Urol Res (2009) 37:345–347
DOI 10.1007/s00240-009-0218-0

SYMPOSIUM PAPER

# Calcium oxalate stone and gout

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Received: 13 September 2009 / Accepted: 16 September 2009 / Published online: 25 September 2009


**Abstract** Gout is well known to be produced by increased uric acid level in blood. The objective of this paper is to assess the relationship between gout and calcium oxalate stone formation in the humans. 48 patients with combination of gout and calcium oxalate stone problem were included. The biochemical values of this group were compared with 38 randomly selected uric acid stone patients with gout, 43 stone patients with gout alone, 100 calcium oxalate stone patients without gout and 30 controls, making a total of 259 patients. Various biochemical parameters, namely serum calcium, phosphorus and uric acid and 24-h urine calcium, phosphorus, uric acid, oxalate, citrate and magnesium were analysed. ANOVA and Duncan's multiple-range tests were performed to assess statistical significance of the variations. The promoters of stone formation, namely serum calcium ($P < 0.05$), phosphorus ($P < 0.05$) and uric acid ($P < 0.05$) and urine calcium ($P < 0.05$), uric acid ($P < 0.05$) and oxalate ($P < 0.05$) were significantly variable in the different groups. The inhibitor citrate ($P < 0.05$) was also significantly variable. Multiple-range test showed that the promoters, namely serum calcium ($P < 0.05$) and urine uric acid ($P < 0.05$) were in a significantly higher range in the gouty patients, gouty uric acid stone patients and gouty calcium oxalate stone patients compared to the non-gouty patients and controls. Urine oxalate ($P < 0.0001$) was in the highest range in the gouty calcium oxalate or gouty uric acid stones patients. The inhibitor urine citrate ($P < 0.001$) was significantly lower in the gouty, gouty uric acid and gouty calcium oxalate patients. Serum uric acid was highest in the non-stone gouty patients, followed by the gouty uric acid stone formers and gouty calcium oxalate stone patients. The high values of promoters, namely uric acid and calcium in the gouty stone patients indicate the tendency for urinary stone formation in the gouty stone patients. There is probably a correlation between gout and calcium oxalate urinary stone. We presume this mechanism is achieved through the uric acid metabolism. The findings point to the summation effect of metabolic changes in development of stone disease.

**Keywords** Gout · Allopurinol · Uric acid stone · Calcium oxalate stone · Biochemistry

## Introduction

Gout is a common metabolic problem manifesting as painful joints of the lower and upper limbs. The pain can be very severe mostly in the lower limb, particularly the big toe. It is well recognised that gout is produced by increased uric acid level in blood. Since elevated uric acid levels in the blood can produce other illnesses, naturally other concomitant conditions have been discussed. Uric acid is the end product of purine metabolism. It may be derived from diet or from tissue break down in the body. It is thus that in malignancy, uric acid levels are seen to be high. Renal stones comprising of uric acid have been associated with high uric acid levels in blood and urine [1–3]. This is well acknowledged.

The role of uric acid metabolism in calcium oxalate urinary stone disease has been debated in recent times. Even

11th international symposium on urolithiasis, Nice, France, 2–5 September 2008 Urological Research (2008) 36:157–232. doi:10.1007/s00240-008-0145-5. http://www.springerlink.com/content/x263655772684210/fulltext.pdf.

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though uric acid stones and gout are known metabolic combinations, much has not been reported about the relationship of gout to calcium oxalate stone disease [4, 5]. This paper has attempted to assess the relationship between gout and calcium oxalate stone formation in the human.

## Methods

259 subjects were included in the study; 48 patients had combination of gout and calcium oxalate stone problem. The biochemical values of this group including serum calcium, phosphorus and uric acid and 24-h urine calcium, phosphorus, uric acid, oxalate, citrate and magnesium were compared with 38 randomly selected pure uric acid stone patients with gout, 43 stone patients with gout alone, 100 calcium oxalate stone patients without gout and 30 controls. ANOVA and Duncan's multiple-range tests were performed to assess statistical significance of the variations.

## Results

The promoters of stone formation, namely serum calcium ($P < 0.05$), phosphorus ($P < 0.05$) and uric acid ($P < 0.05$), and urine oxalate ($P < 0.05$) and uric acid ($P < 0.05$) were significantly variable in the different groups (Table 1). Serum calcium was highest in the patients with gout and uric acid stones (10.4 mg%), followed by the group with gout and calcium oxalate stones. Serum phosphorus was maximum in the group with gout and calcium oxalate stones (4.2 mg%). Serum uric acid was highest in the group with gout alone. Urine calcium was highest in the group with gout and calcium oxalate stones (345 mg/24 h) followed by the group with gout and uric acid stones (304 mg/24 h). Urine phosphorus was also highest in the group with gout and calcium oxalate stones (1,789 mg/24 h). Urine uric acid was highest in the gout alone group (786 mg/24 h), followed by the group with gout and uric acid stones (713 mg/24 h). The urine oxalate was highest in the group with gout and calcium oxalate stones (234 mg/24 h) followed by the group with gout and uric acid stones (212 mg/24 h). It is thus seen that the promoters, namely serum calcium ($P < 0.05$) and urine uric acid ($P < 0.05$) were in a significantly higher range in the gouty patients, gouty uric acid stone patients and gouty calcium oxalate stone patients compared to the other groups. Serum phosphorus ($P < 0.05$) and urine oxalate ($P < 0.0001$) were significantly higher in the gouty stone formers compared to the others.

The inhibitor urine citrate was lowest in the group with gout and uric acid stones (153 mg/24 h) followed by the group with gout and calcium oxalate stones (167 mg/24 h). The citrate level was thus significantly lower ($P < 0.001$) in the gouty, gouty uric acid and gouty calcium oxalate patients.

## Discussion

Various studies on gout and urinary stone problem [4, 5] have identified that gout was associated with more number of calcium oxalate stones than uric acid stones. They recognised that the gout plus calcium oxalate stone group had greater urinary calcium and lower urinary citrate compared to the group of patients with gout and uric acid stones. They concluded that patients with gouty diathesis may form calcium oxalate stones due to increased urinary excretion of calcium and reduced excretion of citrate. The findings of the present study are in perfect agreement with these reports. Hyperuricemia was more in those with uric acid stones than in those with calcium stones.

Negri et al. [6] studied a group of pure uric acid stone formers and that of pure calcium oxalate stone formers and found that patients with calcium oxalate stones had higher 24-h urinary calcium excretion. Increased serum uric acid was a characteristic of uric acid stone formers that resembles patients with primary gout. The findings of the present study agreed with these observations also.

A study on the clinical spectrum of gout in south India [7] identified a higher mean serum uric acid level

**Table 1** Biochemical parameters in different groups studied

| No. | Group | Serum | | | Urine | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Ca (mg%) | P (mg%) | UA (mg%) | Ca (mg/24 h) | P (mg/24 h) | UA (mg/24 h) | Ox (mg/24 h) | Cit (mg/24 h) | Mg (mEq/24 h) | |
| 1 | Gout + calcium oxalate | 9.7 | 4.2 | 6.2 | 345 | 1,789 | 687 | 234 | 167 | 6.3 | 48 |
| 2 | Gout + uric acid | 10.4 | 3.9 | 7.1 | 304 | 1,287 | 713 | 212 | 153 | 7.2 | 38 |
| 3 | Gout alone | 9.3 | 3.8 | 7.4 | 289 | 1,378 | 786 | 175 | 178 | 6.9 | 43 |
| 4 | Calcium oxalate alone | 8.9 | 3.3 | 5.9 | 278 | 1,657 | 634 | 195 | 312 | 5.9 | 100 |
| 5 | Control | 8.3 | 3.4 | 4.8 | 154 | 1,459 | 568 | 156 | 350 | 5.3 | 30 |
| | Significance of variation | * | * | * | * | NS | * | * | * | NS | 259 |

in polyarticular gout than in oligoarticular gout. The mean serum uric acid level was higher in the polyarticular than in the oligoarticular gout. This indicates that higher uric acid levels may indicate severe forms of the disease.

Based on these observations it is suggested that calcium oxalate stone formation is very closely linked to uric acid metabolism and that administration of allopurinol, the drug that reduces production of uric acid in the body would be helpful not only in gout and patients forming uric acid stones, but also in those forming calcium oxalate stones, particularly in those patients who have high levels of uric acid in the blood and urine.

Studies on gout [8–14] indicate that use of diuretics, low-dose aspirin, alcohol abuse, renal insufficiency, hypertension, ischaemic heart disease and obesity are seen frequently in the patients. All these may be related to hyperuricaemia. Further studies are thus indicated in assessing the possible aetiological role of these parameters in urinary calcium oxalate stone formation.

## Conclusion

The high values of promoters, namely uric acid and calcium in the gouty stone patients indicate the tendency for lithiasis in the gouty stone patients. There is probably a correlation between gout and calcium oxalate urinary stone. We presume this mechanism is achieved through the uric acid metabolism. The findings point to the summation effect of metabolic changes in development of stone diseases.

## References

1. Yu T, Gutman AB (1967) Uric acid nephrolithiasis in gout predisposing factors. Ann Intern Med 67:1133
2. Kramer HM, Curhan G (2002) The association between gout and nephrolithiasis: the National Health and Nutrition Examination Survey III, 1988–1994. Am J Kidney Dis 40:37–42
3. Kramer HJ, Choi HK, Atkinson K et al (2003) The association between gout and nephrolithiasis in men: The Health Professionals' Follow-Up Study. Kidney Int 64:1022–1026
4. Khatchadourian J, Preminger GM, Whitson PA, Adams-Huet B, Pak CYC (1995) Clinical and biochemical presentation of gouty diathesis: comparison of uric acid versus pure calcium stone formation. J Urol 154(5):1665–1669
5. Pak CY et al (2005) Physicochemical metabolic characteristics for calcium oxalate stone formation in patients with gouty diathesis. J Urol 173(5):1606–1609
6. Negri AL, Spivacow R, Del Valle E, Pinduli I, Marino A, Fradinger E, Zanchetta JR (2007) Clinical and biochemical profile of patients with "pure" uric acid nephrolithiasis compared with "pure" calcium oxalate stone formers. Urol Res 35(5):247–251. ISSN:0300-5623
7. Porkodi R, Parthiban M, Rukmangatharajan S, Kanakarani P, Panchapakesa Rajendran C (2002) Clinical spectrum of gout in south India. J Indian Rheumatol Assoc 10:61–63
8. Nakayama DA, Barthelemy, Carrera G et al (1984) Tophaceous gout: a clinical and radiographic assessment. Arthritis Rheum 27:468
9. Kumar A, Singh YN, Malaviya AN, Choudhary K, Tripathy S (1990) Clinical profile, therapeutic approach and outcome of gouty arthritis in northern India. J. Assoc. Physicians India 38:400–402
10. McCarty DJ (1994) Gout without hyperuricaemia. JAMA 271:302
11. Fam AG (1998) Gout in the elderly. Clinical presentation and treatment. Drugs Aging 13:229–243
12. Johnson RJ, Kivlighn SD, Kim YG, Suga S, Fogo AB (1999) Reappraisal of pathogenesis and consequences of hyperuricemia in hypertension, cardiovascular disease and renal disease. Am J Kidney Dis 33:225–234
13. Worthmann RL, Kelly WN (2001) Gout and hyperuricaemia. Kelly's Textbook of rheumatology, 6th edn. Saunders, Philadelphia, pp 1330–1390
14. Pak CYC, Poindexter JR, Peterson RD, Koska J, Sakhaee K (2002) Biochemical distinction between hyperuricosuric calcium urolithiasis and gouty diathesis. Urology 60(5):789–794