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LETTERS

Increased xanthine oxidase activity in idiopathic pulmonary arterial hypertension

To the Editors:

Oxidative stress may play a role in the pathogenesis of idiopathic pulmonary arterial hypertension (IPAH) [1–4]. A major contributor to oxidative stress is the endothelium-bound enzyme xanthine oxidase (XO), which is involved in the generation of superoxide anions and peroxynitrite [5]. These reactive oxygen species have been implicated in endothelial dysfunction and vascular damage [5]. *In vivo*, XO is bound to the surface of endothelial cells by glycosaminoglycans and can be released into plasma by heparin bolus injection [6]. XO activity has not been assessed in patients with IPAH, but increased activity of this enzyme is suggested by hyperuricaemia, a common finding in patients with IPAH [7].

In the present study, activity of endothelium-releasable XO was measured in the plasma of 31 treatment-naive patients with IPAH (nine male, 22 female, mean pulmonary arterial pressure 51±13 mmHg) and six healthy controls. In the IPAH patients, the samples were obtained during right heart catheterisation to compare XO activity and haemodynamics. XO activity was determined by using electron spin resonance spectroscopy (ESR), as described elsewhere [6]. XO activity was measured at baseline and 1, 3, 5, 7, 10 and 20 min after intravenous administration of heparin (5,000 IU), and depicted as area under the curve with the values shown as arbitrary units (AU). The present study was approved by the local institutional review board and all patients gave written informed consent.

It was found that XO activity was increased in IPAH patients compared with healthy controls (5,201±2,836 AU *versus* 2,424±1,419 AU, p=0.026, Mann–Whitney U-test). There was no significant correlation between XO activity and haemodynamic parameters, such as right atrial pressure, mean pulmonary arterial pressure, cardiac output, pulmonary vascular resistance, or mixed-venous oxygen saturation, respectively. There was also no correlation between XO activity and plasma uric acid levels. In three patients, however, XO activity was measured again 3 months after introduction of treatment with bosentan, an endothelin receptor antagonist, and was found to be markedly lower than prior to therapy (3,052±747 AU *versus* 8,438±5,695 AU).

These preliminary data suggest that XO activity is elevated in patients with IPAH, which may be a contributing factor to endothelial dysfunction and vascular damage in this disease. Further investigations need to determine whether targeted treatment of pulmonary arterial hypertension with endothelin receptor antagonists [8], or other compounds, such as phospodiesterase-5 inhibitors [9] or prostanoids [10], may improve XO activity and endothelial function in these patients.

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