Analysis of the development of inflammatory process and emphysema after intratracheal administration of elastase in rats

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Introduction

Emphysema is a respiratory disease associated with pulmonary inflammation characterized by alveolar wall degradation. The degradation process is not completely described but may be associated to elastase release from resident or recruited inflammatory cells, leading to elastin destruction, which represents one of the main component of the alveolar wall. The aim of this study was therefore to develop an experimental model of emphysema by intratracheal administration of elastase and evaluate the inflammatory and morphological parameters.

Methods

Male Sprague-Dawley rats were administered via intratracheal route (1 ml/kg) with porcine pancreatic elastase (PPE, 30, 60, 120 or 240 UI/kg). Twenty-four hours after, bronchoalveolar lavage (BAL) were performed by administration of 25 ml of warm saline solution (NaCl 0.9 %). Cell composition of BAL was determined after cytocentrifugation and May-Grünwald Giemsa staining. Gelatinase activity was measured by zymography. In another set of experiments, rats were administered with 120 UI/kg PPE. After 3 months, lungs were harvested, fixed in paraformaldehyde and embedded in paraffin. Sections were stained with hematoxylin-eosin and used for evaluation of pathological changes. Alveolar tissue area and parenchymal destruction were measured with an image analyzer (imageJ) as an estimation of the degree of emphysema. Mean of ten measurements (five by slide separated by 300µM in the tissue). The statistical differences were measured using a non parametric Wilcoxon test (statistica, statsoft®)

Results

The intratracheal administration of PPE induced a marked inflammation characterised by a dose-dependent increase in the total number of cells in the BAL. This increase is mainly due to an influx of neutrophils and to a lesser extent of macrophages. In the long term, the administration of PPE at 120 UI/kg i.t. elicited a destruction of lung parenchyma of at least 20 % in comparison with vehicle-treated animals. The increase in alveoli area of at least 200 % confirmed the development of an emphysema.

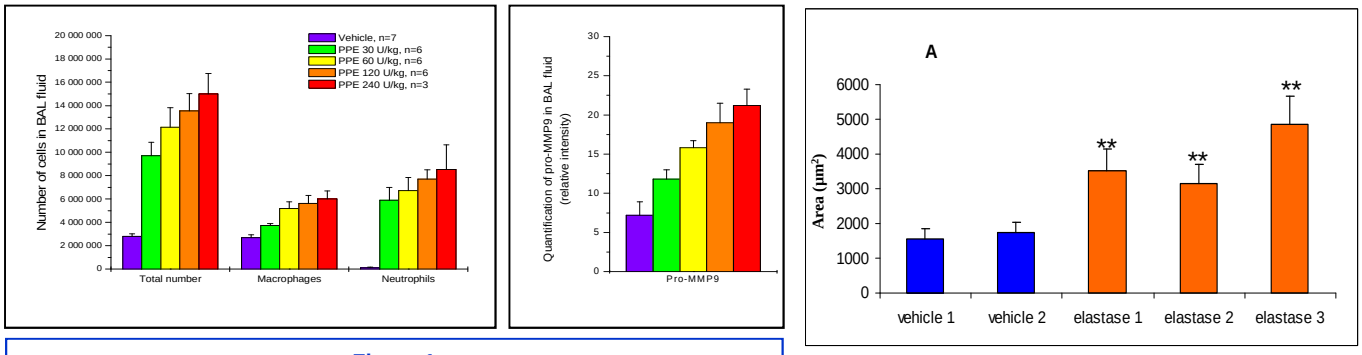

Figure 1

Cell composition and release of pro-MMP-9 in the BAL fluids of rats administered with various doses of PPE.

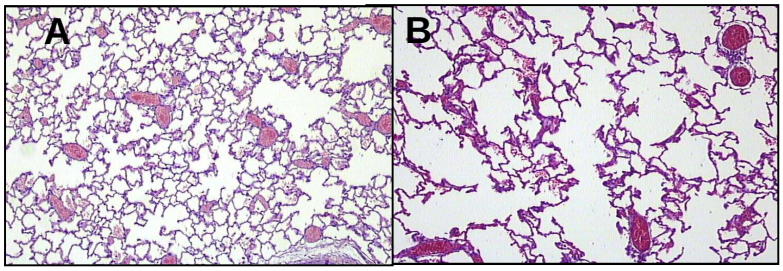

Figure 2

Histological appearance of lungs, 3 months after elastase i.t. administration.
A : vehicle. B : PPE 120 U/kg

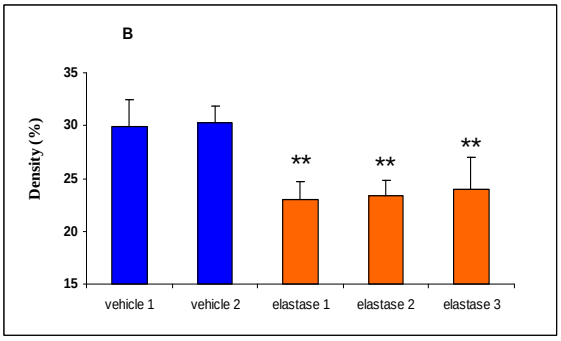

Figure 3

Effect of PPE 120 U/kg on alveolar tissue area (A) and parenchymal destruction (B) (n = 10) ; ** p<0.01

Conclusion

This study shows that the administration of PPE induced alveolar wall destruction associated with an early inflammatory process in airways. This study also suggests that elastase participates in the development of the emphysema