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Blood Uric Acid Levels in Patients With Sleep-Disordered Breathing

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OBJECTIVE: Recurrent hypoxia associated with sleep apnea-hypopnea syndrome (SAHS) leads to an increase in the degradation of adenosine triphosphatase to xanthine and, secondarily, to an increase in uric acid concentrations. The aim of the present study was to determine whether there is a correlation between uric acid levels in peripheral blood and sleep-disordered breathing, independently of known confounding factors.

PATIENTS AND METHODS: We carried out a retrospective cross-sectional study of 1135 patients evaluated for suspected SAHS. For all patients, a medical history was taken using a standardized protocol. In addition, biochemical analysis of venous blood and an overnight sleep study (with either conventional polysomnography or home monitoring) were carried out.

RESULTS: The mean (SD) concentration of uric acid was 6.31 (1.5) mg/dL, and 36% of patients had concentrations above established normal values for their sex. We found a significant correlation between uric acid levels and some sleep study parameters (number of respiratory events, number of desaturations, or the percentage of time with oxygen saturation less than 90%). Those patients with more respiratory events (apnea-hypopnea index or respiratory event index ≥30) had higher uric acid levels than those with mild or no SAHS. However, this difference was not apparent in the univariate analysis of variance, in which body mass index and cholesterol and triglyceride levels were considered confounding factors.

CONCLUSIONS: Uric acid levels are positively correlated with the number of obstructive respiratory episodes and oxygen desaturations during sleep, but this correlation seems to be influenced by other factors, such as obesity.

Key words: Sleep apnea-hypopnea syndrome. Uric acid. Diagnosis.

Valores de ácido úrico en sangre en pacientes con trastornos respiratorios del sueño

OBJETIVO: La hipoxia recurrente del síndrome de apnea-hipopnea durante el sueño (SAHS) origina un aumento de la degradación de adenosintrifosfato a xantina y, secundariamente, de las concentraciones de ácido úrico. El propósito del presente estudio ha sido analizar si existe relación entre los valores de ácido úrico en sangre periférica y los trastornos respiratorios durante el sueño, independientemente de los factores de confusión conocidos.

PACIENTES Y MÉTODOS: Se ha realizado un estudio transversal retrospectivo con 1.135 pacientes evaluados por sospecha de SAHS. A todos ellos se les realizaron una historia clínica protocolizada, un estudio bioquímico de sangre venosa y un estudio de sueño nocturno (polisomnografía convencional o poligrafía domiciliaria).

RESULTADOS: El valor medio (± desviación estándar) del ácido úrico fue de 6,31 ± 1,5 mg/dl, y el 36% de los pacientes presentaban unas concentraciones de uricemia superiores a las establecidas como normales según el sexo. Encontramos una correlación significativa entre los valores de ácido úrico y algunos parámetros de los estudios de sueño (número de eventos respiratorios, número de desaturaciones o el porcentaje de registro con saturación < 90%). Los pacientes con mayor número de eventos respiratorios (índice de apneas-hipopneas o índice de eventos respiratorios ≥ 30) tenían un valor más alto de ácido úrico que aquéllos sin SAHS o con SAHS leve, aunque esta diferencia desapareció al realizar un análisis de la variancia univariante en el que se consideraron factores de confusión el índice de masa corporal y los valores de colesterol y triglicéridos.

CONCLUSIONES: Los valores de uricemia aumentan a medida que lo hacen los episodios respiratorios obstructivos y las desaturaciones durante el sueño, pero este aumento parece condicionado por varios factores, como la obesidad.

Palabras clave: Síndrome de apnea-hipopnea durante el sueño (SAHS). Ácido úrico. Diagnóstico.

Introduction

Obesity is a major medical and public health problem that is currently estimated to affect between 15% and 20% of the population and that increases risk of illness

and death. Among the diseases associated with obesity are those that form part of the so-called metabolic syndrome, such as type 2 diabetes mellitus or lipid metabolic disorder.[1] Obesity has also been associated with elevated plasma concentrations of uric acid and higher frequency of episodes of gout. Furthermore, an excessive accumulation of body fat, especially in the abdominal region, is associated with greater cardiovascular risk, as evidenced by the higher

prevalence of heart disease, cerebrovascular accidents, and high blood pressure in the obese. Obese individuals also have a higher incidence of respiratory diseases. Among the most common of these in such patients are sleep-related breathing disorders, particularly sleep apnea-hypopnea syndrome (SAHS).[2]

Like obesity, sleep-disordered breathing has been associated with increased morbidity and mortality, especially because it leads to a higher frequency of cardiovascular diseases, principally hypertension.[3,4] It is possible that the hypertension attributed to obesity may be due in part to the existence of concomitant sleep-disordered breathing. Sleep-disordered breathing may also play a role in the etiology of some metabolic alterations traditionally associated with obesity, such as hyperuricemia. The repeated episodes of upper airway obstruction that characterize SAHS produce decreases in arterial oxygen saturation repeatedly over the course of the night. Hypoxia promotes the degradation of adenosine triphosphatase to xanthine, which in turn leads to a rise in purine concentrations and in uric acid, the end product of purine catabolism. For this reason, it has been suggested that hyperuricemia may be a marker of inadequate cellular oxygenation.[5] Hasday and Grum[6] evaluated the relation between hyperuricemia and SAHS by studying changes in the urinary excretion of uric acid during the night. In this and subsequent studies it was observed that both the excretion of uric acid and the ratio of uric acid to creatinine increased during the night in patients with SAHS, and it has been suggested that these parameters might be markers of tissue hypoxia in this setting.[5] Furthermore, the use of continuous positive airway pressure reduces the uric acid excreted in urine to normal values.[5,7]

It would therefore seem justifiable to investigate whether uric acid levels could be a simple biological marker of SAHS. The studies carried out with this purpose to date, however, have either included only a small number of patients or have also considered other diseases that might cause chronic hypoxia, such as chronic obstructive pulmonary disease (COPD). Moreover, in these studies uric acid levels were determined by quantitative analysis of urine samples obtained before and after the sleep study, and this can be methodologically complex. We carried out the present study in a large sample of patients referred to our Sleep-Disordered Breathing Unit due to suspicion of SAHS in order to analyze whether there is a correlation between uric acid levels in circulating blood and sleep-disordered breathing, independently of known confounding factors.

Patients and Methods

Study Design and Population

We carried out a cross-sectional retrospective study in a population of 1135 consecutive patients referred to the Sleep-Disordered Breathing Unit of the Medical-Surgical Department of Respiratory Diseases of the Hospital Virgen del Rocio. All patients underwent an overnight sleep study (conventional polysomnography or home sleep study) to investigate initial clinical suspicion of sleep-disordered breathing based on the existence of habitual snoring plus observed apneas during sleep and/or daytime hypersomnolence.

Study Protocol

For all patients, a medical history was taken using a standard protocol including personal characteristics; occupation; use of tobacco, alcohol, or street drugs; as well as relevant surgical, cardiovascular, metabolic and respiratory history. Patients were also questioned about both daytime and nighttime SAHS-related symptoms using a frequency scale (nonexistent, sporadic, or habitual) for each. All patients also underwent a complete cardiorespiratory examination and blood pressure, height, weight, and body mass index (BMI; kg/m^2) were determined. We also measured waist circumference (across the navel, with the patient standing) and hip circumference (across the iliac crests) and calculated the ratio between the 2 measurements (waist-to-hip ratio [WHR]). Either on the same day or a few days after examination in our unit, a complete biochemical analysis was performed on peripheral venous blood extracted from a superficial vein in the arm. Blood samples were processed in the automatic analyzers of our hospital laboratories. We determined, among other things, glucose, triglyceride, and total cholesterol levels. In addition, we measured uric acid concentrations with an in vitro enzymatic colorimetric test (UA Plus, Roche/Hitachi Diagnostics GmbH, Mannheim, Germany). Uric acid concentrations of 7 mg/dL or less in men and 6 mg/dL or less in women were considered normal. In addition to the biochemical study of peripheral blood, we also carried out spirometry (MasterLab/CompactLab 4.2, Erich Jaeger, Würzburg, Germany) and arterial blood gas analysis (IL 1610 Blood Gas System, Instrumentation Laboratory SpA, Milan, Italy).

For overnight polysomnography in our unit's sleep laboratory we used a SleepLab 1.60 polysomnograph (Erich Jaeger GmbH + CO. KG, Würzburg, Germany) that recorded an electroencephalogram, electro-oculogram, submental electromyogram, electrocardiogram, chest and abdominal movements with piezoelectric bands, airflow with an oronasal thermistor, and arterial oxygen saturation by digital pulse oximetry (SpO_2). We analyzed the following events and parameters, defined as follows: a) apnea (absence of oronasal airflow for at least 10 seconds); b) hypopnea (reduction of oronasal airflow by 50% or more accompanied by desaturation and/or arousal); c) desaturation (decrease in SpO_2 of 4% or more compared to previous reading); d) cumulative percentage of time with SpO_2 less than 90% (CT90); e) arousals (according to criteria of the American Sleep Disorders Association[9]); f) apnea-hypopnea index (AHI; number of apneas and hypopneas per hour of sleep); and g) desaturation index (number of desaturations per hour of sleep).

For overnight home cardiorespiratory polygraphy, we used the Apnoescreen I system (Erich Jaeger GmbH + Co. Kg, Würzburg, Germany) that monitored oronasal airflow using a thermistor, SpO_2, heart rate using a finger probe, body position using a mercury sensor, and activity by wrist actigraphy. Polygraphy recordings were processed in a specific data base (Lab4 data base) that allowed them to be analyzed manually in real time. The following events and parameters were studied: a) apnea (absence of oronasal airflow for 10 seconds or more); b) hypopnea (reduction of oronasal airflow by 50% or more accompanied by desaturation and/or arousals); c) desaturation (decrease in SpO_2 of 4% or more compared to previous reading); d) CT90;

e) respiratory event index (REI; number of apneas and hypopneas per hour of recording); and *f)* desaturation index (number of desaturations per hour of recording).

Statistical Analysis

Statistical analysis was performed using version 13.0 of the Statistical Package for Social Sciences (SPSS, Inc. Chicago, Illinois, USA). Results are expressed both as means (SD) and as absolute values and percentages. Qualitative variables were compared used the χ^2 test. Quantitative variables with a normal distribution were compared using the Student *t* test for independent samples. For the comparison of quantitative variables in more than 2 groups, we used analysis of variance (ANOVA), applying Scheffé's method in multiple comparisons. The correlations between quantitative variables were assessed using Pearson's correlation coefficient.

Patients were grouped in terms of the rate of respiratory events (AHI or REI) and uric acid levels in each group were compared. The ANOVA of variance was used to adjust for confounding variables. Significance was set at a value of *P* less than .05.

Results

Of the 1135 patients enrolled in the study, 885 (77.9%) were men and 250 (22.1%) were women. Mean (SD) age was 52 (11.3) years and mean BMI was 32.4 (5.6) kg/m^2. Mean uric acid concentration was 6.31 (1.58) mg/dL (range, 0.9-14.2 mg/dL) and in 36% of the patients uric acid concentrations were above established normal values for their sex. While uric acid concentrations were significantly higher in men than in women (6.58 [1.4] compared to 5.35 [1.5] mg/dL; *P*<.001), we found no significant difference in the percentage of patients with hyperuricemia between men (36.7%) and women (33.6%). Of the 1135 sleep studies (the main results of which are shown in Table 1), 819 (72.1%) used overnight home cardiorespiratory polygraphy, while 316 (27.8%) used overnight polysomnography. Table 2 shows the results obtained in the sleep studies. Patients were classified into 2 groups according to whether or not AHI or REI was 30 or more.

When we analyzed the entire series, we found a significant positive correlation between uric acid levels and some sleep study parameters, such as the number of apneas and hypopneas, the number of desaturations, and CT90. We also found a negative correlation between uric acid, initial SpO_2 in the sleep studies, and PaO_2 (Table 3 and Figures 1-3).

There was also a significant positive correlation between uric acid levels and BMI, WHR, diastolic blood pressure, and cholesterol and triglyceride levels (Table 4 and Figures 4-6).

We divided the series into 4 groups according to the number of apneas and hypopneas obtained by conventional polysomnography or home cardiorespiratory polygraphy: *a)* AHI or REI <5; *b)* AHI or REI ≥5 and <10; *c)* AHI or REI ≥10 and <30; and *d)* AHI or REI ≥30. The number of patients included and uric acid levels for each group are shown in Table 5. As can be observed in this table, patients in the 3 groups

TABLE 1
Results of the 1135 Sleep Studies: Conventional Overnight Polysomnography and Overnight Home Cardiorespiratory Polygraphy*

	Polysomnography Studies (n=316)	Polygraphy Studies (n=819)
AHI-REI	19.5 (22.7)	26.1 (23.5)
Initial SpO_2, %	94.4 (3.1)	93.5 (2.7)
Desaturation index†	11.8 (20.2)	31.1 (26.1)
CT90, %	7.2 (17. 9)	13.1 (20.8)
Minimum SpO_2 %	84.3 (9.6)	73.8 (12

*Data are expressed as means (SD).
AHI indicates apnea-hypopnea index obtained by conventional polysomnography (number of apneas and hypopneas per hour of sleep); REI, respiratory event index obtained by cardiorespiratory polygraphy (number of apneas and hypopneas per hour of recording); SpO_2, arterial oxygen saturation measured by pulse oximetry in sleep recordings; CT90, cumulative percentage of time with SpO_2 less than 90%; minimum SpO_2 lowest SpO_2 value obtained in sleep recordings. †Number of desaturations per hour of sleep (in conventional polysomnography) or per hour of recording (in cardiorespiratory polygraphy).

TABLE 2
Results of the Sleep Studies With Patients Classified According to AHI Obtained by Conventional Overnight Polysomnography or REI Obtained by Overnight Home Cardiorespiratory Polygraphy*

	AHI-REI <30 (n=787)	AHI-REI ≥30 (n=348)
AHI-REI	10.7 (8.4)	54.1 (17.6)
Initial SpO_2, %	94.3 (2.3)	92.2 (3.4)
Desaturation indext	13 (15)	53.6 (23.4)
CT90, %	5.4 (13.9)	24.9 (25)
Minimum SpO_2, %	80.8 (9.7)	67.9 (12.7)

*Results are expressed as means (SD).
AHI indicates apnea-hypopnea index; REI, respiratory event index, SpO_2 arterial oxygen saturation measured by pulse oximetry in sleep recordings; CT90, cumulative percentage of time with SpO_2 less than 90%; minimum SpO_2 lowest SpO_2 value obtained in sleep recordings.
†Number of desaturations per hour of sleep (in conventional polysomnography) or per hour of recording (in cardiorespiratory polygraphy).

TABLE 3
Correlation Between Uric Acid Concentrations, Sleep Study Parameters, and PaO_2 in the 1135 Patients Studied*

	Uric Acid Concentrations, mg/dL	
	R	*P*
AHI-REI	0.184	<.001
Desaturation index†	0.233	<.001
CT90, %	0.156	<.001
Initial SpO_2, %	–0.188	<.001
Daytime PaO_2, mm Hg	–0.1	<.001

*R indicates Pearson's correlation coefficient; AHI, apnea-hypopnea index obtained by conventional polysomnography (number of apneas and hypopneas per hour of sleep); REI, respiratory event index obtained by cardiorespiratory polygraphy (number of apneas and hypopneas per hour of recording); CT90, cumulative percentage of time with arterial oxygen saturation measured by pulse oximetry (SpO_2) less than 90%.
†Number of desaturations per hour of sleep (in conventional polysomnography) or per hour of recording (in cardiorespiratory polygraphy)

with AHI or REI less than 30 had similar uric acid levels, while the mean level of those in the group with 30 or more AHI or REI was significantly higher. In order to adjust this difference for variables that could act as confounding factors, we performed a univariate
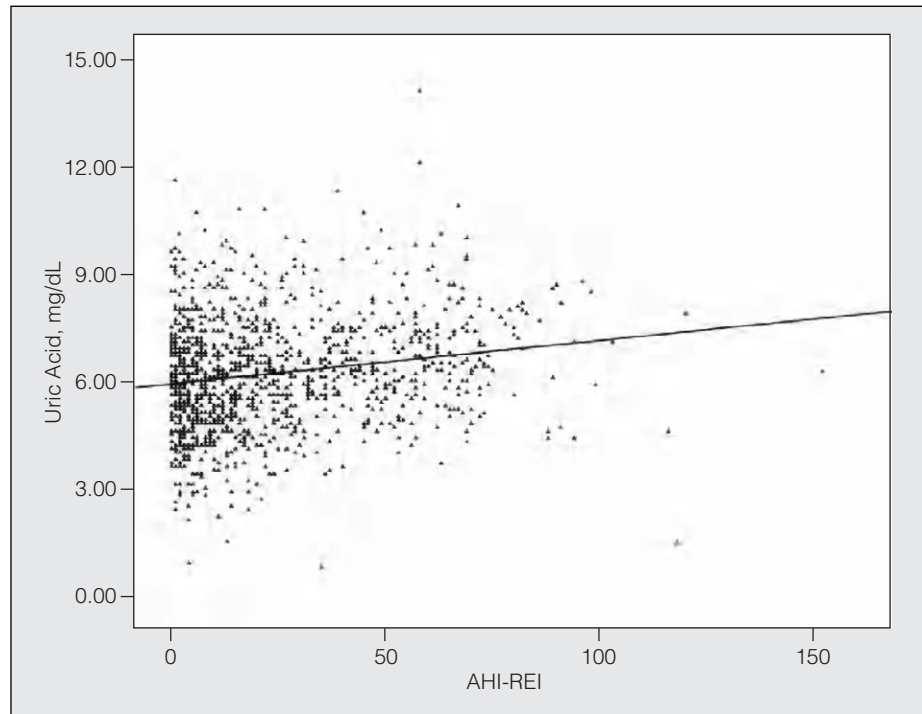
Figure 1. Correlation between uric acid concentrations and AHI obtained by polysomnography or REI obtained by cardiorespiratory polygraphy: AHI indicates apnea-hypopnea index (number of apneas and hypopneas per hour of sleep); REI, respiratory event index (number of events per hour of recording).
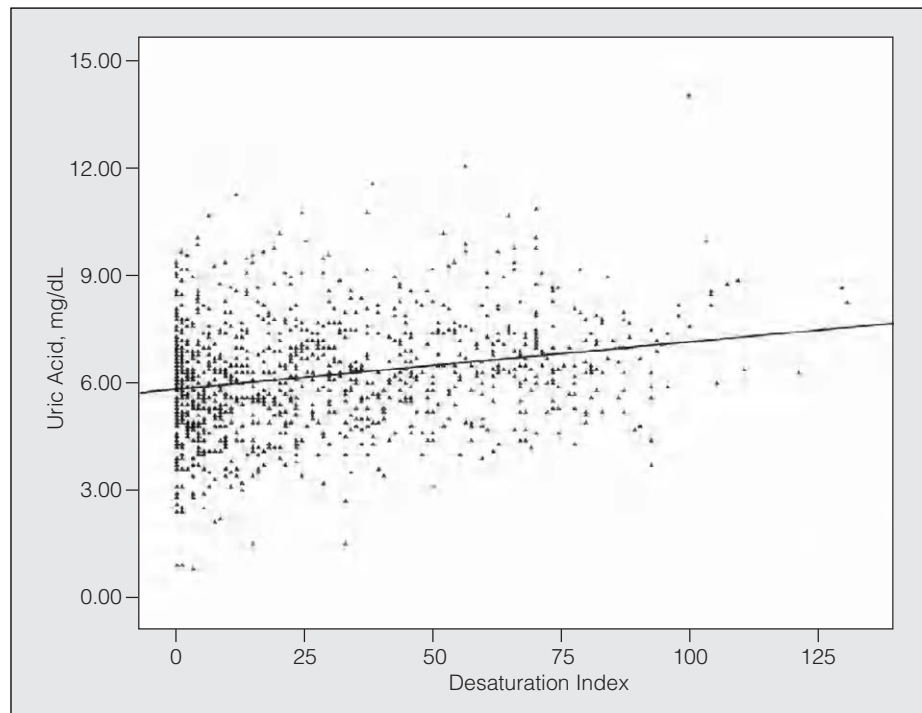

Figure 2. Correlation between uric acid concentrations and desaturation index: number of desaturations per hour of sleep (in conventional polysomnography) or per hour of recording (in cardiorespiratory polygraphy).

ANOVA in which the dependent variable was uric acid and the potentially confounding factors were sex, age, smoking habit, presence of diabetes, systolic blood pressure, diastolic blood pressure, ratio of forced expiratory volume in 1 second to forced vital capacity, BMI, WHR, and cholesterol and triglyceride levels.

When BMI and cholesterol and triglyceride levels were introduced into the analysis, the difference in uric acid levels between the group of patients with an AHI or REI of 30 or more and those with an AHI or REI less than 30 decreased to the point of losing statistical significance (P=.065).
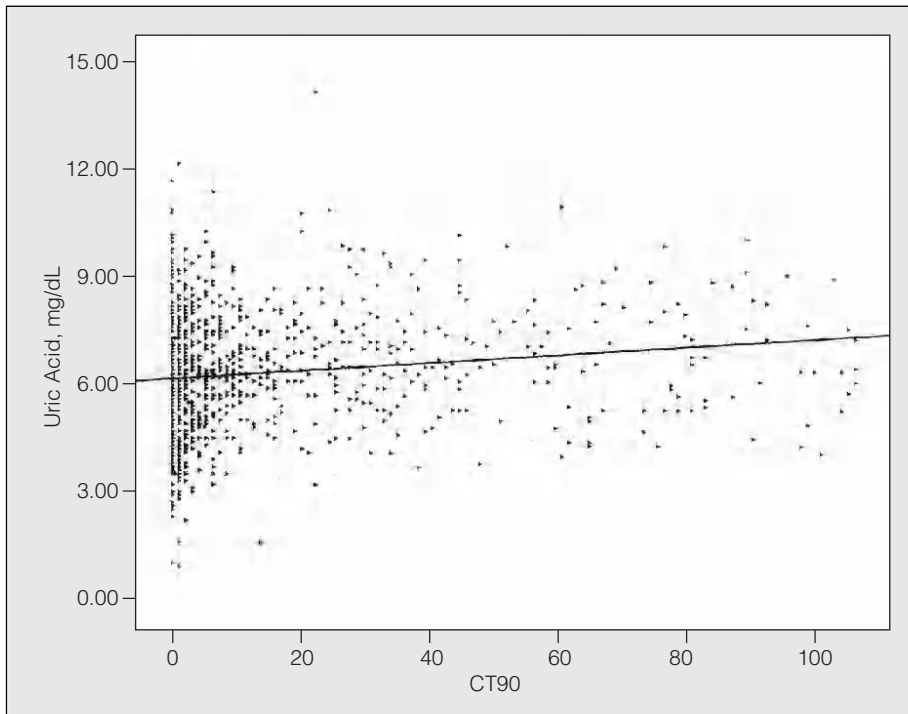
Figure 3. Correlation between uric acid concentrations and cumulative percentage of time with arterial saturation less than 90% (CT90).

Discussion

The results of the present study indicate that patients with severe SAHS (AHI or REI ≥30) have higher levels

TABLE 4
Correlation Between Uric Acid Concentrations in Plasma and Anthropometric Parameters, DBP, and Cholesterol and Triglyceride Levels (n=1135 Patients)[*]

	Uric Acid Concentrations, mg/dL	
	R	*P*
BMI, kg/m^2	0.203	<.001
WHR	0.242	<.001
DBP, mmHg	0.08	<.006
Cholesterol, mg/dL†	0.15	<.001
Triglycerides, mg/dL†	0.24	<.001

[*]*R* indicates Pearson's correlation coefficient; BMI, body mass index; WHR, waist-to-hip ratio; DBP, diastolic blood pressure.
†Values obtained by biochemical analysis of circulating blood.

TABLE 5
Uric Acid Concentrations in Plasma in Each of the 4 Subgroups Established According to AHI Obtained by Conventional Polysomnography or REI Obtained by Cardiorespiratory Polygraphy[*]

AHI-REI	Number of Patients	Uric Acid Concentrations, mg/dL
<5	281	6.03 (1.6)
≥5 and <10	151	6.05 (1.52)
≥10 and <30	355	6.23 (1.54)
≥30	348	6.73 (1.51)†

[*]Uric acid values are expressed as means (SD). AHI indicates apnea-hypopnea index; REI, respiratory event index.
†*P*<.001.

of uric acid in plasma than those with mild to moderate SAHS. However, this difference disappears when the influence of such confounding factors as obesity and cholesterol and triglyceride levels was considered.

In cases of chronic hypoxia, as in COPD, there is an increase in adenosine triphosphate degradation, with a resulting rise in uric acid levels that may be reflected in the higher ratio of uric acid to creatinine in urine described in such cases.[5] A correlation has also been described between uric acid levels and other markers of hypoxia for patients with heart failure.[10,11] It is therefore worth considering whether uric acid might act as a biological marker of deficient cellular oxygenation, such as occurs in patients who experience the repeated desaturations during sleep that characterize SAHS. Several studies have been carried out in recent years on the biochemical alterations and the behavior of some biological markers in sleep-disordered breathing. For example, a decrease in orexin levels[12] and an increase in neuropeptide Y levels (independent of obesity and reversible with continuous positive airway pressure)[13] in SAHS have been described. Furthermore, 2 very recent studies found that hypoxia during sleep can influence circulating leptin,[14] although this hormone seems to be associated more with obesity than with SAHS per se.[13] This improved understanding of the biochemical profile of SAHS has not as yet had practical repercussions, but it would be desirable if the analysis of concentrations of such substances could serve in algorithms to predict the risk of developing sleep-disordered breathing based on the presence of certain biological markers.

Other authors have studied the relation between uric acid and SAHS by evaluating, in small groups of patients, the modifications produced in urinary uric acid
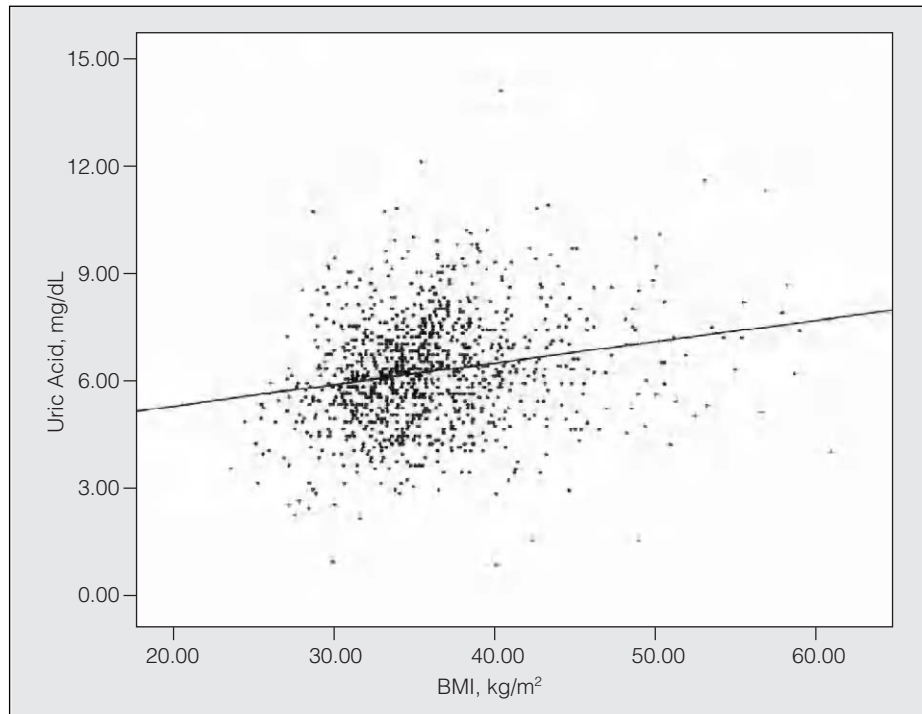
Figure 4. Correlation between uric acid concentrations and body mass index (BMI).
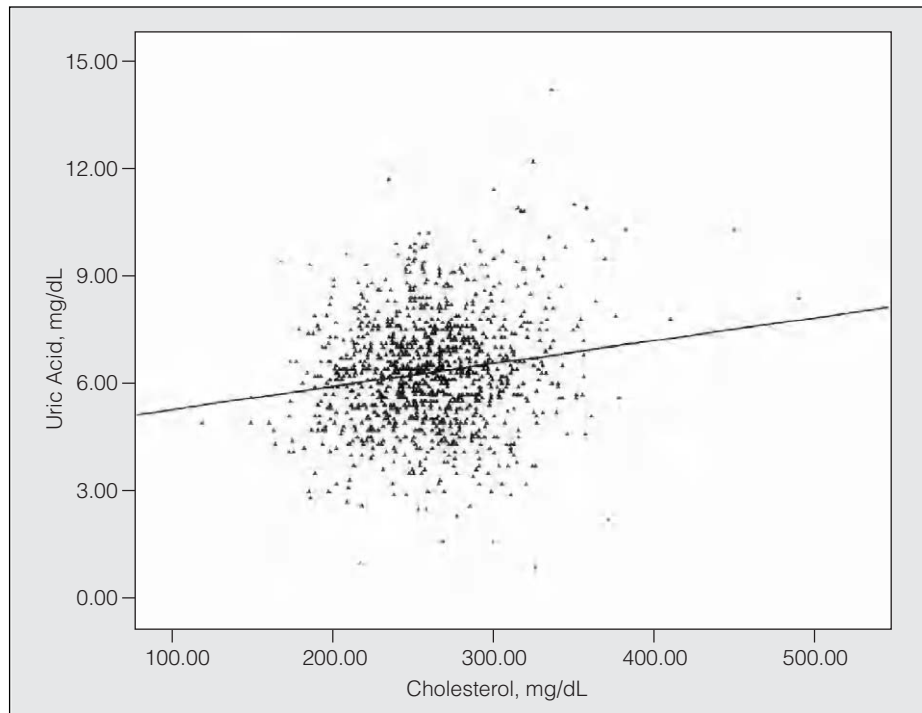

Figure 5. Correlation between uric acid concentrations and cholesterol levels obtained by biochemical analysis of circulating blood.

excretion,[6,7] as well as the changes in the ratio of uric acid to creatinine[5,8] over the course of a night. The advantage of such studies is that the possible influence of confounding factors on uric acid levels is nil, as the changes analyzed are those that occur in each subject. Our study differs from previous ones in that we enrolled a larger population of patients in order to evaluate the possibility that uric acid levels might serve as a biological marker to aid in the diagnosis of SAHS. We therefore had to take into account the influence of other factors that affect uric acid levels, as patients with SAHS generally present significant comorbidity, largely due to their concomitant obesity. Another difference is that ours was a cross-sectional determination of uric acid
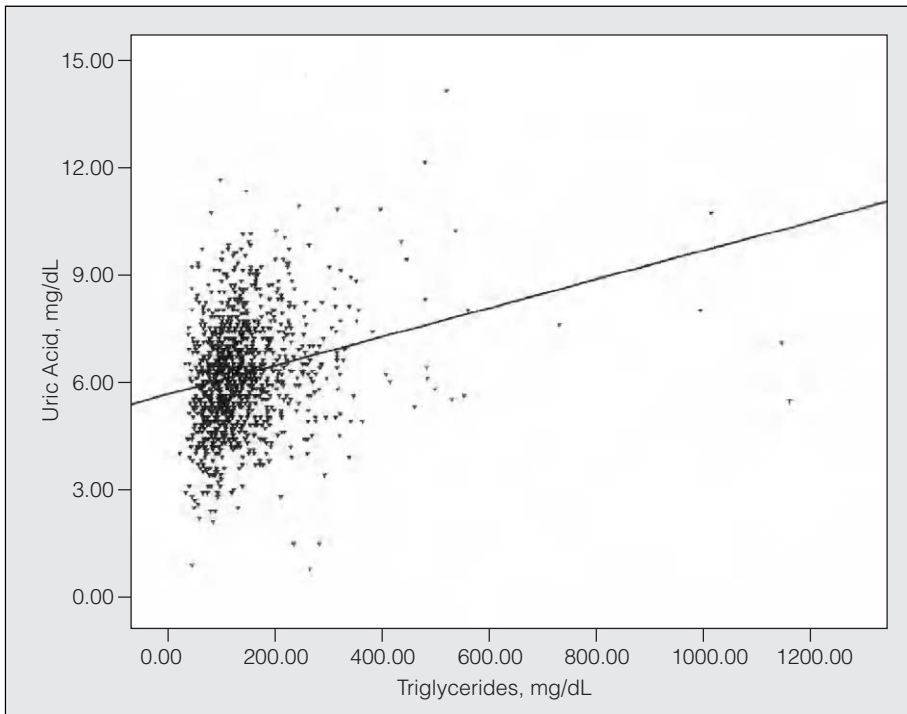
Figure 6. Correlation between uric acid concentrations and triglyceride levels obtained by biochemical analysis of circulating blood.

concentrations in plasma, and this may be methodologically simpler than the calculation of changes in the ratio of the urinary excretion of uric acid to that of creatinine over the course of a night. Furthermore, while uric acid concentrations in both blood and in urine are subject to some degree of variability, the excretion of urate into urine depends directly on glomerular filtration and the level of kidney function.

With regard to the role of hypoxia as a cause of hyperuricemia, we found a significant correlation between uric acid levels and oximetric parameters (desaturation index and CT90), as shown in Table 3. Similarly, lower daytime oximetric values corresponded to higher uric acid levels. While significant, these correlations are statistically weak. This most probably indicates that there are factors other than SAHS involved in these correlations.

As can be seen in Table 5, mean uric acid concentrations rose as the number of respiratory events increased and the effect is more pronounced for the highest AHI or REI values (≥30). However, obesity and a central distribution of body fat also increased significantly with the number of respiratory events.[15] In the univariate ANOVA, the difference in uric acid levels between the group of patients with AHI or REI less than 30 and the group with AHI or REI 30 or more was not apparent when BMI, which probably acted as a confounding factor, was introduced. It is therefore likely that the elevated uric acid levels found in the more severe cases of SAHS were due more to obesity than to SAHS itself. The correlation shown in Table 2 between uric acid levels and central obesity (BMI, WHR) is consistent with this conclusion. The Framingham Heart Study[16] ruled out the possibility that

hyperuricemia might play a causative role in cardiovascular mortality and suggested that uric acid levels are merely a reflection of a patient's cardiovascular risk, which is due to the existence of other more important factors.

The relation between obesity, SAHS, and uric acid levels is complex. On the one hand, the role of obesity as a risk factor for SAHS has been described primarily in cases where there is a pattern of central body fat distribution[17]; on the other hand, obesity can also produce nighttime desaturations that may raise uric acid levels without obstructive events of the upper airway.[18] The univariate analysis revealed other confounding factors in addition to BMI, such as cholesterol and triglyceride levels, that might affect uric acid levels. These parameters are precisely those that are grouped under what is known as the metabolic syndrome, which reflects the association between central obesity and hyperglycemia, hypertension, lipid metabolic disorder, and hyperuricemia.[1] Several studies have found this association between obesity, hyperuricemia, and metabolic alterations and have described higher BMI and cholesterol and triglyceride levels in patients with hyperuricemia.[19-21]

Several studies have described a clear difference in sex distribution among patients evaluated for suspected SAHS.[22,23] In ours, 77.9% of the 1135 patients were men and 22.1% were women. Sex is a factor that must be considered in the study of uric acid in blood. While 7 mg/dL is the limit of solubility of urate in plasma, the upper limit for defining hyperuricemia is usually set at 7 mg/dL for men and at 6 mg/dL for women[19] because estrogens induce an increase in the clearance of urate by the kidneys. Men maintain relatively stable levels of

uric acid throughout life. Their levels are higher than those of women and, while women experience an increase in uric acid levels after menopause, the prevalence of hyperuricemia in higher in men. In our series, as expected, uric acid levels were higher in men, but we found no differences between the sexes in the percentage of patients with hyperuricemia, probably because our patients were suspected of having SAHS and their uric acid levels were higher than those described in series drawn from the general population. Thus, the percentage of patients with hyperuricemia in our series (36%) was higher than that obtained in another study carried out in Spain with 1564 healthy working men, in which a correlation was found between the number of subjects with hyperuricemia and the prevalence of cardiovascular risk factors.[20] Similar results were described in another more recent study, also carried out in the general population, in which uric acid levels increased in proportion to metabolic risk factors.[25]

Certain aspects of the design of our study must be considered. Firstly, while conventional overnight polysomnography is still considered the gold standard for the diagnosis of SAHS, the high prevalence of sleep-disordered breathing[26] and the inadequacy of diagnostic resources available in Spain[27] have led to an ever-increasing emphasis on simpler diagnostic methods in clinical practice. This is the case of cardiorespiratory polygraphy,[28,29] endorsed by the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR)[30] and the American Sleep Disorders Association.[31] In accordance with the important role played today by cardiorespiratory polygraphy in the diagnosis of SAHS, of the 1135 sleep studies carried out in our study, 72.1% used this technique, and only 27.8% used conventional polysomnography. Secondly, the fact that the results obtained by 2 different diagnostic methods were analyzed together might represent a possible limitation, especially for results based on correlation tests. However, while a given AHI value obtained by polysomnography is not exactly equivalent to the REI obtained by cardiorespiratory polygraphy, both procedures make it possible to establish a dichotomous division of the sample according to a particular AHI or REI value. Furthermore, since the increase in uric acid levels was associated primarily with repeated desaturations throughout the night, any hypopneas without associated desaturation that might have gone undetected in the polygraphy studies for lack of neurophysiological criteria (arousals) by which to recognize them are probably not very many. Thirdly, when stratifying the 1135 patients into 4 groups according to AHI or REI values, we also considered low values (0-5 and 5-10) because, although they correspond to a negative diagnosis of SAHS, such mild apnea has been shown to be important in other circumstances. Thus, the results of the Wisconsin Sleep Cohort Study[4] and of the Sleep Heart Health Study[3] confirmed that even very mild cases of sleep-disturbed breathing are associated with the subsequent development of hypertension. This causal relation is independent of any known confounding factors. The final aspect to be considered is that thermistors were used to measure nasal airflow. While widely used in clinical practice, thermistors have the disadvantage of providing only a qualitative estimation of airflow and are therefore unable to detect some hypopneas as well as slight increases in respiratory effort that can lead to arousals. However, this limitation may not be very important in this case, as hypopneas that do not cause desaturations probably do not significantly affect uric acid levels, as we have mentioned above.

In conclusion, in our series we found a positive correlation between uric acid levels and the number of obstructive respiratory events and desaturations during sleep. However, these higher uric acid levels appear to be the result of several factors, particularly obesity, and it seems therefore unlikely that uric acid levels can act as a biological marker in the diagnosis of sleep-disordered breathing.

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