Early biomarkers indicate COPD induced by whole cigarette smoke in live human lung tissue

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Introduction

Cigarette smoke (Cs) inhalation is a main reason to develop chronic obstructive pulmonary disease (COPD). It is characterised by degradation of alveoli, inflammation and mucus hypersecretion. Mechanisms that underline various components of COPD can be modelled in vitro, specifically using cigarette smoke with fresh human lung tissue. The aim of the study is to establish pathological changes of COPD in vital lung tissue by using Cs and cigarette smoke condensate (Csc).

Materials and Methods

Human Precision-Cut Lung Slices (PCLS) were exposed to Csc or whole Cs in an Air-Liquid Interface (ALI) using the in vitro exposure device P.R.I.T.® ExpoCube®. Cytotoxicity, release of cytokines and extracellular matrix (ECM) proteins were analysed. Pharmacological treatments were applied to inhibit inflammatory responses of tissue to Cs.

Results

Concentration dependent cytotoxicity was observed in human PCLS after 24 h Cs submersion exposure and cigarette smoke exposure in ALI culture. EC₅₀ values were determined using WST-1 assay. EC₅₀ values of 196 µg/ml for Csc and 16 µg particles deposited on human lung tissue for Cs were calculated (Fig. 2).

Exposure of human lung tissue to Cs significantly increased the release of pro-inflammatory cytokines (Fig. 5). MMP-9, Pro-Coll1α1 and extracellular RAGE present significant changes in the ECM after Cs exposure (Fig. 6A-C). Increased ratio of MMP-9 to TIMP-1 are biomarkers for an emphysema development (Fig. 6D). Pharmacological intervention reduced the Cs-induced inflammatory cytokines. Dexamethasone significantly reduced IL-1α production (Fig. 6E, F).

Conclusions

Csc and Cs induced concentration dependent tissue injury, early biomarkers of inflammation and changes in ECM proteins in live ex vivo human lung tissue. The exposure of the complex mixture of whole cigarette smoke closely reflects the in vivo situation in human lung tissue.

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