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Oxidative stress and hypoxia-induced pulmonary hypertension

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Keywords

Hypoxia, oxidative stress, pulmonary circulation

Context

Chronic hypoxemia can cause a sustained increase in pulmonary vascular resistance and smooth muscle cell proliferation, leading to pulmonary hypertension (PHT). Hypoxia generates oxidative stress, which may be implicated in pulmonary vascular remodelling. In this study, the relationship between oxidative stress and cardiopulmonary changes was assessed by treating rats with the antioxidant *N*-acetylcysteine (NAC) during 3 weeks of hypoxic exposure.

Significant findings

Rats exposed to chronic hypoxia showed marked increases in pulmonary arterial pressure and right ventricular hypertrophy in comparison with age-matched controls. Treatment with NAC significantly attenuated both the elevation in pulmonary arterial pressure and the right ventricular hypertrophy. Histological assessment of hypoxic rat lung tissue revealed an increase in pulmonary arterial wall thickness that was significantly attenuated by NAC treatment. In the hypoxic rats, levels of phosphatidylcholine hydroperoxide (PCOOH, a marker of oxidative stress) were consistently elevated for the first week of exposure, after which they declined to control levels. Chronic antioxidant treatment reversed this hypoxia-induced elevation of lung PCOOH levels. Lung xanthine oxidase (an important contributor to hypoxia-induced oxidative stress *in vivo*) activity was increased by hypoxia, most significantly during the first 3 days of exposure. Chronic allopurinol treatment decreased PHT, right ventricular hypertrophy, pulmonary vascular remodelling and PCOOH levels.

Comments

This study provides evidence that oxidative stress plays a role in the development of hypoxia-induced PHT and pulmonary vascular remodelling. Although the authors do not address the possible intracellular sources of hypoxia-related oxidative stress or xanthine oxidase activation, the results suggest that pulmonary arterial endothelial cell xanthine oxidase activation during the initial "induction" phase of chronic hypoxia contributes to the development of PHT.

Methods

Morphometric analysis, chemiluminescence-high performance liquid chromotography, fluorometry, chronic hypoxic rat, *in vivo* pressure measurements

Additional information

References

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