

## Effect of Indigenous Drugs on Idiopathic Hyperoxaluria in Stone Formers

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### ABSTRACT

*Idiopathic hyperoxaluria appears to be one of the most important etiological factors in the local stone formers, as significantly higher excretion of oxalate was observed in stone formers as compared to healthy volunteers. Cystone therapy has been demonstrated to bring about marked reduction in urinary oxalate excretion. Hyperoxaluria appears to be of endogenous origin and Cystone probably causes blockade of oxalate synthesis.*

Key words: *Hyperoxaluria; Idiopathic; Primary; Indigenous; Cystone.*

### INTRODUCTION

Until recently, clinical interest in urinary oxalate was practically limited to primary hyperoxaluria. However, a recent and excellent review on oxalate metabolism and renal calculi<sup>4</sup> provides a timely admonition to consider any type of hyperoxaluria quite seriously, since oxalate renders the urine far more propitious to stone formation as compared to any other known stone-forming substance.

Unfortunately, no effective drug is yet available to check hyperoxaluria in human beings. Beneficial effects of several drugs have been reported in the past but none has stood the test of time<sup>1,2,6,11</sup>. In India, several herbal drugs are in vogue for the expulsion of stones or to check recurrence. However, their scientific evaluation, especially in terms of the urine chemistry which is the most important aspect of the disease, has received very little attention.

We wish to report two findings: (a) that hyperoxaluria is an important feature in local stone formers, and (b) that the indigenous drug Cystone is apparently effective in controlling hyperoxaluria. In recent years, India and other developing countries have stressed the evaluation and use of indigenous drugs since these are cheap and readily available if medical care is to be extended to all by 2000 A.D.

We have previously reported the high incidence of urinary stone disease in this region<sup>5</sup>.

### MATERIAL AND METHODS

Thirty two healthy volunteers and 48 stone formers admitted to surgical wards of the General Hospital, R.N.T. Medical College, Udaipur, were selected for this study. All the patients were placed on Cystone treatment (2 tablets, 3 times a day) and were advised to avoid oxalate-rich foods. Forty eight patients returned for check-up after 4 weeks and 14 arrived after 8 weeks.

*Cystone*: This is a patent drug made from indigenous products, marketed by The Himalaya Drug Co., Mumbai, India. The composition of each tablet of Cystone is: *Didymocarpus pedicellata*, 65 mg; *Saxifraga ligulata*, 49 mg; *Rubia cordifolia*, 16 mg; *Cyperus scariosus*, 16 mg; *Achyranthes aspera*, 16 mg; *Onosma bracteatum*, 16 mg; *Vernonia cinerea*, 16 mg; *Shilajeet* purified, 13 mg; and *Hajrul yahood bhasma*, 16 mg.

*Urine collection and oxalate analysis:* The patients were placed strictly on hospital diet for 2 days before the collection of samples. Normal subjects were advised to avoid high oxalate foods during the period of collection of urine samples. A single 24-hour urine sample (from 8 a.m. to 8 a.m. next day) was collected in a 2.5 l bottle containing 10 ml of conc. HCl. In the operated group, urine collection was carried out before surgery. The oxalate was determined by the method of Hodgkinson and Williams<sup>2</sup>.

The same procedures were adopted for urine collection and oxalate analysis after 4 and 8 weeks of Cystone therapy.

The Student 't' test was applied to assess the effect of Cystone on oxalate excretion in stone formers before and after the treatment.

## RESULTS

The excretion of urinary oxalates in normal subjects was  $22.5 \pm 12.66$  mg/24 hr ( $2.06 \pm 1.43$  mg/dl). The value was more than double in stone formers (Table 1), and the difference was statistically significant. After 4 weeks of Cystone therapy, the 24-hour excretion as well as concentration (mg/dl) was significantly reduced (Table 2). Fourteen patients who came for check-ups after both 4 and 8 weeks of Cystone therapy revealed a gradual reduction in oxalate excretion. Eight weeks' Cystone therapy reduced the 24-hour excretion to less than half ( $p < 0.05$ ) and the concentration to almost one quarter ( $p < 0.05$ ; Table 3). Tables 4 and 5 show the numbers of hyperoxaluric subjects in the normal and stone former groups, and the effect of 4 and 8 weeks' Cystone treatment on the latter.

Subjects	Mean $\pm$ SD (mg/24 hr)	Mean $\pm$ SD (mg/dl)
Normal (32)	$22.50 \pm 12.66$	$2.06 \pm 1.43$
Operated (28)	$48.26 \pm 31.28^{\#}$	$3.44 \pm 3.17^*$
Unoperated (10)	$46.97 \pm 23.46^{\#}$	$3.96 \pm 2.45^*$
Spontaneously voided (10)	$47.13 \pm 28.19^*$	$3.39 \pm 3.07$

\* $p < 0.05$  and  $^{\#}p < 0.001$

Oxalate excretion	Stone formers	
	Before treatment (Mean $\pm$ SD)	After treatment (Mean $\pm$ SD)
Mg/24 hr	$47.39 \pm 28.80$	$35.04 \pm 27.12^*$
Mg/dl	$3.46 \pm 2.85$	$2.17 \pm 1.68^*$

Oxalate excretion	Stone formers		
	Before treatment (Mean $\pm$ SD)	After 4 weeks' treatment (Mean $\pm$ SD)	After 8 weeks' treatment (Mean $\pm$ SD)
mg/24 hr	$51.71 \pm 28.44$	$40.34 \pm 31.42$	$24.83 \pm 11.38^*$
mg/dl	$4.78 \pm 3.95$	$1.93 \pm 1.40^*$	$1.24 \pm 0.79^*$

\* $p < 0.05$

Oxalic acid excretion (mg/24 hr)	Normal subjects (32)		Stone formers (48)			
	No.	Percentage	Before treatment		After treatment	
			No.	Percentage	No.	Percentage
40-50	1	3.12	9	18.75	6	12.50
>50	1	3.12	19	39.58	9	18.75

Hyperoxaluria was completely corrected in 46.42% of cases. Severe hyperoxaluria was corrected in 52.64% of cases.

<b>Table 5:</b> Hyperoxaluric stone formers (14) before and after 4 and 8 weeks of Cystone treatment						
Oxalic acid excretion (mg/24 hr)	Before treatment		After 4 weeks' treatment		After 8 weeks' treatment	
	No.	Percentage	No.	Percentage	No.	Percentage
40-50	4	28.57	1	7.14	2	14.28
>50	5	35.71	4	28.57	–	–

Hyperoxaluria was corrected after 4 weeks of treatment in 44.44% of cases. Hyperoxaluria was corrected after 8 weeks of treatment in 77.7% of cases. Severe hyperoxaluria was completely corrected in all 5 patients (100%).

## DISCUSSION

Hyperoxaluria is probably the most insidious factor in stone formation<sup>1,4</sup>. However, there is still controversy over the normal range of urinary oxalate excretion, especially the upper limit, beyond which hyperoxaluria should be considered. Hodgkinson<sup>2</sup> from his own work and several others concluded that the average daily oxalate excretion in the normal population was about 30 mg with a range of 15 to 50 mg/day.

On the basis of the available information and our own experience, we suggest that hyperoxaluria should be classified into three categories, as follows:

- (a) mild hyperoxaluria with a daily excretion of between 40-50 mg.
- (b) severe hyperoxaluria with a daily excretion of between 50-100 mg.
- (c) excessive hyperoxaluria with a daily excretion of >100 mg.

In our two-year study, we have not encountered a single case of primary hyperoxaluria. However, mild or severe hyperoxaluria appears to be a significant feature of local stone formers: 58.33% with uroliths suffered from mild or severe hyperoxaluria. Although sporadic hyperoxaluria due to excessive dietary oxalate is quite possible in this region,<sup>9</sup> it does not appear to represent the cause in the present series as all patients were on a low oxalate (80-150 mg/day) hospital diet, two days prior to urine collection. This implies an enhanced endogenous oxalate production in stone formers.

Hyperoxaluria is one of the important features in Manipuri stone formers also<sup>7,10</sup>. Similar observations have been reported from other countries<sup>4</sup>. This amply underscores the need for an effective drug to control the pathology.

Cystone is widely employed in our country for treating calculus disease. Opinions both in favour and against this drug have been expressed in private discussions and in the scientific literature. It is, however, more important and relevant to evaluate its influence on the urine chemistry, which is at present considered to be the most important investigative aspect of this disease for treatment purposes.

Four weeks' Cystone, therapy in 48 stone formers significantly reduced the 24-hour excretion as well as its concentration per dl ( $p < 0.05$ ). The effect of this drug was more pronounced in the 14 patients who came for check-up after 8 weeks as compared to those after 4 weeks. The effect of this drug became still more evident when only hyperoxaluric uroliths were taken into consideration. Out of 28 hyperoxalurics (9 mild and 19 severe), 13 were completely cured after 4 weeks' treatment. Furthermore, 10 out of 19 severe hyperoxalurics emerged from the danger zone.

Our results indicate that Cystone could prove a promising drug in controlling the propensity of oxaluria. This should decrease the risk of stone formation, recurrence or growth of pre-formed stones. However, it is necessary to verify this effect of Cystone in different stone former populations, especially those who suffer from hyperoxaluria.

## SUMMARY

1. The daily urinary oxalate excretion was determined in normal subjects and stone formers. The values obtained were  $22.50 \pm 12.66$  mg/24 hr ( $2.06 \pm 1.43$  mg/dl) and  $48.26 \pm 31.28$  mg/24 hr ( $3.44 \pm 3.17$  mg/dl), respectively. The difference was statistically significant.
2. The increased excretion of oxalates in stone formers appeared to be of endogenous origin since they consumed low oxalate diet. Our observations suggest endogenous blockade of oxalate synthesis by Cystone.
3. 58.33% stone formers suffered from mild (40-50 mg/24 hr; 18.75%) or severe (>50 mg/24 hr; 39.5%) hyperoxaluria.
4. Cystone therapy revealed a marked reduction in urinary oxalate excretion ( $p < 0.05$ ).

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