BIOMECHANICAL PROPERTIES OF RAT PULMONARY ARTERY IN HYPOXIA-INDUCED PULMONARY HYPERTENSION

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The highly compliant, low resistance pulmonary vasculature is markedly altered with chronic hypoxia. Remodeling involves hypertrophy and hyperplasia of smooth muscle and excessive deposition of connective tissue, with a concomitant rise in pulmonary arterial pressure, i.e., pulmonary hypertension. The hypothesis in this study was that chronic hypoxia alters the contractile properties of smooth muscle in the pulmonary artery, thus contributing to the etiology of pulmonary hypertension. Isometric and isotonic contractility/relaxation experiments were performed using a lever system and excised pulmonary arterial rings from pulmonary hypertensive rats (induced by chronic hypoxia). Hypoxia-induced pulmonary hypertension caused a doubling of the vessel wall thickness with an equivalent and proportionate increase in smooth muscle and connective tissue. Functionally, there was an increase in isometric force but this increase was not proportionate to the increase in smooth muscle. There was a decrease in the optimal resting length and an increase in isotonic shortening ability suggesting vessel lumen narrowing. No difference was detected in the velocity of shortening or isometric relaxation. A decrease in isotonic relaxation was apparent with afterloads relative to optimal resting

tension. These results not only provide functional evidence for the hyperplasia/hypertrophy of pulmonary arterial smooth muscle, but also suggest that a certain population of the newly synthesized smooth muscle may lack contractile function. Velocity of shortening data suggest no change in actomyosin ATPase activity. The lack of distinguishable alterations in overall relaxation suggests no change in phosphatase activity or Ca^{+2}-handling, although a more discriminate analysis of relaxation rate constants showed a slower isotonic relaxation in the hypertensive group suggesting alterations in processes which might prolong relengthening. Increased shortening ability and the slower relaxation when tissue architecture is taken into account suggests that vessel caliber can be affected in such a way as to contribute to the development and/or maintenance of hypoxia-induced pulmonary hypertension. This study provides evidence that, in addition to morphological changes seen in pulmonary hypertension, the tissue mechanics and the biomechanical processes associated with contractility of the pulmonary arterial smooth muscle can additionally play a role in the development and/or maintenance of hypoxia-induced pulmonary hypertension.

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