

Does myoinositol trispyrophosphate protect against the development of the right ventricular heart failure in pulmonary artery banding model in rats. Implications for pulmonary hypertension treatment.

Pulmonary hypertension (PH) is a progressive, fatal disease with poorly understood etiology. In the course of the disease, the lumen of the pulmonary arteries is narrowed as a result of pathologically proliferating smooth muscle cells, which forces the right ventricle (RV) to work harder to pump blood. An overload on RV initially leads to a thickening of its wall, which results in a greater force of contraction, but over time this compensation collapses, leading to RV failure and death of the patient. More and more data indicates that overgrown RV becomes ineffective due to hypoxia.

Myoinositol trispyrophosphate (ITPP) is a compound that increases the release of oxygen from red blood cells. According to our recent studies, ITPP increases the survival of rats in a model of pulmonary hypertension induced by the monocrotaline compound. However, the exact mechanism of ITPP is unknown. It can work by 1) reducing the narrowing of the lumen of the pulmonary arteries or 2) by preventing right ventricular failure.

In this project we will use the rat's pulmonary artery banding (PAB) model for research. This model mimics the effect of pulmonary hypertension on RV without damaging the lungs.

The use of this model will help verify the hypothesis that ITPP reduces mortality and prevents RV failure in the rat PAB model, and moreover will provide evidence that it prevents RV failure by acting directly on itself and not by affecting the pulmonary arteries.

The experiment will be performed on rats, which will be divided into 4 groups. Two will develop pulmonary hypertension, one of which will be given ITPP; the remaining 2 are control groups - with and without ITPP to control the consequences of the treatment on the organism and the effects of ITPP on rats without pulmonary hypertension. After 5 weeks, the following tests will be performed: measurement of pulmonary artery pressure, control of RV function using echocardiography, invasive haemodynamic examination. Finally, tissues will be collected for cellular, histological and molecular biology studies.

The obtained data will help to verify whether ITPP prevents RV failure and reduces mortality in the PAB model, and moreover, whether the mechanism acts directly on RV.

If our study proves the beneficial effects of ITPP on heart failure and survival, this project could be a big step towards the treatment of pulmonary hypertension and cardiovascular disease in general.