Abstract: **P526**

**Signal ways of hypoxia-induced cardioprotection in diabetic heart**

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Introduction. Activation of kinases PI3K/Akt or AMPK is known to exert cardioprotective effects and regulate myocardial metabolism. However, the protective signaling may be disrupted in diabetic heart that may be possible mechanism of insufficient cardioprotective phenomena under diabetes. Some hypoxia-inducible genes as insulin like growth factor IGF-1 and apelin may promote activation of these signal ways, and mediate vasodilatation, cardiac remodeling, regulates glucose uptake to intensify cardioprotection.

Purpose. The aim was to investigate whether hypoxia influences cardioprotective signal ways in heart ventricles of diabetic rats.

Methods. Male Wistar rats aged 6 months, control or with streptozotocin induced diabetes, were exposed to hypoxic preconditioning using mild hypobaric hypoxia séances in barochamber (5600 m, 1 h) or chronic hypoxia of various regimen. In 24 h after hypoxic treatment, changes in protein expression in left and right heart ventricles were examined using Western blotting.

Results. Hypoxic preconditioning intensified PI3K/Akt-mediated cardioprotection by induction of Akt expression and phosphorylation in dependence to intensity of hypoxia regimen. Blockade of PI3-kinase by wortmannin decreased Akt phosphorylation, and abolished cytoprotective effects of preconditioning. Induction of IGF-1 protein in left (LV) and right (RV) heart ventricles was found, the relative expression values were 6-fold and 18.1-fold elevated, respectively. Apelin was induced only in LV. In diabetic rats, PI3K/Akt protection was markedly diminished, but phosphorylation of AMPK markedly elevated after mild hypoxia (2100 m) and reduced after moderate hypoxia (5600 m). IGF-1 expression was 14.4-fold higher in LV, and 35-fold – in RV. After preconditioning, IGF-1 values were diminished in LV and strongly elevated in RV. Besides, hypoxic preconditioning caused apelin induction in both heart ventricles, more pronounced in LV. Chronic hypoxia induced apelin in myocardium only in diabetic rats. After preconditioning or chronic hypoxia, glycemic profile was improved. Thus, hypoxia can improve disrupted protective signaling in diabetic heart with apelin and IGF-1 induction that may support the use of mild hypoxia to optimize cardioprotection in diabetes.