Exposome, genetic traits and functional enzymatic activity as risk factors for COPD

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Chronic obstructive pulmonary disease (COPD) is a multifactorial disease characterized by airflow obstruction that is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles and gases. Cigarette smoke is the main risk factor, but only a small proportion of smokers (15-20%) develop symptomatic disease, this suggests the existence of other risk factors involved in disease onset and progression. This consideration prompt us to perform a multidisciplinary project, with the aim to uncover socio-economic features, biomarkers of genetic damage and susceptibility, and enzymatic activities as risk factors in COPD patients. 229 subjects, all living in the metropolitan area of Bologna, were recruited among outpatients who were undertaking respiratory function tests at the Pneumology Unit of the Sant'Orsola-Malpighi Hospital, Bologna. Patients were classified as mild to very severe COPD according to the GOLD Guidelines. Comprehensive socio-demographic, lifestyle and clinical data, collected by physician interviewers (use of a predefined questionnaire during a routine clinical consultation) revealed that fragility is associated with COPD stage and that comorbidities and the low body mass index are predictors of mortality or hospitalization. Regarding biomarkers of genetic damage, the research has been directed to the evaluation of micronuclei frequency in peripheral blood lymphocytes that may be induced by oxidative stress mechanisms occurring in the evolution of pulmonary chronic-obstructive diseases. Data showed no significant different micronuclei frequencies associated with the disease stage. Interestingly, comparing micronuclei frequency in COPD patients and healthy subjects, all residents in Bologna, we observed a trend for a higher micronuclei frequency in patients. This preliminary evidence suggests that initial alterations in respiratory function are associated with an inflammatory tissue condition that can evoke molecular and cellular alterations such as increased genetic damage. With regard to biomarkers of susceptibility, a case-control study was carried on in COPD patients, aiming to investigate whether polymorphisms of microsomal epoxide hydrolase (mEH) and genes coding for oxidative stress enzymes [(catalase (CAT), glutathione reductase (GR) and peroxidase (GPX), and superoxide dismutase (SOD)] had any bearing on individual susceptibility to COPD onset and severity. DNA of COPD patients and controls was genotyped using PCR-RFLP and PCR-RT techniques. The statistical analysis did not show any significant result about the potential relationship between mEH polymorphisms and COPD risk and severity. Statistical analysis of association with the other analyzed polymorphisms is ongoing. The association of biochemical biomarkers of oxidative stress, associated with exposure to atmospheric pollutants, with COPD risk and severity has been evaluated. Furthermore, the possible influence of polymorphisms in the observed enzymatic activities has been assessed.