

SCREENING FOR BIOCHEMICAL ABNORMALITIES IN UROLITHIASIS PATIENTS

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Background: The significance of biochemical screening in stone formers has been a debated topic. This study was conducted to investigate the frequency of biochemical abnormalities in our urolithiasis patients and to compare the abnormality between the first time and recurrent stone formers so that this information would help in assessing the value of biochemical screening in our practice. **Methods:** Over a twenty-one month period, new and recurrent stone disease patients had one random blood specimen and two random 24-hour urine collections analysed for biochemical abnormalities. Serum was checked for calcium, urate, phosphate and creatinine. The urines were measured for volumes, calcium, oxalate, urate, citrate, cystine and pH. **Results:** Out of total of 113 patients, 83 (73%) had some urinary or blood abnormality. Highest number of abnormalities were in urine. Low volume 33 (39.76%), hypercalciuria 33 (39.76%) and hyperoxaluria 20 (24.1%) were the main urinary abnormalities. Elevated serum creatinine in 10 (12.05%) was commonest blood abnormality. Females had significantly higher frequencies of low urinary volume (48% vs 21%, $p=0.001$), hyperoxaluria (38% vs 11%, $p=0.002$) and hypocitraturia (37% vs 0%, $p<0.001$). There was no significant difference of abnormality rate between first time and recurrent stone formers. **Conclusion:** A high frequency of urinary biochemical abnormality and equal abnormality frequencies among first time and recurrent stone formers highlights the significance of biochemical screening even in cases of initial stone presentation. We feel such diagnostic evaluation would help in providing precise treatment and efficient prophylaxis.

Key Words: Urinary Calculi, Hyperoxaluria, Hyperuricaemia, Citric acid, Oxalic acid, Creatinine.

INTRODUCTION

Over the years, there has been increasing interest in the aetiology of urinary stone formation. The search has also focused on the detection of specific biochemical abnormalities of the blood or in urine that would characterize patients with primary or recurrent urinary calculi. Now, there is convincing evidence that by treating specific biochemical abnormalities stone recurrence rate can be reduced.¹⁻⁶ The treatment measures could either be the "stone clinic effect" that is fluid plus dietary recommendations¹ or drug therapy²⁻⁵ and also combination of medical with shock wave lithotripsy.⁶ Regular metabolic screening for stone disease is not practised by all urologists, especially in the first time stone formers; however the importance of identifying risk factors in the ailment is gaining recognition.^{7,8}

Before deciding on a management protocol for our stone disease patients, we investigated for the presence of biochemical abnormalities in our patients representing a typical UK district general hospital practice. In addition, we also examined the differences of such abnormalities between first time and recurrent stone formers. This assessment was to help us determine whether metabolic screening of our patients would play some role in our management, especially in the case of the first time stone formers.

MATERIAL AND METHODS

Over a period of one year and nine months (March 1995 to December 1996), patients with stone disease presenting to the Departments of Urology & Nephrology at Lister Hospital, Stevenage England, had standardised biochemical screening by looking at a random specimen of blood and two random 24-hour urinary specimens.

The blood specimen check included calcium, urate, creatinine, phosphate and bicarbonate, whilst the urine specimen examination included volume assessment and checking the levels of calcium,

oxalate, urate, citrate; urinary pH and spot cystine were also checked. Each stone screen cost £35.

A low urinary volume was defined as a volume < 1500 ml / 24 hours in both urinary samples. The normal values for other tests were maintained as determined by the standards of the hospital laboratory.

For statistical analysis, Fisher's Exact test was used.

Results

The total number of patients was 113 including 84 (74%) males and 29 (26%) females. The mean age of patients was 49 (range 14-81) years.

The significant finding of the study was the surprisingly high overall frequency of abnormalities. Out of 113 patients, 83 (73%) had an abnormality in either the blood or urine specimen. Males had 69% (n=58) overall abnormalities, whilst 85% females (n=25) showed abnormalities. This gender difference was however not significant (p=0.0894). The highest number of abnormalities was in the urine.

There was no statistical difference of abnormalities between first time and recurrent stone formers. Females had higher frequencies of low urinary volumes, hyperoxaluria and hypocitraturia. Young patients (<35 years) were 17 (20.5%) in number with a mean age of 28 years (range 17-35 years). The abnormalities were present in 14 (86%) patients in this young age group. The main abnormality in this group was low urinary volume (47%). Family history of stone disease was noted in 2 (12%) of the young group.

Among the urinary abnormalities, the most common abnormality was a low urinary volume noted in 33 patients (39.76%). Exactly the same number of patients had hypercalciuria. The next common abnormality was hyperoxaluria noted in 20 patients (24.1%). Citrate assay was available for only 53 / 83 patients and among these 6 were found to have hypocitraturia (11.32%). This was followed by hyperuricosuria in 8 patients (9.64%). A raised phosphate was noted in just one patient (1.2%). There were no abnormalities of cystine. The summary is given in Figure 1.

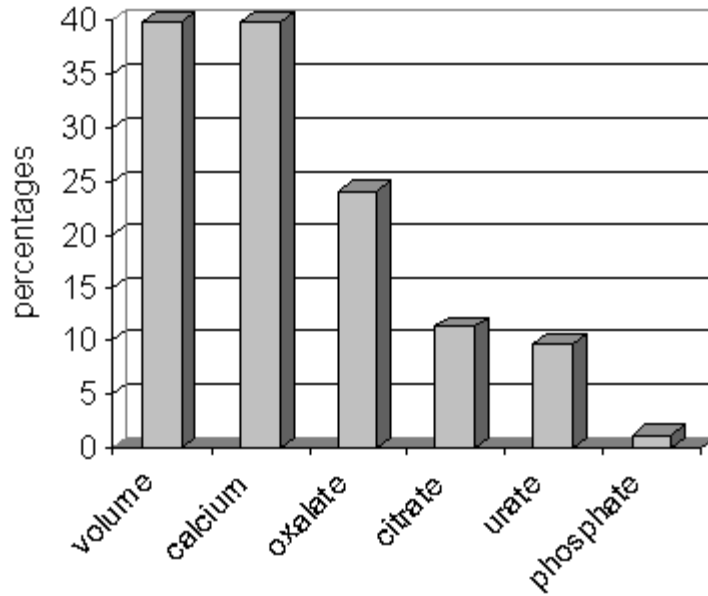


Figure 1: Overall urinary

abnormalities in patients as percentages.

The most common blood abnormality noted was a high serum creatinine in 10 patients (12.05%). Hyperuricaemia was found in 5 patients (6.02%). Only one patient was found to have hypercalcaemia (1.2%). This patient was later found to have primary hyperparathyroidism. Similarly only one person was found to have high serum phosphate who was subsequently also found to have a high urinary phosphate.

A sub-group analysis to compare the urinary abnormalities between males and females was also performed (Table 1). This showed some interesting features including a high occurrence of low urinary volumes in females, which was 48% ($p < 0.001$). The females were also found to have a high incidence of hyperoxaluria at 38% ($p < 0.002$). In addition low urinary citrate was also more common in females at 37% ($p < 0.001$). The male population showed an apparent high rate of hypercalciuria and hyperuricosuria but both these abnormalities were not statistically significant from the similar abnormalities in females.

Table 1: Distribution of urinary abnormalities by gender

Abnormality	Males (percentages)	Females (percentages)
Low volume	21	48*
Hypercalciuria	30	19
Hyperoxaluria	11	38**
Hyperuricosuria	7	2
Hypocitraturia	0	37***

* $p < 0.001$, ** $p < 0.002$, *** $p < 0.001$

In the sub-group analysis of gender related abnormalities, males had an apparent higher frequency of high serum creatinine and of hyperuricaemia but actually this difference between the sexes was statistically not

significant. Similarly, seemingly higher frequency of hypercalcaemia and hyperphosphataemia in females was not significant on a statistical analysis from the male patients frequencies of hypercalcaemia and hyper-phosphataemia.

First time stone formers were in the majority at 53 (63.85%) with recurrent stone formers numbering 30 (36.14.7%). Males were in the majority at 73% as first time stone formers and 83% as recurrent stone formers.

Comparative results here show higher frequencies of low urinary volumes (35%), hypercalciuria (23%), hyperoxaluria (17%) and low citrate (10%) in the first time stone formers, but statistically these differences were not significant when compared to the recurrent stone formers.

Whilst recurrent stone formers showed an apparent higher frequency of hyperuricosuria (4%) but this was also statistically not significant when compared to first time stone formers.

Higher frequency of hyperuricaemia (14%) in the recurrent stone formers was statistically not significant from that of the first time stone formers. Equal frequency of raised creatinine of 6% was noted in each group.

Discussion

With better understanding of stone disease pathophysiology⁹ and impressive results of medical management especially specific treatment,² the importance of diagnostic evaluation of nephrolithiasis has been realised.¹⁰⁻¹² In addition, knowing that majority of first time stone formers (FSF) lead to recurrent stone formation,¹³⁻¹⁶ significance of early biochemical investigation can not be ignored. However not every one is very convinced of its efficacy¹⁷ and it is still not practised by all, especially in the first time stone formers.

The results of our study, by showing a high overall frequency of biochemical abnormalities (73%) in urolithiasis patients and even more surprisingly, almost equal frequencies of various abnormalities between the first time and recurrent stone formers (RSF) has reiterated the importance of diagnostic evaluation, even in patients with first stone episode. One may get an impression from looking at our results that there may have been stone-predisposing dietary habits in our patients, i.e. decreased fluid intake and consumption of foods with a high calcium, oxalate and protein content. The result might also be indicating inadequate medical therapy and random prophylaxis due to the absence of a proper metabolic screening protocol in our practice till recently. Similarity between FSF and RSF abnormalities have also been noted by Yagisawa et al.,¹⁸ when low urinary volume and hypercalciuria was identified in both groups but hypocitraturia was more common in the RSF.

Although relatively higher and significant frequencies of low urinary volumes, hyperoxaluria and hypocitraturia were seen in our female patients but as mentioned before the overall female abnormality rate was not statistically higher than males. Higher incidence of hypocitraturia in females has also been reported in other studies.¹⁹⁻²¹ However other investigators have not found this sex based difference.^{12,22,23}

The findings in our study of low urinary volume and hypercalciuria as the main overall abnormalities, followed by hyperoxaluria and hyperuricosuria are well-known stone disease risk

factors and reported extensively in the past. A large and relatively recent study quite similar to ours with results also fairly similar to ours was conducted by del Valle et al in 1999.²⁴

Other risk factors contributing to renal stone disease are also being identified, which includes plasma phospholipids arachidonic acid content anomaly²⁵ and female obesity.²⁶

The significance of early biochemical screening has also been felt by other investigators by highlighting the cost effectiveness of proper diagnostic evaluation.^{10,27} Depending upon the severity of stone disease, simple and extensive screening methods have been described.²⁸ Our method is more similar to the simpler method already described.

Conclusions

Bearing in mind the above noted observations based on our study results and knowing that most of the biochemical abnormalities if treated can considerably lower the recurrence rate of stone disease, one thus concludes that for rational, efficient and specific urolithiasis management, biochemical screening, particularly urinary screening, should be practised even in the first time stone disease patients. In addition in some cases of initial stone presentation, metabolic evaluation can pick up multi-system pathology responsible for the urolithiasis. Appropriate treatment of the underlying cause in these cases can therefore prevent extra renal complications.

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