Original Article

Hypocitraturia in the treated patients of urolithiasis

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Objective: To determine the frequency of hypocitraturia in the treated patient of urolithiasis in Karachi, Pakistan.

Methodology: This is a cross sectional study was conducted in department of urology at Jinnah Postgraduate Medical Centre Karachi from January to December 2018 for a period of one year. It included 170 patients who had been treated for stone disease and were stone free at the time of study. We measured 24 hours urinary excretion of citrate by enzymatic citrate lyase analysis (Bergmeyer method).

Results: Out of 170 patients, 115 (67.65%) were male while 55(32.35%) were female. Mean age was 39.34±11.87 years. Average urinary citrate level was 262±199 mg/day. Hypocitraturia turned out to be <320mg/day in 119(70%) patients and 51 (30%) patients had normal urinary citrate levels. Hypocitraturia was more in patients with stone size more than 2 cm and disease duration greater than 2 months with significant difference (p=0.001 and p=0.012, respectively).

Conclusion: Hypocitraturia is the most common metabolic disorder and an important risk factor in stone formation particularly in calcium stones. Dietary modifications should also be used in conjunction with medical therapy. (Rawal Med J 202;45:626-628).

Keywords: Hypocitraturia, urolithiasis, pyelolithotomy.

INTRODUCTION

Among the causes of nephrolithiasis, hypocitraturia is a recognized as an important one, particularly in calcium stones. Hypocitraturia is urinary excretion less than 200 mg/day in men, while in females less than 400 mg/day.[1] In urine, citrate chelates free calcium ion forming soluble calcium citrate and resulting in reduction of urinary super saturation of calcium oxalate and phosphates, so inhibiting the both crystal growth and aggregation. It also inhibits monosodium crystallization, and is considered to help prevent urinary stone formation.[2,3]

Urinary citrate has a direct inhibitory action on calcium phosphate precipitation[4] and thus is an important factor for stone formation.[5] In idiopathic stone formers concentration of urinary citrate is low as compared to normal subjects, but there are some studies which have not confirmed this difference.[6] For assessment of urolithiasis, it is important to measure the plasma concentration of metabolites and electrolytes along with 24 hour urine metabolic work up and hormonal assay.[7] There is no consensus on the normal range for urinary citrate. The purpose of this study was to identify urinary citrate levels in previously stone former patients.

METHODOLOGY

This prospective cross sectional study was conducted in the department of urology, Jinnah Postgraduate Medical Centre, Karachi from January 2018 to December 2018. Patients included in this study were stone free after the treatment confirmed on ultrasound and CT KUB while all those patients who had renal diseases, congenital bone diseases, inflammatory bowel diseases and hyperparathyroidism were excluded from the study. Those patients who were on medication like bisphosphonates hormonal therapy, thiazide diuretics, corticosteroids and calcium supplements were also excluded from the study. 24 hour urine was collected on their random diet.

Statistical Analysis: Data were analyzed through SPSS version 22. Effect modifier age, gender, BMI, number of stones, size of stone and duration was controlled through stratification to see the effect of these on outcomes and for post stratification chi square test was applied by taking $p \leq 0.05$ as significant.

RESULTS

Out of 170 patients male patients were 115(67.65%) while 55(32.35%) were female patients. Mean age

was 39.34±11.87 years while BMI was 24.98±4.76 kg/m^2. Average urinary citrate level was 262±199 mg/day (Table 1). Hypocitraturia was found to be less than <320 mg/day in 119(70%) patients. Hypocitraturia was found in 92 male patients and in 27 female patients. There was relevant effect of hypocitraturia observed with respect to gender (p=0.001).

Table 1. Showing variable of the patients (n=170).

Variables	N	Mean	Std. Deviation
Age (years)	170	39.34	11.87
BMI (Kg/m^2)	170	24.98	4.76
Urinary citrate level mg/day	170	262	199
Stone size(cm)	170	3.05	1.35
No. of stones	170	3.14	1.31
Duration of urolithiasis (in months)	170	3.65	1.87

Table 2. Stratification of hypocitraturia with respect to effect modifiers.

Effect modifiers	Hypocitraturia		P-value
	Yes	No	
Age groups			
25-40	81	14	0.001*
41-60	38	37	
Gender			
Male	92	23	0.001*
Female	27	28	
Duration			
2 or less months	47	31	0.012*
More than 2 months	72	20	
BMI Kg/m^2			
≤24	51	19	0.61
>24	69	31	
Stone Size			
<2cm	20	38	0.001*
≥2cm	99	13	
No. of stones			
Single	29	21	0.042*
Multiple	90	30	

Hypocitraturia was found in 52 patients having <24 kg/m^2 BMI, whereas in 69 patients having >24kg/m^2 BMI. There was no significant effect observed with respect to BMI (p=0.61). Stratification for hypocitraturia with respect to age, BMI, size of stone, number of stones, gender showed most of the p-values were significant (p<0.05) (Table 2).

DISCUSSION

Pakistan due to its location in stone belt with hot climate has high prevalence of stone disease. Metabolic disorders such as cystinuria, hypocitraturia, hyperparathyroidism and oxaluria are the well documented risk factor in development of stone diseases and chronic renal insuffiency.[8] The inhibitors for stone formation are small ions and poly anions of high molecular weight such as magnesium, citrate and glycosaminglycans, respectively.[9]

In patients with recurrent urinary tract stones, majority of them have metabolic abnormalities like hyperoxaluria, hypercalciuria, hypocitraturia and hyperuricosuira. In our study, leading metabolic abnormality was found to be the hypocitraturia followed by hypercalciurea. which were same as in another study.[10] Stone formation occurs in those patients who were totally stone free or even with residual stone fragments after pyelolithotomy and PCNL.[1,2] Therefore it is important to start effective treatment for correction of underling metabolic abnormalities in such patients.

Among the stone inhibitors agent, citrate is most important in prevention of stone formation.[11] In normal individuals, mean citrate level is 640 mg/24 hours while 320 mg/day is accepted its lowest limit.[12] Isolated hypocitraturia has been reported in 13% patients while in 15-69% it coexisted with other metabolic abnormalities of calcium.[10,13] In some randomized control trials stone free rates for at least two years was found to be 53.5% while in those with placebo was 35%.[14,15] Patients should be on medical therapy regardless of stone type that can decrease cost of repeated procedures and recommend after PCNL or pyelolithotomy.[16]

In our study, 60% of the patients had decreased urine output which is comparable to international data.[17] We had higher percentage of hypocitraturia (70%), which is compare able to studies from Pakistan.[18,19] Such higher depletion of citrate level in our

population is unclear and seems multifactorial such as usage of high protein diet, usage of added salts, hot climate and decreased fluid intake. Similar results were also seen in the study from Kashmir and india.[20,21]

Another study found that the leading metabolic abnormality was hypocitraturia seen in the 24 hour urine in patients of urolithiasis[22] Some studies had low hypocitraturia as compared to our study, which may be due to the genetic or environmental reasons.[23]

CONCLUSION

Hypocitraturia is an important metabolic risk factor for stone formation especially in calcium stone formers. Correcting this may reduce the stone recurrence following PCNL or pyelolithotomy along with dietary modification.

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