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The therapeutic effect of *citrus aurantifolia swingle* in idiopathic hypocitraturic calcium nephrolithiasis

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ABSTRACT

Mochammad Sja'bani, Mohammad Ismadi, Siti Dawiesah Ismiati, Raja Pingkir Sidabutar, Djoko Rahardjo - ***The therapeutic effect of citrus aurantifolia swingle in idiopathic hypocitraturic calcium nephrolithiasis***

Background: Hypocitraturia is one of the main risks of stone appearance or renal stone recurrence that is easily interfered. A sphere citrus fruit (*Citrus aurantifolia Swingle*) was reported to contain the highest citrate compared to other citrus fruits.
Aims: We aimed to determine the effect of *Citrus aurantifolia Swingle* on the management of hypocitraturia, compared with potassium citrate.
Materials and Methods: Seventy two patients with idiopathic calcium renal stone with hypocitraturia were randomly divided into two groups, therapy and placebo groups. The first group was given potassium citrate treatment (2x20 mEq/day), while the second one was given 2x1.5-g pure lactose. After 6 months, patients without stomachache complaints were given 40ml citrus juice diluted in 2 glasses of water, taken immediately after dinner for 10 days. Observation was done on risk factors in urine collected for 8, 16 and 24-hours, including volume, pH, potassium, magnesium, oxalate, citrate, calcium, sodium, phosphate, sulphate, uric acid, ureum and creatinine. The setting of this study was 1 hospital in Yogyakarta and 2 hospitals in Jakarta.
Results: The increase of urine volume, pH, level and total citrate value, level and total potassium, and the decrease of calcium ratio to citrate urine. The changes of those metabolite levels could lessen the chance of colic and hematuria complaints, as seen after 6 months administation of potassium citrate. Similar results were obtained from the administration of citrus juice, except for calcium level, which was not decreased.
Conclusion: The administration of potassium citrate 2x20mEq/day in 6 months improved patient's complaints and occurrence of renal colic, while consumption of Citrus aurantifolia Swingle in idiopathic calcium renal stone with hypocitraturia was concluded to increase the urine volume, pH level and total citrate value, level and total potassium, and the decrease of calcium ratio to urine citrate.

Key word: renal stone- hypocitraturia- *Citrus aurantifolia Swingle*

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ABSTRAK

Sja'bani - ***Pengaruh pemberian perasan jeruk nipis (Citrus aurantifolia swingle) pada penderita batu ginjal kalsium idiopatik dengan hipositraturia***

Latar belakang: Hipositraturia merupakan salah satu factor risiko yang penting untuk timbilnya batu ginjal kambuh yang mudah dilakukan intervensi. Jeruk nipis local buah sitrus (*Citrus aurantifolia swingle*) dilaporkan mempunyai kandungan sitrat tertinggi diantara buah sitrus.
Tujuan: Menentukan pengaruh pemberian perasan jeruk nipis (*Citrus aurantifolia swingle*) pada terapi hipositraturia disbanding dengan kalium sitrat.
Bahan dan Metode: Dilakukan uji klinik acak terhadap 72 penderita batu ginjal kalsium idiopatik dengan hipositraturia terbagi dalam dua kelompok, kelompok terapi dan kelompok placebo. Kelompok pertama diberikan terapi kalium sitrat (2x20 mEq/hari), sedang kelompok dua diberikan 2x1,5g lactose murni. Sesudah 6 bulan penderita tanpa keluhan nyeri lambung diberikan 40 ml perasan sitrus diencerkan dalam 2 gelas air diminum sesat sesudah makan malam selama 10 hari. Pengamatan terhadap factor risiko air kemih penampungan dalam 8, 16 dan 24 jam, meliputi volume pH, kalium, magnesium, oksalat, sitrat, kalsium natrium, phosphate, sulphat, asam urat, ureum dan kreatinin. Penelitian dilakukan di satu rumah di Yogyakarta dan dua rumah sakit di Jakarta.
Hasil: Ditemukan kenaikan dalam volume PH, nilai dan totl sitrat, nilai dan total kelium, dan penurunan rasio kalsium terhadap sitrat air kemih. Perubahan nilai metabolik diduga dapat mengurangi keluhan kolik dan hematuria yang terjadi sesuah pemberian kalium sitrat selama 6 bulan. Hasilnya serupa dengan pemberian perasan sitrus, dengan tanpa penurunan nilai kalsium.
Simpulan: Pemberian kalium sitrat 2x20mEq/hari selama 6 bulan mengurangi kejadian keluhan kolik penderita, sedang mengkonsumsi *Citrus aurantifolia swingle* pada batu ginjal kalsium idiopatik dengan hipositraturia dapat meningkatkan air kemih dalam volume, nilai pH, nilai dan total sitrat, nilai dan total kalium, serta menurunkan rasio kalsium terhadap sitrat air kemih.

INTRODUCTION

Nephrolithiasis can be classified into renal stone and bladder stone. Renal stones are the most causes of urinary tract abnormality. The proportion of renal stone in Indonesia is closed to those of developed countries, such as The United States, Europe and Australia. In two cities of Java in Indonesia, Yogyakarta and Semarang, the proportion of renal stone has relatively been increasing compared to the proportion of bladder stone since 1974 and 1979 (our unpublished data). Most renal stones consist of calcium oxalate and phosphate or both (65-85%).[1]

Prevention of a new stone appearance was aimed to avoid risk factors. Some clinical test data showed a recurrence in control group without intervention around 10-23%/year. Risk factors such as hypercalciuria, hyperoxaluria, hypocitraturia and hyperuricosuria were reported as the main predisposition factors of calcium renal stone occurrence.[1,2] The role of dietary oxalate in the pathogenesis of calcium oxalate nephrolithiasis is unclear. Significant variation can exist between individuals with respect to the alimentary absorption of oxalate.[3] High level of sodium, sulphate, phosphate and low level of magnesium in the urine also played a role in the occurrence of calcium renal stone.[4,5] The main risk factor easily interfered was hypocitraturia. Hypocitraturia, which could help augment stone formation, could be caused by acidosis, high protein diet and chronic diarrhea.[6,7] Hypocitraturia could be burdened by the presence of high sodium diet intake.[6] The latter was also reported to increase calcium excretion.

The metabolism of sulfur-containing amino acids in animal flesh generates sulfuric acid. As such, dietary animal protein represents an acid load that increases urinary calcium excretion and reduces urinary tract excretion. Dietary protein may also lead to an increase in calcitriol production (possibly induced by an increase in renal mass). A positive association between animal protein consumption and new kidney stone formation has been shown in men but not women.[8]

Renal stone growth was frequently considered occurring in the evening due to food composition, lack of activity and long rest.[7] Citrate excretion in the urine was considered to be highest in the late afternoon and lowest in the morning.[5,7,9] Oxalate and urinary citrate examination to manage renal stone case was reported (Sja'bani M *et al*, 1993,

unpublished data), whereas the follow-up study was never yet reported in Indonesia. An easy, practical and exact method of urine collection should be determined, such as past 22.00-06.00 compared to 24-hour urine collection.

It was considered that the low level of citrate in urine really played a role as a risk factor for idiopathic calcium renal stone to appear, mainly oxalate calcium stone and phosphate calcium stone. The low proportion of citrate level in urine was found frequently in idiopathic calcium stone patients.[10-13] The efforts to increase urine citrate level on renal stone patients with idiopathic calcium type was done at non-random and without comparison. Clinical trial by comparing calcium renal stone patients with hypocitraturia with 12 capsules of potassium citrate divided into 3 dosages/day showed discomfort to most patients.[14] Potassium citrate administration was reported to irritate the stomach. Potassium citrate administered in an empty stomach or given at mealtime was reported to have no compositional difference in urine.[15] The alkali and citrate excretion changes in urine was reported to have reached its peak 2 hours after oral intake and could decrease gradually, and it could be concluded that drug administration with large dosage should be thoroughly examined and administered in the morning and afternoon.[7,9,16] Still, once daily dosage administration was hoped to increase the patient's obedience.

Since potassium citrate material was difficult to obtain and relatively expensive, a cheaper and easier alternative should be sought. A sphere citrus fruit (*Citrus aurantifolia Swingle*) was reported as a fruit easily and cheaply obtained, containing the highest citrate compared to other citrus fruits such as oranges (*Citrus sinensis Osb*), mandarins (*Citrus nobilis Lour*), and lemons (*Citrus limonium*). The citrate content in a citrus fruit was more than 10 times compared to citrate in a mandarin (Sja'bani M *et al*, 1993, unpublished data). Lemon juice administration in calcium stone patients with hypocitraturia was reported,[13] while the study on citrus fruit as an easy and cheap plantation to replace potassium citrate in reducing renal stone risk factor, was not yet reported.

In this study, we investigated the effects of potassium citrate and citrus juice in renal stone complaints and metabolite change in urine from 72 patients with renal stone with hypocitraturia past stone removal by surgery, percutaneous nephrolithotomy (PCN) or lithotripsy.

MATERIALS AND METHODS

Experimental study was done with a double blind randomized clinical trial plan. In the study of citrus administration, a trial study plan was used before and after administration. The study population was idiopathic calcium renal stone patients with hypocitraturia (without primary abnormality; such as hyperparathyroidism, normal calcium and blood uric acid levels, and stone patients accompanied by a history of stone output) past stone removal by surgery, percutaneous nephrolithotomy (PCN) or lithotripsy. They were patients with clean stone or without complaints of broken stone with a diameter of less than 5 mm, patients who did not suffer from systemic disease that needed treatment (such as primary hyperparathyroidism, sarcoidosis, myoma, renal tubulus acidosis and intestine shortening syndrome/had intestine surgery) and patients who were not in pharmacological treatment for stone disease. They were proofed to be stone free by intravenous pielography X-ray, and citrate level was still less than 320 mg in 24-hour urine.

Seventy two patients from 2 centers in Jakarta, namely Cikini, Mediros and Sumber Waras Hospital, and 1 in Yogyakarta namely Panti Rapih Hospital were taken purposively. They were divided into therapy and placebo groups. The first group was given potassium citrate treatment (*extra pure tripotassium citrate monohydrate* DHB, Ph Eur, BP, USP, FCC, E 332 MERCK 64271 Darmstadt, Germany) with a dosage of 2x20 mEq/day each. The second group was given 2x1.5-g pure lactose. Both groups were advised to lessen salt intake, or to consume salty food. The habit of protein intake in both groups was advised not to be changed. After 6 months, patients without stomachache complaints were given 2 pieces of citrus juiced (diameter > 4.5 cm) or more than 40 ml, diluted in 2 glasses of water, taken after evening meals. Observation was done on risk factors in urine collected for 8, 16 and 24-hour, including volume, pH, potassium,

magnesium, oxalate, citrate, calcium, sodium, phosphate, sulphate, uric acid, ureum and creatinine.

The study variable consisted of independent and dependent variables. Independent variable consisted of potassium citrate and citrus juice administration. The independent variable was correlated with dependent variable that were renal stone complaints consisted of colic or renal pain, spontaneous stone output and hematuria. The other dependent variable in urine were pH, volume, magnesium, citrate, sulphate, oxalate, phosphate, calcium, uric acid, potassium, creatinine, sodium and ureum. Dependent variable in urine could be assumed as intermediate variable to dependent variable renal stone complaints.

Following the urine volume measurement, a pH meter microcomputer Hanna type HI 9023 was used to measure the pH. Parathormone level blood serum (intact parathormone/immunoreactive parathyroid hormone iPTH), the level of potassium, sodium (with burnt photometry) calcium inorganic phosphate and magnesium serum (photometry) were examined. Examinations on enzymatic uric acid, ureum, and creatinine in serum and urine were also done. Potassium, sodium, magnesium and calcium urine levels were examined with, as well as spectrophotometer examination for oxalate by Hodgkinson and Williams, citrate by Camp and Farmer and spectrophotometer for sulphate and phosphate.

Patients sent their urine every 3 months, which were obtained by collecting urine from morning past 06.00 and retained until 22.00, while the second urine was retained past 22.00 until 06.00. The collected urine was divided into 3 small bottles, 2 of them were indicated with a label of urine past 06.00 until 22.00 and 1 bottle with urine past 22.00 until 06.00. Twenty four hours retained urine volume was measured by mixing the retained morning and afternoon urine. Its pH value was also determined.

We also provided 6 small bottles for the collected urine. Two bottles contained toluene 0.5 ml (for citrate examination), two bottles contained solid hydrochloride 0.4 ml (for oxalate, magnesium, calcium, potassium, natrium, phosphate and sulphate examination) and two bottles contained no preservative. Each of the bottles was filled with urine 50 ml from retained morning and evening urine.

This study lasted for 6 months to observe potassium citrate administration and 10 days for citrus juice. Citrus juice was given after the study lasted 6 months, in patients without stomachache complaints. Each patient was reexamined and asked to bring the remainder of medicine. Study was done to know the urine composition level.

Chi-square (X^2-test) was used to know the proportion of renal stone occurrence after potassium citrate was administered 2x20 mEq/day or placebo used. *Independent t-test* was used to know the influence of potassium citrate administration 2x20 mEq/day or placebo in urine past 22.00 until 06.00; past 06.00 until 22.00 and 24-hours. *Correlated* analysis was done to know how large was the correlation of each risk factor in the urine towards the proportion of renal stone complaint occurrence. *Logistic regression* analysis was done to identify the main risk factor (odd ratio value) that had a chance of renal stone complaints. *Paired t-test* was done to know the risk factor changes caused by giving 2 citrus fruit juiced.

RESULTS AND DISCUSSION

Potassium Citrate Administration

There were no significant differences in sex, family history and nausea complaints in the first 3 months, while colic complaints and hematuria were found to increase in placebo group in the second 3 months, as seen in TABLE 1.

TABLE 1. Sex, stone history and renal stone complaints on treatment group vs placebo group at baseline, after 3 and 6 months

Variable	Treatment group (%)	Placebo group (%)	N
Baseline	N=37	N=35	
Sex (M/F)	67.6/32.4	74.3/25.7	0.609
Stone history	45.9	34.3	0.345
3 months	N=35	N=32	
Sex (M/F)	68.6/31.4	71.9/28.1	0.796
Stone history	42.9	34.4	0.617
Colic history	0	6.3	0.224
Hematuria history	0	6.3	0.224
Spontaneous stone output	0	0	-
6 months	N=33	N=30	
Sex (M/F)	69.7/30.3	70.0/30.0	1.000
Stone history	42.4	36.7	0.797
Colic history	9.1	33.3	0.028
Hematuria history	9.1	36.7	0.014
Spontaneous stone output	6.1	23.3	0.073

The evening calcium level and 24-hour after 3 and 6 months in potassium citrate therapy group were found significantly smaller compared to evening and 24-hour calcium level in placebo group (P<0.05). The value of total calcium in the morning, evening and 24-hours in the therapy group tended to be smaller compared to the total calcium value in the morning, evening and 24-hours in placebo group, although it the difference was not significant (TABLE 2).

TABLE 2. Risk factors of calcium and potassium after 6 months treatment therapy group vs placebo group

Risk factor of urine	Therapy group mean±SD	Placebo group mean±SD	95% CI
6 months	N=33	N=30	-2.25 ~ 0.01
Morning calcium	8.61±2.15	9.73±2.33	
Morning total calcium	103.15±35.55	111.93±35.13	-26.61 ~ 9.05
Evening calcium	8.20±1.94	9.96±2.33	-2.84 ~ -0.69
Evening total calcium	63.95±27.30	77.80±28.64	-27.95 ~ 0.25
24 hour calcium	8.44±1.8	9.83±2.30	-2.46 ~ -0.31
24 hour total calcium	167.09±58.21	189.72±61.69	-52.84 ~ 7.58
Morning potassium	177.46±43.33	112.61±33.25	45.25 ~ 84.46
Morning total potassium	2077.55±542.01	1291.76±482.86	526.14 ~ 1045.44
Evening potassium	177.37±45.91	111.21±36.56	45.10 ~ 87.20
Evening total potassium	1344.59±559.95	851.27±355.73	254.24 ~ 732.41
24 hour potassium	176.92±37.55	112.07±26.55	48.56 ~ 81.15
24 hour total potassium	3422.12±892.27	2143.03±683.06	875.74 ~ 1682.49

SD: standard deviation CI: confidence interval n= number of patients

Barcelo *et al*. (1993) reported that pH value and total urine citrate were significantly higher caused by the administration of 60 mEq/day potassium citrate in 3 and 6 months compared to placebo.[15] Other reports in the increase of total citrate value and urine pH were reported to be caused by sodium citrate, calcium citrate and magnesium citrate.[17-23] Sakhaee *et al*. (1991) reported that potassium citrate administration 80 mEq/day to eight calcium stone patients for 18 days could raise pH urine value and total citrate urine excretion and decreasing urine calcium excretion.[24] Potassium citrate administration of 60 mEq for 4 weeks to 5 uric acid stone patients, increased citrate level and decreased urine calcium level.[17]

Butz *et al*.(1984) and Preminger *et al*. (1988) reported that the total value of calcium was smaller after potassium citrate administration more than 3 months, based on an unrandomized study.[18,21] The low level of calcium in urine was necessary to prevent stone formation. The ratio of calcium molar to citrate molar could be used to determine the amount of free calcium to oxalate, phosphate complex and formed urinary tract stone.[25]

The calcium ratio value to citrate in the morning, evening and 24-hour therapy group was found significantly smaller compared to calcium ratio value to citrate in placebo group after 3 and 6 months (TABLE 3 and TABLE 4). Calcium ratio value to sulphate and calcium ratio to phosphate remained smaller significantly in the evening urine (from 22.00 until 06.00), as seen from the result of the first and second 3 months. Calcium to citrate excretion ratio value was significantly higher in stone patients compared to normal control.[26,27]

TABLE 3. Risk factor of pH and citrate after 3 months on treatment group vs placebo

Urine risk factor	Treatment groupmean ± SD	Placebo groupMean ± SD	95% CI
3 months	N=35	N= 32	
Morning pH	6.24±0.53	5.55±0.36	0.47 ~ 0.91
Evening pH	6.33±0.53	5.48±0.33	0.63 ~ 1.06
24 hours pH	6.28±0.52	5.53±0.35	0.53 ~ 0.96
Morning citrate	24.19±9.763	14.51±4.08	6.06 ~ 13.31
Morning total citrate	273.62±113.92	157.18± 50.45	73.77 ~ 159.12
Evening citrate	24.78±5.60	14.29±4.15	9.06 ~ 13.91
Evening total citrate	183.23± 60.75	98.01±36.66	60.90 ~ 109.54
24 hours citrate	24.64±6.41	14.39±3.44	7.76 ~ 12.75
24 hours total citrate	456.85±140.99	255.19±73.29	147.23 ~ 256.09

SD: standard deviation CI: confidence interval

Citrus Juice Administration

Twenty-seven out of 33 patients in therapy group and 26 out of 30 patients in placebo group received 2 citrus fruit juiced of more than 40 ml and diluted in 2 glasses for 10 days. Four patients from therapy and 2 from placebo were dropped from citrus juice administration observation due to their disobidience. The final number of patients from therapy group was 27 patients and placebo group was 26 patients. There were 17 patients with hypocitraturia, which all were from placebo group.

The evening volume and total 24-hour urine in therapy and placebo group (P<0.001) presented significant increase. The pH value in therapy group was significantly lower in morning urine (P<0.05). The pH value in evening and 24 hours urine was not significantly different.

The administration of citrus juice to therapy group resulted in the reduction in citrate level in morning urine (P<0.05), evening and 24-hour (P<0.001). The total amount of citrate was significantly smaller in morning urine (P<0.05). In placebo and hypocitraturia group, after citrus juice was given, level and total value of citrate was significantly greater in the morning, evening and 24-hour urine (P<0.01). An increase of total citrate value showed a renal stone risk factor reduction in placebo and hypocitraturia group (TABLE 5 and TABLE 6).

TABLE 4. Risk factor of pH and citrate after 6 months treatment therapy group vs placebo group

Risk factor of urine	Therapy groupMean ± SD	Placebo groupMean ± SD	95%CI
6 months	N=33	N=30	
Morning calcium	8.61±2.15	9.73±2.33	-2.25 ~ 0.01
Morning total calcium	103.15±35.55	111.93±35.13	-26.61 ~ 9.05
Evening calcium	8.20±1.94	9.96±2.33	-2.84 ~ 0.69
Evening total calcium	63.95± 27.30	77.80± 28.64	-27.95 ~0.25
24 hour calcium	8.44±1.98	9.83±2.30	-2.46 ~ 0.31
24 hour total calcium	167.09±58.21	189.72±61.69	-52.84 ~ 7.58
Morning potassium	177.46±43.33	112.61±33.25	45.25 ~ 84.46
Morning total potassium	2077.55±542.01	1291.76±482.86	526.14 ~ 1045.44
Evening potassium	177.37±45.91	111.21±36.56	45.10 ~ 87.20
Evening total potassium	1344.59±559.95	851.27±355.73	254.24 ~ 732.41
24 hour potassium	176.92±37.55	112.07±26.55	48.56 ~ 8.15
24 hour potassium	3422.15±892.27	2143.03±683.06	875.74 ~ 1682.49

SD: standard deviation CI: confidence interval n= number of patients

Citrus juice administration decreased oxalate level value in the evening and 24- hour urine significantly in therapy and placebo group, while evening urine oxalate level value was significantly smaller in hypocitraturia group. There was no significant difference in the total oxalate, calcium, magnesium, sodium value after citrus administrations in three groups. A significant smaller magnesium level value was found in evening and 24 hour urine in three groups (P<0.001). The urine potassium level value in the morning, the evening and 24 hours and total potassium value in the morning and 24-hour in the group who received therapy decreased significantly after receiving citrus juice. Citrus juice administration increased the level and total potassium value in morning, evening and 24 hours urine in placebo and hypocitraturia group significantly (P<0.001). An increase of potassium due to citrus juice administration caused an increase of pH value in urine with the presence of potassium, calcium, magnesium and sodium in urine. Sodium urine level value in the evening and 24 hour were found significantly smaller in therapy group (P<0.001) and placebo group (P<0.05), but total sodium value was found with no difference in therapy and placebo groups before and after citrus juice administration (data not shown).

Sulphate and phosphate level value were significantly smaller (P<0.05) in the evening and 24-hour urine in therapy group, while in placebo and hypocitraturia groups, the phosphate urine level value was smaller. The total sulphate and phosphate values in all urine collection were found to be not significant. A decrease of sulphate and phosphate level was considered to be advantageous to calcium stone patients, although there was no significant difference in total value. This was considered due to urine volume changes. There was no significant difference in uric acid level and total value in morning, evening and 24-hour urine. There was no significant difference in level and total ureum value in the morning, evening and 24-hour urine, in placebo and hypocitraturia groups, except for ureum level value in 24-hour urine in placebo group was significantly smaller (P<0.05). The creatinine level value was smaller in evening and 24-hour urine in therapy group and evening urine in placebo group. There was no difference in total creatinine value in all groups and in morning, evening and 24-hour urine collection (data not shown).

The calcium ratio value to citrate in morning, evening and 24-hour urine tended to increase. The ratio of calcium to citrate in morning, evening and 24-hour urine was significantly smaller in placebo and hypocitraturia groups after citrus juice administration (p<0.01). There was no significant difference in the calcium ratio value to phosphate, sulphate and creatinine in morning, evening and 24-hour urine in therapy group (data not shown).

An increase of urine volume was reported to decrease renal stone occurrence.[28] The volume of urine in patients with renal stone formation were found less than 250-350 ml.[29] The pH value of morning urine was considered smaller as citrus juice

was administered in the evening and such value was equally obtainable with the administration of potassium citrate 20 mEq. Citrus juice administration was considered to influence urine changes in the evening. A higher pH value in the morning, evening and 24 hour was found after the administration of citrus juice in placebo and hypocitraturia groups (P<0.001) (TABLE 7 and TABLE 8).

TABLE 7. Urine volume after 6 months of potassium citrate administration in treatment group vs placebo and after 10 days of citrate administration in treatment group vs placebo in therapy, placebo and hypocitraturia.

Urine Risk Factors	Treatment group (n=27)		95%CI	*P*
	Beforemean ± SD	Aftermean ± SD		
Morning urine volume	1187.04±183.59	1201.11±175.05	-64.44 ~ 36.29	0.571
Evening urine volume	756.67±234.32	874.81±238.70	-147.47 ~ -8.83	<0.001
24 hours urine volume	1943.70±331.84	2075.93±304.37	-177.09 ~ -7.35	<0.001
Morning urine volume	1125.38±199.20	1158.08±186.44	-78.83 ~ 7.45	0.106
Evening urine volume	753.46±178.05	850.38±205.63	-140.97 ~ -88.83	<0.001
24 hours urine volume	18778.85±340.96	2008.46±345.00	-179.97 ~ -79.27	<0.001
Morning urine volume	1044.71±179.17	1098.24±176.79	-93.15 ~ -13.91	0.011
Evening urine volume	704.12±170.26	774.71±182.73	-127.10 ~ -14.08	0.018
24 hours urine volume	1748.82±313.09	1872.94±295.16	185.60 ~ -62.63	0.001

TABLE 8. Urine pH after 6 months of potassium citrate administration in treatment group vs placebo and after 10 days of citrate administration in treatment group vs placebo in therapy, placebo and hypocitraturia

Urine Risk Factors group (n=27)	Treatment	95%CI		*P*
		Beforemean±SD	Aftermean±SD	
Morning pH	6.31±0.49	6.21±0.37	0.002 ~ 0.22	0.047
Evening pH	6.12±0.99	6.23±0.39	-0.46 ~ 0.24	0.526
24 hours pH	6.30±0.49	6.23±0.32	-0.02 ~ 0.17	0.134
Placebo group (N=26)				
Morning pH	5.66±0.31	6.13±0.32	-0.60 ~ -0.35	<0.001
Evening pH	5.64±0.35	6.26±0.29	-0.75 ~ -0.48	<0.001
24 hours pH	5.64±0.33	6.20±0.29	-0.68 ~ -0.43	<0.001
Hypocitraturia (N=17)				
Morning pH	5.64±0.29	6.04±0.33	-0.55 ~ -0.25	<0.001
Evening pH	5.66±0.34	6.19±0.31	-0.69 ~ -0.36	<0.001
24 hours pH	5.64±0.30	6.12±0.31	-0.64 ~ -0.33	<0.001

An increase of pH and urine citrate and a decrease of calcium ratio value to citrate were also found in citrus juice administration. Stomachache side effect and nausea were not found in the two groups of citrate and placebo for 6 months and citrus juice administration for 10 days, when taken while eating or after meals.

Based on this study we suggested the consumption of potassium citrate 2 x 20 mEq/day in more than 6 months for idiopatic calcium renal stone post removal patients with hypocitraturia. This is meant to maintain optimal condition in urine, thus decreasing renal stone complaints. Since we found similar results in metabolite changes in the urine of hypocitraturic nephrolithiasis patients after the

consumption of citrus juice, we also suggest such patients to consume 2 pieces of citrus juice and diluted in 2 glasses of water to be taken immediately after dinner more than 10 days.

CONCLUSION

The administration of potassium citrate 2x20mEq/day in 6 months improved patient's complaints and occurrence of renal colic, while consumption of Citrus aurantifolia Swingle in idiopathic calcium renal stone with hypocitraturia was concluded to increase the urine volume, pH level and total citrate value, level and total potassium, and the decrease of calcium ratio to urine citrate. Such conditions decrease the reccurence of renal stone in patients with post-stone removal. The effect of citrus juice administration for longer duration, as well as the influence of citrus juice administration to patients for other types of renal stones should be further examined.

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