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ROLE OF ORAL PYRIDOXINE (VITAMIN B6) SUPPLEMENTATION IN THE REDUCTION OF HYPEROXALURIA AND PREVENTION OF RECURRENT UROLITHIASIS

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ABSTRACT Our prospective, randomised controlled study was to assess the role of oral pyridoxine (Vitamin B6) supplementation in addition to standard dietary advice, compared against only dietary advice, in the reduction of urinary oxalate levels in patients with urinary calculi along with proven hyperoxaluria. 74 subjects were randomly divided into Interventional Group (n=38) who received oral Pyridoxine 40mg/day with dietary oxalate restriction and Control Group (n=36) who received only dietary oxalate restriction. Both groups were evaluated and statistically compared at the end of 3 months. Interventional group showed statistically significant (p = 0.0001) reduction in 24 hours urinary oxalate levels. Pyridoxine, cofactor in the alanine-glyoxalate-transaminase pathway converts glyoxalate to glycine and reduces oxalate production thereby decreasing hyperoxaluria, risk factor of urolithiasis. Oral Pyridoxine supplementation (40 mg/day) with dietary oxalate restriction can be a prophylactic measure for prevention of recurrence of calcium oxalate urolithiasis.

KEYWORDS : Hyperoxaluria, Pyridoxine supplementation, Prevention of Recurrent Urolithiasis

INTRODUCTION

Urolithiasis is the most common urological disorders with worldwide prevalence of around 1 -5%. [1] It affects 10 % of people over their lifetime and acute renal colic accounts for 1% of all hospital admissions. [2] The mainstay of treatment of this acute phase is NSAIDS for pain management, antibiotics for prevention or treatment of infection and urinary alkalizers. The definitive treatment involves either conservative management with dietary restrictions and hydration therapy, conventional open surgical procedures, or in some cases the newer minimally/ non-invasive procedures such as Percutaneous Nephro Lithotripsy (PCNL) Extracorporeal Shock Wave Lithotripsy (ESWL).

Recurrence of calculi after successful treatment is the other major area of concern with approximately 50% of patients having recurrence within 10 years and 75% within 20 years. [3] The choices of treatment, being limited to either repeat ESWL or surgical procedures for recurrent urolithiasis, doctors are now looking for alternative treatment modalities for both treatment and recurrence. There is evidence that intervention in the form of lifestyle advice and some forms of medical therapy can reduce the rate of stone recurrence; thus, metabolic investigations and medical treatment are both important elements in the clinical management of renal stone disease today. [4,5]

Calcium is the most common cationic constituent of renal stones accounting for 80-95% of calculi; and oxalate, being the commonest anion, hyperoxaluria/ hypercalciuria are the two most important risk factors of urinary stone formation. [6,7] Though these factors contribute to urolithiasis by precipitating calcium oxalate in the urinary tract, hyperoxaluria is in fact a more potent risk factor than hypercalciuria in the genesis of urolithiasis. [8]

The aim of treating patients with recurrent calcium oxalate stone is to correct the abnormalities in urine composition, eliminate risk factors and thereby counteract or stop the formation of new stones. One strategy for preventing recurrence of calcium oxalate stones includes tackling of hyperoxaluria which is a more important factor than hypercalciuria as mentioned above. This can be achieved by supplementation of oral Pyridoxine (vitamin B6), in addition to the standard dietary advice regarding avoidance of oxalate rich foods (e.g. spinach, onions etc.) in these patients. Pyridoxine is a cofactor in the alanine-glyoxalate-transaminase pathway, which converts glyoxalate to glycine, and reduces oxalate production by enzyme induction. It is in this context that our study was designed to assess the role of pyridoxine, in addition to dietary advice, in reduction of hyperoxaluria and thereby prevent recurrent urolithiasis.

MATERIALS AND METHODS

74 patients admitted in Surgical Wards of a tertiary level teaching hospital with urolithiasis and meeting the inclusion criteria were randomly divided into **Interventional Group (n = 38)** and **Control Group (n=36)** by chit method. The sample size was calculated based on the findings of pilot study conducted on 6 patients. The total study period ranged from July 2014 to April 2016. Patients were investigated with Complete blood count, Renal Function Tests, Urine routine and microscopy for calcium oxalate crystals, urinary pH and 24 hours urinary oxalate and 24 hours calcium levels were analysed on admission and at 3 months follow up. Urinary oxalate levels were estimated by Hodgkinson's method and urinary calcium levels were calculated from a kit at Metropolis Laboratory. In our study, hyperoxaluria has been defined as urinary oxalate levels more than 40 mg/day. [9] Patients in Interventional Group received oral supplementation of Pyridoxine tablet 40 mg/day as a single dose in the morning at 10 am in addition to dietary restriction of oxalate rich foods. [10,11] Patients in Control Group received only dietary restriction of oxalate rich foods. Pyridoxine (Vitamin B6) Supplementation was continued for 3 months in patients in Interventional Group. The parameters included for comparison were calcium oxalate crystalluria, 24 hours urinary calcium level and 24 hours urinary oxalate level. The data was tabulated and analysed using SPSS (Statistical Packages of Social Sciences, version 20.)

RESULTS

The results showed that both the groups were comparable at baseline for gender, age, urinary pH, dietary pattern, calcium oxalate crystalluria, 24 hours urinary calcium levels and 24 hours urinary oxalate levels. In our study, there were 40 Males (54.1 %) and 34 Females (45.9 %). It was observed that in general there was significant reduction in 24 hours urinary oxalate excretion in both males as well as females (p = 0.0001) in both groups. The youngest subject was of 17 years and oldest was of 70 years. The mean age of presentation was 42.21 + 14.486 years in interventional group while it was 40.56 + 13.964 years in control group. Urine samples of large majority of patients (95.9 %) had acidic pH. Out of a total of 74 subjects, 89.2 % had a mixed diet. The proportion of patients having calcium oxalate crystalluria reduced from 92.1 % (baseline) to 10.5 % (at 3 months) in Interventional Group and from 97.2 % (baseline) to 36.1 % (at 3 months) in Control Group. In both the groups, the reduction in 24 hours urinary calcium levels at 3 months follow up obtained was statistically significant (p = 0.0001). However, when comparison was done between Interventional Group and Control Group to assess the mean change in 24 hours urinary calcium levels (Interventional Group 10.53

+ 4.76; Control Group 8.36 + 7.8), no significant difference (p = 0.237) was observed. The **reduction in 24 hours urinary oxalate levels** was **statistically significantly (p = 0.0001)** higher in the **Interventional group** compared to Control Group (TABLE 1). In Interventional Group, 24 hours urinary oxalate levels decreased from 51.32 + 9.37 (baseline) to 31.90 + 3.92 (at 3 months follow up). Similarly, in Control Group, 24 hours urinary oxalate levels also decreased from 49.04 + 6.00 (baseline) to 44.16 + 5.85 (at 3 months follow up). However, the mean 24 hours urinary oxalate level of 44.16 in the Control Group at 3 months follow up, was not the desired decrease as the value is still more than 40 mg/day, cut off for labelling patient "hyperoxaluric". When comparison was done between Interventional Group and Control Group to assess the **mean change in 24 hours urinary oxalate levels** (Interventional Group 19.42 + 7.32; Control Group 4.88 + 3.56), **significant difference (p = 0.0001)** was observed (TABLE 2).

TABLE 1: 24 hours urinary oxalate levels (mg/dl) at baseline and at 3 months

24 HOUR URINARY OXALATE (mg/dl)	INTERVENTIONAL GROUP (n = 38)	CONTROL GROUP (n = 36)	Unpaired T-Test, p value
BASELINE	51.32 ± 9.37	49.04 ± 6.00	0.241
AT 3 MONTHS	31.90 ± 3.92	44.16 ± 5.85	0.0001

The values indicate Mean + Standard Deviation

TABLE 2: Comparison of difference in 24 hours urinary oxalate (mg/dl) levels between the groups

DIFFERENCE IN THE 24 HOURS URINARY OXALATE IN mg/dl AT BASELINE AND AT 3 MONTHS	INTERVENTIONAL GROUP (n = 38)	CONTROL GROUP (n = 36)
MEAN	19.42	4.88
STANDARD DEVIATION	7.32	3.56
STANDARD ERROR OF MEAN	1.87	0.59

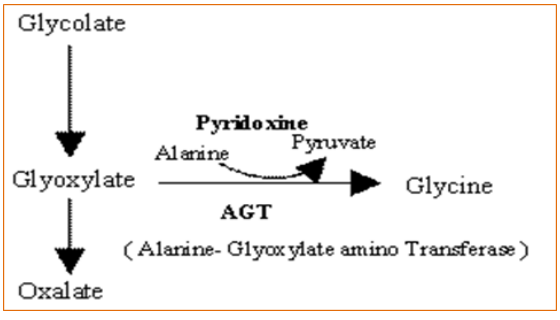
Mann Whitney Test, p = 0.0001 (significant)

DISCUSSION

Nephrolithiasis is a highly prevalent condition with a high recurrence rate. A proper understanding of the metabolic evaluation and medical management of a stone former is important to identify patient specific factors that may be modified in order to reduce the risk for recurrent stone formation. Hyperoxaluria (defined as urinary oxalate levels more than 40mg/day) is an important factor associated with recurrent urolithiasis. Therefore, reduction in urinary oxalate excretion is crucial in preventing recurrence of urinary calculi.

The role of pyridoxine in reduction of urinary oxalate level is established. It is well known that oxalate absorption by the gastro intestinal tract increases markedly in the absence of or with reduced levels of pyridoxine. Pyridoxine is a cofactor in the alanine-glyoxalate-transaminase pathway which converts glyoxalate to glycine, and reduces oxalate production by enzyme induction (FIGURE 1). [12] Pyridoxine deficiency leads to marked increase in endogenous oxalate production. With Pyridoxine supplementation, this pathway is interrupted and results in a lowering of oxalate levels in urine thereby reducing the chances of developing calcium oxalate calculi significantly. [13]

FIGURE 1: Alanine-Glyoxylate Transaminase Pathway [12]



The beneficial role of pyridoxine supplementation in the reduction of hyperoxaluria is proven and most of the results of our study agreed with previous studies that have been done on this subject. [13,14,15,16] However, consensus needs to be reached on the ideal duration of such supplementation as well as optimization of the dose of pyridoxine to be used in such prophylaxis. We used pyridoxine tablet of 40 mg which is readily available and affordable.

CONCLUSION

Oral Pyridoxine supplementation in the dose of 40 mg/day in addition to dietary restriction of oxalate rich foods results in statistically significant reduction of urinary oxalate excretion, decreasing the precipitation of calcium oxalate and thereby reducing the chances of recurrent calcium oxalate stone formation. It can be used as a simple, cheap and easy to implement prophylactic measure for prevention of recurrence of calcium oxalate urolithiasis, thus reducing the cost of healthcare delivery in our country with limited resources with immense overall benefit to the community.

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