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Title: Influence of oral steroid use in difficult-to-control asthma patients on metabolomic profile of oxidative stress in exhaled breath condensate (EXAIR project)

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Body: Difficult-to-control asthma (DCA) remains a pending clinical problem despite recent advances in therapy. It is supposed that intensity of inflammation and oxidative stress is higher in DCA. Aims: Our hypothesis was that oxidative stress metabolomics in exhaled breath condensate (EBC) differs in oral corticosteroid (CS) dependent DCA patients (group OCS, n=10) versus DCA treated by inhaled CS (group ICS, n=10) from severe asthma center and versus healthy controls. Methods: We have used metabolomic analysis of EBC using liquid chromatography and mass spectrometry to detect concentrations of 22 markers of oxidative stress (e.g. malondialdehyde, leukotrienes, 8-isoprostane, o-tyrosine). EBC was taken by a standardized protocol. Results were analyzed together with FEV1, eNO50, blood eosinophils and differences in OCS and ICS subgroups were statistically evaluated. Results: OCS ad ICS did not differ in gender, age (54 vs 53), asthma control test (12 vs 15), FeNO50 (36.5 vs 50) and FEV1 (53 vs 57% predicted) (all $p>0.05$). Peripheral blood eosinophils were higher in ICS group (0.46 vs 0.22 x10/9L, $p=0.03$). 8-isoprostane was significantly higher in ICS group (101.7 vs 54.5 pg/ml, $p=0.002$) only. All other measured markers in EBC did not differ between OCS and ICS, however all markers in EBC of OCS and ICS were higher in comparison to control group (all $p<0.001$). Conclusion: Our data shows increased lipoperoxidation and blood eosinophilia in ICS DCA patients. We speculate that ICS DCA would benefit from earlier chronic oral CS therapy to prevent consequences of oxidative stress, however further data are needed. Support: PRVOUKP.