THE URINARY EXCRETION OF CALCIUM, OXALATE AND INORGANIC PHOSPHATE IN NORMAL AND RENAL STONE FORMING PATIENTS

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ABSTRACT

Background: Nephrolithiasis is a chronic and morbid clinical condition. Hypercalciuria is associated with calcium nephrolithiasis. Hypercalciuria may be due to absorptive, metabolic or renal derangements. Now a days, urinary calcium, oxalate and inorganic phosphate can be determined with rapid enzymatic methods. This study was designed to study the role of calcium, oxalate and inorganic phosphate excretion to understand the etiological factors in nephrolithiasis in this era.

Materials and Methods: This study was conducted from April to September 1996, on 60 indoor patients from various hospitals in Lahore. Thirty normal individuals selected from hospital staff were taken as control. 24 hours urine collection was made while they were on routine diet. The specimens were properly preserved and analyzed by auto analyzer Technicon (R.A 2010) for calcium and inorganic phosphate and for oxalate by Sigma diagnostic kit.

Results: The mean urinary excretion of calcium and oxalate was significantly raised by 26% and 40% respectively in stone formers as compared with the controls. While 24 hours urinary phosphate was significantly reduced in patients as compared with the controls.

Conclusion: The association of high calcium and oxalate excretion in patients as compared to normal subjects, results in a high degree of super saturation of urine with respect to calcium oxalate.

Key words: Nephrolithiasis, calcium, oxalate and inorganic Phosphate.

INTRODUCTION

The association of hypercalciuria with calcium nephrolithiasis has been recognized and the disorder is called idiopathic hypercalciuria. The idiopathic hypercalciuria constitute several pathogenic origin i.e. absorptive hypercalciuria, renal hypercalciuria and fasting hypercalciuria.[1]

Absorptive hypercalciuria is intestinal hyper absorption of calcium which may be due to high intake of calcium or dependent on vitamin D. Renal hypercalciuria is due to impaired renal tubular reabsorption of calcium. Secondary increases in parathyroid hormone may be the cause of compensatory intestinal calcium hyperabsorption by stimulating the renal synthesis of 1,25-dihydroxy vitamins D3. The fasting hypercalciuria in the absence of parathyroid hormone stimulation may represent overproduction or hypersensitivity of a variant of $1,25(OH)_2$ D3.

Some investigators argued that hypercalciuria is primarily due to renal phosphate leak[2,3] Enhanced phosphate excretion is due to increase in renal $1,25(OH)_2$ D3 production which secondarily increase intestinal calcium absorption and bone resorption. These studies have several limitations, first, the number of patients studied were 29 and 15 which are very small in number and represent only mean phosphate excretion. Recently a study do not concur with these studies which showed that hypercalciuria was encountered in 61% of patients but renal phosphate leakage was present in only 2.4 % of patients. These are conflicting reports and it is not necessary that all patients fall into these clear-cut groups. The environment and dietary habits may differ from place to place.[4]

Although calcium excretion is increased in high proportion of patients with nephrolithiasis but there are conflicting reports regarding the excretion of oxalate, some workers have reported that oxalate excretion is with in normal limit,[5,6] but most workers have found raised values.[7,8] The methodology for accurate urinary oxalate determination was not available to earlier workers. The measurement of urinary oxalate is now possible with a rapid enzymatic method, which is very specific and simple procedure for routine clinical use. There is a need to study the role of calcium, oxalate and inorganic phosphate excretion to understand the etiological factors in calculogenisis in this era.

MATERIALS AND METHODS

The study was made on sixty hospitalized patients from various hospitals in Lahore and thirty nor-

Table-1: The overall mean + SE of 24 hours urinary excretion of calcium and phosphate among the subjects.

Variants	Controls	Patients	P Values
Calcium mg /24 hour	210.4+13.76	266+ 23.26	<0.05
Inorganic phosphate mg /24 hour	696.4+60.97	500+36.43	<0.01
Oxalate mg /24 hour	35.93+2.54	51.26+4.35	<0.01

Table-2: The daily excretion of calcium in different subjects.

	Calcium (mg /24 Hour)		
Group	**<250**	**251-300**	**>300**
Controls (n=30)			
M (n=18)	14	12	02
F (n=12)	10	02	—
Patients (=60)			
M (n=17)	15	09	13
F (n=23)	17	02	04

mal healthy controls were selected from the hospital staff and their relatives, from the same area. The study was conducted from April to September 1996. The mean age of the patients was 37.5 years and controls 34.9 years. The male to female ratio was 1.5:1 and 1.6:1 respectively. The urinary calculi were analyzed by quantitative method using E. Merck's urinary kit.[9]

Twenty four hours urine collections were made while the subjects were on normal diet of their own choice. Hydrochloric Acid (1 ml /100 ml of urine) was added to keep calcium, phosphate and oxalate in soluble form as well as to stop auto-conversion of ascorbate to oxalate during storage.

Calcium[10] and inorganic phosphate[11] were determined by automatic clinical analyzer Technicon R.A 2010. The urinary oxalate was determined by using sigma diagnostic kit. The method is simple colorimetry based on coupled enzyme assay, involving oxalate oxidase and peroxidase.[12]

Urinary Calcium excretion more than 300 mg/ 24 Hour and 250 mg /24 Hour in men and women respectively was considered as hypercalciuria. [7,13]

RESULTS

The patients showed a significantly increased 24 hours urinary calcium and oxalate excretion of 266+23.26 mg/24 hour and 51.26 + 4.35 as compared to control group 210.4 +13.76 mg/24 hour and 35.93+2.54 respectively while 24 hours urinary phosphate was significantly ($p<0.01$) reduced in patients i.e. 500+36.43 mg/24 hour as compared to control group 696.4+60.97 mg/24 hour. (Table-1)

DISCUSSION

Calcium and oxalate are the main reason for the renal stone diseases, because 90-95% of the renal stones are calcified stones and majority of calcium calculi contain calcium oxalate as a single salt and reminder as a mixed calculi with calcium phosphate or urate.[14]

In this study 58(96.7%) were calcified stone. Among them 42 (70.00%) were pure calcium oxalate and 25% were mixed type. Most patients with calcium oxalate stone have no discernible disorder of oxalate metabolism. They either have an abnormal production of calcium or oxalate.

Urinary oxalate was also significantly high as compared to controls, and 19 (31.7%) were hyper-calciuria as compared to 2(3.3%) controls. When we compare our findings with earlier studies done in Pakistan, it is found that overall mean daily excretion of calcium is higher. Our results are very similar with various studies done in west who have reported that 30-50 % of renal lithiasis patients were hypercalciuria[15,16] while in overall mean values in earlier studies done in Pakistan, there was no significant hypercalciuria found among the patients and controls. There are several reasons of hyper-calciuria in renal lithiasis such as idiopathic hypercalciuria, sarcoidosis, Cushing's syndrome, malignant tumors, renal tubular acidosis etc.

Absorptive hypercalciuria is most common cause of kidney stones accounting for over half of reported cases.[17] The hyperparathroidism leading to renal lithiasis is not a rare entity in west. In Pakistan, it need further work up for the exact diagnosis of hyper-calciuria especially in recent calculi formers.

In this study urinary phosphate in significantly ($p<0.01$) low in patients as compared to controls subjects. In Pakistan, various studies showed that urinary inorganic phosphate excretion among controls and patients did not have any difference.[18,19] On the other hand, significantly increased excretion of inorganic

phosphate in patients has been reported[2,8] Urinary phosphate concentration may decrease in response to reduce dietary phosphate intake as the plasma phosphate and therefore glomerular filtrate concentration decrease. A decrease urinary phosphate excretion in unilateral obstruction of kidney has also been documented by many workers,[20] whereas, there is increase phosphate excretion by bilateral ureteric obstruction which may be related to hyperphosophaturia.[21] Thus lower urinary phosphate excretion in the calculus patients in the present study may be related to 75% calculi being unilateral. The renal handling of these bivalent ions by the kidney during obstruction is a complicated phenomena because it involves multiple sites and factors, so phosphate excretion can vary according to site of obstruction. It need to be studied in great depth.[22]

CONCLUSION

Daily urinary excretion of calcium and oxalate is significantly increased while that of inorganic phosphate is decreased in most of the stone forming subjects. Hypophoshaturia along-with hypercalciuria and hyperoxalauria seem to be important risk factors in nephrolithiasis.

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