Is the presence of sleep apnoea–hypopnoea syndrome a precursor for gout?

The importance of a relationship between gout and SAHS

This editorial refers to Gout, hyperuricaemia, sleep apnoea–hypopnoea syndrome and vascular risk, by Miguel Cantalejo Moreira et al. on pages 1619–22.

Sleep apnoea–hypopnoea syndrome (SAHS) is characterized by periodic apnoea that is associated with cyclical changes in arterial oxygen saturation (SaO2). In SAHS, Hasday and Grum [1] were the first to measure the overnight change of urinary uric acid secretion and report that it could be a good index of tissue hypoxia. However, the validation of this index has not been confirmed by subsequent studies [2], as this index remained normal in some patients with SAHS who had severe nocturnal arterial oxygen desaturation and because the indexes of overnight urinary uric acid excretion and nocturnal arterial oxygen desaturation did not correlate in those patients. Adenosine in plasma, as an intermediary of such an adenosine triphosphate (ATP) degradation pathway, may be a more sensitive marker of tissue hypoxia than uric acid in urine, although the measurement of plasma adenosine is technically not easy because of its short half-life in plasma [3, 4].

When oxygen supplies are inadequate to meet the oxygen demands of the cells, formation of ATP from adenosine diphosphate is impaired and a net degradation of ATP to adenosine diphosphate (ADP) and adenosine monophosphate (AMP) occurs. This process leads to the release of purine intermediates (adenosine, inosine, hypoxanthine and xanthine) and the purine catabolic end product uric acid. Saito et al. [5] have demonstrated in their study that the index of change in uric acid/creatinine ratio (ΔUA/Cr) did not correspond to the severity of apnoea index (AI) or arterial oxygen desaturation, but that it was significantly linked to the plasma level of adenosine in patients with SAHS. They found that both variables decreased to the range of the ΔUA/Cr normal group with successful treatment of sleep apnoea by nasal continuous positive airway pressure (CPAP). These data indicate that both indexes of the ΔUA/Cr and plasma adenosine during sleep reflect the same purine catabolic pathway associated with tissue hypoxia in these patients.

Sleep-disordered breathing as well as high serum uric acid levels are independent risk factors for cardiovascular disease. However, studies evaluating the relationship between sleep-disordered breathing and hyperuricaemia are limited. Wiener and Shankar [6] examined the 2005–08 National Health and Nutrition Examination survey’s sleep variables and high serum uric acid in 6491 participants aged ≥20 years. They found that snoring more than 5 nights per week, daytime sleepiness and an additive composite score of sleep variables were associated with high serum uric acid in the age- and sex-adjusted model and in a multivariable model adjusting for demographic and lifestyle or behavioural risk factors. This association was attenuated with the addition of variables related to clinical outcomes such as depression, diabetes, hypertension and high levels of cholesterol. The results indicate a positive relationship between sleep variables, including the presence of snoring, snorting and daytime sleepiness, and high levels of serum uric acid.

The strongest evidence for gout resulting from concomitant sleep apnoea is physiological, and it is supported by epidemiological evidence and comorbidities known to be common to both gout and SAHS. The most easily recognized common comorbidity is excess body weight. The relative risk of incident gout in men shows a strong monotonic increase with body weight [7]. Other studies show similar results for SAHS, with each 1% increase or decrease in body weight associated with a 3% increase or decrease in apnoea–hypopnoea index, respectively [8, 9].

In this issue of Rheumatology, Moreira et al. [10] reported that 88.9% of patients with gout and suspicion of SAHS had polysomnography-confirmed SAHS. They have more severe forms of SAHS and greater prevalence of the documented atherothrombotic complications compared with a control group of patients with knee OA and polysomnography-confirmed SAHS. In the group of hyperuricaemic patients with gout, two-thirds had severe forms of SAHS compared with the patients with OA in whom only one-third had severe forms. The authors assumed that the repeated episodes of upper airway obstruction during the night in SAHS conditions decrease saturation of peripheral oxygen (SpO2), which would induce an increase in ATP degradation to xanthine, leading to an increase in uric acid. This would suggest that hyperuricaemia could be a marker of impaired cellular oxygenation. Elevated uric acid has been associated with arterial hypertension, multiple sclerosis and coronary vascular disease.

In this study, almost half the patients with gout and SAHS presented with atherothrombosis, although no patient in the OA group had established vascular disease.
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–dietary control of the CV risk factors, we assumed that hyperuricaemia represents a factor associated with more severe progression of the vascular disease. The data of the current study show that patients with gout and hyperuricaemia have more severe forms of SAHS and atherothrombosis than subjects with OA and SAHS. Moreover, when the apnoea episodes are frequent, the kidney cannot eliminate the uric acid produced. This study also shows the importance of early detection in the presence of SAHS in patients with gout and suspicion of SAHS. The degree of gout amelioration as a function of SAHS treatment needs to be determined, as well as the frequency of gout flares, which will allow reliable diagnosis of concomitant SAHS. Gout flare might be an immediate result of SAHS and therefore gout can be considered to be an early warning of concomitant SAHS. Routine screening of gouty patients for SAHS may be an important step towards reducing the number of patients with gout at risk of developing serious comorbidities of SAHS.

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Lyubomir Marinchev

1Rheumatology Department, MHAT SOFIAMED, Sofia, Bulgaria.

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Correspondence to: Lyubomir Marinchev, Department of Rheumatology, MHAT SOFIAMED, 16 G.M. Dimitrov Blvd, 1797 Sofia, Bulgaria. E-mail: lubommar@gmail.com

References