

## Study of spontaneous crystalluria for the lithiasic patients before and after surgical treatment

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### ABSTRACT

The study of the crystalluria is badly codified examination since it does not emerge always clearly to the eyes of the clinicians because of its difficult interpretation linked most of the time, to the imperfectly conditions of its realization. To check most if the crystalluria could help to predict the composition of the stones, it at the same time we follow the patient to avoid the maximum attempt of stone recurrence, we have studied the urine of 147 lithiasic patients before and after the surgical treatment of their stones, the frequency and the nature of the crystals have been compared to those ones observed in the waking urine in the subject of healthy persons studied in the same conditions.

234 first waking urine of lithiasic subjects before and after surgical interventions were examined using polarization microscopy to look for and identify an eventual crystalluria. Patients were divided into two groups (before and after surgical treatment). The result are expressed in sort of majority crystalluria.

The whole frequency of the positive crystalluria was 94% for the groups, (98.6% before the operation and 86.2 after the operation) about twice more than the one observed in normal subjects. The crystalluria of the nature oxalate of calcium was far away as far as concerns the one of crystalline sort 30.3% before surgical treatment and 25.3% after the treatment. The average pH of the urines of lithiasic subject occurs between 5.59 and 7.66 in the sum is inferior to 7. That means more acid than those of healthy subjects.

The whole results show that the positive crystalluria of lithiasic patients has fall down after the surgical treatment than before the treatment of 98.6% to 86.2%. The crystalline sort of the type weddellite is more frequent for the two sexes before or after the medical treatment, we also notice the total elimination of frequency of urate precipitation for the two sexes after the surgical treatment than before the treatment.

**Key words:** Lithiasic, crystalluria, treatment surgical, calcium oxalate, pH.

### INTRODUCTION

The crystalluria is the expression of an excessive supersaturation of the urine. It can be made profitable to detect certain genetic pathologies and to appreciate the lithogenous urinary anomalies among suffering patients of nephrolithiasis or susceptible to develop a lithiasis. In spite of that, the study of the crystalluria remains an examination can be used in practice daily because of the constraints and technical difficulties of its realization<sup>1</sup>. At a known lithiasic patient, the supervision of the crystalluria in certain conditions, seems as an excellent indicator of the effectiveness

of medical treatment or at the contrary like a prognostic marker of the risk of stone recurrence in a lithiasic patient<sup>2</sup>. WERNESS<sup>3</sup> has well showed that the abundance of the crystalluria were different in the pathologies like the primary hyperparathyroidy with and without lithiasis, the primary hyperoxaluria or the stone recurrence idiopathic calcic lithiasis. Recently the clinical interest to determine crystalline volume was been brought in the follow-up of the patients cystinuric for the detection of the risk of stone recurrence<sup>4</sup> and it was shown in elsewhere for common calcic lithiasis, that the frequency of the crystals in the urine of the wake up was strongly correlate with the risk of stone

recurrence in a lithiasic patient<sup>5</sup>. In this work we have studied the crystalluria of the urines of the waking of 147 lithiasic patients before surgical treatment of their stones and compared with crystalline nature identified in the urines of the same subjects but after surgical operation and this to follow the evolution of the crystalline phases and to determine the supersaturation of the urines which reveal under the influence of the surgical treatment.

### Patients and methods

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234 urines of the wake up were examined about 147 stone formers (that is to say two samples per patient) hospitalized in the service of urology of the university hospitals (Oran, Mostaganem, Mohammadia,) for renal calculi. 147 lithiasic patients about 86 men and 61 women hospitalized before surgical intervention, their average age 43.5 years (extremes 10 years at 80 years). 87 lithiasic patients about 53 men and 34 women who have undergoes an operation where them stones was extracted surgically.

#### Methods

All the urines collected in sterile tubes after the first micturition of the morning are conserved at ambient temperature and are analyzed in the two hours following the emission.

#### Crystalluria

The urine homogenized is taken with the Pasteur pipette and placed in Malassez cell. The identification of nature and the numeration of the urinary crystals and the determination of the average and maximum sizes are to carry out for each crystalline species and separately, for the aggregates were realized using an optical microscope ZEIZ equipped with polarization. The crystals were identified by their morphology and their characteristics in polarized light according to the protocol and criteria's described before<sup>6,7</sup>.

Besides, pH measurement of urine were systematically performed with the pH-meter as of reception at the laboratory. The results of the study of crystalluria were expressed in terms of frequency and nature of the majority species crystalline according to the surgical treatment and the sex of the patients.

## RESULTS

Table 1 gathers the whole of the results relating to the nature and the frequency of the crystalluria for each group of subjects according to the surgical treatment. The positive crystalluria registered at the lithiasic subjects before and after operation was 98.6% and 86.6% respectively in contrary to the witnesses it presented 30% at the direct examination. If we make a difference between the positive of the pure crystals and mixed frequency of the crystalluria one notes generally that the frequency of the pure crystals before and after operation was 41.3% and 38.6% respectively, but the frequency of the associated crystals was 58.6% before operation and 61.3 after surgical treatment.

On the level of the crystals observed individually the crystalline species most frequent in all the studied samples that is to say before or after surgical operation and the calcium oxalate which crystallizes in the form of weddellite (calcium oxalate dihydrate) with a frequency of 35.9% as follows distributes 18.6% before operation, 17.3% after operation. What proves that there is a waning on the level of this majority crystalline species, whereas whewellite (calcium oxalate monohydrate) its recorded global frequency was 19.6% that is before or after surgical treatment, where we notice a fall of his frequency (7.9%) after operation by report/ratio that before operation (11.7%). For the crystals of phosphatic nature its total frequency registered was at the two groups 12.6%, as follows distributes the frequency of the 1st group (subjects not operated) was 4.7% and 7.9% for the 2nd group (subjects operated), which gives sign that the frequency of phosphates is increased after the surgical treatment and this for struvite like the brushite (4.1%, 0.6%) before operation and (5.3%, 2.6%) after operation respectively. The total frequency of the uric acids marked was 9.4% where we see an increase at the level of the frequency (4.0%) of the uric acid dihydrated after intervention than before medical treatment (2.7%) on the other hand the frequency of the anhydrous uric acid it remains constant (1.3%) at the two groups without difference. Finally for complex amorphous urates its frequency before surgical treatment was 2.0%, but after treatment are eliminated completely.

**Table - 1: Frequency of pure and associated crystals for the lithiasic patients before and after the surgical treatment**

Pure crystals	Before operation		After operation		Global crystalluria	
	<i>nombre</i>	%	<i>nombre</i>	%	<i>nombre</i>	%
Cr+	145	98.6	75	86.2	220	94.0
Calcium oxalates	<b>44</b>	<b>30.3</b>	<b>19</b>	<b>25.3</b>	<b>63</b>	<b>28.6</b>
Wh	17	11.7	06	7.9	23	10.4
Wd	27	18.6	13	17.3	40	18.1
Phosphates	<b>07</b>	<b>4.7</b>	<b>06</b>	<b>7.9</b>	<b>13</b>	<b>5.9</b>
Str	06	4.1	04	5.3	10	4.5
Br	01	0.6	02	2.6	03	1.3
Uric acids	<b>06</b>	<b>4.1</b>	<b>04</b>	<b>5.3</b>	<b>10</b>	<b>4.5</b>
UAD	04	2.7	03	4.0	07	3.1
AUA	02	1.3	01	1.3	03	1.3
CAU	03	2.0	00	00	03	1.3
Total	60	41.3	29	38.6	89	40.4
<b>Associated crystals</b>	<b>85</b>	<b>58.6</b>	<b>46</b>	<b>61.3</b>	<b>131</b>	<b>59.5</b>

Cr+ : positive crystalluria, Wh : whewellite, Wd : weddellite, Str : struvite, Br : brushite, AUD : uric acid dihydrated, AUA : anhydrous uric acid, CAU : complex amorphous urates.

**Table- 2: Frequency of crystalluria for the lithiasic patients before and after the surgical treatment according to the sex.**

Pure crystals	Before operation				After operation			
	Men		Women		Men		Women	
	<i>nombre</i>	%	<i>nombre</i>	%	<i>nombre</i>	%	<i>nombre</i>	%
Wh	22	7.5	12	4.1	08	5.3	04	2.6
Wd	32	11	22	7.5	18	12	08	5.3
Str	04	1.3	08	2.7	02	1.3	06	04
Br	02	0.6	00	00	02	1.3	02	1.3
UAD	04	1.3	04	1.3	02	1.3	04	2.6
AUA	02	0.6	02	0.6	02	1.3	00	00
CAU	02	0.6	04	1.3	00	00	00	00
Total	68	23.4	52	17.9	34	22.6	24	16.0
<b>Associated crystals</b>	<b>102</b>	<b>35.1</b>	<b>68</b>	<b>23.4</b>	<b>62</b>	<b>41.3</b>	<b>30</b>	<b>20.0</b>

The associated crystals their frequencies at the men increased after treatment compared to the women which A fell from 23.4% to 20% under the same conditions.

### Sex and crystalluria

At the level of the positive crystalluria registered during this work as far as the sex, we note a very important reduction in the frequencies after treatment than before for the two sexes (58.6%, 41.3% women), (64.0%, 36.0% men). With regard to the pure crystalluria among women one

distinguishes the crystalline species from type calcium oxalate dihydrate and majority with a frequency of 7.5% before operation compared to the other crystalline species registered, for the men was 11,0%. After operation the frequency of this species decreased among women (5.3%) on the other hand it increased at the men (12%). The total

**Table - 3: Correlation between of major crystalline species and medium pH**

Crystals	medium	pH
<b>Pure</b>	Wh	6.03
	Wd	6.02
	Str	7.66
	Br	7.03
	AUD	5.77
	AUA	5.70
	UAC	5.87
<b>Mixed</b>	Wh+UAC	5.59
	Wh+ Wd	6.18
	Wd+ UAC	5.83
	Wh+Str	6.97
	Wh+Br	7.35
	Wh+Wd+ AUD	6.37
	Wh+Wd+Str	7.11

frequency of the crystalline species of type calcium oxalate monohydrate observed at the men was 7.5% for the women was 4.1% before surgical treatment in the contrary we have noticed a fall down of the frequency of this species without difference at the two sexes as shows in the chart table 2. For the other crystalline species observed during this analysis of the urines of the lithiasic subjects before and after medical treatment one noted an increase in the frequencies of the crystals of the type struvite, brushite and uric acid dihydrated exceptionally among women after surgical operation. With regard to complex amorphous urates one has to determine that it has an elimination total of these crystals after surgical operation at the two sexes.

#### Correlation pH crystals

As table 3 shows it the domain of the pH registered according to results of this analysis ranged between 5.59 and 7.66 and at the same time it is more acid in 69% for all the samples studied without difference between before or after medical treatment. The crystals observed either pure or mixed under the microscope found their domain of pH, for the uric acids and the oxalates the pH is inferior than 7 while for phosphates is higher than 7.

## DISCUSSION

The urinary calculi is a frequent pathology which affects approximately 10% of the population of the occidental countries. Its prevalence has increased considerably during 50 last years which have seen the progression<sup>8</sup>. In Algeria as in the other countries the urinary calculi is oxalo-calcic with 61.2%<sup>9</sup>. In the developing countries where the successive epidemiologic data are available, we note the increase in prevalence of the urinary calculi of the adult and the reduction in the prevalence of the vesicle calculi<sup>10</sup>. The examination of the crystalluria observed on the urines at wake up of 147 lithiasic patients either before or after operation show that the frequency of the crystals is overall superior since 94% of the taking away examined containing of the crystals against 60 to 70% at the lithiasic idiopathic<sup>11,12,13</sup>.

The comparison of the urines collected before and after surgical operation highlight a significant fall from 98.6% to 86.2% of the crystalluria after the surgical gesture. The interpretation of this fall of frequency would require complementary investigations to make part it the traumatism renal resulting from the urological treatment of stone, therapeutic measurements engaged after the intervention and from the modification of the alimentary habit of the subject hospitalized since several days and operated recently, who is not any more in situation to nourish itself like a patient not hospitalized in free diet. Under these conditions and being given the very high frequency (98.6%) with which we observe crystals on the taking away before intervention, we can consider that this one is sufficient to detect the biochemical anomalies responsible for the crystalluria and to propose to the clinician an orientation on the composition of stone in complement of the radiological data obtained in addition.

The crystalline species most frequently identified was the weddellite, detected in (18.1%) of the urines. Its calcium-dependent character, well-known today, makes of it a marker of the hypercalciuria of debit or concentration. The comparison of the urines before and after intervention almost did not show a difference in the

frequency of the crystalluria of weddellite, on the other hand whewellite is observed in 10.4% of the urines analyzed with a difference in frequency marked well before operation (11.7%) and after operation (7.9%). Its oxalate-dependent character is well-known also like a marker of the hyperoxaluria. It is remarkable that the presence of whewellite crystals strongly correlates to the dominant presence of whewellite on the level of stones. This form of lithiasis is frequent in Algeria as testifies some the high frequency (48%) to majority whewellite stones observed in the Algerian West<sup>9</sup>. Struvite is directly related to the existence, of a urinary infection with particular germs, was identified in (4.5%) of the studied urines is 4.5% before treatment and 5.3% after treatment what testified to a secondary infection urinary would require an examination cytobacteriologic of urines (ECBU). This variety of lithiasis is that which generally leads to the renal insufficiency, because it can remain ignored a long time and thus arrive at the quiet destruction of the kidneys. Finally for the uric acids and urates their frequencies is relatively very weak compared to the other identified species. Its character is pH-dependent. This type of lithiasis is often frequent and meets more and more in the

industrialized countries<sup>14</sup>. For the mixed crystalluria their frequencies was 59.5% what explains the increase increased in the frequencies of the mixed calculi<sup>15</sup> which often takes its origin in a co-education of the crystalluria.

## CONCLUSION

Our study confirms previous work highlighting a frequency increased of the crystalluria at the subjects lithiasic as compared to the healthy subjects (nonlithiasics)<sup>16,17,18,19,20</sup>. Few work studied the correlation between the crystalluria and urinary stones extracted by the surgical treatment way<sup>21</sup>. The examination of the crystalluria observed on the first urines at wake up of 147 stone formers included in the study presented here shows that the presence of the crystals is overall almost 3 times superior (94%) with that noted at the normal subjects (30%) and that were completely comparable with the frequencies published. The whole of our results shows many parameters are implied in the phenomenon of formation of a crystalluria such as the sex, pH, diet and the surgical treatment this last which seems therapeutic effect used in the prevention of the lithiasic recurrence.

## REFERENCES

- Mbarki M., Jabrane. J., Ossama A., Daudon M. Etude de la cristallurie des sujets diabétiques. *Prog. Urol*, **15** 420- 426 (2005).
- Daudon M. Critères d'interprétation d'une cristallurie. *L'Eurobiologiste*. Tome XXVII, 203 (1993).
- Werness PG., Bergert JH., Smith LH. Crystalluria. *J. Cristal Growth*, **53**: 166-181 (1981).
- Daudon M., Cohen-Solal F., Barbey F., Gagnadoux M.F., Knebalmann B., Jungers P. Cystine crystal volume determination: a useful tool in the management of cystinuric patients. *Urol. Res*. **31**: 207-211 (2003).
- Daudon M., Hennequin C., Boujelben G., Lacour B., Jungers P. Serial crystalluria determination and the risk of recurrence in calcium stone formers. *Kidney. Int*, **67**: 1934-1943 (2005).
- Daudon M., Cohen-Solal F., Lacour B. Etude de la cristallurie : réalisation pratique et signification clinique. *Feuillets de biologi*, **43**: 31-53 (2003).
- Daudon M., Jungers P., Lacour B. Intérêt clinique de l'étude de la cristallurie. *Annal. Biol. Clin*, **62**: 379-393 (2004).
- Daudon M. Epidémiologie actuelle de la lithiase rénale en France. *Annales d'Urologie*, **39**: 209-231 (2005).
- Harrache D., Mesri Z., Addou A., Semmoud A., Lacour B., Daudon M. Analyse des calculs urinaires de l'adulte dans l'Ouest algérien par spectroscopie infrarouge à transformée de Fourier. *Eurobiol*, **31**: **69** (1997).
- Asper R. Epidemiology and socioeconomic aspects of urolithiasis. *Urol. Res*, **12**: 1-5 (1984).
- Leusmann DB., Blascheke W. Result of 5035

- stones analyses: a contribution or epidemiology of urinary stone disease. *Scand. J. Urol. Nephrol*, **24**: 205-10 (1990).
12. Yoshida O., Terai A., Okada Y. National trend of the incidence of urolithiasis in Japan From 1965 to 1995. *Kidney. Int*, **56**: 1899-904 (1999).
  13. Daudon M., Jungers P. Clinical value of cristalluria and quantitative morphoconstitutional analysis of urinary calculi. *Nephron Physiol*, **98**: 31-6 (2004).
  14. Jungers P. Les calculs urinaires. *Ed, Herman Paris*. ISBN 270.56 60 712. France (1987).
  15. Réveillaud R.J., Daudon M., Protat M.F., Ayrole G. Analysis of urinary calculi in adults. Attempt of correlations between morphology and composition. *Eur. Urol*, **6**: 161-165 (1980).
  16. Daudon M., Protat M.F., Réveillaud R.J., Rouchon M. Etude de la cristallurie spontanée par spectroscopie infrarouge. Recherche de corrélation entre les cristaux, calculs, les germes et le sexe des malades. *Ann. Biol. Clin*, **41**: 199-207 (1983).
  17. Hallson P.C., Rose G.A. Crystalluria in normal subjects and in stone formers with and without thiazide and cellulose phosphate treatment. *Br. J. Urol*, **48**: 515-524 (1976).
  18. Kacem B., Kaid-omar Z., Daudon M., Semmoud A., Lacour B., Bougeard D., Addou A. Comparison of crystalluria in patients drinking either free or controlled water intake. *Biosciences. Biotech. Research. Asia*, **2**(2): 93-98 (2004).
  19. Robertson W.G., Peacock M. Calcium oxalate crystalluria and inhibitors of crystallization I recurrent renal stone formers. *Clin. Sci*, **43**, 499-506 (1972).
  20. Werness P.G., Bergert J.H., Smith L.H. Crystalluria. *J. Crystal Growth*, **53**, 166-181 (1981).
  21. Kaid-Omar Z., Daudon M., Attar, A., Semmoud A., Lacour B., Addou A. Corrélation entre cristalluries et composition des calculs. *Prog*, **9**, 633 (1999).