Summary

Monitoring of airway inflammation in patients with various types of bronchial obstruction. Monitoring of oxidative stress biomarkers in exhaled breath condensate of patients with severe refractory asthma.

Background: Asthma is chronic inflammatory disease associated with bronchial hyperreactivity. Various cells plays and cellular products are involved in asthma pathogenesis. Oxidative stress plays also a significant role in mechanisms of asthma via action of reactive oxygen (ROS) and nitrogen (NOS) species. These free radicals develop from inflammatory airway reaction and from exogenous exposure of air-pollution (ozone, cigarette smoke). ROS and NOS and its products cause damage of bio-membranes, proteins and nucleic acid. Several studies showed correlation of asthma severity to intensity of oxidative stress.

Aim of the study: The main goal of the study was to describe differences in concentrations of various markers of oxidative stress in exhaled breath condensate of severe refractory asthma (SRA) patients and healthy controls (HC). Secondary aim was to show correlation of oxidative stress intensity to severity of eosinophilic inflammation described by peripheral blood eosinophilia or exhaled nitric oxide concentration.

Methodology: We harvested exhaled breath condensate in 40 SRA patients and 19 HC according to recommended technique (Jaeger EcoScreen). Samples were studied by liquid/gas chromatography and mass spectrometry. We studied markers of oxidative damage of lipids: malondialdehyd (MDA), 4-hydroxy-trans-nonenal (HNE), 4-hydroxy-trans-hexenal (HHE), cysteinyl leukotriens, 8-isoprostane and markers of protein damage: nitro-tyrosine, orto-tyrosine, chloro-tyrosine and markers of nucleic acid damage: 5-hydroxymethyl uracil, 8-hydroxyguanosin a 8-hydroxy-2'deoxyguanosin. All results were correlated to currently used methods eosinophilic inflammation assessement (eosinophils in peripheral differential blood count (EC), exhaled nitric oxide (FeNO). Eosinophilic inflammation was considered as EC>4% and FeNO≥30 ppb.

Results: We have shown statistically significantly higher concentrations of all tested oxidative stress markers in SRA vs. HC (all $p<0.001$). Higher concentration of HNE was found in non-eosinophilic SRA (EC<4%) versus eosinophilic SRA (48.5 vs 41.1 ng/ml, $p=0.034$) and similar results of HHE versus eosinophilic SRA (52.6 vs. 48.9 ng/ml, $p=0.006$). ROC analysis of HNE showed limit of 31,97 ng/ml as 94,7% sensitivity a 95% specificity for differentiation of SRA vs HC (AUC 0.9895, $p<0.0001$). Other tested markers of oxidative stress were correlated neither to EC, nor to FeNO and systemic steroid therapy, age, body-mass-index.

Conclusion: We have proved significantly higher concentrations of oxidative stress markers in SRA than in HC. Non-eosinophilic SRA was associated with higher concentration of HHE and HNE, which could indicate increased lipoperoxidation of ω-6 resp. ω-3 unsaturated fatty acids. Increased lipoperoxidation could play a role in pathogenesis of noneosinophilic asthma phenotype. Other tested markers of oxidative stress were correlated neither to EC, nor to FeNO.