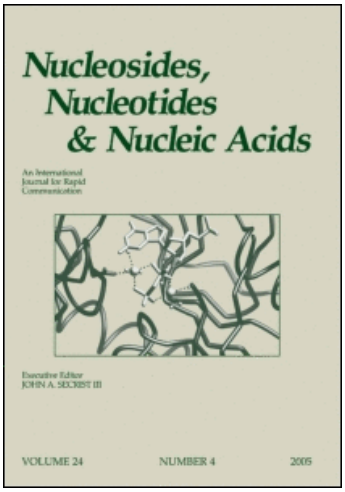

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URIC ACID METABOLISM IN PATIENTS WITH PRIMARY GOUT AND THE METABOLIC SYNDROME

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□ *Forty-four patients (40 males) with a mean age of 58 years were included in this pilot study. Mean serum urate concentration in patients with and without the metabolic syndrome (MS) was 8.8 mg/dL and 8.1 mg/dL, respectively. Urinary uric acid excretion was 543 mg/day/1.73m^2 in the former and 609 mg/day/1.73m^2 in the latter. Uric acid to creatinine ratio was 0.37 mg/mg in patients with the MS and 0.42 mg/mg in those without the MS. Mean serum urate increased from 8.6 mg/dL in subjects with three or more MS components to 10.3 mg/dL in those with five MS components. Serum urate was markedly lower in patients with mild MS (9 patients, 8.6 mg/dL) as compared to severe MS (10 patients, 9.2 mg/dL). In contrast, urinary uric acid to creatinine ratio was 0.42 mg/mg in patients with gout and mild MS and 0.33 mg/mg in gout patients with severe MS. Uric acid underexcretion appears to be more severe in gout patients with the MS. This disturbance appears to be related to the severity of the MS.*

Keywords Gout; MS; uric acid; hyperuricemia

INTRODUCTION

Gout is commonly associated to pathological conditions such as obesity, high blood pressure, dyslipidemia, and metabolic syndrome (MS).[1] Increasing evidence suggests that uric acid may play a role in the MS. The elevated level of serum urate observed in the MS has been attributed to hyperinsulinemia, since insulin reduces renal excretion of uric acid.[2] However, hyperuricemia is prior to hyperinsulinemia Hyperuricemia, however, often precedes the development of hyperinsulinemia.[3] Studies in animal models have shown that decreasing uric acid levels can prevent or reverse features of the MS.[4]

The relation between uric acid and cardiovascular disease is observed not only with hyperuricemia.[5] However, in patients with MS, mean serum urate

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levels are approximately 0.5–1.0 mg/dL higher compared with controls.[1,6,7] Serum urate increases with the number of components of the syndrome,[7–9] even when adjusted for several confounding factors such as age, gender, creatinine clearance, and alcohol and diuretic use. In our population-based study,[1] we found a graded increase in serum urate levels with increasing number of MS components; mean serum urate increased from 4.6 mg/dl in individuals with no components of the MS to 5.9 mg/dl in patients with three components. Serum urate, however, did not increase further in patients with more than three components of the MS. However, we do not know whether serum urate is increased in gouty patients with MS.

An increased serum urate concentration due to uric acid underexcretion is a common feature in patients with the MS. Patients with primary gout frequently show MS characteristics. We aimed to assess whether uric acid metabolism is more severely disturbed in patients with primary gout and the MS.

MATERIALS AND METHODS

Patients with primary gout, according to Wallace criteria, were examined to assess whether they also suffered MS (ATP III criteria, MS $\geq$ 3 criteria). Patients with secondary gout and enzyme defects were not included. Uric acid metabolism was studied under a purine-free diet. Allopurinol was discontinued for at least 3 months in those patients receiving this drug. Colchicine prophylaxis (0.5 mg/day) was administered to all patients. Twenty-four hour creatinine clearance was used to assess the completeness of urine collection; only values within 20% of the Modification of Diet in Renal Disease Study (MDRD) formula to assess glomerular filtration rate were considered adequate. Patients with the MS were classified into two groups according to the severity of the MS components.

Forty-four patients were recruited from the Vascular Risk Unit at the Division of Internal Medicine at La Paz University Hospital, Madrid, Spain. Caucasian subjects, aged $\geq$ 18 years, with primary gout according to Wallace criteria[10] were admitted into the study after informed consent was obtained. All patients underwent a thorough clinical evaluation to establish or rule out the diagnosis of MS, according to ATP III criteria.[11] Serum urate concentration and uric acid excretion were obtained from a purine-restricted intake diet. The severity of MS was established according to a progressive increase in the components and classified into two groups.

RESULTS

Forty-four subjects (40 males) with a mean age of 58 years were included in the study. Mean serum urate concentration was 8.8 mg/dL in patients without MS (20/44). Mean serum urate concentration in gouty subjects with

TABLE 1 Serum uric acid (SUA) and Urine uric acid (UUA) in gouty patients with or without MS

		SUA (mg/dL)	UUA (mg/24h/1.73 $m^{2)}$
GOUT with MS	N = 20	8.8 ± 1.8	543 ± 210
GOUT without MS	N = 24	8.1 ± 1.4	609 ± 240

N, number of patients; MS, metabolic syndrome.

MS was 8.1 mg/dL (Table 1). Urine acid excretion was lower in the MS group (543 mg/24h/1.73 m^2).

Serum urate increased with the number of components of the defined MS. However, did not decrease in patients with less than three components of the MS (Figure 1).

According to the severity of the MS (Table 2), patients were classified into two groups and serum urate was measured. In the mild MS group, mean serum urate was 8.6 mg/dL; in the Severe MS group, mean serum urate group was 9.2 mg/dL. Among the gouty subjects without MS, mean serum urate was 8.1 mg/dL. In contrast, urinary uric acid to creatinine ratio was 0.42 mg/mg in patients with gout and mild MS and 0.33 mg/mg in gout patients with severe MS.

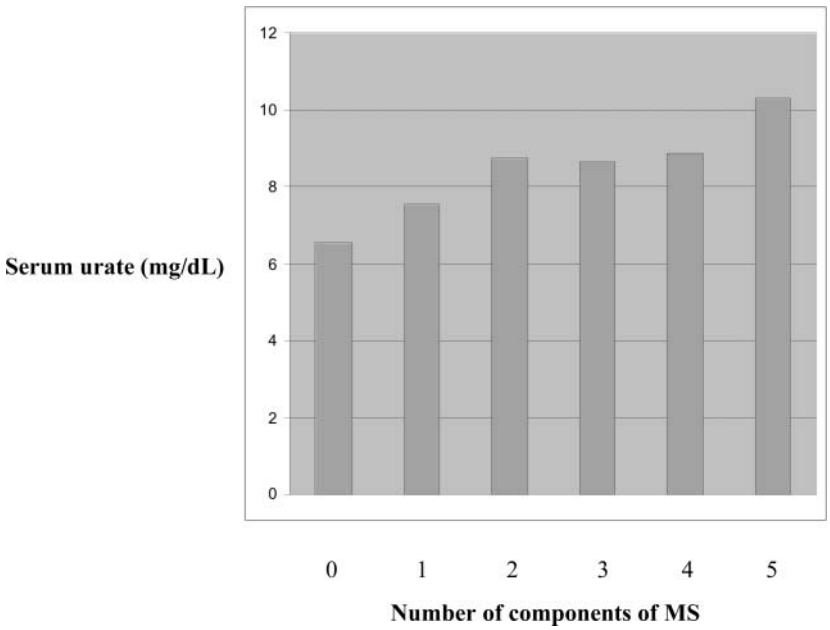

FIGURE 1 Serum urate concentration according to number of components of metabolic syndrome.

TABLE 2 Score for the severity of the MS

MS criteria according to ATPIII	1 point	2 points	3 points
Waist circumference (cm) (Male >102, Female > 88)	102–110	111–119	>120
Triglycerides (mg/dL) (Male and female ≥ 150)	150–180	181–200	>201
HDL cholesterol (mg/dL) (Male < 40, Female < 50)	40–35	34–30	<29
Fasting plasma glucose (g/dL) (Male and female ≥ 100)	100–125	126–150	>151
Hypertension (Male and female ≥ 130/85 mmHg)	No = 0 points	Yes = 2 points	
4–7 points: MILD stage	Serum Urate	mean 8.6	SD 1.4
> = 8 points: SEVERE stage		mean 9.2	SD 2.1
No MS		mean 8.1	SD 1.4

DISCUSSION

In this preliminary study, mean serum urate increases from 8.6 mg/dL in subjects with three MS components to 10.3 mg/dL in those with five components of the MS. Serum urate has a graded increase with increasing number of MS components, as we found in our population-based study.[1] However, serum urate did increase in gouty patients with more than three components of the MS too. We observed in our population study[1] that serum urate did not increase according to the components of the MS in non-gouty subjects.

Thus, urine acid excretion was lower in the MS group (543 mg/24h/1.73 m^2) than non-MS group (609 mg/24h/1.73 m^2). And urinary uric acid to creatinine ratio was 0.42 mg/mg in patients with gout and mild MS and 0.33 mg/mg in gout patients with severe MS. Diminished uric acid excretion is reported in patients with the MS[6] and appears to reflect impaired renal uric acid excretion mediated by hyperinsulinemia enhanced proximal tubular sodium reabsorption.[5,12] Reduced uric acid excretion due to enhanced sodium reabsorption has also been reported in conditions such as obesity and hypertension,[13] the two most common diseases associated with the MS.

Hjortnaes[7] investigated the association between serum urate levels and the metabolic syndrome in a population of patients with manifest vascular disease to determine whether serum urate levels convey an independent risk for vascular disease in patients with the metabolic syndrome. The metabolic syndrome was present in a half of patients. Serum urate levels were higher in 214 patients with the metabolic syndrome than in 217 patients without (0.36 ± 0.08 mmol/L vs. 0.32 ± 0.09 mmol/L). And serum urate concentrations increased with the number of components of the metabolic syndrome (0.30 mmol/L to 0.38 mmol/L) adjusted for age, sex, creatinine clearance, and alcohol and diuretic use. They demonstrated that elevated serum urate levels were strongly associated with the metabolic syndrome and in patients without the metabolic syndrome, elevated serum urate levels were associated with increased risk for vascular disease.

Although our pilot study has a reduced number of patients, we have observed that uric acid underexcretion appears to be more severe in gout patients with the MS. This disturbance appears to be related to the severity of the MS. We need a longitudinal study to verify this hypothesis to clarify the pathogenesis of the gout related to MS.

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