Urinary Risk Factors for Recurrent Calcium Stone Formation in Thai Stone Formers

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Objective: *To survey the urinary risk factors associated with recurrent calcium stone and the contribution of renal tubular acidosis to the prevalence of recurrent calcium stone formation in Thai recurrent stone formers.*
Material and Method: *There were 86 consecutive recurrent calcium stone formers. Three-day dietary record, serum biochemical parameters, first morning urine pH, and two 24-hour urine collections were obtained from each subject. Urinary risk factors for calcium stone formation were determined from the average of the 2-day urine collection. Normal controls were 34 subjects matched for aged, sex, and weight, and without a history of renal stone formation.*
Results: *Seven patients (8.1%) were diagnosed as incomplete renal tubular acidosis (iRTA). Among the 79 idiopathic calcium stone formers (ISF), 69.6%, 15.2%, 10.1%, 7.2% and 1.3% of patients were hypocitraturia, hypercalciuria, low urinary volume, hyperuricosuria and hyperoxaluria, respectively. The common combinations of risk factors were hypocitraturia plus low urine output (8.9%) or plus hypercalciuria (7.6%). There were significant differences between ISF and normal controls in urinary oxalate excretion (0.16 ± 0.01 vs 0.12 ± 0.01, $p < 0.05$), urinary calcium/citrate ratio (4.49 ± 0.50 vs 2.83 ± 0.34, $p < 0.01$) and ion activity product for calcium oxalate stone (0.46 ± 0.03 vs 0.33 ± 0.03, $p < 0.05$). Urinary citrate in ISF varied directly with net alkaline absorption ($r = 0.34$, $p < 0.005$) and urinary potassium ($r = 0.54$, $p < 0.001$). There were significant correlations between urinary calcium excretion and both sodium excretion ($r = 0.42$, $p < 0.001$) and urea excretion ($r = 0.41$, $p < 0.001$) in ISF. There were seven (8.1%) with incomplete renal tubular acidosis. Patients with iRTA tended to have less urinary citrate and higher calcium/citrate ratio than did ISF, but hypercalciuria was uncommon.*
Conclusions: *Hypocitraturia was the most common urinary risk factor found in Thai recurrent idiopathic calcium stone formers followed by hypercalciuria and low urinary volume. Almost one-fourth of the stone formers had multiple risk factors. Hypocitraturia might result from low potassium and low alkaline intake. iRTA was common among recurrent calcium stone formers. Determination of morning urine pH should be a part of the investigations for urinary risk factors to avoid overlooking the diagnosis of iRTA.*

Keywords: *Urolithiasis, Renal stone, Hypocitraturia, Hypercalciuria, Hyperoxaluria, Hyperuricosuria*

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A high prevalence of urolithiasis has been reported in Thailand, 17-20% of the general rural population in northeastern of Thailand[1,2]. The hot climate in the tropics and a percutaneous loss of fluid, resulting in less urine output, may be an important risk factor for urinary tract stone formation. A systematic approach to determine the risk factors for stone formation in Thailand, as well as in the nearby countries, has rarely been done. Given the differences in lifestyle, composition of the diet, environment, and racial factors, it is unlikely for Thai stone formers to have the same risk factors for urinary tract stone formation as what have

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been found in most Western populations. For example, the average dietary calcium intake is around 10 mmol/day in Thais[3], whereas it is 20-30 mmol/day in Western populations[4]. Protein intake also is lower in the Thai population[3]. The variation in dietary compositions between populations will definitely result in a marked difference in urinary constituents. Thailand is in a transition period. The changing economic conditions have brought about a great alteration in the diet, particularly in the composition of animal protein. This may result in alterations in the urinary constituents of the Thai population in a less predictable way. Moreover, an unusually high prevalence of renal tubular acidosis (RTA), both the classical (RTA) and the incomplete (iRTA) forms, has been reported in Thailand[1,5]. RTA is a disease caused by renal acidification defect, which causes a very active stone disease if it is left untreated[6]. The contribution of RTA to the prevalence of recurrent urinary tract stone in unselected Thai recurrent stone formers is still unknown. It is uncertain if an investigation to rule out RTA should always be a part of the metabolic work up of a recurrent renal stone. The authors, therefore, conducted the present study to explore the spectrum of urinary risk factors for urinary tract stone formation and the contribution of RTA to the prevalence of recurrent urinary tract stone formation in Thai recurrent calcium stone formers.

Material and Method

Subjects

All recurrent calcium stone formers who presented to the Ramathibodi Hospital Stone Clinic from July 2000 to November 2001 were enrolled in the present study. A recurrent stone former was defined as a patient who presented to the clinic with symptomatic urinary tract stone plus the evidence of a previous stone formation, including 1) history of passing a stone, 2) presence of a stone on a previous KUB X-ray or ultrasound, or 3) history of operation for urinary tract stone. A patient with serum creatinine greater than 180 umol/L, chronic diarrhea, urinary tract infection, short bowel syndrome, or concurrent usage of drugs that affect acid-base status and calcium metabolism was excluded from the present study. Eighty-six recurrent stone formers participated in the present study. The analysis of stone content was based on a stone analysis using infrared spectroscope or the presence of a calcium stone on KUB X-ray.

Normal controls included 34 healthy volunteers who had no history of renal stone formation, no demonstration of urinary tract stone by KUB X-ray or ultrasound at the time of the present study, and no concurrent systemic illness.

Blood sample, urine analysis, urine culture, and two 24-hour collections of urine samples were obtained from each subject in both the normal control group and the stone former groups. Each subject was instructed to maintain his usual dietary habits during the two days of 24-hour urine collection and blood samples. If urinary tract infection were diagnosed, 24-hour urine collection would be postponed until the infection was cured. For a patient who had extracorporeal shockwave lithotripsy (ESWL) or an operation done to remove urinary tract stone, the investigation would be postponed for at least 2 months. A 3-day dietary record was obtained from each patient after the patient had been given instructions provided by a dietitian. Food composition was determined by INMUCAL (Mahidol) computer program[7]. The total energy intake in the presented patients was 1577.0 $\pm$ 47.3 kcal/day, carbohydrate 231.2 $\pm$ 7.9 g/day (59.2 $\pm$ 0.9% of total calories), protein 60.1 $\pm$ 2.4 g/day (15.4 $\pm$ 0.4% of total calories) and fat 44.3 $\pm$ 1.8 g/day (25.4 $\pm$ 0.7% of total calories). The calcium intake was 10.11 $\pm$ 0.65 mmol/day and dietary fiber was 8.6 $\pm$ 0.4 g/day.

In order to make a diagnosis of incomplete renal tubular acidosis iRTA, first morning urine pH was determined in all stone formers. If morning urine pH was higher than 5.5, the patient would undergo a short acid loading test (0.1 g/kg/d of oral NH_4Cl) and urine pH was measured after taking oral NH_4Cl for 4-6 hours. A patient who had normal baseline serum electrolytes and failed to acidify urine (pH < 5.5) in the presence of systemic acidosis (blood pH < 7.35) after the acid loading test was diagnosed as iRTA[8].

The present study was approved by the Ramathibodi Hospital Ethic Committee. Written informed consent was obtained from each subject.

Biochemical Determinations

Two 24-hour urine collections were obtained from each patient in the out patient department. Urine samples were collected in clean polyethylene containers with toluene as a preservative[9]. The urine samples were acidified immediately after complete collection and frozen at -20 C and analyzed within 1 month. Blood samples were taken after an overnight fast. Serum and urinary electrolytes (sodium (Na), potassium (K), chloride (Cl), bicarbonate), creatinine, uric acid, urea, calcium (Ca), and phosphate (P) were determined by using a Technicon Auto Analyzer. Urinary magnesium (Mg) was determined by atomic

absorption spectrophotometry, urinary citrate (Cit) by citrate lyase technique[10], and urinary oxalate (Ox) by high performance liquid chromatography (HPLC) technique[11]. For the oxalate assay, the inter-assay coefficients of variation averaged 4%, whereas the averaged recovery of oxalate was 93%. Net gastrointestinal alkaline absorption (Alk-Ab) was calculated according to the formula[12]:

$$(Na + K + Ca + Mg) - (Cl + 1.8 \times P)$$

where electrolyte excretion are expressed in mEq/day, except P, which is expressed in mmol/day with an average valence of 1.8.

Risk of calcium oxalate stone formation was determined by using Tiselius's index[13], in which the ion activity product was estimated by an index called AP(CaOx):

AP (CaOx) index

$$= 1.9 \times Ca^{0.84} \times Ox^{1.0} \times Mg^{-0.12} \times Cit^{-0.22} \times V^{-1.03}$$

Urinary excretions of calcium (Ca), oxalate (Ox), magnesium (Mg) and citrate (Cit) are expressed in mmol/L, and urine volume (V) is expressed in liters. Complete collection of 24-hour urine sample was verified by the amount of urinary creatinine of greater than 80% of appropriate creatinine excretion. The appropriate urinary creatinine excretion was estimated using the formula[14]:

Urinary creatinine excretion

= (140-age) x BW x 1.77 umol/d (for male)

= (140-age) x BW x 1.50 umol/d (for female)

The average amount of each urine constituent from the two 24-hour urine collections was used for further analysis.

Statistical Analyses

Data are presented as mean ± standard error of mean (SEM) for continuous variables and as percentage for categorical variables. An unpaired student's *t*-test or Mann Whitney U test were employed to compare group means, and a Chi-square test or Fisher exact test were used to compare categorical number of two independent samples. A *p*-value of less than 0.05 was considered statistically significant. Pearson's correlation coefficient and linear regression were applied to determine correlation between two independent variables. All computations were performed using the SPSS software package for Windows, version 9.0 (SPSS, Chicago, IL, USA).

Results

Of the 86 patients enrolled, 79 were diagnosed as idiopathic calcium stone formers (ISF), and seven were diagnosed as incomplete renal tubular acidosis iRTA. Patient characteristics and serum biochemical parameters for ISF, patients with iRTA, and normal controls are shown in Table 1. There was no significant difference in patient characteristics among ISF, patients with iRTA, and normal controls. There was no abnormality in serum biochemical parameters among ISF and patients with iRTA. The 24-hour urinary constituents are shown in Table 2. There were no significant differences in urinary biochemical parameters between ISF and normal controls, except urinary oxalate, calcium/citrate ratio, ion activity product for calcium oxalate stone [AP(CaOx)], and fractional excretion of calcium (FE calcium). The percentages of patients whose uri-

Table 1. Subject characteristics and serum biochemical parameters for idiopathic calcium stone formers (ISF), iRTA, and normal controls

	ISF	iRTA	Normal controls
N	79	7	34
Age (yr)	49.5±1.4	47.0±3.2	42.6±1.9
Gender (M:F)	42:37	4:3	14:20
Weight (kg)	62.6±1.0	65.1±4.0	62.2±2.1
Serum biochemical parameters (mmol/L)			
Sodium	141.1±0.2	141.3±0.5	140.3±0.5
Potassium	4.4±0.1	4.3±0.2	4.3±0.1
Chloride	107.0±0.2	106.7±0.9	106.3±0.5
Bicarbonate	23.7±0.3	23.5±1.7	23.3±0.6
Calcium	2.6±0.3	2.4±0.1	2.4±0.1
Phosphate	1.1±0.2	1.1±0.1	1.1±0.1
Creatinine (umol/L)	84.7±2.5	106.9±26.7	80.0±4.1

Data were presented as mean ± SEM

Table 2. 24-hour urinary constituents for idiopathic calcium stone formers (ISF), iRTA, and normal controls

Urine constituents(mmol/day)	ISF (n = 79)	iRTA (n = 7)	Normal controls (n = 34)
Sodium	171.3±7.4	169.0±22.0	160.6±9.8
Potassium	35.7±1.5	34.4±2.2	36.1±2.3
Chloride	171.2±6.7	178.8±19.2	164.3±9.5
Calcium	4.81±0.26	4.70±0.89	4.06±0.35
Phosphate	18.82±0.67	16.62±3.94	18.08±1.10
Magnesium	3.74±0.17	3.26±0.39	3.54±0.22
Citrate	1.62±0.12	1.04±0.22	1.86±0.18
Oxalate	0.16±0.01#	0.19±0.02	0.12±0.01
Uric acid	3.24±0.10	3.18±0.23	3.29±0.17
Urea	288.80±10.3	275.6±27.4	267.6±15.4
Creatinine	10.20±0.35	9.54±1.01	10.25±0.56
Alkaline absorption (mEq/d)	19.01±2.67	10.60±9.72	15.10±2.83
Volume (L)	1.90±0.09	2.19±0.29	1.87±0.15
Calcium/Citrate ratio	4.49±0.50*	6.92±2.03	2.83±0.34
AP(CaOx)	0.46±0.03#	0.43±0.11	0.33±0.03
FE calcium	0.017±0.001#	0.020±0.004	0.013±0.001

Data were presented as mean ± SEM
Significant difference from normal controls * at p value < 0.01, # at p value < 0.05 by Unpaired t-test

Table 3. Percentages of subjects with abnormal urinary risk factors for renal stone formation

	Normal limit (mmol/d)	ISF		iRTA		Normal controls	
		No.	%	No.	%	No.	%
Hypocitraturia	> 2.0	55	69.6	7	100	19	55.9
Hypercalciuria	> 7.50 for male > 6.25 for female	12	15.2	2	28.6	3	8.8
Low urinary volume	< 1.5 liter/day	27	34.2	2	28.6	16	47.1
	< 1.0 liter/day	8	10.1	-	-	4	11.8
Hyperoxaluria	< 0.44	1	1.3	-	-	-	-
Hyperuricosuria	> 4.80 for male > 4.50 for female	6	7.2	-	-	2	5.9

nary constituents were abnormal are shown in Table 3. Hypocitraturia was the most common abnormality found in ISF of all the stone formers (69.6%). The distribution of urinary citrate in recurrent ISF is shown in Fig. 1. Female stone formers tended to have higher urinary citrate excretion than male stone formers, but the difference was not significant (1.81 ± 0.16 vs 1.45 ± 0.17 mmol/day, $p > 0.05$). Urinary citrate/creatinine excretion (mmol/mmol) was 0.22 ± 0.02 and 0.14 ± 0.03 in normal females and males, 0.24 ± 0.02 and 0.12 ± 0.01 in female and male stone formers, respectively. However, females had significantly higher citrate/creatinine excretion than males in both normal controls ($p < 0.05$) and ISF ($p < 0.001$). Urinary citrate in ISF varied directly with net alkaline absorption (r = 0.34, $p < 0.005$) and urinary potassium (r = 0.54, $p < 0.001$) as shown in

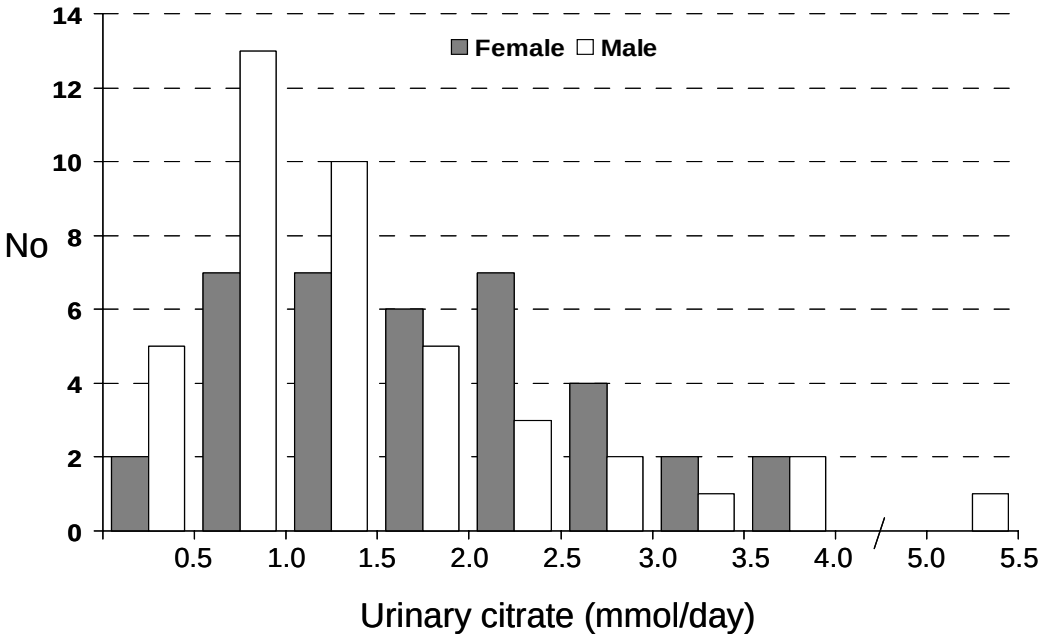

Fig. 1 Distribution of urinary citrate excretion in recurrent calcium stone formers (ISF) between male and female

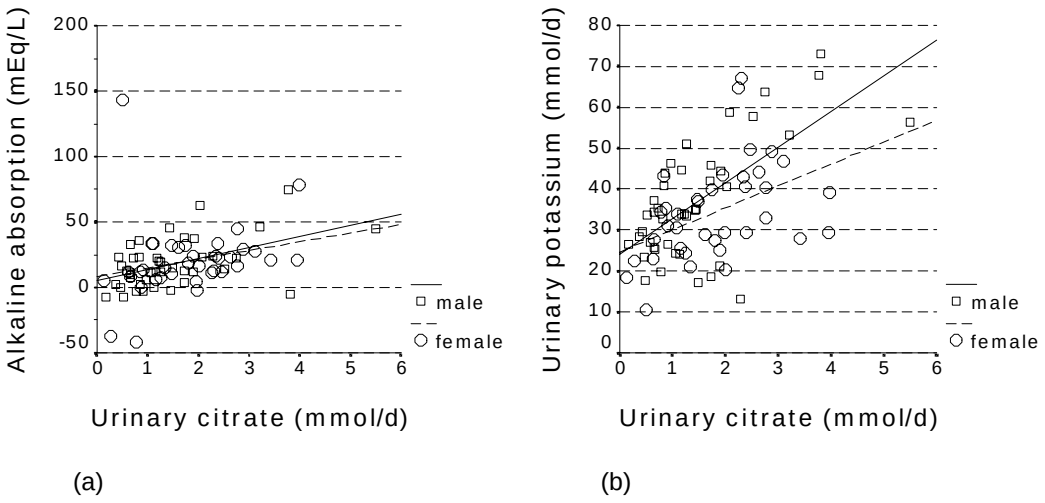

Fig. 2 The relationship between urinary citrate excretion and (a) alkaline absorption, and (b) urinary potassium in recurrent calcium stone formers (ISF)

Fig. 2, but not with body weight. Urinary calcium excretion tended to be higher in ISF than in normal controls, but the difference was not significant. Hypercalciuria was the second most common abnormality found in ISF, 16.7% in males and 13.5% in females. The distribution of urinary calcium in recurrent ISF is shown in Fig. 3. However, if the cut-off levels for hypercalciuria were reduced to 6.25 mmol/day (250 mg/day) in males and to 5.00 mmol/day (200 mg/day) in females, the percentages of patients with hypercalciuria would become 23.8% for male and 37.8% for female stone formers. There was significant correlation between urinary calcium excretion and sodium excretion ($r = 0.42$, $p < 0.001$) as well as between urinary calcium excretion and urea

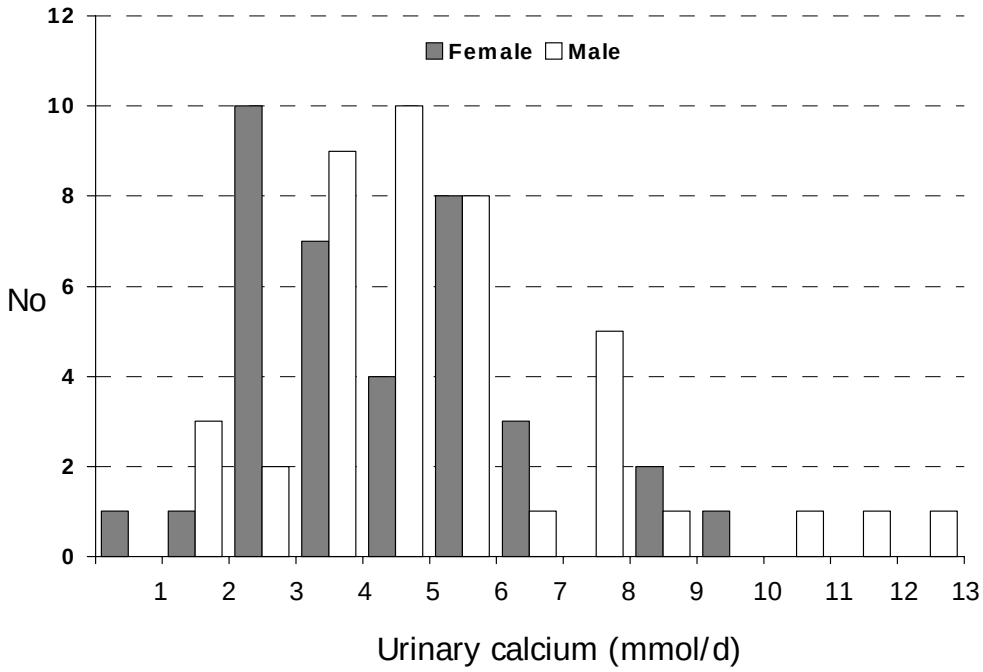

Fig. 3 Distribution of urinary calcium excretion in recurrent calcium stone formers (ISF)

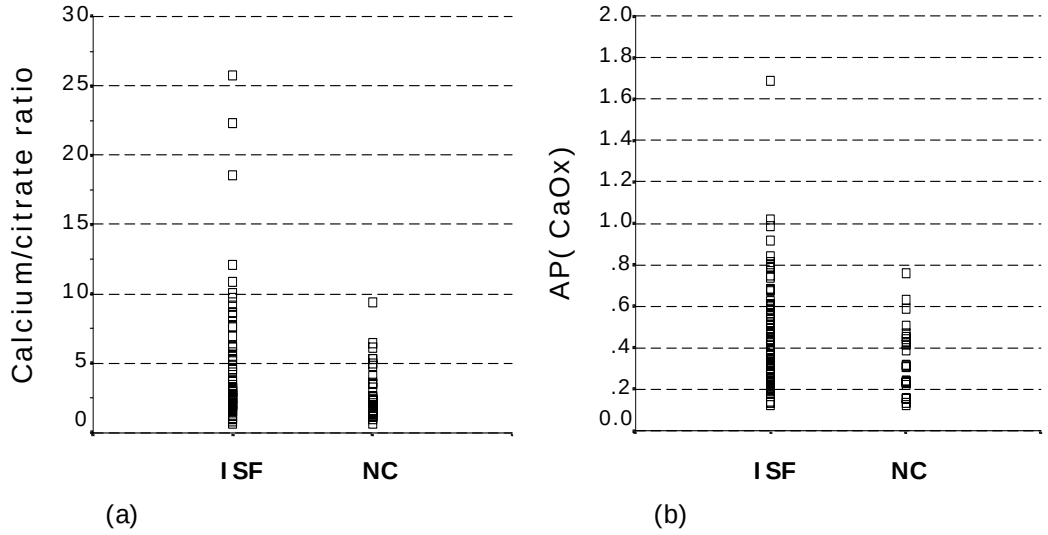

Fig. 4 (a) Urinary calcium/citrate ratio and (b) AP(CaOx) for individual subjects of recurrent calcium stone formers (ISF) and normal controls

excretion (r = 0.41, $p < 0.001$), but correlation between urinary calcium excretion and calcium intake (r = 0.09, $p > 0.05$) was not significant. Low urinary volume was the third most common abnormality found in ISF. 10.1% of patients had urine volume excretion < 1 liter/day. The urinary excretion of oxalate was significantly higher in ISF than in normal controls. However, there was only one patient with hyperoxaluria. Correlation between urinary calcium excretion and oxalate excretion (r = 0.072, $p > 0.05$) was not significant. The ion activity product [AP(CaOx)] and calcium/citrate ratio for calcium oxalate stone in ISF were elevated markedly

above the value found in normal controls. The distribution of calcium/citrate ratio and AP(CaOx) for ISF and normal controls is shown in Fig. 4. There were six (7.2%) ISF with hyperuricosuria. Significant correlation between urinary uric acid excretion and urea excretion ($r = 0.76$, $p < 0.001$) was found. No risk factors for urinary tract stone formation were identified in 18 patients. Twenty patients (25.3%) had more than one risk factor for urinary tract stone formation. The total energy intake in the presented patients was 1577.0 $\pm$ 47.3 kcal/day, carbohydrate 231.2 $\pm$ 7.9 g/day (59.2 $\pm$ 0.9% of total calories), protein 60.1 $\pm$ 2.4 g/day (15.4 $\pm$ 0.4% of total calories), and fat 44.3 $\pm$ 1.8 g/day (25.4 $\pm$ 0.7% of total calories). The calcium intake was 10.11 $\pm$ 0.65 mmol/day and dietary fiber was 8.6 $\pm$ 0.4 g/day.

Seven patients with iRTA (8.1% of all recurrent stone formers) were diagnosed by short acid loading test. These patients had normal serum electrolytes. The urinary constituents for iRTA patients are shown in Table 2. There were two iRTA patients with hypercalciuria but the mean calcium excretion in iRTA was also comparable to those in normal controls and ISF. Patients with iRTA tended to have less urinary citrate, higher calcium/citrate ratio, and higher FE calcium than ISF, but the differences were not significant.

Discussion

In the present study, common urinary risk factors for urinary tract stone formation in Thai recurrent calcium stone formers were identified. Hypocitraturia was the most common abnormality found in ISF, almost 70%, followed by hypercalciuria, 15%, and low urine output, 10%. Hyperuricosuria and hyperoxaluria were less common. Almost one-fourth of ISF had multiple risk factors. The two common combinations of risk factors were hypocitraturia/low urine output and hypocitraturia/hypercalciuria. The findings were rather different from what have been reported from studies in Western populations. Most reports from studies in Western countries demonstrated that hypercalciuria was the most common risk factor for urinary tract stone formation, accounting for 60% of stone formers[15].

Urinary citrate excretion in the presented patients was very low compared with the normal value of what has been reported from other studies done in Western populations[16]. The presented data was in the range of what was reported in other studies in Thai populations, 0.69-1.82 mmol/day[1,2,17,18]. If the normal cut-off value for urinary citrate were greater than 2.0 mmol/day[19], 69.6% would have hypocitraturia. Minisola et al found urinary citrate excretion (mmol/mmol of urine creatinine) of 0.43 $\pm$ 0.13 and 0.23 $\pm$ 0.08 in normal females and males, and 0.28 $\pm$ 0.17 and 0.16 $\pm$ 0.09 in female and male stone formers, respectively[20]. Both male and female stone formers had lower urinary excretion of citrate than did their counterpart normal controls. In the present study, however, citrate excretion in both ISF and normal controls were comparable. The urinary citrate excretion in normal controls in the present study was also lower than the normal value reported in the Minisola et al study[20]. These findings indicate that hypocitraturia is very common in Thai populations, even in subjects without a history of stone formation. This may be an explanation for the very high prevalence of stone disease in Thailand. In ISF, there was a significantly positive correlation between urinary citrate and urinary potassium as well as urinary citrate and urinary alkaline absorption. It has been postulated that hypokalemia may cause hypocitraturia by the mobility of potassium into extra-cellular, and may lead to intracellular acidosis, resulting in an increase in citrate metabolism in the renal tubular cell[21]. There was no subject with hypokalemia in the present study. The relatively low urinary potassium found in ISF might reflect low potassium intake and indicate indirectly that the majority of the presented subjects might have subclinical potassium deficiency or marginal potassium store in the body. The alkaline absorption in our ISF was also less than what has been reported from studies in Western populations[16], indicating indirectly that low alkaline intake might be another cause of low citrate excretion in the presented ISF. The low urinary citrate found in the present study was unlikely a result of poor handling of specimens as tremendous efforts have been made to instruct all subjects to handle specimens with great care, and the complete collection of specimens were confirmed by the amount of creatinine excretion. The preservation of specimens and analytical technique were performed according to standard methods[22].

Hypercalciuria was the second most common abnormality found in the presented ISF, 16.7% in males and 13.5% in females, if hypercalciuria was defined as urinary calcium excretion > 7.50 mmol/day in males or > 6.25 mmol/day in females[23]. These findings were rather different from what have been reported from studies in Western populations. The incidences of hypercalciuria reported from most studies in Western countries ranged from 50-70% of stone formers[15]. The averaged urinary calcium excretions were also lower in the presented subjects, both in ISF and in normal controls, than in Western populations. The cause of

a prevalence of hypercalciuria found in the presented patients should be the result of a low dietary calcium intake in the presented populations, which is supported by the low calcium intake estimated from the dietary record. The averaged calcium intake in the presented population was approximately 10 mmol/day. However, an abnormality in calcium metabolism among the presented ISF cannot be excluded due to the tendency of having higher calcium excretion in ISF than in normal controls. If the cut-off levels for hypercalciuria were reduced to 6.25 mmol/day in males or to 5.0 mmol/day in females as suggested by Curhan et al[4], the percentages of the presented patients with hypercalciuria would increase to 23.8% for male and 37.8% for female stone formers. The fractional excretion of calcium was also higher in ISF than in normal controls, indicating possibly higher calcium leakage from the kidney. However, the mechanism of higher fraction excretion of calcium in the presented ISF cannot be determined from the present study. There was significant correlation between calcium excretion and sodium excretion or urea excretion. It has been demonstrated that an increase of sodium intake inhibits net renal tubular calcium reabsorption and increases urinary calcium excretion[24], and that an increase in dietary protein intakes augments urinary calcium excretion[25]. Restriction of sodium and protein intake in our ISF with hypercalciuria should still be encouraged in the presented patients in order to reduce urinary calcium excretion. Given the low urinary citrate commonly found in the presented patients, reduction in urinary calcium (despite being in the normal range) may still provide additional benefit in the prevention of recurrent stone formation, especially in a patient with a high calcium/citrate ratio.

Low urinary volume was another common abnormality found in the presented ISF. Low urine output might reflect low fluid intake that may lead to volume depletion or insensible loss of fluid due to the persistently high ambient temperature in Thailand. A high fluid intake should always be a part of the nutritional modification to reduce the risk of nephrolithiasis[26]. Hyperuricosuria was less common. It was found in only 7% of ISF. Urinary excretion of uric acid varied directly with urinary urea, indicating a dietary origin.

Urinary oxalate excretion was significantly higher in our ISF than that found in normal controls. However, there was only one patient with hyperoxaluria if hyperoxaluria was defined as urinary oxalate excretion > 0.44 mmol/day[27]. The prevalence of hyperoxaluria was very low compared to that found in Western populations. The prevalence of hyperoxaluria in Western populations has been reported to vary from 15% to 50% among the patients with ISF[28]. Low oxalate intake may cause low urinary oxalate in the presented ISF.

The urinary calcium/citrate ratio was significantly higher in ISF than that found in normal controls. The high urinary calcium/citrate ratio should result mainly from low urinary citrate excretion rather than from high urinary calcium excretion. The cut-off level of urinary calcium/citrate ratio was around 10 mmol/mmol, as shown in Fig. 4. The AP(CaOx) in ISF was also elevated markedly above the value found in normal controls. The cut-off level of AP(CaOx) was approximately 0.8 as shown in Figure 4. The cut-off level for AP(CaOx) in our ISF was markedly below the value for stone formers reported from studies in Western populations, ranging from 1.5-2.0[13]. There was considerable overlap of both urinary calcium/citrate ratio and AP(CaOx) indices between normal controls and ISF. The cut-off value for urinary calcium/citrate ratio and AP(CaOx) associated with low sensitivity and specificity, indicating limited value for discrimination between stone formers and normal subjects. Both indices should be more helpful in the monitoring of treatments in stone formers rather than in the identifying of subjects at-risk of renal stone formation.

In the present study, seven patients with incomplete renal tubular acidosis iRTA were diagnosed after the short acid-loading test. These patients had normal serum electrolytes, making it easy for the diagnosis of iRTA to be overlooked. Therefore, determination of the first morning urine pH should be a part of the investigation of a recurrent stone former in order to provide a clue for the diagnosis of iRTA, especially in a geographical area where RTA is prevalent. Patients with iRTA tended to have less urinary citrate and a higher calcium/citrate ratio than ISF. Only two iRTA patients had hypercalciuria. The mean urinary calcium excretion in iRTA was comparable to those of ISF and normal controls. The reported prevalence of hypercalciuria in RTA has varied from 3% to 36% in Western populations[29]. The authors' previous studies of RTA patients also demonstrated comparable calcium excretion with that found in normal controls[30]. However, subjects with iRTA tended to have higher renal calcium leakage. Urinary phosphate excretion in iRTA patients was also comparable to those found in ISF and normal controls. Patients with iRTA excreted urinary citrate only 60% of the amount of normal controls, which was also lower than the amount that found in ISF. This resulted in a higher calcium/citrate ratio in iRTA than what was found

in either of the other two groups. However, considerable overlaps of their urinary parameters between iRTA and ISF were found, making it impossible to discriminate between their two conditions based on the urinary findings alone. The present findings suggest against the role of hypercalciuria and hyper phosphaturia as major risk factors for stone formation in iRTA patients. Extremely low urinary citrate excretion and persistently high urinary pH should be the major risk factors for stone formation in iRTA patients.

Conclusion

Hypocitraturia was the most common urinary risk factor found in Thai recurrent ISF followed by hypercalciuria and low urinary volume. Almost one-fourth of the stone formers had multiple risk factors. The most common combinations of risk factors were hypocitraturia plus low urine output or hypocitraturia plus hypercalciuria. Incomplete renal tubular acidosis was common among recurrent calcium stone formers. Determination of morning urine pH and acid loading test as being indicated should be a part of the investigations for urinary risk factors to avoid overlooking the diagnosis of iRTA.

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ปัจจัยเสี่ยงทางระบบทางเดินปัสสาวะที่ทำให้เกิดนิ่วชนิดแคลเซียมออกซาเลตซ้ำ ในผู้ป่วยชาวไทยที่เคยเป็นนิ่วมาก่อน

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วัตถุประสงค์: *เพื่อทำการสำรวจหาปัจจัยเสี่ยงทางระบบทางเดินปัสสาวะที่ทำให้เกิดนิ่วชนิดแคลเซียมออกซาเลตซ้ำ และหาอุบัติการณ์ของภาวะ renal tubular acidosis (RTA) ในผู้ป่วยชาวไทยที่เคยเป็นนิ่วมาก่อน*

วัสดุและวิธีการ: *ทำการศึกษาในผู้ป่วยชาวไทยที่เคยเป็นนิ่วมาก่อน (ISF) จำนวน 86 คน การศึกษานี้ได้จดบันทึกรายการอาหาร ที่รับประทานเป็นเวลา 3 วัน ทำการเจาะเลือดตรวจหา serum biochemical parameters ต่าง ๆ วัด pH ของปัสสาวะ ในตอนเช้า และเก็บปัสสาวะ 24 ชั่วโมงเป็นเวลา 2 วัน และได้ศึกษาในกลุ่มคนปกติที่ไม่เคยมีประวัติเป็นโรคนิ่วจำนวน 34 คน ซึ่งมีเพศ อายุ น้ำหนักใกล้เคียงกับกลุ่มผู้ป่วยชาวไทยที่เคยเป็นนิ่วมาก่อน (ISF)*

ผลการศึกษา: *พบว่ามีผู้ป่วย 7 คนที่เป็น incomplete renal tubular acidosis (iRTA) หรือ 8.1% ของผู้ป่วยโรคนิ่วทั้งหมด ส่วนผู้ป่วยที่เคยเป็นนิ่วมาก่อน (ISF) จำนวน 79 คนตรวจพบว่ามีภาวะ hypocitraturia 69.6% ภาวะ hypercalciuria 15.2% ภาวะ low urinary volume 10.1% ภาวะ hyperuricosuria 7.2% และภาวะ hyperoxaluria 1.3% ปัจจัยเสี่ยงที่ทำให้เกิดนิ่วที่พบร่วมกันเป็นส่วนใหญ่ในกลุ่มผู้ป่วย ISF คือ ภาวะ hypocitraturia ร่วมกับ ภาวะ low urine output (8.9%) หรือ ร่วมกับภาวะ hypercalciuria (7.6%) กลุ่ม ISF พบว่ามี urinary oxalate excretion (0.16 $\pm$ 0.01 vs 0.12 $\pm$ 0.01, $p < 0.05$), urinary calcium/citrate ratio (4.49 $\pm$ 0.50 vs 2.83 $\pm$ 0.34, $p < 0.01$) และ ion activity product for calcium oxalate stone (0.46 $\pm$ 0.03 vs 0.33 $\pm$ 0.03, $p < 0.05$) สูงกว่ากลุ่มคนปกติอย่างมีนัยสำคัญทางสถิติ นอกจากนี้ยังพบความสัมพันธ์ระหว่าง urinary citrate กับ net alkaline absorption ($r = 0.34$, $p < 0.005$) และ urinary potassium ($r = 0.54$, $p < 0.001$), urinary calcium excretion กับ urinary sodium excretion ($r = 0.42$, $p < 0.001$) และ urea excretion ($r = 0.41$, $p < 0.001$) ในกลุ่ม ISF ด้วย ส่วนในกลุ่ม iRTA มีแนวโน้มว่า urinary citrate ต่ำกว่าในกลุ่ม ISF และ calcium/citrate ratio สูงกว่าในกลุ่ม ISF*

สรุป: *ปัจจัยเสี่ยงทางระบบทางเดินปัสสาวะที่พบบ่อยในกลุ่มผู้ป่วยชาวไทยที่เคยเป็นนิ่วมาก่อน ISF คือภาวะ hypocitraturia รองลงมาคือ ภาวะ hypercalciuria และ low urinary volume การวัด morning urine pH เป็นสิ่งที่ควรปฏิบัติ เพื่อช่วยในการวินิจฉัยภาวะ iRTA*