Original Article

Randomized single-blind clinical evaluation of Safoof-e-Pathar phori in urolithiasis patients

Abstract

Objective: Safoof-e-Pathar phori (SPP), a unani polyherbomineral formulation, used for antilithiatic activity since long time. This study was aimed to evaluate the clinical efficacy of SPP in adult human patients with urolithiasis. The study was a randomized, placebo-controlled, and single-blind, clinical trial. **Materials and Methods:** Forty-five patients who have stone size below 15 mm in the age group of 15–55 years with diagnosis of calcium oxalate renal calculi were taken in the study. Out of which, only 30 patients fulfilled the criteria and completed the study. Twenty patients received SPP (Group I) and ten patients were given placebo (Group II) for 2 months. The patients were investigated for routine, hemogram, blood urea, serum creatinine, calcium, phosphorus, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, and uric acid levels at definite time intervals. Similarly, routine and microscopic urine examination was done with radio-imaging KUB and ultrasound KUB examination, etc., which were repeated on completion of the study. **Results:** All patients received the same dosage of SPP or placebo for a 2-month period. On starting SPP, symptomatic relief was reported by patients. The disappearance of stones was noted in patients as confirmed by X-ray KUB and Ultrasound KUB examination. Totally, 56.67% of patients showed reduction in size of stone and 49.31% showed litho expulsive effect. **Conclusion:** The use of SPP in the treatment of calcium oxalate stone as noninvasive remedy for the urolithiatic patients is validated and proved. Since the dose of formulation is too high, further study on dose reduction followed by preclinical evaluation may be attempted for development of scientific data.

Key words:
Calcium oxalate, Safoof-e-Pathar phori, urolithiasis

Introduction

Urolithiasis affects 1–5% of population in industrialized countries with a progressive decline in incidence of western countries. The incidence of urolithiasis is higher in developing countries (including India) than in industrialized countries. It has been hypothesized that the main source of dietary proteins being cereals is an important etiological factor.[1] The Northern and Northwestern regions of India can be described as an endemic stone-forming belt due to a dietary pattern rich in cereals and pulses.[2] The present study was planned to evaluate the efficacy and safety of Safoof-e-Pathar phori (SPP), a polyherbal formulation in urolithiasis.

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SPP is a unani polyherbomineral formulation and has been used in unani system of medicine for its antiurolithiatic

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activity. It is a powdered formulation which contains six different plant/mineral constituents: Pathar phori (*Didymocarpous pedicellata*), kulthi (*Dolichos biflorus*), revand chini (*Rheum emodi*), namak turb (*Raphanus sativus*), jawakhar (potassium carbonate), and shora qalmi (potassium nitrate).[3]

Materials and Methods

Study design

This study was a randomized, placebo-controlled single-blind. The clinical trial approved by the Ethics Committee of Jamia Hamdard, New Delhi.

Inclusion criteria

Forty-five patients, in between 15-65 years, of either sex, were diagnosed as a case of urolithiasis below the size of 15 mm by ultrasonographically or radiologically were taken into the study. A written informed consent was signed by all the patients.

Exclusion criteria

The study was not conducted on the patients requiring immediate surgery, acute renal failure, pregnant or lactating women, hepatic or renal or cardiac disease having severe hydronephrosis, and those unwilling to give informed consent.

Study procedure

All included patients were stratified by diagnosis (renal calculi) and from each stratum, patients were randomized to receive SPP or placebo.

A baseline history was obtained to determine the patient's eligibility for enrollment in the trial, to compare the study groups, and to describe the study population. The baseline assessment included personal data, description of symptoms, and details of past medical history, after which all patients underwent a complete clinical examination.

All patients were investigated for routine hemogram and blood urea, serum creatinine, sodium, potassium, calcium and phosphorus, and uric acid levels. In all patients, routine and microscopic urine examination was done.

All patients also underwent Abdominal X-ray KUB ultrasound KUB examination. All these investigations were repeated for 60 days.

All patients received the same dosage of SPP or placebo (4.0 g, twice daily) for 60 days.

Primary and secondary outcome measures

The predefined primary outcome measures included the effect on urinary excretion of stone formation inhibitors, change in the number and size of stones, and spontaneous passage of stone and secondary measures were symptomatic relief and to prevent urinary tract infection..

Adverse events

All adverse events reported or observed by patients were recorded with information about severity, date of onset, duration, and action taken regarding the study drug. Relation of adverse events to study medication were predefined as "unrelated" (a reaction that does not follow a reasonable temporal sequence from the administration of the drug), "possible" (follows a known response pattern to the suspected drug but could have been produced by the patient's clinical state or other modes of therapy administered to the patient), and "probable" (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient's clinical state).[4]

Patients were allowed to voluntarily withdraw from the study if they had experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For patients withdrawing from the study, efforts were made to ascertain the reason for dropout. Noncompliance (defined as failure to take <80% of the medication) was not regarded as treatment failure, and reasons for noncompliance were noted.

Statistical analysis

Statistical analysis was done for the drug and placebo groups to compare baseline characteristics with regards to age, blood urea, serum creatinine, calcium, and phosphorus levels using the "unpaired *t*-test," both by "assuming and not assuming equal variances." One-way ANOVA test followed by Dunnett's multiple comparison and unpaired '*t*' test for evaluation of symptomatic scores.

Results and Discussion

Forty-five patients were enrolled in the study, out of which four patients were excluded from the study and 11 patients were lost to follow-up. Both the drug and placebo groups were statistically comparable.

The demographic data of the patients on entry [Table 1] indicated that twenty-five males and five female patients with a mean age of 26.80 ± 10.15 years were included in the study. Out of the 30 subjects, 20 subjects received SPP and 10 subjects received placebo in a random fashion. With SPP treatment, a statistically significant ($P < 0.001$) symptomatic relief from intermittent abdominal pain (74%) and low backache (54%) was observed [Table 2].

There was also an improvement in the frequency and flow of urine though it was not significant. Urine analysis indicated statistically significant ($P < 0.001$) improvement

in microscopic hematuria, pus cells, and crystalline sediments [Table 3].

The disappearance of the calculi as seen by ultrasonography was noticed in 10 out of 20 patients, treated with SPP ($P < 0.001$) and a decrease in the size of the stone in remaining subjects. In patients treated with placebo, out of 10 patients, there was no disappearance of stone in any patient. The disappearance of the calculi by plain X-ray KUB and ultrasound KUB was seen in 10 out of 20 patients treated with SPP ($P < 0.001$); there was decrease in the size of the stone in another ten subjects. In patients treated with placebo, out of 10 patients, there neither disappearance nor any reduction in size of stone [Table 4].

The study showed statistically significant reduction in the calculi size from 10.42 ± 3.28 to 3.98 ± 5.17 (56.67%) at the end of the treatment in SPP group ($P < 0.0001$) as compared to placebo [Table 5]. There were no changes observed in the hematological parameters. There were no adverse effects either reported or observed during the study.

There are a number of options for treatment of urinary calculi, including surgery, endoscopic procedures such as ureteroscopy, percutaneous nephrolithotomy, and extracorporeal shockwave lithotripsy.[5] Patients invariably prefer to have a medical therapy for advantage of convenience. Medications such as calcium channel blockers, alpha-adrenergic blockers, and steroids are used, but adverse effects compromise their long-term consumption. On the other hand, some herbal remedies have been used to treat urinary stone disease although scientific principles have been lacking. With the understanding of many pathophysiological features underlying stone disease and the mechanism of herbal remedies that can have a role in the formation and treatment of urinary stone, phytotherapy might be an alternative treatment with an effective, safe, and acceptable options. Although some oral medications have positive effects, they are not effective in all patients. Oral citrate is one of the most widely used medical therapies for preventing urinary stone disease.[6] However, this drug is not tolerated by all patients, and some patients are still active stone formers during this therapy.[7] Due to adverse effects of these drugs, alternative treatment modalities comprised herbal remedies have been the mainstay of medical therapy for thousands of years, especially in Eastern civilizations.[6] Use of medicinal plants as a source of relief and cure from various illness is as old as humankind itself. Even today, medical plants provide a cheap source of drugs for majority of olds population. Plants have provided and will continue to provide not only directly usable drugs but also a great variety

Table 1: Demographic data on patients on entry

Parameters	Safoof-e-Pathar phori	Placebo
Means age in years	26.80 ± 10.15	26.80 ± 8.70
Male: female	17:3	7:2
Smokers	11	15
Alcoholics	8	12
Diet (vegetarian: nonvegetarian ratio)	12:8	16:6
Pain	20	10
Low backache	15	8

Table 2: Effect of Safoof-e-Pathar phori on clinical symptoms of urolithiasis

Parameters	Safoof-e-Pathar phori ($n=20$)		Placebo ($n=10$)	
	On entry	End of 2nd month	On entry	End of 2nd month
Pain				
Present	20	9	10	8
Absent	0	11	0	02
Low backache				
Present	20	8	08	06
Absent	0	12	02	04
Decrease in urinary frequency				
Present	06	4	03	03
Absent	14	16	07	07

$P<0.0001$ as compared to on entry value

Table 3: Effect of Safoof-e-Pathar phori on urine analysis

Parameters	Safoof-e-Pathar phori ($n=20$)		Placebo ($n=10$)	
	On entry	End of 2nd month	On entry	End of 2nd month
Microscopic hematuria				
Present	14	0	07	05
Absent	06	20	03	05
Urinary infection (microscopy evidence)				
Present	13	02	06	06
Absent	07	18	04	04

$P<0.0001$ as compared to on entry value

Table 4: Effect of Safoof-e-Pathar phori on radiological investigation

Parameters	Safoof-e-Pathar phori ($n=20$)		Placebo ($n=10$)	
	On entry	End of 2nd month	On entry	End of 2nd month
X-ray abdomen showing renal calculi				
Present	20	07	10	10
Absent	0	13	0	00
Renal ultrasonography showing renal calculi				
Present	20	10	10	10
Absent	0	19	0	00

$P<0.0001$ as compared to on entry value

Table 5: Effect of Safoof-e-Pathar phori on calculi size

Parameters	On entry		End of 2nd month	
	Safoof-e-Pathar phori ($n=20$)	Placebo ($n=10$)	Safoof-e-Pathar phori ($n=20$)	Placebo ($n=10$)
Calculi size in mm	10.42±3.28	10.11±4.1	3.98±5.17	11.29±6.1

$P<0.0001$ as compared to on entry value

of chemical compounds that can be used as starting points for the synthesis of new drugs with improved pharmacological properties.[8] World Health Organization (WHO) has also emphasized development and utilization of herbal drugs and traditional medicines for the benefit of the world population, in terms of cost-effectiveness and side effects of the drugs. WHO has also estimated that about 80% of the population living in the developing countries relies on traditional medicines for their healthcare needs.[9]

SPP is an polyherbal formulation and has been used since long time for the management of urolithiasis or renal calculi.[10]

Herbs such as *D. pedicellata* has been shown to have diuretic activity.[11] Another plant *D. biflorus* contains a dipeptide pyroglutamylglutamine responsible for diuretic activity which is 2–3 times more potent than acetazolamide.[12] *R. emodi* is used for the anti-inflammatory, analgesic effects and found antioxidant potential in this.[13]

Conclusion

The present study indicates that SPP is an effective and safe alternate in the management of urolithiasis. It brings about significant symptomatic relief and helps in expulsion of stone or reducing the size of the renal stones. No clinically significant adverse reactions were reported or observed during the study period. A further study in a larger population will be required to confirm the evidence seen in the present clinical study.

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Conflicts of interest

There are no conflicts of interest.

References

1. Polinsky MS, Kaiser BA, Baluarte HJ. Urolithiasis in childhood. Pediatr Clin North Am 1987;34:683-710.
2. Teotia M, Teotia SP. Kidney and bladder stones in India. Postgrad Med J 1977;53 Suppl 2:41-51.
3. Ahmad W, Zaidi SMA, Mujeeb M, Ansari SH, Ahmad S. HPLC and HPTLC methods by design for quantitative characterization and *in vitro* anti-oxidant activity of polyherbal formulation containing *Rheum emodi*. J Chromatogr Sci 2014;52:911-8.
4. Ravichandran G, Bhardawaj VS, Kolhapure SA. Evaluation of the clinical efficacy and safety of "Anti-Dandruff Shampoo" in the treatment of dandruff. Antiseptic 2004;201:5-8.
5. Heilberg IP, Schor N. Renal stone disease: Causes, evaluation and medical treatment. Arq Bras Endocrinol Metabol 2006;50:823-31.
6. Gürocak S, Küpeli B. Consumption of historical and current phytotherapeutic agents for urolithiasis: A critical review. J Urol 2006;176:450-5.
7. Mattle D, Hess B. Preventive treatment of nephrolithiasis with alkali citrate – A critical review. Urol Res 2005;33:73-9.
8. Potterat O, Hosttettman K. Plant source of natural drugs and compounds. In: Nierenberg WA, editor. Encyclopedia of Environmental Biology. Vol. 13. London: Academic Press Inc.; 1995. p. 139-53.
9. World Health Organization (WHO). World Health Organization Monographs on Selected Medicinal Plants. Geneva: World Health Organization; 2002.
10. Anonymous. Qarabadeen Majeedi All India Unani Tibbi Conference Delhi; 1986.
11. Chopra RN, Nayar SL, Chopra LC. *Didymocarpous pedicellata*. In: A Glossary of Indian Medicinal Plants. 4th ed. New Delhi: National Institute of Science Communication; 1996a. p. 96.
12. Anonymous. The Unani Pharmacopoeia of India. Vol. 1. New Delhi: Ministry of Health and Family Welfare, Dept. of AYUSH, Govt. of India; 2007. p. 58-9.
13. Anonymous. The Unani Pharmacopoeia of India. Vol. 1. New Delhi: Ministry of Health and Family Welfare, Dept. of AYUSH, Govt. of India; 2007. p. 91-2.