



## Evaluation of Efficacy and Safety of Renomet, a Polyherbal Formulation in the Treatment of Urolithiasis: A Double Blind Randomized Study

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### ABSTRACT

Nephrolithiasis is one of the most commonly occurring disorders in India. Although this disorder is seen in any age group, young and middle aged individuals are the most common sufferers. The treatment of nephrolithiasis is mostly diuretics or surgical procedure. However, commonest complaint of patients where the stones have been removed surgically is recurrence. Therefore a need was felt to evaluate the efficacy of Renomet, a poly herbal product in the treatment of nephrolithiasis. Seventy four patients between 35-60 years of age and fulfilling inclusion criteria were included in the trial. All the patients had multiple stones up to 9 mm in size and had past history of renal stones surgically removed. They were divided in to two groups after obtaining the informed consent and administered either Renomet or a commercially available herbal formulation at the dose of 1 tablet twice daily for 6 weeks. Patients were asked to report for any side effect during the treatment period. At the end of the trial, patients in the Renomet treated group were found to be symptom free and about 98% of them had passed the stone. Whereas in the herbal supplement (CAHP) group only 68% patients had passed stones. The average size of the stone in group A and B at the time of recruitment were  $8.88 \pm 0.26$  and  $7.10 \pm 0.88$  respectively. After 6 weeks of treatment with Renomet Group A, dysuria and hematuria improved in all (100%) and pain abdomen improved in 98.6% cases. In group B, after 6 weeks of treatment with CAHP, pain abdomen was still present in 8.7%, hematuria in 3.26% and dysuria in 14.99% of cases. The average size of the stone reduced to  $4.1 \pm 0.22$  in group A, while in group B the size reduced to  $5.56 \pm 0.43$ .

**Keywords:** Renomet, nephrolithiasis, calcium oxalate, *Saxifraga lingulata*, *Tribulus terrestris*, *Dolichos biflorus*.

### INTRODUCTION

Nephrolithiasis, or kidney stone disease, is a condition in which individuals form calculi (stones) within the renal pelvis and tubular lumens. [1] Stones form from crystals that precipitate (separate) out of the urine. Stone formation may occur when the urinary concentration of crystal-forming substances (calcium, oxalate, uric acid) is high and/or that of substances that inhibit stone formation (citrate) is low. [2] Although nephrolithiasis may occur at any age, onset is more common in young and middle-aged adults. Lifetime prevalence is estimated at 13 percent for men and 7 percent for women [3] and after an episode of stone occurrence and

removal, the spontaneous 5-year recurrence rate is about 35 to 50 percent. [4] Medical conditions that increase the risk of nephrolithiasis include primary hyperparathyroidism, [5] obesity, [6] diabetes, [7] and gout. [8] Dietary factors associated with increased risk of nephrolithiasis include low fluid intake and high dietary calcium. However, evidence is mixed for diets with increased animal protein, low dietary magnesium, low dietary potassium, and increased sodium. [9-11] With respect to fluid intake, different beverage types appear to have different impacts on the risk of nephrolithiasis. [12-13] It is estimated that at least 10% of the population in the industrialized part of the world is afflicted by urinary tract stone disease. Kidney stones are common in industrialized nations with an annual incidence of 0.5% to 1.9%. [14] In India upper and lower urinary tract stones occur frequently but the incidence shows wide regional variation. [15] The incidence of renal calculi is comparatively low in the

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southern part of country compared to other parts.<sup>[16]</sup> The prevalence of urolithiasis is as high as 7.6% in Satpura part of Maharashtra.<sup>[17]</sup> A high and progressively increasing incidence of urolithiasis has been reported in Udaipur and some other parts of Rajasthan in the western part of India.<sup>[18]</sup> With its varied etiology and high rate of recurrences, urolithiasis provides a medical challenge. Many studies from India have also documented that calcium oxalate forms the major constituent of renal calculi disease. The increase incidence of stone formation is mainly attributed to changes in life style, mostly sedentary habits and an unhealthy dietary plan. Increase in body weight is also an issue in developed and underdeveloped countries. Major risk factors that contribute to stone formation and its recurrence include "classic" risk factors in the urine (low urine volume, hypercalciuria, hyperoxaluria, hyperuricosuria and hypocitrauria). Many factors like- climate, race, ethnicity, age, sex, body weight is also responsible for this boom. Western countries have also encountered this problem,<sup>[19]</sup> affecting 1 person in 1,000 annually and the incidence is increasing in tropical developing countries too.<sup>[20]</sup> The peak age of onset is in the third decade, and prevalence increases with age until 70. The prevalence of calculi ranges from 4 to 20 percent<sup>[21]</sup> in the Afro-Asian belt. Other reports suggested that kidney stone disease is uncommon before the age of twenty years. Men are at greatest risk of developing kidney stones with incidence and prevalence rates between 2-4 times that of women.<sup>[22-24]</sup> Men have higher oxalate concentrations than in women.<sup>[25]</sup> Such high incidence of calcium oxalate stones have been attributed to major consumption of cereals like millet, which are high in calcium and phosphate, beside factors like lack of animal proteins and increased consumption of oxalate rich vegetables.<sup>[26]</sup> Once a patient suffers from the first episode of urinary calculi, the chance of recurrence is high (30% in next 10 years for calcium stone former).<sup>[27]</sup> Nephrolithiasis often is incidentally identified in asymptomatic patients who undergo plain radiographs or computed tomographic imaging for another indication.<sup>[28]</sup> Small stones generally pass through the urinary tract without symptoms. While larger stones may cause symptoms, more than 90 percent of stones  $\leq 5$  mm in diameter still passes through the urinary tract without intervention, as compared to spontaneous passage of approximately 50 percent of stones 5 to 10 mm in diameter.<sup>[29]</sup> Potential symptoms of nephrolithiasis include: urinary symptoms such as dysuria, hematuria, and urgency; renal colic with severe abdominal and flank pain, nausea and vomiting, urinary tract obstruction and infection and acute, though generally transient, impairment in renal function. Large struvite stones remain in the renal pelvis and may not cause pain. Some studies have suggested that nephrolithiasis also may increase the risk of chronic kidney disease.<sup>[30]</sup> Nephrolithiasis also may lead to hospitalizations and procedure-related morbidity. Direct medical expenditures for nephrolithiasis in the United States have been estimated at \$2.1 billion annually.<sup>[31]</sup> Renal stone was well known in olden times in Ayurveda. Ashmari was correlated to urolithiasis. Sushruta, the father of surgery, has elaborately described the etiopathogenesis, symptomatology, and management of ashmari by drugs, paramedical therapy and surgery. Kulattha, Varun, and Pasanbhed are among the herbs which were used by ancient and recent practitioners in ayurvedic medicine. Researchers and Ayurvedic practitioners have proposed that these

ayurvedic herbs have lithotriptic and lithopreventive properties. After a thorough survey of the incidence and prevalence of nephrolithiasis in our state, we had decided to conduct a clinical trial to prove the safety and efficacy of an herbal product Renomet in Nephrolithiasis and compared it with another commercially available herbal product. Renomet, a polyherbal formulation contains *Saxifraga lingulata* 150 mg, *Tribulus terrestris* 100 mg, *Dolichos biflorus* 100 mg, *Crataeva nurvala* 100 mg.

## MATERIALS AND METHODS

Patients of renal calculus and fulfilling the inclusion criteria were included in this study after obtaining informed consent from them. Total of 74 cases who fulfilled the following inclusion criteria were included in the study:

1. Patient with renal calculus proved on X-ray KUB and urine showing calcium oxalate crystalluria
2. Serum creatinine  $< 2$  mg%
3. Patient not taking any other lithotriptic agent
4. Stone size up to 9 mm

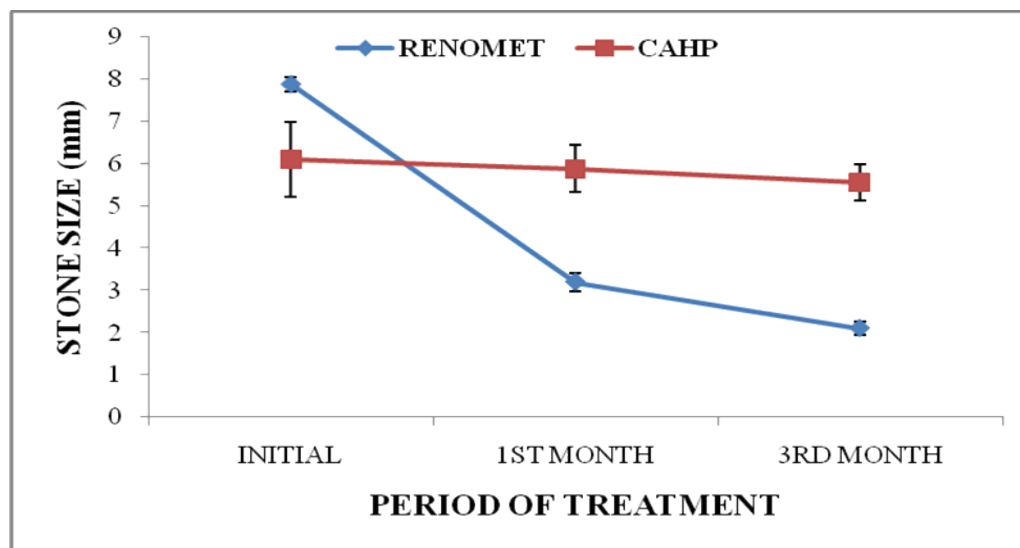
Patients with serum creatinine  $> 2$ mg%, stone size  $> 9$ mm or with radiological evidence of hydronephrosis (grade 3 or above) were excluded from study. Patients were randomly divided into two groups, group A was given Renomet at the dose of 1 tablet twice daily and group B received commercially available herbal product at the dose of 1 tablet twice daily for 6 weeks. All the patients were thoroughly examined. All of them were subjected to base line urine, hematological, biochemical and radiological investigation. Patients were followed up for a period of 6 weeks. Patients in both the groups were evaluated and reassessed for any improvement or deterioration of symptom. Patients had undergone investigation at the time of recruitment and at the end of 6 weeks. Clinical improvement with radiological evidence of reduction and absence of calculus or history of passage of stone in urine was taken as criteria for improvement.

## RESULTS AND DISCUSSION

Nephrolithiasis often is incidentally identified in asymptomatic patients who undergo plain radiographs or computed tomographic imaging for another indication.<sup>[32]</sup> Small stones generally pass through the urinary tract without symptoms. While larger stones may cause symptoms, more than 90 percent of stones  $\leq 5$  mm in diameter still passes through the urinary tract without intervention, as compared to spontaneous passage of approximately 50 percent of stones 5 to 10 mm in diameter.<sup>[33]</sup> Increasing water intake should increase urine volume and lower the urinary concentration of all crystal-forming substances. Dietary restrictions are also important in preventing or at least delaying the recurrence of renal calculi.<sup>[34]</sup> Reducing dietary oxalate may lower urinary oxalate and the risk of calcium oxalate stones; reducing dietary animal protein and other purines may lower urinary uric acid and the risk of uric acid stones; and increasing dietary calcium to bind intestinal oxalate and thereby lower urinary oxalate and the risk of calcium oxalate stones are some of methods adopted to reduce formation of stones.<sup>[35]</sup> Currently, in the management of urinary stones surgical procedures and extra corporeal shock wave Lithotripsy are commonly employed. The major drawback of these procedures is recurrence of stones.<sup>[36]</sup> The plant products and

**Table 1: Showing various parameters before and after treatment with Renomet and CAHP**

Parameters (mg%)	Renomet			CAHP		
	Initial	30 days	45 days	Initial	30 days	45 days
Creatinine	1.22 ± 0.12	0.91 ± 0.1	0.97 ± 0.16	0.87 ± 0.11	0.88 ± 0.14	0.90 ± 0.13
Urea	26.8 ± 1.31	26.6 ± 2.12	25.18 ± 1.61	26.2 ± 2.1	29.17 ± 2.11	28.67 ± 2.31
Calcium	8.75 ± 1.22	8.12 ± 2.16	7.9 ± 1.11	9.23 ± 1.4	9.43 ± 2.68	8.79 ± 2.13
Phosphorus	3.16 ± 0.23	3.45 ± 0.12	4.14 ± 0.31	4.01 ± 1.12	4.34 ± 1.01	4.07 ± 0.97
Uric Acid	3.87 ± 0.33	3.78 ± 0.45	4.12 ± 0.41	4.23 ± 0.87	3.99 ± 1.02	4.12 ± 0.91
Hemoglobin	12.2 ± 1.12	11.77 ± 1.01	12.67 ± 1.34	11.12 ± 0.88	11.23 ± 1.12	12.1 ± 0.78

**Fig. 1: Showing response of Renomet and CAHP on renal stone size in patients suffering from urolithiasis****Table 2: Showing size of stones before and after treatment with Renomet and CAHP (Value in mm)**

Group	Initial	30 days	3 <sup>rd</sup> Month
Renomet(Group A)	8.88 ± 0.17	6.2 ± 0.21	4.1 ± 0.26*
CAHP(Group B)	7.10 ± 0.88	6.88 ± 0.56	5.56 ± 0.43**

Each value Mean ± SEM, \*p<0.001, \*\*p<0.05

derivatives of their active compounds as such may not replace these procedures but may surely help in decreasing the recurrence rate of renal calculi. The main drawbacks in the development of a standard drug may be the multicausal nature of urolithiasis, different biochemical disorders that leads to urolithiasis and different chemical varieties of renal stones.<sup>[37]</sup> During this study one thing that was clearly observed was the fact that patients who had undergone surgical procedure previously for removal of stone refused to undergo similar procedure again and again. For them any therapy that would remove renal stone and would prevent recurrence would be preferred. After 6 weeks of study the data was analysed which show the following:

The age of patients ranged from 35-60 years. Mean age in both groups was well matched and no statistical difference was noted. Most common presenting feature was the subjective feeling of pain abdomen in 95-100% patients in both groups. Other common symptoms were nausea, vomiting, dysuria and hematuria. In group A there were 40 patients and in group B the number of patients was 36. At the time of recruitment, the symptoms of patients in group A were as follows: pain abdomen was present in 100%, hematuria in 12.14% and dysuria in 100% of patients at presentation and in group B pain abdomen was present in 100% cases, hematuria in 14.12% and dysuria 98% cases. The average size of the stone in group A and B at the initiation of the study was 8.88 ± 0.26 and 7.10 ± 0.88 respectively. After 6 weeks of treatment with Renomet, dysuria and

hematuria improved in all (100%) and pain abdomen improved in 98.6% cases. In group B, after 6 weeks of treatment with CAHP, pain abdomen was still present in 8.7%, hematuria in 3.26% and dysuria in 14.99% of cases. The average size of the stone reduced to 4.1 ± 0.22 in group A, while in group B the size reduced to 5.56 ± 0.43.

In group A, 98% of patients passed the stones but in group only 68% patients passed stones.

Nephrolithiasis carries significant morbidity and imposes tremendous financial burden on healthcare system. With changing lifestyles and climate, its prevalence has shown a rise over decades, e.g., 37% rise in USA from 1976 to 1994.<sup>[38]</sup> Life-time risk of urolithiasis varies from 1-5% in Asia, 5-9% Europe, 10-15% USA and 20-25% middle-east; lowest prevalence is reported from Greenland and Japan.<sup>[39]</sup> The situation is not unlikely to be similar in various geographical regions worldwide making it alarming enough to lay more stress on preventive aspect of urolithiasis.

The present study clearly shows that Renomet a multiherbal product is safe and effective in not only reducing the size of stones but is also effective in eliminating the stones. About 98% patients in the Renomet treated group passed stones within the treatment period and became symptom free. Reduction of stone size was more or less similar in both the groups; patients in Renomet treated group were symptomatically better indicated by complete remission of symptoms. Patients who continue to have stones and hematuria were referred for definitive treatment. However, a bigger trial with more number of patients in various geographical locations is necessary to fully evaluate the efficacy of this product in controlling recurrence.

#### CONFLICT OF INTEREST STATEMENT

We declare that we have no conflict of interest.

## ACKNOWLEDGEMENT

We convey our sincere thanks to Matxin Labs, Bangalore for providing necessary support, medicines and other help to successfully complete this study.

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