Protective effects of soluble ubiquinol in monocrotaline model of pulmonary hypertension in rats

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Objective: Due to its high antioxidant activity ubiquinol (U) potentially could be used for the treatment of cardiovascular diseases coupled with the development of oxidative stress and inflammation. There are several papers, showing the positive effect of ubiquinol on endothelium-dependent vasodilation. Pathogenesis of pulmonary hypertension (PH) is associated with inflammation and endothelial dysfunction. Effects of ubiquinol on PH development has not been studied before. Therefore, the aim of this work was to investigate the possible effects of ubiquinol on PH development in experiments on rats.

Design and method: Experiments was performed on male Wistar rats divided into 3 groups. All animals were subcutaneously injected with a solution of monocrotaline (MCT) (60 mg/kg, 0.5 ml) on the first day of the experiment. On 7th and 14th days after the start of experiment animals of the group 1 were injected with a solution of solubilized U (30 mg/kg, iv), group 2 – with vehicle (V) and group 3 - physiological saline, (PS) in appropriate volumes. On the 21st day after MCT injection rats of each group were anaesthetized (urethane, 1.2 g/kg) and systolic right ventricular pressure (SRVP) and arterial blood pressure were measured. For testing vascular reactivity phenylephrine (PE) (6 µg/kg) and sodium nitroprusside (SNP) (6 µg/kg) were injected iv. After decapitation of narcotized rats the weight of right ventricle (RV) was measured and RV hypertrophy (RVH) was calculated as RV weight/body weight. 

Endothelium-dependent vasodilatation (evoked by acetylcholine (ACh) of isolated segments of pulmonary and systemic vessels were investigated as well.

Results: PH developed in all groups of animals 3 weeks after injection of MCT, that was confirmed by the increase in SRVP and RVH. Differences between of SRVP levels between groups (44.4 mmHg for U-group, 45.7 mmHg for V-group, and 44.5 mmHg for PS-group ) were not significant Values of RVH demonstrated a significantly lower degree of hypertrophy development in U group compared to PS group (0.00076 vs 0.00085, p<0.05). The response of systemic blood pressure to intravenous injection of SNP in group U was 5.27% higher than in PS group and 18.29% higher than in the V group. A similar pattern was found for reaction to PE, that shows the capability of U to restore reactivity of blood vessels of systemic circulation to vasoactive factors. Study of reactivity of isolated segment of pulmonary artery at ACh showed that in group U compared with V-group there was a statistically significant increase in vasodilator response to ACh at concentrations of 10-7M(23% vs 17.2%), 10-6M (30.3% vs 25.1%), 10-5M (36.9% vs 30.9%) (p<0.05 for all).

Conclusions. Double intravenous administration of ubiquinol on an MCT model of PH on rats was able to inhibit the degree of RVH, being one of the major symptoms. In addition, it contributes to the restoration of reactivity of both systemic and pulmonary vessels.