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Analysis of urinary calculi composition by infrared spectroscopy: a prospective study of 625 patients in eastern China

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Abstract Urolithiasis is a common urologic disease whose prevalence is about 1–20% and increasing throughout the world. The recurrence rate after treatment is more than 50%. Urinary stone analysis is important in determining the possible etiology and the pathophysiology of stone formation. A better understanding of the stone composition may help prevent urinary stone formation. From March 2007 to December 2008, physical analysis of urolithiasis in patients who lived in eastern China for more than 5 years and underwent surgery or shock wave lithotripsy in our hospital or passed their stones spontaneously was carried out using the Fourier transform infrared spectroscopy (FT-IR). Clinical and demographic findings were evaluated and compared with the stone components. Stone analysis was performed in 625 patients. The FT-IR evaluation showed that 234 (37.4%) were pure, and the most frequent was calcium oxalate (33.9%), followed by calcium phosphate (2.7%), and uric acid (0.8%). 391 (62.6%) were mixed stone, calcium oxalate (43.2%) was the most commonly major component, followed by calcium phosphate (16.3%), cystine (1.3%), uric acid (1.1%), and struvite (0.6%). Uric acid ($p = 0.029$) was the major component found more frequently in men, while struvite ($p = 0.037$) was more frequent in women. Uric acid ($p = 0.031$) was more common in lower urinary tract stones, and its formers with the mean age of 55 years were older than those with other components ($p = 0.039$). In eastern China, the most commonly found pure stone was calcium oxalate, while the most frequent mixed stone was calcium oxalate and calcium phosphate mixture. Stone location, gender, and age may influence stone component.

Keywords Urolithiasis · Epidemiology · Stone composition · Infrared spectroscopy

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Introduction

Urolithiasis is a common urologic disease whose prevalence is about 1–5% in Asia, 5–9% in Europe, 13% in North America, 20% in Saudi Arabia and increasing throughout the world [1–4]. The recurrence rate after treatment is more than 50% at a mean follow-up of 7 years [5]. Urinary calculi analysis is important in determining the possible etiology of stone formation and the pathophysiology of urolithiasis, as previously reported [6]. Fourier transform infrared spectroscopy (FT-IR), X-ray diffraction, simultaneous thermal analysis, polarized light microscopy, and scanning electron microscopy have been used in urinary stone physical analysis. FT-IR is now considered a standard method of stone analysis as it is very sensitive, selective, special for all components and requires minimal sample volume since it was first used in 1955 [7, 8].

We studied the characteristics and distribution of urinary stones using FT-IR and examined the relationship between

stone composition, location, age, and gender which has never been reported in China.

Materials and methods

From Mar 2007 to Dec 2008, physical analysis of urolithiasis in patients who lived in eastern China for more than 5 years and underwent ureteroscopy, shock wave lithotripsy, PCNL, open surgery or passed spontaneously was performed using the FT-IR (BRUKER TENSOR 27, Germany). Clinical and demographic findings were evaluated and compared with the stone components.

The stone samples were washed with distilled water and dried for 24 h at 60°C. The whole stones were cut in half along a plane, and samples were obtained from the core to the surface. When the stones were obtained in a fragmented form, all the fragments were obtained in order to establish their original intact form as far as possible. Dried stone powder sample was homogenized with dried potassium bromide of spectroscopic purity at a sample concentration of 1%. The mixed powder was ground into micrometer level in an agate pestle, and pressed to suitable disk with a diameter of 13 mm, and thickness of about 1 mm. The spectral range was set from 4,000 to 400 cm^{-1} and resolution was set at 4 cm^{-1}. We performed 32 scans for infrared data acquisition. Sample spectrum matched against computerized infrared database of stone components so as to identify and quantify the compositions of stone. The result was analyzed by chi-square test and *t* test using SPSS 13.0 statistical software. Statistical significance was defined as $p < 0.05$.

Results

Stone analysis was performed in 625 patients (449 males and 176 females) with a mean age of 47.0 (range 20–92) years. The majority of the stones were removed by lithotripsy or open surgery and the rest were passed spontaneously. Upper urinary tract stones were found in 574 patients, with 204 in kidney and 370 in ureter, while lower urinary tract stones were found in 51 patients, with 43 in bladder and 8 in urethra.

The FT-IR evaluation showed that 234 (37.4%) were pure stone, and the most frequent was calcium oxalate (33.9%), followed by calcium phosphate (2.7%) and uric acid (0.8%). 391 (62.6%) were mixed stone, calcium oxalate (43.2%) was the most commonly found major component, followed by calcium phosphate (16.3%), cystine (1.3%), uric acid (1.1%), and struvite (0.6%). (Table 1).

Calcium oxalate was detected in 586 stones (93.8%), it contained more than 50% of stone composition in 482 stones (77.1%) (whewellite in 305, weddellite in 177). 33.9% were pure calcium oxalate stone, 34.2% were calcium oxalate mixed with calcium phosphate and 9.0% were mixed with uric acid or protein. Calcium phosphate was found in 340 stones (54.4%), it contained more than 50% of stone composition in 119 stones (19%), mixed calcium phosphate stone were in 102 (16.3%) while pure calcium phosphate stone in 17 (2.7%). Uric acid was detected in 10.2% of the stone (64), it was major component in 1.9%, all of them were from males.

Uric acid ($p = 0.029$) was more frequently the major component in men as well as more common in lower urinary tract stones ($p = 0.031$), and its formers with the mean age of 55 years were older than those with other components ($p = 0.039$), whereas struvite ($p = 0.037$) was more frequent in women (Tables 2, 3).

Table 1 Relative proportion of urinary stone components

	Total no.	Constituents	No.	%
Pure	234 (37.4%)	Calcium oxalate monohydrate (COM)	169	27.0
		Calcium oxalate dihydrate (COD)	43	6.9
		Calcium phosphate (CaP)	17	2.7
		Uric acid (UA)	5	0.8
Mixed	391 (62.6%)	Calcium oxalate (CaOx) + CaP	214	34.2
		CaP + CaOx	94	15.0
		CaOx + UA	36	5.8
		CaOx + Protein	20	3.2
		CaP + UA + Struvite	8	1.3
		Cystine + CaOx/CaP	8	1.3
		UA + CaOx/CaP	7	1.1
		Struvite + CaOx/CaP/UA	4	0.6
Total			625	100.0

Discussion

As is well known, an accurate analysis of the stone composition may provide a scientific basis for the best choice of management and prevention and may help us study the mechanism for the formation of urinary stones [9]. There are many methods of stone analysis, such as chemical analysis and various physical analyses, which provide valuable information for the etiology, pathology, and physiology of urolithiasis. Among these, FT-TR is one of the most common ways to determine the urinary stone composition all over the world [8], which allows an accurate, efficient, precise quantitative method of stone analysis and separate zonewise analysis of the stone nucleus, external, and

Table 2 Distribution of urinary stone according to the gender of patients and location of stones

Constituents	No. (%)	Gender		*p* value	Location		*p* value
		Male (%)	Female (%)		UUT (%)	LUT (%)	
COM	305 (48.8)	220 (49.0)	85 (48.3)	0.874	286 (49.8)	19 (37.3)	0.085
COD	177 (28.3)	125 (27.8)	52 (29.5)	0.670	162 (28.2)	15 (29.4)	0.857
CaP	119 (19.0)	85 (18.9)	34 (19.3)	0.912	106 (18.5)	13 (25.5)	0.221
UA	12 (1.9)	12 (2.7)	0	0.029[a]	9 (1.6)	3 (5.9)	0.031[a]
Cystine	8 (1.3)	6 (1.3)	2 (1.1)	0.841	7 (1.2)	1 (2.0)	0.652
Struvite	4 (0.6)	1 (0.2)	3 (1.7)	0.037[a]	4 (0.7)	0	0.550
Total	625 (100)	449 (100)	176 (100)	0.100	574 (100)	51 (100)	0.165

[a] Chi-square test

$p < 0.05$

Table 3 Distribution of urinary stone according to the age of patients

Constituents	Age range	Age		*p* value
		Yes	No	
COM	20–92	47.0 ± 14.8	47.0 ± 13.8	0.966
COD	22–85	47.1 ± 13.1	46.9 ± 14.8	0.904
CaP	20–80	46.0 ± 14.1	47.2 ± 14.4	0.408
UA	30–75	55.4 ± 17.1	46.8 ± 14.2	0.039[a]
Cystine	23–76	47.0 ± 19.1	47.0 ± 14.3	0.998
Struvite	37–59	47.8 ± 9.2	47.0 ± 14.3	0.915

[a] *t* test

$p < 0.05$

internal layers. It is in effect a fingerprint of the constituent materials [10].

The main component of urinary calculi in industrialized countries is calcium oxalate, about 75–90% of urinary stones, followed by calcium phosphate or uric acid [11–13]. Our study showed that calcium oxalate was detected in 93.8% of the stones, which was major component in 77.1%. In south east of Asia, calcium oxalate stone was most commonly encountered in 68–80% followed by calcium phosphate [10, 14, 15]. Our findings are in agreement with these data.

The most commonly occurring urinary calculi are comprised of calcium oxalate and the pathogenesis of calcium oxalate calculi was poorly understood until quite recently. It may be associated with metabolic or genetic factors. Randall theorized that mineral depositions were initially located on the renal papillae before the development of calcium oxalate calculi, also known as Randall's plaque, which is considered an ideal site for an overgrowth of calcium oxalate and calcium phosphate to develop into calculi [16]. Randall's plaque was investigated in almost 100% calcium oxalate stone formers and 43% others [17]. The investigators have previously demonstrated that Randall's plaque is composed of apatite, a common crystalline phase of calcium phosphate. These deposits are thought to serve as initiating nidus for urinary crystal attachment and development into calculi [18]. However, we found only 44.4% (214/482) of calcium oxalate as pure or main component of calculi were mixed with calcium phosphate. Conversely, 79% (94/119) of calcium phosphate containing more than 50% of stone composition were mixed with calcium oxalate. In the sample we obtained, more than 70% was randomized fragmented sample from URL or ESWL rather than a sequential sample from the core to the surface, which may be the reason for this finding.

Maurice [19] demonstrated that correlations between the crystalline phase of the phosphates and the cause of calculi. The crystalline phase of 74% calcium phosphate is carbapatite: it can result from metabolic disorder (such as hypercalciuria, primary hyperparathyroidism, tubular acidosis) or chronic urinary tract infection, but the latter etiology is still debated. The carbonate rate of carbapatite above 15% was commonly related to urinary tract infection with urea-splitting bacteria. Conversely, the carbonate rate was frequently less than 10% in cases induced by metabolic disorders. Carpentier [20] found that the carbonate rate in those showing bacterial imprints on scanning electron microscopy was significantly greater than in those without a visible bacterial imprint and the close relationship between urinary tract infection and etiology of calcium phosphate was proved. Due to different cause of calcium phosphate, our data showed no significant difference between gender, location or age, and calcium phosphate stone rate.

The etiology of uric acid stone is still unknown. It may be related to insulin resistance, molecular, and genetic factors, which could influence urinary pH, and uric acid metabolism, and excretion [21]. A low urinary pH is the most significant element in the generation of uric acid stones with hyperuricosuria caused by purine metabolic disorder, that thereby induce the formation of calcium stones. When the amount of urine reduces, the sudden rise

of uric acid in the urine may also initiate the uric acid stone. It is reported that the incidence of uric acid stones is 5–9.7% of all kidney stones in the United States, and 17–25% in Germany, and as high as 18–40% in Israel [21]. In our study, uric acid stones make up 1.9% of all stones. These distinct geographical and ethnic variations in the incidence of uric acid stone development are compatible with environmental or genetic susceptibility in some populations [22]. Our data showed uric acid stone patients with the mean age of 55 years were older than that with other components. Daudon et al. [23] studied the data based on 27,980 urinary stones (from 19,442 males and 8,538 females) analyzed by infrared spectroscopy between 1976 and 2001. They found an increasing prevalence of uric acid stones with age in both genders. UA represented less than 2% of stones in patients under 30, and rose to 11.6% in the age class 50–59 years and in 40% aged 80 years or more in males. The proportion of uric acid stone rose continuously with age from 0% in the age class 10–19 years to 27.3% in patients aged 90 years or more in females. Their data showed a higher prevalence of uric acid stones in patients over 50 years in both genders. Hyperuricemia, low urine pH, reduced ammoniagenesis and insulin resistance characteristic of metabolic syndrome could be factors in uric acid stone in older patients.

The stone composition is different in terms of the different genders, which may relate to the different diet, anatomical structure, and metabolic disorder. Females suffered urinary tract infection more frequently compared with the males, which causes urine pH increase, and easy precipitation of magnesium ammonium phosphate. Daudon found that UA stones were about twice as frequent in males as in females in all age classes [23] and in non-diabetic patients [24], which could be associated with fast-absorbed sugars and lipids. Hereby, uric acid stones are more frequently detected in males, over against magnesium ammonium phosphate in females.

In conclusion, physical analysis of urinary stone with FT-IR provides important information on stone composition, distribution, and risk factors. The most commonly found pure stone was calcium oxalate, while the most frequent mixed stone was calcium oxalate and calcium phosphate mixture in eastern China. The result of this study may be associated with regional of residence, genetic factors, and nutrition. This finding shows a view of the present epidemiology of urinary stone composition in eastern China and may help improve our understanding of the pathophysiology of urolithiasis in the Chinese population.

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