The role of nitric oxide and cholinergic pathways in the cardiovascular and lung functional changes following chronic hypoxia

Chronic hypoxia results in pulmonary hypertension (PHT) and bronchial hyperresponsiveness (BHR) via the involvement of the vagal pathway and/or via airway and pulmonary vascular remodelling. We aimed at characterizing whether inhibiting these pathways protects PHT and lung functional changes following chronic hypoxia. Rats were exposed for 21 days to: room air (C, n=9), hypoxia (11 % O2, HC, n=8), hypoxia with concomitant daily treatment with sildenafil (20 mg/day, HS, n=7) or an anticholinergic, tiotropium (18 µg/day, HT n=8). End-expiratory lung volume (EELV) was determined plethysmographically. Lung responsiveness was assessed by forced oscillations during iv methacholine provocation, and the equivalent dose causing 200% increase in airway resistance (ED200) was determined. The right ventricular hypertrophy (RVH)-index was calculated. The pulmonary arterial wall thickness [(Dex-Din)/Dex, AWT] was measured on lung sections.

Hypoxia led to PHT and increased EELV with no significant effect of any of the treatments, which in contrast prevented hypoxia-induced BHR (Figure). These findings suggest that the pathophysiological mechanisms of the hypoxia-induced cardiovascular and lung functional changes are mainly dissociated. Stimulating the NO-pathway or inhibiting the vagal tone has a beneficial effect on BHR without preventing hypoxia induced PHT. Grant support: OTKA K81179; ERS LTRF172-2011.