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INDUCED SPUTUM METALLOPROTEINASES AND THEIR INHIBITORS IN RELATION TO EXHALED NITROGEN OXIDE AND SPUTUM NITRIC OXIDES AND OTHER INFLAMMATORY CYTOKINES IN COPD PATIENTS

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An inappropriate MMP/TIMP balance in chronic inflammation may lead to disturbances in the turnover and remodeling of pulmonary extracellular matrix, as can occur in asthma and COPD. The aim of this study was to assess sputum levels of MMP-1, MMP-2, MMP-3, TIMP-1 and TIMP-2, and MMPs/TIMPs ratios in relation to exhaled NO (eNO) and sputum NOs (nitrates and nitrites) and IL8 obtained from COPD patients, healthy non-smokers, and healthy smokers. Higher levels of TIMP-1 (118.9 ng/ml) and TIMP-2 (3.75 ng/ml) were found in COPD patients than in healthy smokers (17.7 ng/ml, $p<0.03$; 0.51 ng/ml, $p>0.05$, respectively) and healthy non-smokers (84.6 ng/ml, $p>0.05$; 1.61 ng/ml, $p>0.05$, respectively). We observed significant positive correlations between concentrations of NOs and MMP-1, MMP-2, MMP-3 and TIMP-2 ($r=0.37$, $p<0.02$; $r=0.60$, $p<0.0001$; $r= 0.56$, $p<0.0004$ and $r=0.47$ $p<0.004$, respectively) in COPD patients.IL8, MMP-2, MMP-3 and TIMP-2 levels in induced sputum were negatively correlated with airway obstruction, i.e., FEV1/FVC ($r= -0.61$, $p<0.00009$; $r=-0.41$, $p<0.01$; $r=-0.38$, $p<0.02$; $r=-0.49$, $p<0.002$).The correlation between NO and metalloproteases and their inhibitors and IL8 suggests an important role of the reactive form of nitrogen oxide in airway remodeling in COPD. Our study indicated the potential pathogenic role of stromelysin-1 (MMP-3) in COPD.