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Prediction of successful treatment by extracorporeal shock wave lithotripsy based on crystalluria-composition correlations of urinary calculi

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ABSTRACT

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Objective: To provide correlations between crystalluria and chemical structure of calculi *in situ* to help making decision in the use of the extracorporeal shock wave lithotripsy (ESWL).

Methods: A crystalluria study was carried out on 644 morning urines of 172 nephrolithiasis patients (111 males and 61 females), and 235 of them were *in situ* stone carriers. After treating by ESWL, the recovered calculi have been analyzed by Fourier transform infrared spectroscopy and their compositions were correlated to the nature of urinary crystals.

Results: We obtained successful treatment for 109 patients out of 157 and 63 patients out of 78 with stones had a treatment failure (33.2%). The correlations showed that for the overwhelming crystalluria containing calcium oxalate dihydrate (COD) with mixed crystals without calcium oxalate monohydrate, we should have 68% to 88 % success rate. However, the obtained result was 79%. Similarly, for crystalluria with COD + calcium oxalate monohydrate ± carbapatite, the prediction was 11% to 45% and the result was approximately 39%. When the majority of crystalluria was calcium phosphate, the prediction of 50% to 80% was confirmed by 71% success rate. For those majority containing magnesium ammonium phosphate hexahydrate (struvite) ± diammonium urate ± COD, we predicted between 80% to 100%, and the result gave a success rate of 84%.

Conclusions: The analysis of crystalluria of morning urine can help to know the composition of calculi *in situ* and can predict the success rate of ESWL for maximum efficiency.

1. Introduction

Currently, extracorporeal shock wave lithotripsy (ESWL) has become the treatment of choice for urinary stones. It allows treating without intervention or endoscopic procedure. Sometimes other methods are associated to the ESWL such as the percutaneous surgery in order to obtain complete calculi extraction. A radiological control after surgery can highlight stone fragments not evacuated by the patients[1-3]. The total or partial removal of calculus or its fragments determines the criterion of successful treatment like the conventional surgery

where the persistence of a calculus, even small, was considered as a treatment failure. One difficulty of treatment by ESWL is the total elimination of fragments which depends on the urinary flow, the location of the calculus, its initial size, compositions and its ability to resist fragmentation. The most sensitive urinary calculi compositions to ESWL are calcium oxalate dihydrate (COD), carbapatite (CA), magnesium ammonium phosphate hexahydrate [struvite (ST)] or uric acid (UA). However, the calcium oxalate monohydrate (COM), brushite (BR) and cystine calculi are much more resistant to ESWL[4]. It would therefore be useful to know in advance the nature of urinary calculi *in situ* so as to propose the best treatment. The radiographic appearance of urinary calculi allows to some extent the prediction of their nature[5], but it is often of a limited reliability[6-9]. Kaid-Omar *et*

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al.[10,11] have correlated the crystalluria of preserved urines for 48 h at 4 °C with the composition of the calculi with a prediction in most cases. This study had not been validated at that time due to lack of lithotripter and the open surgery was the primary mode of treatment[10-12]. Moreover, crystalluria was not performed on the morning urine.

The aim of this work is to propose correlations between crystalluria of morning urine at room temperature and *in situ* composition of urinary stones recovered after fragmentation by ESWL. Correlations provide a basis for predicting the success rate for this type of treatment. Such correlations may assist the clinician in the choice of the therapeutic strategy to adopt and avoid complications for patients and persistence of residual fragments recognized as sources of recurrence[13].

2. Materials and methods

2.1. Patients

The urology department of Oran University Hospital has acquired a lithotripter shock wave Electroconductives (Sonolith Praktis) equipped with a dual tracking system with fluoroscopy and ultrasound. From May 2006 to June 2011, the hospital received 2360 patients with nephrolithiasis, 1884 (79.8%) of them were treated with ESWL, 397 patients (16.8%) underwent conventional surgery, and 79 patients (3.4%) had spontaneous expulsion. Our study focused on 172 patients, 111 males and 61 females, a sex ratio of 1.82. The mean age was 41.6 years. The youngest was 12 years and the oldest was 70 years. All patients underwent a study of crystalluria on morning urine before ESWL treatment and fragment calculi analysis by Fourier transform infrared spectroscopy (FTIR). Radiological and/or ultrasound tests prior to ESWL treatment helped to clarify calculi number and topography. A total of 235 calculi were identified with a ratio of 1.36 per patient.

2.2. Crystalluria

Study of urinary crystals on the first morning urine was performed with an optical microscope equipped with the polarization. Several morning urine were collected from patients between 4 and 9 days before being processed by ESWL. In total, 644 samples were examined with an average of 3.7 per patient urine. The urine was stored at room temperature and examined within 2 h after urination. After homogenization of urine by gentle stirring and turning, a sample was taken by using a Pasteur pipette, transferred to a Malassez cell and immediately examined under the microscope[14]. This analysis included a review of cytology, a count of any crystal species crystalline under a

magnification of 400 times, a pH measurement and density measurement[15].

2.3. Extracorporeal lithotripsy

The average size of the stones treated with ESWL ranged from 6 mm to 25 mm. The evacuation of fragments is neither always complete nor immediate. Radiological examination days after the intervention often revealed fragments which were not removed from the patients[16]. The assessment of the ESWL results was made by reading the ultrasound or radiography of the abdomen without preparation or by intravenous urography carried out in the third month. The outcome criteria were defined as follows: (i) the absence of residual fragment (ARF) confirmed by the abdomen without preparation and/or the presence of one or more fragments which were smaller than 4 mm on ultrasound was considered as a treatment success; (ii) the presence of one or more residual fragments (PRF) which were bigger than 4 mm highlighted during the last consultation was considered as a failure.

2.4. Urinary calculi

The calculus is an essential element of etiological diagnosis of the disease, since it is virtually the only witness during the course of lithogenic biochemical disorders which is responsible for its formation. Its analysis is very important from the clinical point of view. We performed a morphological analysis by using a dissecting microscope and spectroscopic study by FTIR allowing a quick way to determine the molecular composition and crystallinity of the calculus[17,18].

3. Results

3.1. Anatomical location

The distribution of calculi based on their anatomical location and the sex of patients are given in Table 1 which shows the absence of laterality for the kidney (38.7% in the left kidney against 37.0% in the right kidney) or for the ureter (14.5% in the right ureter against 9.8% in the left ureter).

Table 1
Anatomical location by sex of patients.

Location	Males		Females		Total		Ratio M/F
	n	%	n	%	n	%	
Left kidney	63	40.9	28	34.6	91	38.7	2.25
Right kidney	58	37.7	29	35.8	87	37.0	2.00
Left ureter	15	9.7	8	9.9	23	9.8	1.87
Right ureter	18	11.7	16	19.7	34	14.5	1.12
Total	154		81		235	100.0	1.85

The accurate location of calculi in the kidney or the ureter (Table 2) showed that 52.3% were located in the pelvis, 23.4% in the calyx and 24.3% in the ureter with a predominance of lumbar ureter ($P < 0.001$).

Table 2

Distribution of urinary stones in terms of anatomical site.

Location of calculi	Number of calculi	frequency (%)
Calyceal stone	Superior	11
	Median	24
	Inferior	20
Renal pelvis	123	52.3
Iliac ureter	11	4.7
Lumbar ureter	39	16.6
Pelvic ureter	7	3.0
Total	235	100.0

3.2. Urine

Out of 644 analyzed morning urine samples, 493 had a positive crystalluria (76.5%). Twenty two (12.8%) out of the 172 patients included in the study, have never presented any crystals in their urine. Table 3 summarizes the frequencies of the different identified crystals. Calcium oxalate was the most common major compounds (35.4%), COD representing 25.0% of cases and 10.4% of cases were COM. Calcium phosphates formed the majority in 22.1% of cases with a predominance of amorphous calcium carbonate phosphate (ACCP, 15.1% of cases), BR representing 7.0% of cases. Amorphous urates complex (AUC) was observed in 19.8%, ST in 11.6%, and UA in 7.0% of cases, ammonium urate acid (AUA) and cystine respectively in 2.9% and 1.2% without any significant differences between sexes.

Table 3

Frequency of the majority urinary crystals before ESWL. %.

Lithogenic crystals in urines	Males	Females	Total
Calcium oxalate	COD	27.0	21.3
	COM	10.0	11.5
Calcium phosphate	ACCP	15.3	14.8
	BR	6.3	8.2
ST	10.8	13.1	
AUA	4.5	0.0	
AUC	18.0	23.0	
UA	7.2	6.5	
Cystine	0.9	1.6	

3.3. ESWL

All patients were treated with 1 to 3 ESWL sessions with an average of 2.01 per patient. The distribution of locations of 235 calculi present in 172 patients according to the result of treatment success (ARF) and failure (PRF) was shown in Table 4. The results also showed that 66.8% of calculi have been totally eliminated

since there was no residual fragment and 33.2% had residual fragments after treatment. Out of 172 patients, 109 (63.3%) were successful (ARF) and 63 (36.7%) had a failure (PRF).

Table 4

Distribution of stones treated with ESWL.

Location of calculi	PRF	%	ARF	%	Total
Kidney	44	24.7	134	75.3	178
Calyceal stone	Superior	3	27.3	8	72.7
	Median	11	45.8	13	54.2
	Inferior	15	75.0	5	25.0
	Pelvis	15	12.2	108	87.8
Ureteral stone	34	60.3	23	39.7	
Lumbar ureter	23	59.0	16	39.0	
Iliac ureter	4	36.4	7	63.6	
Pelvic ureter	7	100.0	0	0.0	
Total	78	33.2	157	66.8	235

The results in Table 4 showed that the ESWL was more effective for kidney stones than those of the ureter (ARF = 75.3% versus 39.7%). In the kidney, the act has proved particularly effective for pelvis calculi (87.8% ARF) and the upper calyx calculi (ARF = 72.7%). The iliac ureteral stone (63.6%) seems to have been fragmented more efficiently than those in the lumbar ureter, but due to the small number of cases, the difference is not statistically significant. The locations leading to the higher proportion of failures were the kidney with the lower calyx (ARF = 25.0%) and those of the pelvic ureter (ARF = 0).

3.4. Analysis of recovered calculi

All fragments of calculi were recovered and analyzed by FTIR spectroscopy. Table 5 shows the compositions of these calculi. After treatment, 51.6% of evacuated calculi consisted of calcium oxalate (40.8% COM and 10.8% COD); 21.6% consisted of CA and 15.3% consisted of ST. Uric acid anhydrous (UAA) accounted for 6.4% and 5.1% of AUA. Calculi recovered by surgery due to a total or partial failure had a different composition than the foregoing. Table 5 shows that 66.7% of calculi were composed of calcium oxalate (COM 50.0% and COD 16.7%). And 18.0% of calculi were calcium phosphates, 7.7% of UAA, 3.8% of ST, 2.5% of cystine and 1.3% AUA.

Table 5

Compositions of urinary stones obtained after successful ESWL. n (%).

Main constituents	Number of calculi	ARF	Number of calculi	PRF
Calcium oxalates	COM	17 (40.8)	39	(50.0)
	COD	64 (10.8)	13	(16.7)
Calcium phosphates	CA	34 (21.6)	13	(16.7)
	BR	0 (0.0)	1	(1.3)
ST	24 (15.3)	3	(3.8)	
UAA	10 (6.4)	6	(7.7)	
AUA	8 (5.1)	1	(1.3)	
Cystine	0 (0.0)	2	(2.5)	
Total	157 (100.0)	78	(100.0)	

Table 6

Correlations of crystals-urinary stones and prediction of success.

Lithogenic crystals	Number	Compositions of calculi	Success obtained after ESWL	% of success in relation to the major constituents	
COD ± COM (N = 43)	12	COD + CA + COM ± ACCP	10	If composition of stone prevails in COD (86.1% of success)	
	10	COD + COM + CA	9		
	8	COD + CA + COM + PROT	6		
	6	COD + CA + ACCP	6		
	4	COM + COD + CA + ACCP	1		In COM (25%)
	2	UA + COM + COD	2		In UAA (100%)
	1	BR + COM + COD	0		
Total	43		34 (79.1%)		
COD ± COM (N = 18)	2	COD + CA + ACCP + COM	1	In COD (57.1%)	
	2	COM + COD + WIT + trace of proteins	0		
	3	COD + BR + CA	1		
	2	COD + COM + UAA + CA	2		
	4	COM ± COD ± CA ± ACCP ± UAD	1		In COM (16.7%)
	3	UAA + COD + CA	0		
	2	CA + COM + COD	2		In CA (100%)
Total	18		7 (38.9%)		
Phosphates (N = 38)	21	CA + COD ± ST ± UAA	17	In CA (80.9%)	
	11	COD ± CA ± ACCP ± WIT ± trace of proteins	7		In COD (69.2%)
	3	COM + CA + ACCP	1		In COM (33.3%)
	1	BR + CA + ACCP	0		
	2	COD + CA + ST + trace of proteins	2		
Total	38		27 (71.05%)		
ST ± ammonium urate (N = 25)	22	ST + CA ± COD ± PROT ± UAA	18	In ST (81.8%)	
	1	COD + CA + COM	1		
Total	2	CA + COD + PROT + COM	2		
	25		21 (84%)		
AUC + COD ± COM (N = 34)	11	COM ± COD + CA + trace of proteins	4	In COM (25.8%)	
	2	COM + COD + UAD	0		
	13	COM + COD + apatite	4		
	5	COM + COD	0		
	2	UA + COM + trace of proteins	2		In UA (100%)
	1	ST + CA + COD + COM	0		
Total	34		10 (29.4%)		
UA ± COD ± AUC (N = 12)	3	UAA ± COM + PROT	3	In UAA (100%)	
	2	UAA + PROT + COD	2		
	3	UAD + UAA + COM + COD	3		
	4	COM ± COD + CA ± WHIT ± PROT	2		In COM (50%)
Total	12		10 (83.3%)		
Cystine (N = 2)	2	Cystine	0	In cyst (0%)	

3.5. Correlations between crystalluria, composition calculation and prediction of success

Results summarized in Table 6 highlighted several profiles of crystalluria. Pure or dominant crystalluria of COD but not COM were associated mainly with COD calculi. The crystalluria which contained COM with or without COD was associated with COM calculi. Calcium phosphate crystalluria was present with phosphate-rich calculi. The AUC crystalluria majority associated with or not with COD/COM were correlated with COM calculi. As for crystalluria which were mainly UA associated with or not with COM and AUA complex, they were present in the urine of patients who had high uric acid calculi. Cystine was observed in two patients who had pure cystine calculi.

4. Discussion

Currently, the first act of choice for the removal of urinary calculus is the ESWL. This is a recently used technique in the University Hospital of Oran, but that is already widely established in the world. It allows more than 80% fragmentation of renal calculi. Its effectiveness remains high despite the disposal problems that may arise as a result of the act and expose the patient to one or more additional actions for the treatment of residual fragments[19]. The success of the ESWL depends on several parameters such as the size, the anatomical location, the shape and the compositions of the calculus[20], hence it is important to develop methods and/or techniques to predict *in situ* the compositions before offering the ESWL treatment[5-7,10]. Two studies have examined the correlations

of urine crystalluria with the nature of urinary stones. The first proposed by Cohen *et al.*[21] focused on the prediction of the compositions of calculi before lithotripsy correlated with crystalluria nephrolithiasis of subjects before the treatment. In this study, the correlation was limited to the differentiation of chemical species and distinction of pure or mixed crystalluria; the latter appeared to correspond to less fragmented calculi which required in half of the cases an additional percutaneous surgery[7]. A study by Kaid-Omar *et al.*[10] examined the correlations between crystalluria and *in situ* compositions of calculi, but the results could not be validated because of the absence of lithotripter at the time in the University Hospital of Oran. In addition, the study focused on urine crystalluria stored for 72 h at 4 °C, which can be a disadvantage in the logistics of sample collection or in the nature of observed crystals after cold storage as compared to those of fresh urine. It seemed more relevant in this work to correlate the crystalluria of morning urine on direct examination before the ESWL with the compositions of stones recovered after treatment. Indeed, crystalluria remains the image of biological urinary anomalies leading to lithogenic process. It allows to assess the level of supersaturation of urine which represents major therapeutic targets in the prevention of recurrent nephrolithiasis[14,22]. It also provides evidences on the predominant nature of the calculus[14].

In our study, the overall incidence of positive crystalluria of morning urine from nephrolithiasis subjects was 76.5%. The most frequently observed crystalline species (crystal) was COD which was detected in 25.0%; its calcium-dependent character makes a marker for hypercalciuria of flux or concentration[23]. Over 80% of these patients had calcium-dependent calculi riching in COD (Table 6). We can consider that the radio-opaque calculi associated with COD crystalluria without COM have a calcium-dependent structure and are therefore potentially friable and may be subject to treatment by ESWL.

The crystalluria COD with or without COM of 43 patients were correlated with major COD calculi with a success rate of 86.1%.

The pure COD crystalluria or mixed with COM of 18 lithiasic patients were correlated with major calculi COD and COM in 13 cases. Out of 7 patients who had major calculi COD, 4 (57.1%) were successful. For the 6 patients who had major calculi COM, only one success (16.7%) was recorded.

Phosphatic crystalluria of 38 patients were correlated with major phosphate calculi COD and COM. Out of 21 patients who had major carapatite calculi, 17 (80.9%) were successful. However, for the 3 subjects who had the majority COM, there was one success (33.3%). The case with a major BR resulted in failure, as the predictable result of COM and BR are known to be difficult to the ESWL treatment.

Calcium phosphates are dependent on crystalline species of the phosphaturia, calciuria and pH of urines. These latter two factors are largely predominant[8].

Pure cystine crystalluria of 2 subjects were correlated to pure

cystine calculi where no success was recorded. COM calculi, BR and cystine are more resistant to the ESWL treatment which resulted with the highest level of residual fragments[4]. By their mineral nature they may respond poorly to shock waves[4-10], making their treatment more complex with a subsequent increased risk of letting fragments capable of forming a new lithogenesis[4,11,16,17].

ST crystalluria with or without ammonium urate was found in 25 patients and correlated with ST-rich calculi. Such cases indicated the presence of infection composed mainly of struvite calculus. Out of 22 subjects who exhibited crystalluria correlated with the majority of ST, 18 (81.8%) had a successful treatment.

The crystalluria of UAC + COD ± COM of 34 nephrolithiasis were correlated with major COM calculi. Out of 31 subjects with major COM crystalluria, 8 cases (25.8%) showed a success. These results were expected given the resistance of COM to the ESWL treatment.

The crystalluria of UA ± COM ± UAC ($n = 12$) were correlated with major UA and COM calculi. A 100% success was noted for all calculi which showed a majority of compositions of anhydrous or UAD. However, for the major whewellite calculi the success was only 50%.

The presence of COM in urine can be seen as an indicator of oxalo-dependent calculus major COM whose resistance to modern urological treatments lithotripsy is often greater than COD calculi. Based on previous studies, the success rate of ESWL for calculi type COD and COM is 80% and 35% respectively, reflecting the fact that the hardness of the stones is an important factor in the resistance to the ESWL treatment[5,7].

In our work on 43 crystalluria correlated with major COD calculi, the success rate was 77.3%. This result confirms the ease of this type of calculi to be treated by ESWL and confirms the literature data. The success rate for the 18 crystalluria which was correlated with major COM calculi was 38.9%, a result close to the figures given in the literature (35%)[11]. The COM is a marker of debit or concentration of hyperoxaluria whose presence in the urine depends on both its content of calcium oxalate and oxalate molar ratio. However, the predominant type of calculi in Western Algeria is undoubtedly COM with a frequency of 50.3%[12], which may represents an important factor in treatment failure with ESWL. The *in situ* presence of other resistant calculi, even in small proportions may lead the surgeon to undertake another treatment strategy without risk to the patient and his kidney.

The study highlighted the prediction rate of successful treatment as compared with success rate after ESWL. Indeed, for crystalluria type COD + mixed (no COM), the prediction rate of success was 68%–88% and the result was 79.1%. For crystalluria of COD + COM (± CA), the prediction was 11%–45% and the result represented 38.9%. For those of calcium phosphates, we predicted between 50% and 80% and the result was 71.05%. Predicting the success rate of crystalluria type ST ± DAU ± COD was 80%–100% and we obtained 84%. As for crystalluria with AUC ± UAD ± COD, we predicted 20%–30% success and the success rate was 29.4%. Finally, the

predicted result of crystalluria type UAD ± COM was not consistent with the success rate obtained after treatment. Thus, the success rate was 83.3% and the prediction was 40%–50%.

Extracorporeal lithotripsy can now treat the majority of urinary stones. It can be considered as the first-line treatment for stones which are smaller than 2 cm in size. The risk of failure is increased especially when it comes to uneasily friable calculi.

To increase the success rate of this treatment, we have proposed correlations between crystalluria of morning urine and the compositions of stones *in situ*. Thus, from the identification of the major types of crystals presenting in the urine, it is possible to predict the success rate of lithotripsy and therefore avoid situations which may present post-treatment risks.

Conflict of interest statement

We declare that we have no conflict of interest.

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