Concise report

Gout, hyperuricaemia, sleep apnoea–hypopnoea syndrome and vascular risk

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Abstract

Objective. This study aimed to evaluate cardiovascular (CV) and atherothrombosis risk factors in patients with gout and hyperuricaemia with suspected sleep apnoea–hypopnoea syndrome (SAHS) compared with a control group of subjects with knee OA and SAHS.

Methods. Clinical information on CV risk factors and atherothrombosis was collected in a rheumatology department in patients with gout and hyperuricaemia and suspicion of SAHS. Confirmation polysomnography that registered apnoea–hypopnoea index (AHI) and oxygen saturation during sleep (SaO₂) was performed. The control group consisted of patients with OA and polysomnographically confirmed SAHS.

Results. In the gout patient group (54 patients, 48 men), CV risk factors were found in 77.8% and evidence of atherothrombosis in 46.3%. In the OA group (36 patients, 27 men), CV risk factors were found in 66.7% and evidence of atherothrombosis in 0%. SAHS diagnosis was confirmed by polysomnography in 88.9% of patients. AHI showed mild, moderate and severe SAHS in 12%, 26% and 66% of the gout patients and 45%, 24% and 30% of the OA patients, respectively. SaO₂ was 90.18% in the gout group and 91.26% in the OA group.

Conclusion. Patients with gout and hyperuricaemia and suspicion of SAHS had polysomnographically confirmed SAHS in 88.9% of cases. These patients had more severe forms of SAHS and a greater prevalence of documented atherothrombotic disease compared with a control group with OA.

Key words: gout, sleep apnoea–hypopnoea syndrome, uric acid, cardiovascular risk, atherothrombosis.

Introduction

Hyperuricaemia has been associated with cardiovascular (CV) diseases and risk factors [1]. Gout prevalence has increased in recent decades [2]. On the other hand, the prevalence of sleep apnoea–hypopnoea syndrome (SAHS) is approximately 3% [3] and is also associated with different CV risk factors [4]. Its association with metabolic syndrome is especially seen with the severity of the SAHS [5]. Uric acid has been related to different hypoxia markers [6]. Few studies have been carried out on the joint relationship of gout and SAHS in the same individual as well as its association with CV risk. The current study has been developed to determine these associations.

Methods

Patients between 35 and 75 years of age were recruited from the outpatient clinic of a rheumatology department between January 2009 and January 2011. The study was approved by the ethics committee of the University Hospital of Fuenlabrada and prior to data collection all patients read the information sheet of the study and signed the consent document. All the patients who fulfilled the following three enrolment criteria were selected: (i) having an established diagnosis of monoarticular or polyarticular gout, (ii) having hyperuricaemia and (iii) presenting symptoms suggestive of SAHS. The gout diagnosis was established based on the finding of monosodium urate crystals in SF in at least two different measurements...
according to the diagnostic criteria of the American Rheumatism Association [7], as well as by those of the Sociedad Española de Reumatología [7], and based on the criterion having the greatest evidence of diagnostic recommendation of gout [8]. The symptoms questioned in order to consider diagnostic suspicion of SAHS were snoring, daytime sleepiness and morning headache, according to the National Consensus Document on sleep apnoea–hypopnoea [9]. Information was obtained on the clinical history and complete physical examination in all the patients regarding uricaemia levels and the following CV risk factors: arterial hypertension (AHT), obesity, dyslipidaemia, diabetes mellitus (DM) and smoking habit. The presence or absence of atherothrombotic and heart disease was studied. Established atherothrombotic disease was defined as when the patient had suffered from, or evidence was found of, ischaemic heart disease, cerebrovascular accident and atheromatosis [10]. Heart disease was defined as signs of left ventricular hypertrophy, heart failure or a medical history of cardiac arrhythmias.

Hyperuricaemia was defined as uricaemia levels >7.0 mg/dl. AHT was defined as blood pressure levels ≥140 mmHg systolic and/or 90 mmHg diastolic if measured in the physician’s office or levels of 130–135 mmHg systolic and/or 85 mmHg systolic for ambulatory monitoring or home self-measurement by the patients, or when the patients were receiving anti-hypertensive treatment, according to the criteria of the European Society of Hypertension/European Society of Cardiology [11]. If the patient had DM and/or chronic renal disease, AHT levels >135/85 mmHg were considered. Obesity was considered as a BMI ≥30 kg/m², according to the Sociedad Española para el Estudio de la Obesidad (Spanish Society for the Study of Obesity) [12]. Dyslipidaemia was defined as low-density lipoprotein cholesterol levels ≥130 mg/dl in subjects with more than two CV risk factors or with levels >100 mg/dl in subjects with atherothrombosis or DM [13]. DM was defined as having two measurements on different days of fasting glucose ≥126 mg/dl and/or casual glucose drawn at any time of the day ≥200 mg/dl and/or receiving glucose-lowering drugs and/or insulin treatment, according to the criteria of the American Diabetes Association [14]. A patient was considered to be a smoker if, at the time of the clinical questioning, the patient reported tobacco consumption (one or more cigarettes/week). Established atherothrombotic disease was considered to exist if the patient presented ischaemic heart disease and/or cerebrovascular accident or transient ischaemic attack and/or peripheral arterial disease and/or arterial vascular alteration in imaging tests [12]. Left ventricular hypertrophy was determined by ECG criteria.

Sleep studies

Questionnaires used for patients with high suspicion of SAHS were administered to all the patients. A confirmation diagnosis was made using a polysomnography. The polysomnography registered SaO₂ by a pulsioxymeter and the apnoea–hypopnoea index (AHI). The AHI was defined as the sum of the number of apnoeas plus hypopnoeas divided by hours of sleep. SAHS was defined as an AHI > 15 or as AHI > 5 accompanied by symptoms [15]. According to the AHI, mild SAHS was defined as an AHI between 5 and 9 (with symptoms), moderate between 10 and 30 and severe as AHI ≥ 30.

Control group

A control group was established with patients who had knee OA and SAHS diagnosed by polysomnography, attended in a rheumatology department. The same clinical variables, CV risk factors and involvement or not of atherothrombotic and cardiac conditions were collected in all the patients.

Results

A total of 54 patients (48 men and 6 women) with gout, mean age (upper–lower limits) of 52.95 (35–75) years, were included. Of these, 34 patients were diagnosed with polyarticular gout (34 men) and 20 with monoarticular gout (14 men). The mean baseline level of uric acid was 8.4 (7.6–11.4) mg/dl. In the study group (gout), CV risk factors were found in 77.8% of the patients. The control group was made up of 36 patients with OA (27 men and 9 women), with a mean age (upper–lower limits) of 54.82 (41–82) years. In the control group (OA), CV risk factors were found in 66.7% of the patients (Table 1). Atherothrombotic disease was present in 46.3% of the gout group patients and 0% of the control group patients. In contrast, heart disease was observed in 27.8% of the control group patients and 5.5% of the gout group patients (Table 2).

Polysomnography confirmed the SAHS diagnosis in 48 patients (88.9%). The mean AHI was 55.96 episodes per hour. Severe SAHS (AHI > 30) was present in 33 patients (66%), moderate SAHS (AHI > 10 and ≤ 30) in 15 patients (26%) and mild SAHS (AHI < 10 in 3 patients and < 5 in 3 patients) in 6 patients (12%). The mean oxygen saturation during sleep in the total sample of the gout group was 90.18% (86–93%). In the control group with OA, severe SAHS was found in 11 patients (30%), moderate in 9 patients (24%) and mild in 16 patients (45%). Oxygen saturation in the control group was 91.84% (89–95%).

<table>
<thead>
<tr>
<th>TABLE 1 CV risk factors in the two groups</th>
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<tbody>
<tr>
<td><strong>Gout group, n (%)</strong></td>
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<tr>
<td>-------------------------------</td>
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<tr>
<td>Without CV risk factors</td>
</tr>
<tr>
<td>With CV risk factors</td>
</tr>
<tr>
<td>1 factor</td>
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<tr>
<td>2 factors</td>
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<tr>
<td>3 factors</td>
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<tr>
<td>4 factors</td>
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<td>5 factors</td>
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Table 2  Vascular involvement (atherothrombotic and cardiac) in the two groups

<table>
<thead>
<tr>
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<th>Gout group, n (%)</th>
<th>Control group, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without atherothrombic and cardiac involvement</td>
<td>26 (48.1)</td>
<td>29 (80.5)</td>
</tr>
<tr>
<td>With atherothrombic involvement</td>
<td>25 (46.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>IHD</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>CVA</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>RAS</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>AA</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>With cardiac involvement</td>
<td>3 (5.5)</td>
<td>10 (27.8)</td>
</tr>
<tr>
<td>LVH</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>CI</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

IHD: ischaemic heart disease; CVA: cerebral vascular accident; RAS: renal artery stenosis; AA: aortic atheromatosis; LVH: left ventricular hypertrophy; CI: cardiac insufficiency.

Discussion

The data from the current study show that 88.9% of patients with monoarticular or polyarticular gout with hyperuricaemia and suspicion of SAHS had polysomnographically confirmed SAHS. Patients with monoarticular or polyarticular gout and suspicion of SAHS compared with a group of patients with knee OA and polysomnographically confirmed SAHS have more severe forms of SAHS and greater prevalence of the documented atherothrombotic disease.

In the series of hyperuricaemic patients with evaluated gout and suspicion of SAHS, two-thirds had severe forms of SAHS compared with the patients with OA in whom only one-third had severe forms. It has been observed that the repeated episodes of upper airway obstruction produced during the night in SAHS conditions some decreases in SpO₂, which would induce an increase in adenosine triphosphate degradation to xanthine, and then a rise in purine concentrations and its end product uric acid [16]. This suggests that hyperuricaemia could be a marker of impaired cellular oxygenation. In an observational study performed in 1135 patients with suspicion of SAHS, it was observed that patients with an AHI > 30 had higher uricemia levels. However, the authors could not rule out certain confounding variables [17]. In the current study, subjects showing a higher number of apnoeas/hypopnoeas are those patients with hyperuricaemia with gout vs those with knee OA. It has not been well established whether uric acid is a good marker of the oxidative stress produced in SAHS [18]. However, treatment with allopurinol improves the endothelial vascular dysfunction produced by the hypoxia [19], which reaffirms the role of uric acid in SAHS.

Hyperuricaemia has been associated with CV disease [1]. Atherothrombosis is the most important cause of mortality in Western countries [17]. The appearance of vascular disease is strongly conditioned by the presence of CV risk factors that when associated with each other, as in the case of hyperglycaemia, obesity, dyslipidaemia and AHT, constitute metabolic syndrome. The importance of the syndrome lies in that it identifies patients who have an elevated risk of developing atherothrombosis and DM. Elevated uric acid has been associated with AHT, metabolic syndrome and coronary vascular disease. In the current work, almost half of the patients with gout and SAHS presented with atherothrombosis, while no patient in the OA group with established vascular disease was found. However, the prevalence of CV risk factors is elevated in both groups (77.8% and 66.7%, respectively), and although the current study did not evaluate the grade of pharmacological or dietary control of the CV risk factors, it can be considered that hyperuricaemia could represent a factor associated with more severe progression of vascular disease [10, 18].

The data of the current study show that patients with gout and hyperuricaemia have more severe forms of SAHS and already established vascular lesions (atherothrombosis) than subjects with OA and SAHS. Thus, when the apnoea episodes are very frequent, the kidney cannot eliminate the uric acid production [19, 20]. The information highlighted by this study shows the importance of early detection of the presence of SAHS in patients with gout and suspicion of SAHS.

Conclusions

The data of the current study show that patients with gout with hyperuricaemia and suspicion of SAHS show polysomnographically confirmed SAHS in 88.9% of cases. Patients with monoarticular or polyarticular gout and suspicion of SAHS compared with a group of patients with knee OA and polysomnographically confirmed SAHS have more severe forms of SAHS. Patients with monoarticular or polyarticular gout and suspicion of SAHS compared with a group of patients with knee OA and polysomnographically confirmed SAHS show a higher prevalence of documented atherothrombotic disease.

Rheumatology key messages

- The apnoea–hypopnoea index is more severe in gout patients than in controls.
- An excess of vascular risk was found in gout patients compared with controls.
- The relationship between SAHS and gout could be an important public health problem.

Disclosure statement: The authors have declared no conflicts of interest.

References