

ISOFORM-SPECIFIC ALTERATIONS OF ADRENORECEPTORS IN MONOCROTALINE-INDUCED MODEL OF PULMONARY HYPERTENSION

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Pulmonary arterial hypertension is a chronic and progressive disease characterized by vascular proliferation and remodelling of small pulmonary vessels contributing to increased pulmonary vascular resistance and, ultimately, to right ventricular failure and death if untreated. In left ventricular failure, long-term hyperactivity of sympathetic nervous system is associated with downregulation of α and β adrenoceptor (AR) isoforms, disease progression and unfavourable prognosis. However, little is known about alterations of AR isoforms in pulmonary arterial hypertension and in right ventricular failure. Therefore, we determined the relative expression of both α and β AR in pulmonary artery, aorta, right and left ventricle in the monocrotaline (MCT) model of pulmonary hypertension not only in relation to disease progression (1, 2, 4 weeks after MCT application) but also to end-stage disease (animals sacrificed at 4 weeks or after acute deterioration – humane endpoint). We used 12 weeks old male Wistar rats, which were subcutaneously injected with 60 mg/kg MCT. Controls were treated with saline. Relative expression of ARs was determined by RT-qPCR. β 1-AR underwent significant subtype-specific downregulation in the right ventricle, but not in the left ventricle, 4 weeks after MCT application, which correlates with significantly elevated BNP levels and hypertrophy of the right ventricle. In contrast to β 1-AR, the relative expression of β 2-AR remained unchanged. Significant downregulation of β 1 and β 2-AR in the lungs was observed already from the first week after MCT application. More profound effects were seen in rats with end-stage disease. α 1_A and α 1_B receptors were downregulated after 2 and 4 weeks in the pulmonary artery. Experimental data indicates that alternations in expression of ARs may contribute to maladaptive processes, such as pulmonary and ventricular remodelling and disease progression.

Key words

pulmonary arterial hypertension, right heart failure, sympathetic nervous system, adrenoceptors