

EVALUATION OF CLINICAL EFFICACY OF *BRYOPHYLLUM PINNATUM* SALISB FOR TREATMENT OF LITHIASIS

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ABSTRACT

In the present study, clinical efficacy and safety profile of juice of *Bryophyllum pinnatum* Salisb for treatment of lithiasis by performing a non comparative open clinical study was accessed. Patients of lithiasis having <10 mm stones were treated with fresh leave juice of *B. pinnatum* in a single dose of 10 ml/day × 30 days by oral administration. The clinical response was graded as effective, moderate or ineffective by comparing the pre and post treatment ultra-sonographs and x-rays. During the experimental phase 24-h urine samples were collected at baseline and on day 30 of the trial periods and analyzed. Urine analysis data were used to calculate the relative urinary super-saturations of calcium oxalate, uric acid and calcium phosphate. Data were assessed statistically by analysis of variance. Among the 23 patients who underwent the treatment, 64% patients had medium renal stones (<10mm in diameter) and 36% had small sized (<5mm in diameter) stones at different locations. A clinical effective improvement was observed in 87% patients. Remaining 13% patients also showed moderate improvement. Out of five patients of cololithiasis three patients showed effective improvement and two patients showed moderate improvement. Biochemical assays showed that oxalate excretion and super-saturation of calcium oxalate was decreased in treated patients. Therefore, fresh juice of *Bryophyllum pinnatum* may be oral treatment option to treat lithiasis.

Keywords: Lithiasis, *Bryophyllum pinnatum*, Anti-lithiasis, Medical prophylaxis

INTRODUCTION

In industrialized countries 10% of men and 3% of women have renal stones at some time in their life¹⁻². Having a family member with a history of stones doubles these rates. Peak incidence occurs in people aged 35-45 years, but the disease can affect anyone at any age. Most active emergency departments treat an average of at least one patient with acute lithiasis every day depending on the hospital's patient population. The treatment of patients with urinary stones has two aspects: firstly, dissolving or surgically removing stones and secondly preventing recurrence. Recurrence of most types of stone is now preventable with dietary and medical measures. Dissolution of existing stones is difficult, since the urine has to be made under-saturated with the concerned salt or acid continuously for several days or weeks. Cystine, uric acid, magnesium ammonium phosphate and calcium phosphate stones may be dissolved by this technique but it is extremely difficult with calcium oxalate stones which are found in most of the cases. The main alternative to dissolve the stone is surgical removal which may be necessary if there is ureteric or intrarenal obstruction. With most types of treatments, there is a high risk of recurring stones³. Furthermore, all surgical operations including exotic methods like mechanical vibration of the patient ultrasonic lithotripsy, urethral and intrarenal irrigation carry a risk of introducing infection.

About 80% of the world population is dependent (wholly or partially) on plant based drugs⁴. Ayurveda, an ancient Indian traditional system of medicine reported the use of *Bryophyllum pinnatum* Salisb. (Synonym: *Kalanchoe pinnata* Lam.) to remove stones irrespective of their nature and location. Plant was described as Phashanbhed, which mean to dissolve the stones. In Ayurveda, plant is used for the treatment of Ashmari (kidney stone)⁵. *Acolypha indica* is also reported to have antilithiatic activity⁶. *B. pinnatum* is a perennial herb of family Crassulaceae, growing widely and used in folkloric medicine in tropical Africa, India, China, Australia and tropical America. A number of active compounds have been identified in *B. pinnatum*⁷⁻⁸. In traditional medicines the leaves of the plant have been reported to possess antimicrobial⁹⁻¹⁰, anti ulcer, anti inflammatory, analgesic¹¹⁻¹³ and anti-hypertensive¹⁴ activities. In present study, clinical trials for the treatment of lithiasis were undertaken.

MATERIAL AND METHODS

Plant Material and Juice Preparation: Fresh leaves of *B. pinnatum* were collected and juice was prepared. Fresh juice of leaves was prescribed for every dose to the patients.

Patients: Twenty three patients in the age ranged from 25 to 55 years of both gender were voluntarily involved after their consent before start up of study. 50% patients had a well-documented history of persistent or recurrent stones despite intermittent treatments. The patients who had stones <10 mm in size were included in the study. The patients having severe complications were advised for hospital treatment.

Diagnosis: Ultra-sonographs and x-rays were carried out on all patients before and after treatments. Stone size was recorded arbitrarily from the ultra-sonographs and x-ray films as medium (longest diameter <10 mm), and small (5-2 mm). Patients having large stones (diameter >10mm) were referred to hospital treatment and were not included in the study. Different clinical symptoms such as burning and painful micturation, pain in flank were recorded. All the volunteers were monitored every week.

Treatment: The patients who had kidney stones <10 mm in size were treated with the 10 ml/day × 30 days oral doses of juice of *B. pinnatum*. The patients were asked to drink fresh juice early in morning with empty stomach. During the experimental phase patients were allowed to take their regular diets and to keep a record. An antibiotic (cotrimoxazole) was prescribed to control bacterial infection in some cases, according to therapeutic doses. The clinical response was graded as effective, moderate or ineffective by comparing the pre and post treatment ultrasonographs and x-ray films.

Urine Samples: 24-h urine samples were collected at baseline and on day 30th of the trial periods and analyzed. Oxalate, citrate, phosphate, urate and creatinine in urine samples were measured by using commercially available assay kits. Urine analysis data was used to calculate the relative urinary super-saturations of calcium oxalate, uric acid and calcium phosphate using the computer algorithms. Urinary pH and volume were routinely measured for each sample. All data were assessed statistically using ANOVA, with differences considered statistically significant at P<0.05.

RESULTS

Patients: Ultra-sonographs and x-ray films study revealed that seventeen patients were of nephrolithiasis and four of urolithiasis. The five patients had multiple stones including recurrent cololithiasis. Fifteen patients of lithiasis had multiple unilateral and bilateral stones. Rest of the penitents had only one stones of medium sized.

Stones: Among the 23 patients, 64% of the patients had medium renal stones (<10mm in diameter) and 36% had small sized (>5mm in diameter) stones. During the study twenty patients passed stones or "gravel"; and three had a size reduction. A clinical effective improvement was observed in 87% patients. Remaining 13% patients also showed moderate improvement. For cololithiasis three patients showed effective improvement and two patients showed moderate improvement.

Urine Samples: Table 1 and 2 presents the mean urinary variables and the computed risk indices. The ingestion of juice produced three

statistically significant changes in urine composition that were not present at baseline. Oxalate excretion was observed to be decreased relative to first day. Citrate excretion was found to be significantly increased (all $P < 0.001$) which has well defined role in binding calcium and inhibiting calcium oxalate crystallization. Therefore, it is reasonable to presume that high urine citrate levels could dissolve the calcium oxalate stone. Phosphate excretion was found to be decreased relative to the control ($P=0.0112$).

The relative super-saturation of calcium oxalate decreased significantly after consuming juice tended to be significantly lower than that on base line ($P=0.001$). Several urinary risk factors were also altered significantly, i.e. pH and total urine volume increased, while calcium excretion and the relative super-saturations of brushite and uric acid decreased. Creatinine clearance was not significantly different at the baseline and after treatment although greater clearance in treated group was noticed.

Table 1: Comparison of urinary variables for the control and juice regimens

Variable	Before Treatment	After Treatment	P
pH	6.05±0.08	6.41±0.06	0.013
Volume, ml/24 h	1504.0±114.6	1905.0±71.91	<0.001
Oxalate, mmol/24 h	0.16±.002	0.10±0.005	<0.001
Citrate, mmol/24 h	1.83±0.28	3.25±0.18	0.001
Urate, mmol/24 h	3.32±0.14	2.72±0.18	0.102
Creatinine, mmol/24 h	13.12±0.63	14.91±0.54	0.745
Phosphate, mmol/24 h	28.23±2.12	32.18±1.76	0.0112

Table 2: Comparison of relative super-saturation of urinary variables for the control and juice regimens

Variable	Before Treatment	After Treatment	P
Brushite	1.64±0.17	0.650±0.13	<0.001
Uric acid	2.00±0.21	0.106±0.18	<0.001
Ca Oxalate	4.88±0.23	1.250±0.20	<0.001

DISCUSSION

B. pinnatum is a well characterized drug in the traditional medicinal system of India to treat and prevent lithiasis effectively. Till date plant was studied for its different properties but not for its anti-lithiasis properties. The regular fresh juice of *B. pinnatum* based medical prophylaxis effectively dissolved the stones in 87% patients and remaining patients showed moderate improvement. In this study, it was demonstrated that regular medical prophylaxis effectively dissolves the stones regardless of its position, nature and previous treatments. Biochemical investigations showed that the ingestion of juice favourably and uniquely altered three key urinary risk factors, i.e. oxalate excretion decreased, while citrate excretion increased. The reduced oxalate excretion after drinking juice is important as it is a key risk factor in calcium oxalate stone formation. In the present study, drinking juice increased urinary citrate. It is noteworthy that plant is reported for considerable high levels of citric acid, malic acid and malate, which might be helpful to increase urine citrate levels. This is an important finding, as citrate is universally regarded as an effective inhibitor of calcium oxalate stone formation¹⁵. Urinary phosphate was observed to be reduced favorably which is a risk factor for brushite and apatite saturation. The relative super-saturation of calcium oxalate decreased significantly and the increase in pH, suggesting dilution effects. The studies suggest that juice may have antilithogenic properties (with respect to the relative super-saturation of calcium oxalate). The significantly higher urine volumes produced by the juice is an indication of fluid compliance and gives confidence in these data. Indeed, other significant changes during treatment (in relative super-saturations of brushite and uric acid) may be attributed to urinary dilution effects. The assessment of drug dose in case of kidney patients is also important to avoid the consequences¹⁶.

CONCLUSIONS

It may be concluded from the study that taking fresh juice of *B. pinnatum* favorably remove the medium and small sized stones

regardless of its position and nature by altering important risk factors for stone formation, and as such it deserves to be considered as therapeutics in managing this disease. However, study lacks the long term follow ups which are required to clarify the exact role of the plant juice for preventing the lithiasis. But it also provides possibility of developing a non-toxic and low cost alternative for treating or preventing lithiasis.

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