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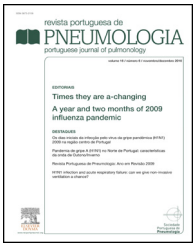

ORIGINAL ARTICLE

Urinary uric acid excretion as an indicator of severe hypoxia and mortality in patients with obstructive sleep apnea and chronic obstructive pulmonary disease

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KEYWORDS
Uric acid;
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Abstract
Objective: Uric acid (UA) is the end product of adenosine triphosphate degradation, and could increase due to hypoxia. We investigated the association of UA metabolites with nocturnal hypoxemia, apnea-hypopnea index (AHI), noninvasive mechanical ventilation (NIMV) usage and five-year mortality.
Materials/subjects and methods: We obtained urinary specimen before and after the night polysomnography in order to measure UA excretion and overnight change in urinary UA/creatinine ratio (ΔUA/Cr) in 75 subjects (14 controls, 15 chronic obstructive pulmonary disease (COPD) without nocturnal hypoxemia (NH), 15 COPD with NH, 16 obstructive sleep apnea syndrome (OSAS) without NH, 15 OSAS with NH). Percentage of time spent below SaO_2 of 90% (T90%) for >10% of sleep time was considered as nocturnal hypoxemia. Patients were contacted after 5 years with a questionnaire including information on the use of NIMV treatment (*n*: 58) and urinary specimen analysis (*n*: 35).
Results: T90% was found to be significantly correlated with UA excretion (coefficient: 0.005, 95%CI: 0.003–0.007) and ΔUA/Cr (coefficient: 0.8, 95%CI: 0.3–1.2) after adjustments for age, gender, body mass index and apnea-hypopnea index. Median and IQR (interquartile range) of baseline UA excretion were 0.79 (0.51–0.89) and 0.41 (0.31–0.55) in 10 deceased and 58 surviving patients, respectively ($p = 0.001$). UA excretion median and IQR of baseline and 5 years of NIMV treatment were 0.41 (0.36–0.57) and 0.29 (0.23–0.37), respectively ($p = 0.01$).
Conclusion: UA excretion, as a marker of tissue hypoxia, may be useful in the management of OSA and COPD patients.

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Introduction

Obstructive sleep apnea is characterized by recurrent episodes of partial (hypoapnea) or complete (apnea), obstruction of the upper airway during sleep, and is associated with episodes of arousal and/or oxyhemoglobin desaturation.[1] Uric acid (UA), which is the end product of adenosine triphosphate (ATP) degradation, increases in body fluids in the case of increased anaerobic metabolism induced by cellular hypoxia.[2–5] Increased levels of ATP degradation products in body fluids were reported in clinical conditions with tissue hypoxia, such as infant respiratory distress syndrome,[6,7] exercise[8–12] and acute respiratory failure.[13,14] Hasday and Grum reported that the overnight change in urinary UA/creatinine ratio (ΔUA/Cr) could reflect tissue hypoxia in obstructive sleep apnea syndrome (OSAS).[15]

Hypoxemia occurs during sleep in the case of OSAS, and during both sleep and daytime in the case of chronic obstructive pulmonary disease (COPD). Since sleep-associated hypoxemia has been implicated in the pathophysiology of several abnormalities of COPD and OSA syndrome, urinary UA, as a marker of tissue hypoxia, may be useful in defining the higher risk groups in relation to these two diseases.[16,17]

In this study, the correlation of urinary UA and ΔUA/Cr with nocturnal hypoxemia and apnea-hypopnea index (AHI) was investigated in a follow-up study including patients with COPD and patients with OSA syndrome. Additionally, these patients were contacted 5 years later and the correlation between first night UA measurements and mortality and the correlation between the change in UA levels during five years and use of noninvasive ventilation (NIV) treatment were investigated.

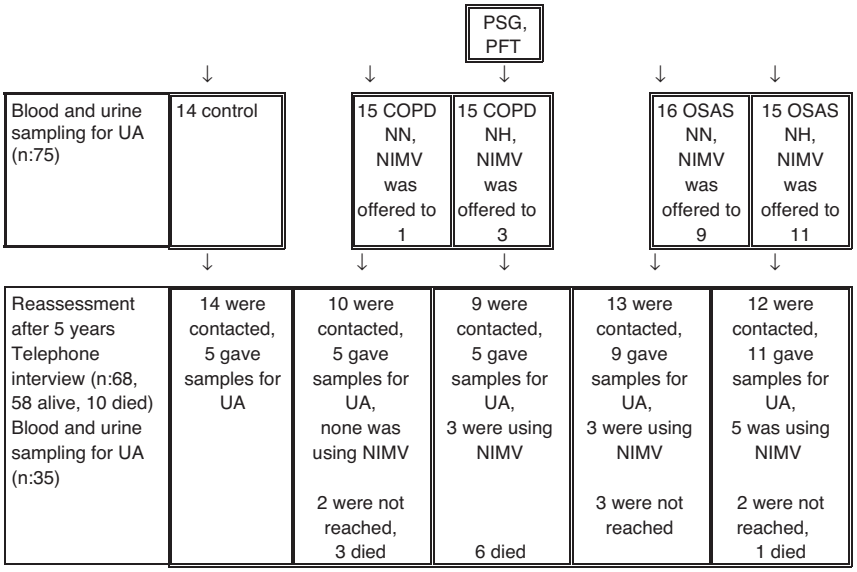
Material and methods

Patient selection

The study enrolled 75 patients, including 31 cases with OSA syndrome, 30 with COPD, and a control group including 14 subjects who were eligible and gave informed consent to participate in this prospective follow-up study. The diagnostic criteria for OSA and CPAP (continuous positive airway pressure) treatment were determined according to the standard criteria published by the American Academy of Sleep Medicine (AASM).[18] The criteria are defined below. OSA patients displayed at least two of the following three symptoms: snoring, witnessed apnea, and excessive daytime sleepiness. Their AHI score was 5 or higher in the overnight polysomnography (PSG).[18] CPAP treatment was given if AHI > 30 or AHI between 5 and 30 with a cardiovascular co-morbidity. OSAS patients did not have COPD defined by spirometry.

Patients were routinely called after 3 months and 1 year periods to our outpatients clinic. For reassessment after 5 years patients were contacted by telephone interview ($n = 68$, 58 alive, 10 died). 35 of them agreed to give uric acid samples (blood and urine) (Fig. 1). The compliance of CPAP use was evaluated after follow-up.

The recruitment criteria for COPD included a history of 10 or more pack-years of smoking or a history of biomass exposure, a forced expiratory volume in one second (FEV 1) of less than 80% of the predicted value after bronchodilator use and a ratio of FEV 1 to forced vital capacity (FVC) of 0.7 or less after bronchodilator use.[19] The condition of the patients was graded according to the stages of disease defined by



PSG: polysomnography, PFT: Pulmonary function tests, UA: Uric acid, NIMV: Non invasive mechanical ventilation, OSAS NN: Obstructive sleep apnea syndrome nocturnal normoxemic, OSAS-NH: Obstructive sleep apnea syndrome nocturnal hypoxemic, COPD-NN: Chronic obstructive pulmonary disease nocturnal normoxemic, COPD-NH: Chronic obstructive pulmonary disease nocturnal hypoxemic.

Figure 1 Flowchart of the study procedures. PSG: polysomnography, PFT: pulmonary function tests, UA: uric acid, NIMV: non invasive mechanical ventilation, OSAS NN: obstructive sleep apnea syndrome nocturnal normoxemic, OSAS-NH: obstructive sleep apnea syndrome nocturnal hypoxemic, COPD-NN: chronic obstructive pulmonary disease nocturnal normoxemic, COPD-NH: chronic obstructive pulmonary disease nocturnal hypoxemic.