

## Efficacy of Herbal Preparation(Cystone) in Management of Urinary Stone Disease

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### ABSTRACT

**Objective:** To evaluate the efficacy of herbal medicine cystone, in reduction of renal and ureteric stone size.

**Methodology:** This observational follow up study was conducted in Urology Department, Madinah Teaching Hospital, associated with University Medical and Dental College, Faisalabad after obtaining the ethical approval from the mentioned institute during March 2018 to December 2018. One hundred and ninety two patients coming to urology outpatient clinic, fulfilling the inclusion criteria were recruited in the study. Out of which 27(14.06%) were lost in follow up and were excluded from study. Out of remaining 165 patients, 99 were male and 66 female patients. All patients with renal stones who were freshly prescribed with oral Tablet cystone twice a day for four weeks were enrolled in the study and were followed for stone size with ultrasonography followed for the duration of four weeks Patients were followed till the primary endpoint.

**Results:** One hundred and seven (64.84%) patients cleared the stone, 10 (6.06%) patients had their stone size reduced, 17(10.3%) patients had their stone size unchanged and 31 (18.78%) patients had their stone size increased. No significant adverse effects were noted during the study that required the patients to stop the treatment. There was significant decrease in stone size from initial mean stone size  $1.57 \pm 0.08$  mm to end point stone size  $0.69 \pm 0.09$  mm after treatment with cystone (p- value 0.000).

**Conclusion:** The mean stone size was reduced after using this herbal preparation for one month.

**KEYWORDS:** Renal stone, Ureteric stone, Cystone.

### INTRODUCTION

Urinary stone disease and its recurrence rates have been rising at an alarming rate globally. It is a common challenging health problem affecting all ages, genders and races throughout the world with an incidence of 12%.<sup>1</sup> It is one of the most prevalent urologic diseases in south Asia with prevalence of 5%–19.1%.<sup>2</sup> This growing trend is because of lifestyle modifications including lack of physical activity, poor dietary habits

and global warming due to the industrialization and modernization in the societies.<sup>1</sup> Formation of urinary stones is a complex and multifactorial process. It depends on intrinsic factors such as age, gender, heredity factors and extrinsic factors like climate, geography, dietary, mineral composition, and water intake contributes in calculogenesis.<sup>1</sup>

Majority of the urinary stones are composed of oxalates, calcium salts and phosphates crystal. Renal stones are the consequence of nucleation of crystals, causing their rapid growth and aggregation that can interact with some intrarenal structure of urinary tract leading to the accumulation within the kidney and renal collecting tubular system leading to further aggregation and secondary nucleation to form the clinical stone. Saturation and super saturation of urine with respect to stone chemical constituents favors nucleation and the growth of crystals, hence further facilitate stone formation. However some studies have reported the presence of inhibitors of crystal formation in the urine that suppresses calculogenesis in normal healthy individual.<sup>3</sup> Stone recurrence remains to be a serious health problem globally and measures for its prevention is debatable and required to understand its logistic mechanics.<sup>1</sup> Previous studies have reported strong association of renal stones with metabolic

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syndrome including diabetes mellitus, hypertension or adiposity.<sup>2</sup> It was estimated that 2 to 3% of the end-stage renal cases are attributed to the urolithiasis.<sup>1</sup> Urolithiasis is treated by the various methods, which may range from the conservative approach, dissolution therapy, minimally invasive procedures like extracorporeal shockwave lithotripsy and invasive techniques like percutaneous nephrolithotomy or open surgery. Despite new mode of treatments have been introduced in decades, current treatments under practice have customary issue related to the poor patient compliance, cost effectiveness of the treatment and adverse effect profile. Therefore, an effective, pocket friendly, safe treatment owing the good patient compliance is highly desirable which could also play pivotal role in prevention for stone growth. As intervention for the urinary stone disease has significant burden on the society, resources and health system, hence, cost effective oral therapy is easiest.<sup>4</sup> Cystone, which is an oral herbal formulation used for treating urolithiasis in various parts of the world, is being studied since 1954 in Indian subcontinent as well as middle east. Each tablet contains extracts of *Saxifraga ligulata*, *Cyperus scariosus*, powder of purified *Shilajeet* and *Hajrul yahood* bhasma, *Achyranthes aspera*, *Onosma bracteatum*, and *Vernonia cinerea* and *Didymocarpus pedicellata*.<sup>5</sup> These herbal constituents have various effects on urine composition. Numerous previous studies have shown its beneficial effects on renal stones, although some showed conflicting data.<sup>3</sup> Hence, this study was aimed to observe patients with urolithiasis, already taking treatment with cystone to evaluate its efficacy in decreasing the renal and ureteric stone size.

## METHODOLOGY

This observational follow up study was conducted in Urology Department of Madinah Teaching Hospital from March 2018 to December 2018. Ethical approval was taken from University Medical and Dental College, The University of Faisalabad with the vide no. TUF/Dean/2018/32. Patients with age ranging 15-75 years, presenting with renal and ureteric stones in which immediate surgical intervention was not absolutely indicated or the patients were not willing for active surgical intervention or other extracorporeal shockwave lithotripsy and were recently prescribed tablet cystone for treating renal stones were eligible to participate in study. The patients who were taking cystone tablet twice daily were enrolled in this observational follow up study after consenting their data to be used for research purpose.<sup>6</sup> Benefits and risks

were clearly explained to participants and anonymity was assured. All patients underwent routine diagnostic tests of urinary stones including ultrasound, X-ray, Computed Tomography Urography (CTU), Intravenous Urography (IVU) and renal profile. Stone size and location were recorded. The patients requiring immediate intervention, deranged renal functions, obstructing renal stones, patients having food or drug allergy, pregnant ladies and patients who lost in follow up were excluded from the study. The study's primary endpoint was stone size after four weeks of regular use of medication. Secondary end point was development of stone or drug related complications like obstructive uropathy, fever, pyuria, vomiting, haematuria or severe pain with vomiting, itching, rash, drug allergy and overall compliance to the treatment. Patients were followed weekly for assessment for duration of four weeks. During follow up patients were evaluated for colicky pain at loin, abdominal pain, hematuria, dysuria, nausea/vomiting, pain on micturition, tenderness in the lumber regions, fever/chills, and loss of appetite in addition to the evaluation of stone size. Repeat ultrasonography were performed at endpoint for estimation of stones size in centimeters (in longitudinal axis). Subjects with the absence of stones were enquired about expulsion of stones through urine passage. Findings of these patients were also confirmed on computed tomography.

**Statistical analysis:** was performed by SPSS 22. Continuous variables were expressed as mean and standard deviations. Categorical variables were shown in frequencies and percentages. Mean was compared by Paired Sample t Test. p value  $\leq 0.05$  was considered significant.

## RESULTS

A total of 192 patients were recruited in the study. Twenty seven patients were lost in the follow up. Remaining 165 patients out of whom there were 99(60%) male and 66(40%) were female. Study participants were followed weekly for the duration of

**Table 1: Paired Sample t Test Showing Change In Renal Stone Size ( n= 165)**

Initial stone Size(cm)	End point stone size (cm)	Mean difference (cm)	95% Confidence Interval of the Difference	P value
Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD		
1.57 $\pm$ 0.08	0.69 $\pm$ 0.09	0.87 $\pm$ 1.06	0.711-1.038	0.000*

Endpoint refers to the analysed parameter change from baseline at 4 weeks, cm= centimetres p value  $\leq 0.05$  was considered significant.

four weeks for repeated assessments. Mean age of presentation was  $37.94 \pm 13.42$  years. Mean  $\pm$ SD of the initial renal stone size was  $1.57 \pm 0.08$  and endpoint stone sizes was  $0.69 \pm 0.09$  cm. Mean difference in initial and end point stone size was  $0.87 \pm 1.06$  cm, difference was statistically significant (p-value 0.000). Over all mean stone size was reduced. At end point in 107(64.84%) of patients, stones were not seen on renal scan, of these patients more than half (60%) were confirmed removal of stone through urine, while rest were unaware of removal. 10(6.06%) patients had their stone size reduced, 17(10.303%) patients had their stone size unchanged and 31(18.78%) patients had their stone size increased.

## DISCUSSION

Urinary calculi form as a result of physicochemical or genetic derangements leading to super-saturation of the urine with stone forming salts or less commonly from recurrent urinary tract infection with urease producing bacteria.<sup>7</sup> Although not fatal in most of the patients, urolithiasis is a main cause of morbidity resulting in hospitalization, leading to the days off from work.<sup>8</sup> If conservative approach or invasive therapy is not preferred by the patient, they usually turn to medical therapy. Although some oral medications may provide relief from pain, they may be ineffective in some patients. Oral citrate is most commonly used medical treatment for preventing urinary stone disease.<sup>9</sup> However, all the patients do not tolerate this drug and may still form stones while taking the treatment.<sup>10</sup> Owing to the cumbersome side effects of the oral medications, alternative herbal treatments have been used as therapy for thousands of years, especially in Eastern civilizations.<sup>9</sup> Plants with medicinal qualities have been used for various illnesses since the beginning of humanity. Cystone is a herbal treatment, developed for management of urinary stone disease. It was developed in 1943 and since then being used for the treatment of urolithiasis and UTI. The literature evidences showed pharmacological properties of the ingredients of cystone including antimicrobial, anti-inflammatory and antioxidant properties.<sup>11, 12</sup> It also acts as an antispasmodic agent having diuretic and lithotropic properties.<sup>13,14</sup>

Current study showed that significant reduction in size of the renal calculi at primary endpoint of fourth week of treatment with the cystone as compare to initial point of treatment. ( $0.69 \pm 0.48$  versus  $1.57 \pm 1.07$ ) Current results are in accordance with Palaniyamma study that also reported significant decrease in size of renal calculi.<sup>7</sup> However, 10(6.06%) patients had their

stone size reduced using cystone, 17(10.303%) patients had their stone size unchanged while 31(18.78%) of the patients had their stone size increased. In 107 (64.84%) of subjects stones were not identified with the scanning, reflecting expulsion/dissolution of kidney stones, more than half of these patients were self-reported the removal of stone in passage of urine. In previous study by Erickson et al, patients were followed for one year and stone volume was precisely measured pre and post cystone treatment with three dimensional CT scanning. Erickson reported increased stone volume and burden in those patients, suggesting no overall beneficial effect of using cystone herbal preparation.<sup>14</sup> These findings of Erickson was against to our results. Disparity between our results and Erickson might be because of duration of follow up. In our study we just observe our patients on cystone for follow up period of only one month whereas in Erickson study it was of long duration of one year,<sup>15</sup> might be stone volume in his study was increased due to use of cystone drug for long duration by his study participants. While other previous studies have reported that cystone was safe and effective in the treatment of urinary stone disease, with significant relief in clinical symptoms, decrease in stone size, and increased in urinary volume.<sup>5,16</sup> The efficacy of cystone forte can be attributed to synergistic activity of all these herbs present in the formulation in the treatment of urolithiasis.<sup>5</sup> The meta-analysis of 50 clinical studies showed that cystone is helpful in the treatment of Urolithiasis taking into account the symptomatic relief, clearance of stones, increased urinary volume, and reduction in the stone forming constituents in urine with minimal side effects.<sup>17</sup>

**Limitations:** Small sample size and short duration of the study is our limitation. It should be conducted on a broader scale for a long duration with control group following strict protocol to validate the results to be implemented on overall population.

## CONCLUSION

The mean stone size was reduced after using the herbal preparation for one month whereas spontaneous clearance of urinary stones was seen in more than half of the subjects.

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**Conflicts of Interest:** None.

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**Author's Contribution:**

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<b>Dr. Muhammad Sohail</b>	Study design, manuscript writing, Reviewed and approved the manuscript.
<b>Dr. Muhammad Tahir Bashir Malik</b>	Data collection, manuscript writing, compiling and analysis of data, interpretation of results, formulate tables. Reviewed and approved the manuscript.
<b>Dr. Hanan Noor</b>	Study design, data analysis write up and interpretation of results. Revising manuscript critically for important intellectual content
<b>Dr. Muhammad Saifullah</b>	Data analysis, manuscript writing, Revising manuscript critically for important intellectual content
<b>Dr. Muhammad Akram Malik</b>	Data collection, revised manuscript and approved it

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