

Change of Voltage-gated Potassium Channel 1.7 and NADPH Oxidase 4 Expressions in Monocrotaline-induced Pulmonary Arterial Hypertension Rat Model

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Introduction: An abnormality of potassium channel expressions influences the function of vessels, including vascular tone and rates of proliferation. Diverse potassium channels, including voltage-gated potassium (Kv) channels, have been involved in pathological changes of in pulmonary arterial hypertension (PAH). However, the exact therapeutic importance of Kv1.7 is currently not clear. Therefore, we investigated whether Kv1.7 channel expressions change in the lung tissues of monocrotaline (MCT) -induced PAH rat model and this change is caused by the endothelin (ET)-1 and reactive oxygen species (ROS) pathways.

Methods: The rats were separated into two groups: the control (C) group and the monocrotaline (M) group (MCT 60 mg/kg). A hemodynamic study was performed by catheterization into the external jugular vein to estimate right ventricular pressure (RVP) and pathological changes were investigated in the lung tissues. Changes of protein and RNA expression levels were confirmed by western blot and polymerase chain reaction analysis respectively.

Results : MCT caused increased RVP, medial wall thickening of the pulmonary arterioles and increased protein expressions of ET-1, endothelin receptor A (ERA) and NADPH oxidase (NOX) 4. Decreased Kv1.7 channel expression was detected in the lung tissues. Inward rectifier channels 6.1 channels was also increased in the lung tissues. We confirmed ET-1 increased NOX4 protein expression level and decreased glutathione peroxidase-1 protein expression level in pulmonary artery smooth muscle cells (PASMCs). Thus, ET-1 increased ROS level in PASMCs.

Conclusions : Kv1.7 contributes to MCT-induced PAH and this change might be caused by the ET-1 and ROS pathways.