# Assessment of Small Airway Dysfunction and Z-Alpha1-Antitrypsin Polymers in Exhaled Breath Condensate in Healthy PiZZ Subjects

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Introduction: Z-alpha1-antitrypsin (Z-AAT) polymers can be found in the bronchial epithelium of PiZZ subjects (Respir Res, 2014 Sep 14;15:112), playing a potential pro-inflammatory role in the airways. The IL8-mediated neutrophil cell recruitment induced by these polymeric aggregates could act as an underlying pathogenetic factor for developing neutrophilic-related airways diseases, such as Neutrophilic Asthma. Our study aimed to evaluate the presence of small airways dysfunction and the potential correlation with Z-AAT polymers, documented via Exhaled Breath Condensate (EBC), in healthy PiZZ subjects, comparing the results with healthy PiMM subjects. Methods: We enrolled 17 asymptomatic non-smoker subjects: 9 PiZZ and 8 PiMM, as controls, with no obstructive spirometric pattern (i.e., normal FEV1/VC ratio). All subjects underwent complete Pulmonary Function Tests (PFTs). EBC was collected in PiZZ subjects. In order to find and quantify the Z-AAT polymers, we performed ELISA tests. Results: The PiZZ subjects had normal lung volumes and DLCO values. However, In comparison with PiMM subjects, the single breath test $N_2$ wash-out revealed significant differences regarding the phase III slope (1.5±0.4 $N_2$/L vs. 1.1±0.3 $N_2$/L) and the closing volume/vital capacity ratio (14.3±4.5 % vs. 9.5±5.3 %) ($p<0.05$) in PiZZ subjects. The ELISA test detected the presence of Z-AAT polymers in 4 PiZZ patients. No correlations were found between polymers levels and any functional respiratory parameter. Conclusions: PiZZ healthy subjects show functional findings suggesting small airways dysfunction when compared to healthy PiMM subjects. Surprisingly, Z-AAT polymers were found only in 4 PiZZ subjects, probably due to the sampling methodology. New studies are needed to understand better the correlation between EBC Z-AAT polymers, sputum examination, and neutrophilic inflammation-related small airway impairment in Z-AAT subjects.

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