Serum and pulmonary uric acid in pulmonary arterial hypertension

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Shareable abstract (@ERSpublications)
Uric acid (UA) level is associated with poor prognosis in PAH. Local UA production is increased in the remodelled pulmonary vasculature, and inhibition of UA incorporation in PA-SMCs reduces their proliferation and mildly reduces experimental PH. https://bit.ly/2Ll5qXM

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Abstract

Previous studies have suggested an association between uric acid (UA) and the severity of pulmonary arterial hypertension (PAH), but it is unknown whether UA contributes to disease pathogenesis.

The aim of this study was to determine the prognostic value of circulating UA in the era of current management of PAH and to investigate the role of UA in pulmonary vascular remodelling.

Serum UA levels were determined in idiopathic, heritable or anorexigen PAH at baseline and first re-evaluation in the French Pulmonary Hypertension Network. We studied protein levels of xanthine oxidase (XO) and the voltage-driven urate transporter 1 (URATv1) in lungs of control and PAH patients and of monocrotaline (MCT) and Sugen/hypoxia (SuHx) rats. Functional studies were performed using human pulmonary artery smooth muscle cells (PA-SMCs) and two animal models of pulmonary hypertension (PH).

High serum UA levels at first follow-up, but not at baseline, were associated with a poor prognosis. Both the generating enzyme XO and URATv1 were upregulated in the wall of remodelled pulmonary arteries in idiopathic PAH patients and MCT and SuHx rats. High UA concentrations promoted a mild increase in cell growth in idiopathic PAH PA-SMCs, but not in control PA-SMCs. Consistent with these observations, oxonic acid-induced hyperuricaemia did not aggravate MCT-induced PH in rats. Finally, chronic treatment of MCT and SuHx rats with benzbromarone mildly attenuated pulmonary vascular remodelling.

UA levels in idiopathic PAH patients were associated with an impaired clinical and haemodynamic profile and might be used as a non-invasive indicator of clinical prognosis during follow-up. Our findings also indicate that UA metabolism is disturbed in remodelled pulmonary vascular walls in both experimental and human PAH.