Original Article

Prospective randomized clinical trial comparing phytotherapy with potassium citrate in management of minimal burden (≤8 mm) nephrolithiasis

Iqbal Singh[1], Ishu Bishnoi, Vivek Agarwal, Shuchi Bhatt[2]

Departments of Surgery, [1]Urology, and [2]Radiodiagnosis, University College of Medical Sciences (University of Delhi) and GTB Hospital, Delhi, India

Abstract

Aim: To compare efficacy and tolerability of phytotherapy (PT) vs. potassium citrate (KC) in patients with minimal nephrolithiasis. To compare and assess changes in value of certain serum ($Ca^{2}+$, PO_4^{3-}, uric acid [UA]) and urinary (24-hr Ca^{2+}, PO_4^{3-}, UA, citrate, oxalate, and urine pH) parameters in patients being treated with PT or KC.

Materials and Methods: After clearance by the local institutional ethics committee, 60 patients of nephrolithiasis who had consented for the study, were enrolled (as per entry criteria) and randomized into citrate therapy (group-I) or PT (group-II). PT was administered as a nutritional supplement, using a lupeol-based extract (Tablet Calcury™, two tablets twice a day). They were monitored for the changes in the serum and urinary biochemical, radiological, and clinical parameters (efficacy and tolerability) as per protocol.

Results: Group-I patients demonstrated favorable changes in certain biochemical parameters (decreased serum calcium, urinary UA/oxalate, increased urinary citrate and pH) along with significant symptomatic improvement (decrease in visual analogue pain score with increased stone clearance/reduction in stone size). Four (13.3%) patients of group-I had mild upper gastrointestinal discomfort which was controlled with antacids. Group-II patients had favorable changes in biochemical parameters (decreased serum UA and increased urinary citrate) along with significant symptomatic improvement (reduction/clearance in the stone size), but without any noticeable side effects.

Conclusions: Medical therapies with both KC and PT (with lupeol extract using Calcury™) were effective in reducing the stone size and symptoms of nephrolithiasis. It appeared that KC was biochemically efficacious in producing some favorable biochemical changes with some side effects, whereas PT was probably clinically efficacious in hastening stone expulsion (<8 mm) without any observed adverse events. Although both the medical therapies were not effective in all aspects, we believe that PT using lupeol-based extract (Calcury™) may be used as an alternative form of medical therapy in select patients with minimal nephrolithiasis. Long-term randomized placebo-controlled trials are needed to better define the precise role of lupeol-based PT *vs*. citrate therapy in minimal nephrolithiasis.

Key Words: Medical therapy, nephrolithiasis, phytotherapy, potassium citrate

Address for correspondence:
Dr.(Prof.) Iqbal Singh, F-14 NDSE-2, New Delhi - 110 049, India. E-mail: iqbalsinghp@yahoo.co.uk

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INTRODUCTION

About 15% of the population is globally affected by nephrolithiasis, if neglected it can cause obstructive uropathy, sepsis, and renal failure.[1] Based on the stone burden and composition, and the patient's general condition,[2] treatment includes minimally invasive (interventional) therapy and/or medical management. Medical therapy for nephrolithiasis

comprises dietary manipulation, fluid intake, drug manipulation for certain stones, and phytotherapy (PT) (plant extracts).[3-5] The benefit of potassium citrate (KC) in the dissolution of some renal stones is proven,[6-9] though with certain limitations.[6,10] Scientists have also explored the use of alternative herbal medicines (PT) for nephrolithiasis,[5,11-13] with both experimental studies[11-16] and some human trials[17-19] showing good results. Plant extracts with renal antilithogenic efficacy include lupeol[12-17] (*Crataeva nurvala*), aspartic acid-saponins (*Tribulus terrestris*) and sterols-alkaloids (*Boerhaavia diffusa* and *Dolichos biflorus*).[5,12,17,20] Calcury™, Cystone™, and Distone™, which contain one or more of these herbal compounds, appear to act by inhibiting crystallization, causing diuresis and stone expulsion,[11-17] without noticeable side effects.

MATERIALS AND METHODS

The study was approved by the Institutional ethics committee. The entry criteria included adult patients of symptomatic nephrolithiasis with renal stone burden (≤8 mm), as determined by ultrasound/X-ray KUB, presenting to our outpatient clinic from November 01, 2008 to December 31, 2009. Patients with chronic renal failure, extensive comorbidity, sepsis, and prior metabolic abnormalities were excluded. A prior screening visit was performed in eligible patients, comprising history examination, urine analysis, electrocardiography, and X-ray/USG KUB. ECG was performed as per protocol in all our patients, due to some reports of hyperkalemic cardiac arrhythmias occurring in patients following prolonged unmonitored ingestion of KC.[21] Patients, who had consented (with the option to exit at any stage) for this trial, were instructed to follow a one-week unrestricted diet with avoidance of known antilithogenic agents (like pyridoxine, sodium cellulose phosphate, carbonated beverages, soda, citrus juices, and any other citrate- or magnesium-based preparations) and controlled fluid intake to ensure a urine output of at least 2l per day. As per our protocol, symptomatic treatment of pain and discomfort with analgesics was not given to either group. A total of 60 patients were prospectively randomized in a simple unrestricted (randomization table produced by www.randomization.com accessed on September 22, 2008) equivalent parallel clinical trial design and were assigned to be allocated equally into either the KC (group-I) or the PT (group-II) by the 2nd author. The 1st author was double blinded to these two groups while analyzing their outcome parameters. The stone composition was not known before the study enrollment. Group-I patients were prescribed KC syrup (10 ml dissolved in a glass of water, thrice a day after meals) and group-II patients were prescribed PT as a nutritional supplement with Tablet Calcury™ (Lupeol-based extract), two tablets twice a day. Patients were monitored for compliance and adverse events as per protocol. Compliance was checked by instructing patients to bring the empty carton/bottle every week and to take the prescription in front of a resident (refills were given against an empty carton). Serum biochemistry (S.Ca, PO_4, uric acid [UA]), 24-hour urine (Ca, PO_4, UA), and X-ray KUB and USG-KUB were done on 0, 30th, and 90th day, while 24-hour urinary citrate and oxalate were monitored on the 0 and 90th day. The primary efficacy parameters assessed were reduction in size/number of stones and stone passage during therapy, with favorable changes in the urinary parameters like decreased 24-hour Ca, PO_4, UA and normalization of serum Ca, PO_4, UA and urine pH (6.8-7.2). The secondary efficacy parameters recorded were reduction in the pain symptoms, by using the Visual Analogue Scale (VAS). Tolerability was recorded by noting the incidence of side/adverse events and the patient's compliance to the administered therapy.

Summary statement of statistics: PASS™ (Power analysis and sample size software package-2008 for windows) was used to compute the sample size in this trial. Using PASS™-based equivalence test of means with two one-sided tests on data from a parallel-group design with sample sizes of 27 in the reference and 27 in the treatment group, 80% power at 5% significance level was achieved when the true difference between the means was 0.25, with a SD of 0.80 and with equivalence limits of -0.80 and 0.80 [Table 1]. Based on this, we used a sample size of 30 patients in each group in this trial. For quantitative tests like reduction in the stone size, biochemical tests and stones passage, *t* test was used, whereas for qualitative tests like VAS, we used the chi-square test.

RESULTS

Demographic profile

The age range was 18 to 55 years, and the mean age±SD was 31.03±13 and 28.73±8.31 years in group (I) and (II), respectively. Recurrent stone formation was detected in 15 of

Table 1: *Depicting the power analysis of two-sample t test for testing equivalence using differences

P	N1	N2	EL	EU	D	S	Alpha	Beta
0.8009	27	27	-0.80	0.80	0.25	0.80	0.0500	0.1991

P: Power Is the probability of rejecting non-equivalence when the means are equivalent, N1: Reference group sample size; N2: Treatment group sample size, EL, EU: Lower and upper equivalence limits. It is the maximal allowable differences that result in equivalence, D: It is the true difference anticipated actual difference between the means, S: Is the average standard deviation within the two groups, Alpha: Is the probability of rejecting non-equivalence when the means are non-equivalent, Beta: Is the probability of accepting non-equivalence when the means are equivalent, *PASS™: Power analysis and sample size software package-2008 for windows was used

60 (25%) patients, with six and nine patients from group (I) and (II), respectively.

Stone profile

Of 60 patients with stones (≤8 mm), 15 patients had bilateral nephrolithiasis (30 renal units), whereas 45 patients had unilateral nephrolithiasis (45 renal units). In group-I, 37 of 60 renal units had nephrolithiasis while in group-2, 38 of 60 renal units had nephrolithiasis. The number of renal units with stones ≤5 mm was 12 and 14 in groups I and II, respectively; hence, the overall % of renal units with stones ≤5 mm was 12+14/37+38=26/75=34% renal units. Thus, the remaining majority of renal units (66%) had stones >5 mm. The overall mean stone size was (5.5-6.5 mm), whereas in the two groups, it was 6.22±1.52 mm (I) and 5.52±1.8 mm (II), which were comparable.

Serum electrolytes

There was no significant difference in the mean serum sodium and potassium levels in both groups. Both groups had normal mean serum Ca levels at 0, 30th, and 90th day. The change in serum Ca was insignificant in both groups (P=0.7 and 0.16 in group (I) and (II), respectively). The mean±SD of serum PO_4 in both groups at 0, 30th, and 90th day was within normal limits. In both groups, the mean serum PO_4 decreased at 30th and 90th day, which was insignificant (P>0.05). In group (I), the decrease in serum PO_4 on the 30th and 90th day was 0.5 and 0.8%, respectively, while in group (II), this was 2.2 and 6.8%, respectively. The difference in the decreased mean serum PO_4 was insignificant (P>0.05). Both groups had normal mean serum UA levels at 0, 30th, and 90th days. The overall serum UA mean±SD at day 0 was 4.27±1.15, while in group I and group II, this was 4.14±1.1 and 4.41±1.22 mg%, respectively. The overall mean±SD of serum UA at the 90th day was 3.47±0.84 mg%. Statistical analysis (Dukey's test) suggested a significant decrease in serum UA in both the study groups (P<0.05) to the tune of 18 and 19% in groups (I) and (II), respectively.

Urinary parameters

All the patients had a normal mean urine pH at day 0 (pH=6-8). The overall mean urinary pH±SD level at day 0 in the 60 patients was 6.89±0.34, while in the group (I) and (II), this was 6.85±0.32 and 6.93±0.35, respectively. The overall mean urinary pH±SD level at 90th day in the 60 patients was 7.06±0.24, while in the group (I) and (II), this was 7.05±0.25 and 7.06±0.23, respectively. In both groups, the mean urinary pH increased at 30th and 90th day to the tune of 3 and 1.9% in group (I) and (II), respectively, over 90 days. This increase in the mean urinary pH was statistically significant in group (I), whereas it was insignificant in group (II). The change in the urinary 24-hour Ca level on the 30th and 90th day was statistically insignificant (P>0.05) in both the groups. The mean urinary 24-hour PO_4 on the 0, 30th, and 90th day were within normal limits in both groups. Both the groups had normal mean 24-hour urinary Ox levels on the 0 and 90th day, though it showed a decreasing trend after therapy. This decrease in the urinary Ox value was significantly higher in the group-I (7.8%) *vs* (3.2%) in group-II. The mean 24-hour urinary citrate levels in both the groups on the 0 and 90th day were within normal limits. Both groups showed a significantly increased 24-hour urinary citrate level on the 90th day, which was to the tune of 45 and 26% in group (I) and (II), respectively. The biochemical parameters are depicted in Table 2.

VAS score

The mean VAS score was 6.9 and 6.8 in group (I) and (II), respectively, which decreased significantly in both the groups

Table 2: Mean values of various biochemical parameters evaluated in both groups

Parameter	Day-0	Day-30	Day-90	*P* value (sig. <0.05)
S. calcium (I)	9.727±0.137	9.857±0.123	9.953±0.127	0.16
S. calcium (II)	9.813±0.137	9.973±0.123	9.920±0.127	0.70
S. phosphate (I)	3.567±0.138	3.547±0.114	3.537±0.113	0.90
S. phosphate (II)	3.640±0.138	3.560±0.114	3.393±0.113	0.31
S. uric acid (I)	4.137±0.209	3.873±0.182	3.363±0.153	0.001 (S)
S. uric acid (II)	4.410±0.209	3.867±0.182	3.567±0.153	0.001 (S)
Urinary pH (I)	6.85±0.06	7.07±0.04	7.05±0.04	0.01 (S)
Urinary pH (II)	6.93±0.06	7.05±0.04	7.06±0.04	0.59
U.24h calcium (I)	146.63±15.41	151.87±13.70	148.23±11.89	0.88
U.24-h calcium (II)	143.40±15.41	142.07±13.70	137.87±11.80	0.65
U.24-h phosphate (I)	440.40±35.49	433.10±26.99	444.17±22.24	0.99
U.24-h phosphate (II)	447.10±35.49	452.97±26.99	443.90±22.24	0.80
U.24-h uric acid (I)	547.46±38.42	473.70±30.34	442.76±27.37	0.02 (S)
U.24-h uric acid (II)	452.26±38.42	451.13±30.34	407.10±27.37	0.16
U.24-h oxalate (I)	24.78±1.25	-	22.85±0.85	0.04 (S)
U.24-h oxalate (II)	23.92±1.23	-	23.14±0.83	0.83
U.24-h citrate (I)	2.58±0.52	-	3.74±0.79	0.01 (S)
U.24-h citrate (II)	2.78+0.62	-	3.52+1.03	0.02(S)

(I)-Denotes potassium citrate group, (II)-Denotes phytotherapy group, (S) -Significant *P* value

by 90th day of therapy to the tune of 75.36 and 73.97% in group (I) and (II), respectively.

X-ray KUB

15 patients had stones in both renal units, and of the 60 patients (120 renal units), stone burden was present in (15×2+45=75) 75/120 (62.5%) renal units. Of these 75 renal units, complete stone clearance was attained in 36 (16 and 20 from group I and II, respectively) renal units. The % decrease in the stone size on the 30th and 90th day was 30 and 64.14% in group (I), respectively, and 33.15 and 64.31% and in group (II), respectively. The overall decrease in the stone size by the 90th day of therapy was significant (P<0.05). X-ray KUB could detect calculi in 23 of the 60 patients (14 group-I and 9-group-II), with an overall sensitivity and specificity of 38.33 and 100%, respectively. After the 90th day of therapy, 6 of the 14 patients (43%-group-I) and 4 of the 9 (44%-group II) had radiological (X-ray KUB) evidence of persistent nephrolithiasis. Thus, complete stone clearance was seen in 13 of the 23 (55.95%) patients, of which 8 of 14 (57%) and 5 of 9 (55.56%) were from group (I) and (II), respectively. The VAS and USG findings are depicted in Table 3.

Tolerability

Four patients (13.33%) in the group-I developed side effects like mild upper gastrointestinal disturbances where drug dose was maintained with additional antacid therapy. No other adverse effects were noticed in this group. No side effects or adverse effects were noticed in group-II. The overall drug compliance was 100% in both the groups.

Table 3: Depicting the mean values of VAS and USG in both the study groups

	Day-0	Day-30	Day-90	*P* value
VAS (I)	6.90±0.24	3.83±0.33	1.70±0.33	0.01 (S)
VAS (II)	6.80±0.24	3.33±0.33	1.77±0.33	0.01 (S)
USG KUB (I)	6.22±0.27	4.32±0.36	2.29±0.40	0.01 (S)
USG KUB (II)	5.52±0.27	3.69±0.36	1.97±0.39	0.01 (S)
USG KUB (II)	5.52±0.27	3.69±0.36	1.97±0.39	0.01 (S)

(I)-Denotes potassium citrate group, (II)-Denotes phytotherapy group, (S)-Significant *P* value; VAS: Visual analogue scale, USG: Ultrasonography

DISCUSSION

Medical therapy implies the administration of drugs to eliminate renal stone(s) which includes KC, potassium magnesium citrate, vitamin B_6, diuretics, allopurinol, sodium cellulose phosphate, and PT using plant-herbal extracts. The mechanism of action of these drugs includes dissolution, altering the formation of stones or hastening their expulsion, and prophylaxis.

Various factors may predispose to recurrence of various types of renal stones; like dietary factors, untreated metabolic disorders, dehydration, recurrent urinary tract infection, and malformed kidneys.[2,4,22-26] According to Tiselius,[27] any metabolic evaluation for calcium stone formers must comprise 24-hour urinary Ca, Ox, citrate, magnesium, and creatinine testing. Others[2,27,28] have similarly recommended that first-time and recurrent renal stone patients should be comprehensively evaluated with 24-hour urinary Ca, PO_4, UA, Ox, citrate, creatinine, and serum Ca, PO_4, UA, creatinine, and parathyroid hormone.

KC acts by inhibiting CaOx crystallization by forming bicarbonate which binds to Ca, directly inhibiting CaOx formation and promoting increased release of some urinary proteins that inhibits CaOx crystallization.[5-7,10] KC inadvertently also increases $CaPO_4$ crystallization and stone formation by alkalizing the urine,[3,5,6,10] due to which it is contraindicated in known $CaPO_4$ stone formers.[6,10]

Our study suggested that changes in the serum Ca and PO_4 values after 30th and 90th day of therapy were not significant (P>0.05). Many studies[5,7-9,29] have failed to detect significant changes in the serum Ca and PO_4 levels with KC therapy, which appears to be in concordance with the mechanism of action of KC.[6,7,11] Various human studies[17,19,30] evaluating the use of PT for nephrolithiasis and many experimental studies[11-16] investigating the possible mechanism of action of PT with lupeol extract of *Crataeva nurvala* failed to detect any significant effect on the serum levels and intrinsic metabolism of Ca and PO_4.

There was significant decrease (P<0.05) in mean serum UA level by 19% and 18% in group-(I) and (II), respectively. Thus, both our patient study groups showed a near equal efficacy in reducing serum UA levels. Published literature on KC therapy[5,7-10,31] and PT[17-19,32,33] has not demonstrated any effect on the serum UA levels. The reason(s) for the decline in the serum UA levels in our study are difficult to ascertain; however, we conjecture that this could be related to the general effect of KC on UA metabolism; alkalizing the urine by converting UA into urate ion and this urate ion passes into urine without its crystallization, thus decreasing the concentration of UA.[6,10] The decreased serum UA in group (I) may be possibly due to the spontaneous passage of urate ions, leading to shift of more UA into the urine, patient's increased fluid intake, and decreased intake of animal protein.[25,26,34] Similarly, mean serum UA values also decreased in the PT group (II) possibly because of PT-induced diuresis, altered metabolism of stone formation, and patient's increased fluid and reduced animal protein intake. The decline in serum UA levels may be beneficial as it may lower the risk of UA stones; however, the urinary UA and pH levels may be other more critical criteria than serum UA

alone.[25,27,34] In patients with hyperuricemia due to high animal protein intake with a normal pH, the decrease in the serum UA level is proportionate to the decrease in the urinary UA,[33] which we believe may lower the risk of renal stone formation.

There was an increase in the urinary pH by 0.2 (3%) and 0.1 (1.96%) in group I and II, respectively, which was statistically significant ($P<0.05$) in group (I) and insignificant ($P>0.05$) in group (II). KC alkalinizes the urine by its intrahepatic conversion into potassium bicarbonate by cytochrome P_{450} and its subsequent urinary excretion.[5,6,10] Long-term treatment with KC (60 meq/day) has demonstrated an elevation in the urinary pH by 0.7 units.[6] In our study, the rise in the urinary pH was 0.2 and 0.1 in the groups (I) and (II), respectively. Various published studies[5,8,9,31] have also similarly demonstrated that KC significantly increases the urinary pH. In a study conducted by Pak *et al*.,[9] the authors documented that with KC therapy, urinary pH had increased from 5.62 to 6.55 over 4 months. Others have suggested that with KC therapy, it may be advisable to monitor urinary pH to a target level of 6.8 to 7.2 for effectively inhibiting nephrolithiasis.[6,10,12] In a critical review by Mattle and Hess[35] that reviewed 46 KC studies, the authors concluded that in at least 13 of these studies evaluated for changes in the urine pH, there was a demonstrable significant ($P<0.05$) increase in the urinary pH by 1 to 3% over 3 months. Thus, our observed rise in the urinary pH with KC therapy was similar to reports of others.[5,8,9,31] Increased urinary pH can lead to inhibition of CaOx and UA stones.[5,6,10] There was some increase in the urinary pH (by 1.96%) with PT; we believe that this may be due to increased diuresis and urinary citrate excretion,[11-15,36-38] though some PT studies[18,19,37,38] have not revealed evidence of the same.

The change in mean urinary 24-hour Ca and PO_4 was insignificant ($P>0.05$). Studies on KC[9,35] failed to detect significant changes in the 24-hour urinary Ca and PO_4; however, in a review by Mattle and Hess,[35] the authors concluded that urinary Ca decreased by 8 to 40% in 9 studies, whereas it increased by 15.4% in one study. Experimental studies with PT have shown decreased CaOx and $CaPO_4$ crystallization;[11-16,36-40] however, PT studies in human beings have not shown any significant changes in the urinary Ca and PO_4 levels.[17-19,32,33]

The decrease in the urinary 24-hour UA on the 90th day by 19% in group-I (significant, $P<0.05$) and by 10% in group-II (insignificant, $P>0.05$) is probably due to KC-induced alkalization of urine that converts UA into urate ions.[5,6,10] A rise in the urinary pH to 6 has been shown to decrease the UA concentration by 50%.[3,6] Trinchieri *et al*.[8] also showed significant dissolution of UA stones with KC therapy, while PT is not known to have any effect on the urinary UA.[17,19]

Although there was a decrease in the 24-hour urinary Ox by 7.8% (significant) and 3.6% in groups I and II, respectively, in this study, other studies[9,32,35] with KC therapy failed to detect any significant change in urinary Ox levels. The observed decrease in the urinary 24-hour Ox levels in patients of group-I may be due to the possible inhibitory action of KC on CaOx crystallization. PT may also directly act by decreasing the renal CaOx crystals, by causing diuresis by its intrinsic natural urinary mucoprotein inhibitory effect.[11-16,33,36,37] PT has been documented in experimental studies to inhibit Ca-Ox crystallization.[11-16] PT studies conducted on human beings so far have not shown any conclusive evidence of change in the urinary Ox.[17-19]

There was a significant ($P<0.05$) increase in the urinary 24-hour citrate levels (45 and 26% in groups I and II, respectively). Published studies have documented that KC therapy benefits by directly augmenting the urinary citrate concentration, by balancing the renal handling of citrate concentration[5,6,10] (favorable for hypocitraturia), and thereby preventing CaOx and UA stone formation. Long-term treatment with KC at doses of 60 mEq/day has shown to raise the urinary citrate levels by approximately 400 mg/day.[6,10] Therapeutic studies[9,31,35] with KC have demonstrated a significant increase in the 24-hour urinary citrate. In a study with KC therapy,[9] the authors documented a significant increase in urinary citrate (from 319 to 601 mg/day) over 4 months. PT with grape juice, cranberry juice, and lemonade juice has also demonstrated to maintain urine output and perhaps block renal stone formation.[38,39] However, PT with extracts from *Crataeva nurvala, Tribulus terrestris,* and *Boerhaavia diffusa* has not shown any evidence of significant effect on the urinary citrate levels.[17-19] In our study, however, PT was associated with a significant rise (26%) in the urinary citrate levels; probably this may have been due to an unknown mechanism(s) augmenting urinary citrate excretion or may have been due to a variation in the composition of various herbal preparations.

Comparative studies of KC therapy with placebo have also shown a significant reduction in the stone size and in preventing stone recurrence.[8,9,31,35] In a review,[35] the authors documented complete stone clearance in 66% of their patients after one year of KC therapy. The decrease in size and passage of stone is explained by inhibition of CaOx and UA crystal formation by KC.[5,6,10] Various published studies of PT in human beings have found significant reduction in stone size.[17-19,32,33] Patankar *et al*.[33] documented 33.04% reduction in stone size (in the 5-10 mm stone group patients) and 11.25% reduction in stone size (in >10 mm stone group patients). Experimental PT studies investigating their possible mechanism have shown that plant extracts may directly inhibit CaOx crystallization, increase natural stone inhibitors (mucoproteins), and hasten stone expulsion by diuresis[5,12-17]

There was a significant ($P<0.05$) decrease in the VAS (from 6.9 and 6.8 to 1.77 and 1.70) in group I and II, respectively. This may be due to decreased stone size/expulsion, with favorable urinary pH that may have decreased the pain symptoms. It is also possible that the decreased VAS score in patients with refractory stones may also in part be due to a placebo effect; however, this could not be substantiated due to lack of a control group. Therapy with conventional medicines[9,31,35] and PT (human studies)[17-19,32,33] have demonstrated significant benefits in nephrolithiasis.

In group (I), 4 of 30 (13.33%) patients developed mild upper gastrointestinal (GI) disturbance (KC therapy was safely maintained with antacids). Pak *et al*.[9] had also documented similar side effects in 33.3% of their cases who received KC therapy over 2 to 4 years. KC therapy may cause upper GI disturbances[7,9,32,35] like gastritis, nausea, vomiting, and adverse events due to hyperkalemic cardiac arrhythmias[21] and tingling.[5,6,10] Studies on the use of PT in human beings have not documented any side/adverse event.[17-19,32,33] It is believed that PT may supplement conventional medicines for managing nephrolithiasis.[40] The limitations of the current study include short duration, lack of a control group (not used as we believe that it may be unethical to deny treatment to symptomatic patients), and omitting noncontrast CT scan for documenting nephrolithiasis (due to its high cost).

CONCLUSIONS

Therapy with both PT using a lupeol-based extract (Calcury™) and KC appeared to be efficacious clinically, in respect of reduction in the renal stone size and in improving symptomatology of nephrolithiasis. PT may be probably more effective clinically than KC in hastening expulsion of small stone fragments (<8 mm). KC therapy may be more effective biochemically in alkalinizing the urine, decreasing the urinary 24-hour oxalate and UA excretion, and in increasing the urinary citrate excretion; thus, it may be more effective in preventing recurrent renal stones and may be associated with some side effects. Although both the medical therapies were not effective in all aspects, we believe that PT with lupeol-based extract (Calcury™) may be used as an alternative form of medical therapy in select patients with minimal nephrolithiasis. Larger long-term placebo-controlled randomized trials are definitely needed to better define the role of lupeol-based PT in the management of nephrolithiasis.

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