Abstract Group: 7.1. Paediatric Respiratory Physiology

Keyword 1: Orphan disease  Keyword 2: Inflammation  Keyword 3: Biomarkers

Title: Oxidative stress in serum of patients with alpha-1 antitrypsin deficiency

Prof. Dr Francisco 11523 Dasí Francisco.Dasi@uv.es 1,2, Dr. Mónica 11542 Amor monichi5@hotmail.com MD 1,3, Dr. Francisco 11558 Sanz fr.sanz@gmail.com MD 4, Prof. Dr Pilar 11564 Codoñer-Franch pilar.codoner@uv.es MD 5,6, Ms. María Mercedes 11567 Navarro-García mer_navarro2002@yahoo.es 1 and Prof. Dr Amparo 11579 Escribano aescribano@separ.es MD 1,3,6. 1 UCIM, Fundación Investigación Hospital Clínico Valencia/INCLIVA, Valencia, Spain, 46010 ; 2 Physiology, University of Valencia. School of Medicine, Valencia, Spain, 46010 ; 3 Pediatric Neumology, Hospital Clínico Universitario Valencia, Valencia, Spain, 46010 ; 4 Neumology, Hospital General Valencia, Valencia, Spain ; 5 Pediatric Gastroenterology, Hospital Dr. Peset Valencia, Valencia, Spain and 6 Pediatrics, Obstetrics and Gynecology, University of Valencia. School of Medicine, Valencia, Spain.

Body: Background: Oxidative stress (OE) has been shown to be a contributing factor in the development of liver and lung damage in animal models of alpha-1 antitrypsin deficiency (AATD). Rationale and aims: In humans, AAT shows a high degree of variability and it has been proposed that emphysema progression is heavily influenced by the antioxidant defenses of the lung. We hypothesize that those patients with low AAT levels and high OE levels will be more prone to develop severe emphysema. The aim of this study is to determine in serum the OE profile of children with AATD and study the association with the AAT phenotype. Methods: Forty-seven children diagnosed with AATD were prospectively included in the study. Patients were classified in three risk groups of developing lung disease: low (MM, MS; SS), intermediate (MZ; SZ) and high risk (ZZ). The OE status was evaluated in serum by monitoring the total glutathione, oxidized vs reduced glutathione ratio (GSSG/GSH) and the oxidation products 8-hydroxydeoxyguanosine (8-OHdG), malondialdehyde (MDA) and protein carbonyl (PC). Results: High-risk (ZZ) patients showed significantly higher GSSG/GSH ratio, 8-OHdG, MDA and PC but lower levels of total glutathione than the low-risk group. Interestingly, intermediate-risk (MZ and SZ patients) patients showed OE values between high and low risk patients. Conclusions: OE is increased in serum of high-risk (ZZ) AATD patients, indicating that OE could be an important contributing factor in the development of lung disease when AAT levels are low. Our results open up a new strategy to use OE parameters as biomarkers of lung disease progression. Funding Sources: Supported by SVN, GVA AP-096/11, ISCIII PI11/02884 grants.