Urinary Mucoprotein Excretion in Stone Formers and the Effect of an Indigenous Formulation on its Excretion

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ABSTRACT
We have observed statistically significant elevation of urinary mucoprotein levels in stone formers as compared to normal population. These results suggest that mucoprotein is one of the important risk factors in the etiology of urinary calculus disease in Udaipur region. Cystone, a formulation of indigenous medicines has been found to progressively reduce the mucoprotein excretion in thirty eight stone formers. Three months therapy in seven patients significantly reduced it and brought down its excretion to almost within normal range.

Keywords: Mucoproteins; Stone formers; Indigenous drug; Cystone; Therapy.

INTRODUCTION
In the last decade increasing attention has been given to urinary excretion of mucoproteins. They contain a relatively larger content of carbohydrates (Harper, 1979) and have a specific property of inducing calcium phosphate and calcium oxalate crystalluria and crystal aggregation (Pinto et al., 1980). Although excreted only in small amounts, these are considered to exert a substantial influence on the etiopathogenesis of stones.

Boyce and Swanson (1955) were the first to report the increased urinary mucoprotein excretion in calculus disease, but major interest arose only recently with the reports of Bichler et al., (1976) and Hallson and Rose (1979). Their work was further supported by Pinto et al., (1980) and Scurr et al., (190). Very recently Rose and Sulaiman (1982) presented lucid proof of the stone promoting behaviour of mucoproteins.

Various studies indicate that urinary mucoproteins behave as double risk factors. Firstly, they increase the process of crystal formation and aggregation which may serve as a “seed” for stone formation and, secondly they provide an architectural frame-work on which crystalloids hasten the process of stone growth.

Cystone*, a patent herbal drug formulation manufactured by The Himalaya Drug co., Mumbai, India, is claimed to maintain crystalloid-colloid balance and to dissolve the stone matrix, thereby disintegrating the stone.

(*Cystone composition: Didymocarpus pedicillata 65 mg; Sexifrage legulata 40 mg; Rubia cardefolia 16 mg; Cyperus scariosus 16 mg; Achyranthes aspera 16 mg; Onosma bracteatum 16 mg; Vernonia cineria 16 mg; Shilajeet purified 13 mg and hajrul yahood bhasma 16 mg)

We have been examining the usefulness of various indigenous drugs in urolithiasis. In this project, we have also undertaken clinical trials on Cystone and have observed that it decreases the concentration of some of the stone promoting crystalloids (Singh et al., 1983 and Pendse et al.,
1984). In the present paper we report urinary mucoprotein excretion in normal men and stone formers and the effect of Cystone therapy on the latter.

**MATERIAL AND METHODS**

In the present study 18 healthy persons and 115 radiologically proven stone formers were selected. The normal men took their routine diet and patients were given standard hospital diet. During the period of study oxalate rich foods were avoided and only vegetarian food was permitted. In the stone former group urine samples were collected before and after Cystone therapy. In all the patients Cystone was given at a dose of 2 tablets three times a day for conservative treatment. The patients were advised to report back for further check-ups after a specified period unless they developed any serious complication requiring urgent attention.

Forty five patients were advised to report after 12 and 24 weeks for follow-up. Only seven patients turned up after 12 weeks and none of them returned after 24 weeks despite repeated reminders.

Therefore, we could not ascertain their clinical or biochemical profile thereafter. Another group of 70 patients were placed on the same therapy and were advised to return for check-ups after 4 and 8 weeks. Thirty eight patients turned up for both of these follow-ups.

Two 24 hours urine samples were collected from all the normal subjects and seven stone formers who came for check-ups after 12 weeks. A single 24 hours urine sample was collected from the other 38 stone formers who came for follow-ups after 4 and 8 weeks.

The urine samples were collected in 2.5 litre bottles containing sodium azide as preservative. The samples were sent to the biochemistry laboratory immediately after collection. The urinary output was measured. The samples were mixed and analysed for creatinine (Natelson, 1971) and mucoproteins. The procedure for determination of seromucoids by tyrosine content as described by Natelson (1971) was suitably modified for the determination of urinary mucoproteins.

**RESULTS AND DISCUSSION**

Kachmar and Grant (1976) reported that in man, urinary mucoprotein excretion is about 79 mg/24 hours. Bichlet *et al.* (1976) reported it to be 55.9 ± 6.2 mg/24 hours in males and 42.2 ± 8.2 mg/24 hours in females. Anderson and Maclagon (1955) reported higher normal values (146 ± 7.5 mg mucoprotein in 24 hours in males and 106 ± 6.4 mg/24 hours in females). In our series the mucoprotein excretion in normal subjects ranged from 21.45 to 112.8 mg/24 hours with a mean excretion of 59.01 ± 5.20 mg/24 hours (Table 1). In stone formers the excretion ranged from 24.2 to 399.0 mg/24 hours with a mean excretion of 103.53 ± 11.72 mg/24 hours. The excretion in stone formers was significantly higher than that in normal subjects (*p*<0.05).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal subjects (Mean ± SE)</th>
<th>Stone formers (Mean ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (ml/day)</td>
<td>1,059 ± 120</td>
<td>1,394 ± 106</td>
</tr>
<tr>
<td>Mucoprotein (mg/day)</td>
<td>59.0 ± 5.2</td>
<td>*103.5 ± 117</td>
</tr>
</tbody>
</table>

No significant difference was observed in urinary output of the two groups. These observations suggest that mucoprotein might be one of the etiological factors in stone formation in the local population.

The urinary output, mucoprotein and creatinine excretion of seven stone formers before and after 12 weeks of Cystone therapy are given in Table 2. Cystone therapy decreased the mucoprotein

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*Table 1: 24 hour urinary output and mucoprotein excretion in 18 normal subjects and 45 stone formers*

*Table 2: Urinary output, mucoprotein and creatinine excretion of seven stone formers before and after 12 weeks of Cystone therapy*
excretion from 79.15 ± 8.04 to 55.40 ± 7.49 mg/24 hours (p<0.05). Urinary output increased but it was not statistically significant.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Initial (Mean ± SE)</th>
<th>3 month follow-up (Mean ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (ml/24 hours)</td>
<td>1,302 ± 195</td>
<td>1,598 ± 172</td>
</tr>
<tr>
<td>Mucoprotein (mg/24 hours)</td>
<td>79.1 ± 8.0</td>
<td>*55.4 ± 7.4</td>
</tr>
<tr>
<td>Creatinine (mg/24 hours)</td>
<td>1,121.2 ± 143.5</td>
<td>1,133.7 ± 133.6</td>
</tr>
</tbody>
</table>

* *p<0.05

Even 4 and 8 weeks of Cystone therapy progressively decreased the mucoprotein excretion (Table 3). In this group urinary output was also significantly higher. The level of significance (‘t’ and ‘p’ values) can be seen from Table 4.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Initial (Mean ± SE)</th>
<th>I follow-up (4 weeks) (Mean ± SE)</th>
<th>II follow-up (8 weeks) (Mean ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (ml/24 hours)</td>
<td>1,357 ± 20</td>
<td>1,518 ± 92</td>
<td>1,745 ± 93</td>
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<tr>
<td>Mucoprotein (mg/24 hours)</td>
<td>108.0 ± 14.6</td>
<td>75.2 ± 8.5</td>
<td>55.7 ± 3.6</td>
</tr>
<tr>
<td>Creatinine (mg/24 hours)</td>
<td>971.8 ± 83.0</td>
<td>993.1 ± 69.9</td>
<td>1,219.9 ± 78.0</td>
</tr>
</tbody>
</table>

Table 4: Statistical evaluation of urinary output and mucoproteins before and after 4 and 8 weeks of Cystone therapy in 38 stone formers

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Initial vs I follow-up</th>
<th>'t'</th>
<th>'p'</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume:</td>
<td>Initial vs II follow-up</td>
<td>2.024</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>I follow-up vs II follow-up</td>
<td>6.080</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mucoprotein:</td>
<td>Initial vs I follow-up</td>
<td>2.634</td>
<td>&lt;0.01</td>
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<tr>
<td></td>
<td>Initial vs II follow-up</td>
<td>4.046</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>I follow-up vs II follow-up</td>
<td>2.277</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Among these 45 stone formers, one patient with right ureteric calculus spontaneously voided it during the course of treatment. We did not have any evidence that Cystone pulverised the stone in any of these patients during the therapy period. However, it should be mentioned that the desired effect of the drug on disintegration of calculi is supposed to be achieved after 4-6 months (or even longer) of therapy. Despite our best efforts we have found that clinical trials of such a long duration are not feasible here.

**SUMMARY**

1. The urinary output, and mucoprotein and creatinine excretion in 18 normal subjects and 45 stone formers before and after Cystone therapy were measured.

2. The urinary mucoprotein excretion in normal subjects and stone formers was 59.01 ± 5.20 and 103.53 ± 11.72 mg/24 hours respectively. In the latter group the excretion was significantly higher (p<0.05).

3. In seven stone formers 12 weeks of Cystone therapy significantly decreased the mucoprotein excretion (p<0.05).

4. In 38 stone formers, Cystone therapy progressively decreased the urinary mucoprotein excretion and increased urinary output. These differences were statistically significant.
REFERENCES