[1]. It may then be useful to optimise the urological treatment, to have a prior knowledge of the crystalline composition of the stones, especially calcic stones[2,3] by considering the composition of earlier collected stones from patient and the biological anomalies characterised in the urine samples. From this point of view, we have sought the correlations which might exist between the composition of the observed crystalluria cases stored in a cold place and the composition of the stones collected from patients.

Patients

The study is concerned with 295 lithiasic patients of whom 162 men of average age 39.2 years and 133 women of average 39.2 years. All the stones were either extracted surgically (213 cases), or spontaneously expelled under diuresis treatment (76 cases), or evacuated following an extra-corporeal lithotripsy (6 cases). For each patient, on average three urine samples at wake up were analysed for crystalluria. The collected stones were subjected to qualitative and semi-quantitative analysis consisting of a morphological examination and an FTIR spectrometry

EXPERIMENTAL

Equipment

Zeiss polarisation optical microscope equipped with oculars allowing a x 10 magnification and 10 and 20 times magnifying lenses.

Zeiss binocular optical microscope with magnification ranging from 10 to 25 times.

Fourier transform infrared Perkin-Elmer (Spectrum one) spectrometer. 13 mm in diameter potassium bromide pastille making device.

Methods

Crystalluria

First patient urine at waking was analysed qualitatively and quantitatively for crystalluria with a polarised light optical microscope. Samples were stored at + 4 °C during 48 hours prior to examination. The analysis performed in a Malassez cell consisted of a cytological study, a crystal count by crystalline species under a x 400 magnification. When optical examination would not allow to conclude for a certainty about the nature of the observed crystals, further identification was performed by infrared spectrophotometry via the potassium bromide disc technique[4] made from centrifugation residue collected on membrane or low porosity filter.

Besides, pH measurements of urine were systematically performed as the samples were examined microscopically.

Stones

The stones collected were subjected to a morpho-constitutional analysis. Every stone was analysed morphologically by noting the superficial and internal organoleptic characteristics based on Daudon classification[4-7], and subjected to a sequential analysis of the core at the surface by FTIR spectrophotometry[4] by using the potassium bromide disc technique. In the final stage of the analysis, a stone powder was systematically made to enable quantitative analysis of the various constituents of the potential mixtures.

RESULTS

Crystalluria

Examination of urine at waking stored at + 4°C for 48 hours showed positive crystalluria in 92.6% of the samples. The most frequent crystalline species was weddellite (46.7%), followed by amorphous complex urates and phosphates (Table -1).

Table - 1 : Frequency of observed crystals as major constituent in urine samples

Major Constituent	Frequency (%)
Calcium oxalate	47.4
• Weddellite·	46.7
• Whewellite	0.7
Calcic phosphates	12.5
• Carbapatite	5.4
• amorphous calcium phosphates	4.4
• Brushite	2.7
Struvite	6.8
Purines	2.7
• Ammonium acid urate	2.3
• Complex amorphous urates	20.3
• Uric acids	7.1
Others	3.6

Complex amorphous urates account for 20.3% of the cases, phosphates are identified in 12.5%, uric acids and struvite in 7.1 and 6.8 % of the cases, respectively. Whewellite is present in only 0.7% of the crystalluria cases observed.

Stones

The analysis of the 295 stones showed that the major constituent was whewellite in 55% of the cases, followed by weddellite in 24.4%. Carbapatite acounted for 9.9%, struvite for 6.4% and anhydrous uric acid for 4.3% of the cases (Table II).

Table - 2 : Frequency of major constituent of the urinary stones

Major constituents	Frequency (%)
Calcium oxalates	79.4
• Whewellite	55.0
• Weddellite	24.4
Carbapatite	9.9
Struvite	6.4
Anhydrous uric acid	4.3

Table - 3 : Relationship between the nature of crystalluria and nature of stones

Crystalluria Nature	Frequency (%)	Nb	Composition of Stones	Observations
Weddellite pure or	49	46	* C2 + CA ± C1	* Stones with majority
mixed (without	29,8	28	* C1 + ca	constituent of:
Whewellite)	10,6	10	* C1 + C2 + apatites	- weddellite : 49%
(N = 94)	4,2	4	* CA + C1	- whewellite : 40.4%
	2,1	2	* AU0 + AU2 + C2	*Stones rich in:
	1,1	1	* calcite	- weddellite : 61.7%
	3,2	3	* Others (without C2)	- whewellite : 42.5%
Weddellite +	78,2	36	* C1 ± C2 ± CA	* Stones with majority
Whewellite (±CA)	17,4	8	* C2 + C1	constituent of:
(N = 94)	2,2	1	* PAM + C1 + CA	- whewellite : 80.4%
	2,2	1	* C1 + WK	- weddellite : 17.4%
Calcic	35,1	13	* C1 + CA ± WK	• Stones rich in calcic
Phosphates	35,1	13	* CA + C1 ± PAM ±	phosphates :
(N = 37)	21,6		PACC	-702%
	8,1	8	* C2 ± CA ± C1	
		3	* Others	
Struvite ±	51,8	14	* PAM ± UrAm ± CA	* Stones with majority
Ammonium urate	14,8	4	* C1 + C2 + CA ±	constituent of:
± Weddellite	11,1		PAM	- struvite: 62.9%
(N = 27)	11.1	3	* CA ± PAM	* Stones containing struvite:
	11.1	3	* C2 + PAM + CA	92.6%
		3	* PAM + C2 ± UrAm	
Complex	60	12	* C1 + C2 ± CA	* Stones with majority
Amorphous	20	4	* CA ± PACC ± C2	constituent of
Urates ± AU2 ± C2	20	4	* AU0 + C2 ± AU2	- whewellite : 60%
(N = 20)				
Dihydrated uric	47,6	10	* C1 ± C2 + CA	* Stones with majority
acid ±	28, 6	6	* AU0 + AU2	constituent of
Whewellite ±	9,5	2	* C1 + AU0 + CA	- whewellite : 57.1%
Weddellite	9,5	2	* C2 + C1	* Stones with majority
(N = 21)	4,7	1	* PAM + CA + C1	constituents of
				- uric acids : 28.6%
Complex	86	43	* C1 + CA ± C2	* Stones with majority
Amorphous	10	5	* C2 ± C1 ± CA	constituent of
Urates + C1 ± C2	4	2	* CA + C2 + C1	- whewellite : 86%
(N = 50)				* Rich in whewellite: 100%

AU0 = Anhydous uric acid - AU2 = uric acid dihydrated - CA = Carbapatite - C1 = Whewellite - C2 = Weddellite - ACP = amporphous calcium phosphates - PAM = Hexahydrated ammonium-magnesium phosphate - UrAm = ammonium Acid urate – WK = Whitlockite.

Relationships between crystalluria and stones

The observation of the nature of the crystalluria cases and stone composition shows that several crystalluria profiles may be outlined (Table -3). Thus, the dominant or pure crystalluria cases of weddellite were assocaited with stones where weddellite was pure or the major constituent in 49% of the cases. The same thing was observed with whewellite in 83.3% of the cases, including the case where complex amorphous urates represented the dominant species of crystalluria.

Besides, urates associated with dihydrated uric acid and weddellite were correlated with stones where whewellite was the major constituent in 60% of the cases. Uric acids (pure or mixed with other compounds such as oxalates and complex amorphous urates) were combined with stones containing uric acid in only 28.6% of the cases and with stones where whewellite was the major constituent in 57.1 of the cases.

Struvite crystalluria cases were observed among patients presenting infection stones with ureasic crystals made up of major constituent of struvite in 62.9% of the cases, but in 92.6% of the cases, crystalluria containing struvite was associated with a stone also containing struvite.

As for phosphocalcic crystalluria, it was present in patients bearing stones rich in calcium phosphate or where the latter was the major component in 70.2 and 35.1% of the cases, respectively.

DISCUSSION

The use of crystalluria to predict the composition of stones before lithotripsy was proposed in 1992 by Cohen *et al.* who worked on urine samples freshly produced[8]. These authors have reported an excellent correlation between the nature of the stone assessing the study of post-lithotripsy urine samples and crystalluria observed prior to treatment. However, the correlation was limited to chemical species differentiation and to distinction of pure and mixed crystalluria, the latter appearing to correspond to stones less well fragmented having required in half of the cases further percutaneous surgery[8]. In particular, the authors did not differentiate between the crystalline species and did not distinguish whewellite from weddellite, since they have very different behaviours towards an extra-corporeal lithotripsy[9,10].

An earlier work[11] consisted of a correlative study between the nature of crystalluria before and after surgical treatment and the composition of the urinary stones of 75 patients. The crystalluria study at + 4°C showed the importance of this examination for determining the nature of the stones formed in a given patient when no earlier collected-stone analysis is available. The advantage of storing in a cold place is that it artificially increases the frequency and abundance of crystalluria, which represents an obstacle to the clinical exploitation of the results, when comparison between lithiasic patients and normal people is sought, but an advantage when characterising of a given patient profile is tried. In earlier publications by various authors, the frequency of spontaneous crystalluria, in healthy subjects as well as in lithiasics, is lower than that observed in urine stored in a cold place[11-13]. Some studies have shown the increase in frequency of crystallisation by storing at + 4°C[14]. In a study comparing both experimental procedures, Nguyen et al. have observed a global crystalluria frequency from 48.9 to 96.7% in non treated lithiasic patients. Likewise, in a control subjects group, these authors observed an increase in crystalluria from 14% on direct examination to 42% after storing in a cold place. In our study, the frequencies of crystalluria observed at + 4°C in lithiasic patients before surgery (97.3%) and in control subjects (50%) were quite comparable to those published by Nguyen et al. on samples stored at + 4°C[14].

The experimental procedure consisting in examining urine samples between 48 and 72 hours after storing in a cold place has an undeniable advantage over the direct examination procedure since conveying and storing times, which must be as short as possible, are now no longer limiting factors. In fact, an interesting characteristics of crystalluria developed after storing in a cold place is the good stability of the existing crystalline species over a storing period of several days, which allows easy handling of samples.

In our study, the most widely observed crystalline species was weddellite, observed in 46.7% of the urine samples (Table -1). Its calcium-dependent characteristics, now well-known, makes it a good indicator of output-or-concentration hypercalciuria[15,16]. Nearly two-thirds of these patients had a calcium-dependent lithiasis where weddellite was the majority or the rich constituent. On the basis of these results, confirming earlier results[4], it seems reasonable to consider that a radio-opaque stone associated with a weddellite crystalluria without whewellite shows a calcium-dependent structure, hence potentially fragile and accessible to urological treatments by endo- or extra-corporeal lithotripsy.

Unlike weddellite, the monohydrated calcium oxalate or whewellite is an indicator of output or concentration hyperoxaluria, the presence of which in urine depends both on its oxalate content and the calcium/oxalate molar ratio. The simple existence of whewellite crystals allows the confirmation of hyperoxaluria. On the other hand, if the molar ration Ca/Ox is high, (>14) involving the simultaneous existence of hypercalciuria, there may be absence of whewellite[5, 16]. This explains the non constant presence of whewellite in crystalluria cases. However, the high frequency of whewellite observations (32.5%) in urine samples of lithiasic patients as compared with those of 61 control subjects (2.3%, results submitted for publication) shows evidence of hyperoxaluria frequency in the patients and suggests that the latter plays an important role in the formation of stones.

It is noteworthy that the presence of whewellite crystals correlates well with the dominant presence of whewellite in the stones. In fact, out of 110 patients whose urine contained whewellite crystals, 92 (i.e. 83.6%) had a stone where whewellite was the major constituent. This form of lithiasis is frequent in Algeria as testified by a recently published work showing that 48% of the observed stones in the west of Algeria had whewellite as the major component[17]. The presence of whewellite in urine may then be considered as an indicator of an oxalo-dependent stone where whewellite was dominant, the resistance of which to modern urological treatments by lithotripsy is often higher than that of wheddellite stones, which may require a special treatment strategy.

The patients who had a crystalluria where dihydrated uric acid, known as a pH dependent species[18,19], was the major constituent had a uric acid major component stone in 28.6% of the cases, and rich in uric acid in 38.1% of them.

The complex amorphous urates, which are more urico-dependent than pH-dependent are not well correlated with uric lithiasis since only 5.7% of the patients with a complex amorphous urates crystalluria had uric acid-containing lithiasis. These results confirm the literature data on the determining role of acid urine pH (but not uraturia) as a main factor of uric lithiasis[20,21].

Struvite, a recognised indicator of ureasic germs infections[22], was identified in 27 crystalluria cases. In 92.6% of the cases, it was correlated with the presence of an infection stone or a secondarily infected stone containing struvite, justifying in all cases a special therapeutic treatment consisting of antibiotics supply to inhibit germ spreading during the urological operation.

Conclusion

The examination of crystalluria in urine at waking stored at + 4 °C emerges as a simple means (easy to perform from the clinical viewpoint) of advising the clinician about the nature of the in situ stones, enabling him to optimise the choice of treatment method. Further studies are under way to clarify the significance of this examination which is not very invasive and of simple execution, as an indicator, by itself or associated with other investigating means, of the efficacy of treatments and diets for the prevention lithiasic recurrence.

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