MITOCHONDRIAL PERMEABILITY TRANSITION PORE BLOCKER PREVENTS RIGHT VENTRICULAR MITOCHONDRIAL DAMAGE IN MONOCROTALINE-INDUCED PULMONARY HYPERTENSION

Poster Contributions
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Background: In pulmonary arterial hypertension (PAH), right ventricular hypertrophy maintain cardiac output until right heart failure developed. Recent studies revealed that mitochondria are key roles in the pathophysiology of heart failure. Mitochondrial permeability transition pore (MPTP) is a critical role in cell death and emerged as a critical target for cardioprotection. But it is not well known about mitochondrial dysfunction in PAH. The aim of this study was to evaluated the protective effects of cyclosporine A (CsA), one of MPTP blocker, and morphological changes of mitochondria and MPTP related proteins of hypertrophied RV in monocrotaline (MCT) induced PAH.

Methods: Eight weeks old Sprague Dawley rats were randomized to control, MCT (60 mg·kg-1) and MCT plus cyclosporine A (10 mg·kg-1·day-1) treatment groups. Four weeks later, right ventricular hypertrophy and morphological changes of right ventricle were done. Western blot and RT-PCR for MPTP related proteins, were performed.

Results: Right ventricular hypertrophy was significantly increased in MCT group compared to that of the controls (0.51±0.08 vs. 0.30±0.05), but RV hypertrophy was more increased in CsA treatment groups (0.56±0.02). CsA treatment did not change MCT-induced pulmonary arteriole hypertrophy and RV fibrillar hypertrophy. In transmission electron microscopy, cristae and matrix of RV mitochondria was swollen, loss of integrity, and disrupted in MCT group, but CsA treatment prevented mitochondrial disruption. In western blot, CypD and caspase-3 were significantly increased in MCT group, but were not attenuated in CsA treatment. There were no significant differences in ANT and VDCA expression. In RT-PCR, the expression of ANT1, VDCA and CypD were not significant between three groups.

Conclusion: MPTP blocker, CsA, reduces MCT induced right ventricular mitochondrial damage. However, MPTP blocking does not reverse pulmonary pathology although it may reduce RV dysfunction in pulmonary arterial hypertension.