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Original Article

Orthosiphon Versus Placebo in Nephrolithiasis with Multiple Chronic Complaints: A Randomized Control Trial

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Nephrolithiasis in the communities of Northeast Thailand frequently presents with multiple chronic health complaints, i.e. myofascial pain, back pain, dyspepsia, arthralgia, headache, fatigue, frank paresthesia, dysuria and any of these aggravated by purine-rich food (PRF). We assessed the efficacy of Orthosiphon in treating subjects with at least two active symptoms and negative for urine white blood cells. Subjects were randomly allocated to two groups. Crude extract of Orthosiphon given in a capsule (equivalent to 1.6–1.8 g of dried leaves of Orthosiphon) two times a day to Group 1 ($n = 36$) and a placebo to Group 2 ($n = 40$) for 14 days. The medication for each subject was packed and its code kept secret until the data analysis. Both groups were asked not to consume any of 25 purine-rich foods (PRFs) during treatment. The primary measure was the reduced sum of active severity symptoms as recorded using the visual analog scale before and after therapy (i.e. on day 7 and 14). The data on 76 subjects were processed. The mean of the total scores (95% CI) of the symptoms in each group were decreased significantly ($P < 0.001$); 185.6 (153.3, 218.0) to 94.7 (58.2, 131.2) in the Orthosiphon group and 196.1 (164.4, 227.8) to 89.6 (62.8, 116.5) in the placebo group. When comparing between groups, no statistically significant difference was found. The mean consumption in PRFs was significantly decreased ($P < 0.001$) in both groups; however, Orthosiphon did not have additional benefit over placebo at 7 and 14 days of treatment during which they reduced these foods.

Keywords: chronic fatigue – dyspepsia – myofascial pain – purine rich – renal stone

Introduction

Nephrolithiasis is a common health problem among the rural dwellers of Northeast Thailand. The prevalence of stone cases varies between reports according to the instruments used (range 0.38–16%) (1,2). Besides having kidney stones, affected persons have multiple chronic health complaints (MCHCs): (i) myofascial pain; (ii) back pain; (iii) dyspepsia; (iv) arthralgia; (v) headaches; (vi) fatigue; (vii) frank paresthesia; (viii) dysuria and, (ix) any of these symptoms are aggravated by drinking alcoholic beverages or eating fermented or purine-rich foods (PRFs) (3). These complaints (i.e. dyspepsia, myofascial pain, back pain, arthralgia) are among the common complaints in the out-patient departments (OPDs) of the sub-district health centers and community hospitals. Due to limited resources, patients are treated according to their symptoms and thus likely to revisit, leading to overcrowded OPDs.

A recent survey showed that 93.4% of rural dwellers consumed bamboo shoots or some PRF at least once a week and the prevalence of aggravated symptoms by PRF was 43.3% (4). Searching for an effective treatment

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of MCHC is essential for the patient as well as for reducing the workload at health centers. In another study, patients with kidney stones with MCHC, positive for white blood cells in the urine, were treated with antibiotics for 2 months plus *Orthosiphon grandiflorus* (OG) or sodium potassium citrate according to the treatment groups. More than 90% of both groups reported a dramatic reduction in symptoms (i.e. myofascial pain, arthralgia, dyspepsia and fatigue) without other pharmaceutical products (3). Similarly, Nirdnoy and Muangman (5) observed that drinking an infusion (tea) made from OG caused an increase in urinary pH and the tendency to increase excretions of both K and citrate. They questioned whether the outcome was the effect of the antibiotic or the OG via a correction of K and citrate which are depleted in Northeast Thais suffering from nephrolithiasis (6).

Plant-based systems continue to play an essential role in the primary healthcare of 80% of the world's population. Several of the effective anticancer agents in current use are derived from nature. The search for novel antitumor agents from natural sources is ongoing with botanists, marine biologists and microbiologists teaming up with chemists, pharmacologists, toxicologists and clinicians in the investigation of coral reefs, rainforests for novel bioactive compounds. Over 50% of the anticancer drugs approved by the United States Food and Drug Administration since 1960 originally derived from natural resources, especially from terrestrial plants (7).

Recently, much attention has been directed toward extracts and biologically active compounds extracted from popular plant species. The aqueous extract of leaves of *Indigofera suffruticosa* obtained by infusion showed strong inhibitory activity against *Staphylococcus aureus*, *Trichophyton rubrum and Microsporum canis*. This study suggests that the aqueous extracts of leaves can be used in the treatment of skin diseases caused by dermatophytes (8). An *in vitro* study showed that an aqueous extract of *Orthosiphon aristatus* has an antibacterial activity against two serotypes of *Streptococcus mutans* (MIC 7.8–23.4 mg/ml) (9). Another study revealed that *Orthosiphon stamineus* extract inhibited spore-germination in six of nine fungal species tested (viz. *Saccharomyces pastorianus*, *Candida albicans*, *Rhizopus nigricans*, *Penicillium digitatum*, *Fusarium oxysporum* and *Trichophyton mentagrophytes*) (10).

Orthosiphon is found throughout Southeast Asia. It is called 'java tea' in Indonesia and 'Yha Nhuard Maw' (cat's whiskers) in Thailand. It grows to about 1 m in height and produces white to light-violet flowers. Orthosiphon has been used as herbal tea for centuries in Southeast Asian countries. Traditionally, it is used to treat gout, rheumatism, diabetes, hypertension and renal stones.

Side effects of Orthosiphon are rare. According to the Thai traditional medicine, the people believe that the Orthosiphon infusion may have high concentration of potassium and should not be used in the patients with concurrent cardiac diseases.

This study aimed to evaluate the effect of OG versus a placebo for the treatment of nephrolithiasis in patients suffering from MCHC and testing negative for white blood cell in the urine.

Materials and Methods

Trial Design, Funding and Ethics Approval

Our study was a prospective, concealed, randomized, controlled trial conducted over a 2-week period. The research was supported by Khon Kaen University and the protocol was approved by the Ethics Committee of Khon Kaen University (HE 471224). Written, informed consent was obtained from the patients who met the inclusion criteria.

Patients

Free, ultrasound checks for renal stones were announced through local health workers and village headmen in 15 villages. Participants joining the study were interviewed for their chronic health complaints, received an ultrasound examination and underwent urinalysis (using a urine strip). All of the subjects were asked about the presence of nine chronic symptoms: (i) multiple myofascial pain; (ii) back pain or lower abdominal pain; (iii) dyspepsia; (iv) poly-arthralgia; (v) single-side headache; (vi) fatigue; (vii) frank paresthesia; (viii) dysuria at least once a year and, (ix) any of these symptoms were aggravated by PRF.

The inclusion criteria comprised: (i) patients with renal stones or having a hyperechoic focus suspected of being a stone; (ii) having five or more of the nine variables of MCHC; (iii) having at least two active symptoms and, (iv) being between 20 and 65 years of age. Subjects were excluded if they had: (i) a stone obstruction; (ii) heart disease; (iii) known chronic renal failure; (iv) were pregnant or, (v) had any other severe illness. Patients with white blood cells in the urine, using a strip read by a portable urine analyzer (UriluxS, Roche, Basel, Switzerland), were also excluded from this study but entered into another.

Randomization

Subjects were stratified by the number of their active symptoms: those with two–four symptoms were assigned to Group A, and those with more than four symptoms to Group B. In each group, running numbers were listed according to the time sequence, viz. A01, A02, A03, . . . , A50 in Group A and B01, B02, B03, . . . ,B50 in Group B.

Within each group, patients were allocated to G1 (the OG group) or G2 (the placebo group) by block of six. For example, every six consecutive participants were enrolled in each group (A, B), three subjects by coin toss to the OG group and three to the placebo group. Thus, each running number in each subgroup belonged to the code of either OG or placebo. The medication was prepared according to the code. Thereafter, the codes were concealed and not opened until the data analysis phase.

Treatment

The placebo and OG extract were filled into identical-looking capsules. The placebo contained the dried ground vegetable Ipomoea Aquatica Forsk. To prepare the OG extract, dried leaves of OG were ground in a mechanical mill and put in hot water (kept at 70–80°C for 20 min. The infusion was separated in a container and put on a water bath. The temperature of the infusion was kept at 70–80°C for 36 h until it nearly dried then it was mixed with a prepared mixture, and left in the chamber for 48–72 h at 40–50°C until dried. This dried mixture was ground and capsules filled with it. Each capsule of OG extract equaled 1.6–1.8 g of the dried leaves.

Therapies consisted of 20 minute health education for the MCHC and encouraged them to stop consuming the 25 PRF items during the trial period. Group 1 took one capsule of OG two times a day while Group 2 took the placebo.

The Adverse Effects of Treatments

Adverse effects in this study were defined as: any new symptoms that occurred during treatment, or old, inactive symptoms which became active during treatment.

The Purine-Rich Foods

PRFs in this study included: bamboo shoot (*Gigantochloa albociliata*, *Bambusa sp*., *Thysostachys siamensis Gamble*), tops of *Calamus rotang Linn*; leaf shoot of coconut (*Cocos nucifera Linn*); young leaves of *Acacia pennata*; common local mushrooms [*Pleurotus sajor-caju* (*Fr*.) *Singer*, *Lentinus squarrosulus Mont*., *Volvariella volvaceae*, *Termitomyces fuliginosus Heim*]; fermented boiled flour in noodle form; all kinds of fermented fruits or vegetables; alcoholic beverage; grasshoppers [*Locusta migratoria manilensis* (*Meyen*), *Patanga succincta* (*Linnaeus*)]; queen or larva of red ant (*Oecophylla smaragdina*); silk worm (*Philoamia ricini Boisd*); all kinds of crickets (*Acheta testacea, Acheta bimaculatus De Geer*, *Bracytrupes portentosus Licht*.); beef or buffalo meat (*Swamp buffalo*); a local small freshwater fish (*Rasbora tornieri*); shellfish (*Sinotaia ingallsiana*, *Pila polita*); cuttlefish (*Sepia pharaonis*); squid (*Loligo peali*); chicken (*G.gallus domesticus*); duck (*Anseriformes anatidae*); adult, small /larva of frog (*Rana tigerina*) and ricefield rat (*Rattus argentiventer*).

Measurements

The main outcome measure was the sum of score of each patient's active symptoms on the visual analog scale (VAS). Each symptom had a maximum score of 100 and a minimum score of 0. The VAS was performed by each patient under supervision at the beginning (on day 0) and upon follow up (at day 7 and 14). The second outcome was the score on the general feeling of illness. Data on daily PRF intake were collected, retrospectively, through interviews on days 0, 7 and 14.

Data Analysis

Data were expressed as means and 95% confidence intervals (95% CI), medians and inter-quartile ranges (IQRs). A comparison of results between groups was performed using unpaired *t*-tests for normal distributions or the Mann–Whitney U-test for skewed distributions. Before and after within groups analyses were done using the paired *t*-test or the Wilcoxon signed ranks test (WSRT) for normal or skewed distributions, respectively. A probability of $P < 0.05$ was considered statistically significant.

Results

Eighty-seven subjects agreed to participate in the study, of whom six in the OG and five in the placebo group were lost. Four subjects in the OG declined to join because of the adverse effects: dizziness, myofascial pain, fatigue and palpitation. Two subjects from the OG group and three from the placebo group felt unchanged and quit in the second week. Two subjects in the placebo group moved out of province and we lost contact with them. Seventy-six subjects had complete data portfolios and were analyzed, on an intention to treat basis. (Fig. 1).

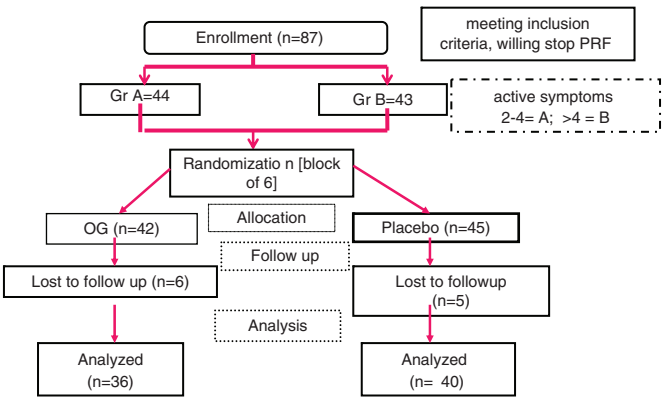

Figure 1. Details of MCHC patients enrolled in the study.

Table 1. Baseline characteristics and mean scores by VAS scale for 76 patients

Characteristic	OG[a] gr. ($n = 36$)	Placebo ($n = 40$)	*P*-value
Age (>45)	29 (80.0%)	32 (80.0%)	0.95[†]
Sex (female)	22 (64.5%)	27 (67.5%)	0.56[†]
Renal stone positive	22 (71.0%)	29 (80.6%)	0.36[†]
Urine red blood cell positive	9 (25.7%)	7 (17.5%)	0.39[†]
Aggravated by PRF[b]	27 (79.1%)	36 (94.7%)	0.08[†]
No. of MCHC[c] *mean(95%CI)*	6.7 (6.1,7.9)	7.5 (6.7,7.3)	0.22[‡]
No. of Active sym. *mean (95%CI)*	3.8 (3.3,4.2)	4.1 (3.6,4.7)	0.31[‡]
Gen feeling *mean (95%CI) of VAS*	52.6 (47.2,58.0)	50.3 (42.5,58.1)	0.71[‡]
MCHC[d] *mean (95%CI) of VAS*	185.6 (154.4,216.8)	196.1 (163.7,228.5)	0.64[‡]

[a]*Orthosiphon grandiflorus*; [b]Purine rich food; [c]Multiple chronic health complaint; [d]Sum of VAS scores of MCHC.
[†]Chi-square tests.
[‡]Mann–Whitney test U.

Baseline Patient Characteristics

The mean age of the 76 participants was 53.7 years (55.6 for OG and 53.8 for placebo); 36 were in the OG group and the 40 in placebo group. Table 1 shows the patients' baseline characteristics by treatment groups, which were similar. Most of the participants were women (64.5 and 67.5%) over 45 years of age (80.0 and 80.0%, respectively). In the OG and placebo groups, the respective mean (95% CI) of the MCHC variables was 6.7 (6.1, 7.9) and 7.5 (6.7, 7.3), and of active symptoms (95%CI) 3.8 (3.3, 4.2) and 4.1 (3.6, 4.7). For the OG and placebo groups, respective renal stone detection was 71.0 and 80.6% and for red blood cells (RBCs) in the urine 25.7 and 17.5%. The positive history for symptoms aggravated by PRF was 79.1 and 94.7%, respectively. The mean (95% CI) VAS score for general feeling of illness between the OG and placebo groups was 52.6 (47.2, 58.0) and 50.3 (42.5, 58.1), respectively. For total MCHC symptoms, the respective mean (95%CI) VAS score for the OG and placebo groups was 185.6 (154.4, 216.8) and 196.1 (163.7, 228.5) points.

Main Outcomes: Sum of VAS Scores of MCHC

In the OG group, the median (IQR) of the sum of VAS scores of the MCHC symptoms was 109.5 (114.3) at day 7 and 68.0 (125.8) at day 14, which were significantly decreased (*P*-value < 0.001, WSRT) from the value on day 0 [166.5 (130.8)] (Table 2). The respective mean (95% CI) sum of VAS scores on day 7 and 14 was 119.0 (88.3, 149.7) and 94.7 (58.2, 131.2), which was 64.1 and 51% of the value on day 0 [185.6 (153.3, 218.0)].

Table 2. VAS scores of general feeling of illness for 76 patients by treatments

Group	VAS score of general feeling of illness			
		Day 0	Day 7	Day 14
OG[a] ($n = 36$)	Median (IQR[b])	50 (12.8)	34 (20.8)*	27 (37.5)*
	Mean (SD)	52.1 (16.4)	35.5 (18.9)	31.3 (24.5)
	95% CI	46.5,57.5	29.1,41.9	22.9,39.5
Placebo	Median (IQR)	50.0 (35.0)	32.0 (44.0)*	15 (38.0)*
($n = 40$)	Mean (SD)	50.3 (24.1)	36.5 (24.1)	26.2 (24.4)
	95% CI	42.5,58.2	28.7,44.3	18.3,34.1
P-value[§]		0.779	0.928	0.374

[a]*Orthosiphon grandiflorus*; [b]Inter-quartile range.
*$P < 0.001$ compare before and after by Wilcoxon Signed Ranks.
[§]Compared between groups by Mann-Whitney U.

Table 3. Total VAS scores of MCHC for 76 patients by treatments

Group	Total VAS scores			
		Day 0	Day 7	Day 14
OG	Median (IQR[a])	166.5 (130.8)	109.5 (114.3)*	68.0 (125.8)*
($n = 36$)	Mean (SD)	185.6 (95.6)	119.0 (90.7)	94.7 (107.9)
	95% CI	153.3,218.0	88.3,149.7	58.2,131.2
Placebo	Median (IQR)	186.5 (104.5)	101.5 (119.0)*	79.5 (94.7)*
($n = 40$)	Mean (SD)	196.1 (99.2)	129.6 (92.7)	89.6 (83.9)
	95% CI	164.4–(227.8)	100.0–159.3	62.8–116.5
P-value[†]		0.747	0.689	0.791

[a]Interquartile range.
*$P < 0.001$, comparing before and after by Wilcoxon Signed Ranks.
[†]Compared between groups by Mann–Whitney U.

In the placebo group, the median (IQR) of the sum of VAS scores for MCHC symptoms was 101.5 (119.0) on day 7 and 79.5 (94.7) on day 14, significantly decreased (*P*-value < 0.001, WSRT) from the beginning [186.5 (104.5)] (Table 3). The respective mean (95% CI) of the sum of VAS scores on day 7 and 14 was 129.6 (100.0, 159.3) and 89.6 (62.8, 116.5), which was 66.1 and 45.7% of the value before treatment.

There was no statistically significant difference for the OG versus placebo groups for the beginning, day 7 and day 14 of treatment (Table 3). Instead, in both groups, each symptom of the MCHC, as a VAS score, at day 7 and 14 was significantly decreased (*P*-value < 0.05, WSRT) from day 0. Figure 2 illustrated the VAS scores at day 0, 7 and 14 for myofascial pain, arthralgia, dyspepsia and back pain.

The General Feeling of Illness

In the OG group, the median (IQR) of the VAS scores for the general feeling of illness was 34 (20.8) at day 7 and 27 (37.5) at day 14, both significantly decreased

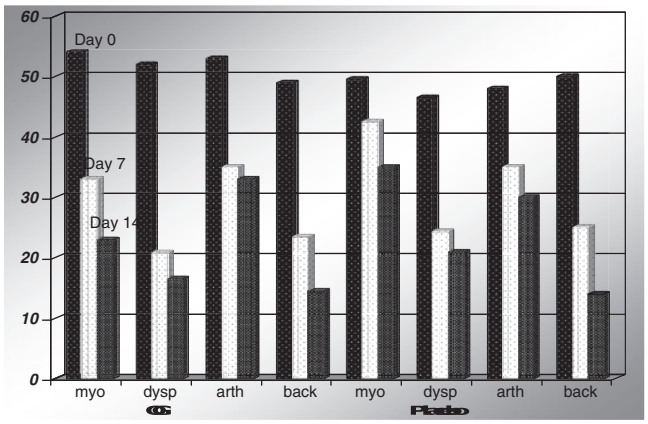

Figure 2. VAS scores of myofascial pain dyspepsia arthralgia back pain of OG, placebo group on day 0, 7 and 14 of treatment.

(P-value < 0.001, WSRT) from day 0 [50 (12.8)] (Table 2). The respective mean (95% CI) of the VAS scores for the general feeling of illness on day 7 and 14 was 35.5 (29.1, 41.9) and 31.3 (22.9, 39.5), which was 68.1 and 60.1% of the value in day 0 [52.1 (46.5, 57.5)].

In the placebo group, the median (IQR) of the sum of VAS scores of the general feeling of illness was 32.0 (44.0) on day 7 and 15 (38.0) on day 14, both significantly decreased (P-value < 0.001, WSRT) from the beginning [50.0 (35)] (Table 3). The respective mean (95% CI) of the sum of VAS scores of the general feeling of illness on day 7 and 14 was 36.5 (28.7, 44.3) and 26.2 (18.3, 34.1), which was 72.6% and 52.1% of the value before treatment [50.3 (42.5, 58.2)]. There was no significant difference between groups in the VAS scores on the general feeling of illness on days 7 and 14 of treatment.

Adverse Effects

The adverse effects in the first and second week of treatments were 27.8 and 2.8% for the first and the second week in the OG group, and 17.5 and 17.5% in the placebo group for the first and the second week, respectively (Table 4). There was a significantly difference ($P = 0.03$, Fisher exact Chi-Squared) when compared between groups in the second week. When compared within the same group at the first and second week, the reported adverse effects were reduced significantly in the OG group ($P < 0.01$, WSRT). The adverse effects reported during the treatments included myofascial, fatigue, back pain, abdominal pain, arthritis, gastrointestinal disturbance and headache; most of which are the symptoms included in the MCHC variables, but were inactive in the pretreatment period.

Purine Rich Foods

The frequencies of PRF consumptions over the seven previous days were reviewed retrospectively at the beginning of the trial and when the subjects came to follow up on day 7 and 14. Table 5 shows the median (IQR) and mean (95%CI) of PRF consumption the week before treatment and during the first and the second week of treatment.

In the OG group, the mean frequency of consumption of bamboo shoot and of the 25 kinds of PRF before treatment was 3.9 and 14.2 times/person/week but this dropped to 0.1 and 1.3 times 0.1 and 1.3 times/person/week during the first and second weeks, respectively.

For the placebo group, the respective mean frequency of eating bamboo shoots and the other kinds of PRFs was 3.6 and 11.4 times/person/week in the week before treatment and 0.4 and 0.9 times and 0.1 and 0.7 times/person/week during the first and second week, respectively.

Both groups significantly ($P < 0.001$, WSRT) reduced the intake of PRFs during the first and second week to < 10% of the frequencies before treatment. There was no significant difference in the frequencies of PRF consumptions between groups during the first and second weeks of treatment (Table 5).

Table 4. Reported adverse effects in the first and second week of treatments

Adverse effect and details	OG[a] gr. ($n = 36$)		Placebo gr.($n = 40$)	
	Day 0–7	Day 8–14	Day 0–7	Day 8–14
Reported adverse effects	10 (27.8%)**	1 (2.8)*	7 (17.5)	7 (17.5)*
Details[b] Myofascial	3	1	4	1
Fatigue	4	0	2	1
Back/abdominal pain	2	1	0	2
Arthritis	1	0	1	0
Sleep problem	2	0	1	0
Gastrointestinal disturbance	1	0	1	3
Headache	0	0	1	0
Others[c]	0	0	0	3

[a]Orthosiphon grandiflorus; [b]A subject had ≥ 1 symptoms; [c]Paresthesia, urticaria, and dizziness.
*$P = 0.03$ by Fisher exact Chi-Square.
**$P < 0.01$ compared within group by Wilcoxon Signed Ranks Test.

Discussion

This study was a double blind, randomized control trial with strict concealment, and it was the first to reveal a method of treating MCHC as a syndrome, the common presentation among the rural dwellers of Northeast Thailand. These groups of patients had renal stones (mostly small) or suspected of having stones, detected as hyperechoic foci on ultrasonography. All of the participants were negative for white blood cells in the urine.

Table 5. Mean (95%CI) of purine-rich foods consumption per week in 76 patients

Type of PRF	Period	OG[a] gr. ($n = 36$)		Placebo gr. ($n = 40$)		p-value[c]
		Median (IQR[b])	Mean (95%CI)	Median (IQR)	Mean (95%CI)	
Meat/chicken *(times/wk)*	Before	5.0 (6.0)	6.0 (3.8,8.2)	3.0 (5.0)	4.0 (2.8,5.2)	0.26
	Week1	0.0 (0.0)*	0.3 (0,0.7)	0.0 (0.0)*	0.3 (−0.1,0.7)	0.70
	Week2	0.0 (0.0)*	0.3 (0,0.5)	0.0 (0.0)*	0.2 (0.1,0.4)	0.76
Bamboo shoot *(times/wk)*	Before	3.0 (3.75)	3.9 (2.7,5.2)	3.0 (2.0)	3.6 (2.7,4.6)	0.88
	Week1	0.0 (0.0)*	0.1 (−0.4,0.2)	0.0 (0.0)*	0.4 (−0.2,1.0)	0.68
	Week2	0.0 (0.0)*	0.1 (0,0.2)	0.0 (0.0)*	0.1 (0,0.3)	0.93
All PRF[d] (times/wk)	Before	9.5 (12.8)	14.2 (9.7,18.7)	9.0 (8.0)	11.4 (8.1,14.7)	0.49
	Week1	0.0 (1.0)*	1.3 (0,02.6)	0.0 (0.0)*	0.9 (0.2,2.0)	0.29
	Week2	0.0 (1.0)*	1.3 (−0.3,2.9)	0.0 (1.0)*	0.7 (0.3,1.0)	0.56

[a]*Orthosiphon grandiflorus*; [b]inter-quartile range; [c]compared between groups by Mann-Whitney U; [d]Purine rich foods.
*$P < 0.001$ compared before and after by Wilcoxon Signed Ranks Test.

The study revealed that the PRF reduction can lessen the severity of the symptoms to approximately one-half by the end of the second week of treatment. When PRF consumption was restricted, the OG (3.2–3.6 g/day) did not have any additional benefit over placebo in the treatment of MCHC symptoms at day 7 or 14 after treatment. This suggests that when the rate of uric acid, or other waste compound, production was low, OG did not have additional benefit over placebo for the excretion.

People suffering from joint pains and myofascial pain feel better when they use Orthosiphon, even when they do not restrict any particular kinds of food. Accounts of this experience are anecdotal but have been reported in many countries for a long time. One study (3) indicated that when the authors did not ask for PRF restrictions, both OG plus antibiotic and sodium potassium citrate plus antibiotic dramatically reduced the MCHC symptoms associated with nephrolithiasis among patients positive for urine white blood cells. This information plus the data from our present study suggests: (i) Orthosiphon can reduce the symptoms even when there are no restrictions on the types of food eaten and, (ii) when consumption of PRFs are restricted, Orthosiphon does not have any additional effect over placebo.

Some foods (i.e. grasshoppers, red ant larvae, silk-worms, crickets, bamboo shoots, frogs and their larvae and ricefield rats) are unfamiliar to people in other parts of the world, but for the rural, subsistence dwellers of Northeast Thailand, these foods are common. Data from a random survey in the rural communities in Khon Kaen revealed that during 1 week, more than 9 out of 10 persons consumed at least once of the following PRF: bamboo shoot, fermented food, meat or insects; and 4 out of 10 reported having their symptoms aggravated by these foods (4). Most of the 25 kinds of restricted foods in the study, PRFs as well as the fermented foods and alcoholic beverages, usually cause pain in patients diagnosed as gout.

Restriction of the foods over our 2-week research period was practicable for the 76 participants, but it would not be easy to maintain compliance for much longer (and certainly not lifelong) without repeated education and public health information. Nevertheless, the study indicates that MCHC patients could relieve their own problems if they decided to restrict particular kinds of foods.

In order to create effective management guidelines for MCHC patients, further research should focus on: (i) will the symptoms completely disappear if the PRF restrictions are prolonged? (ii) Can the OG significantly relieve MCHC symptoms more than the placebo in patients who do not restrict PRF intake? (iii) What is the precise mechanism relating this effect to MCHC variables? (iv) What is the regional variation in the prevalence of MCHC and its association with PRF intake in communities with a different prevalence of renal stones?

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