Invasive but repetitive lung function measurements in rodent models of pulmonary fibrosis

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Introduction

The bleomycin-induced pulmonary fibrosis in rodents is a standard model to test efficacy of drugs to be developed for idiopathic pulmonary fibrosis (IPF). We have modified this model and used invasive but repetitive lung function measurements to monitor the development of bleomycin-induced lung injury and fibrosis. Histological examination is a qualitative method to assess IPF, but lung function testing provides repetitive direct measurements without destruction of the organism.

Methods

Treatment protocol (Fig. 1):
- Animals: Male Wistar WU rats, 10 weeks old
- Induction of lung fibrosis: bleomycin aerosol intratracheally on Day 0 (single-dose regimen) or on Day 0 and 1 (two-dose regimen) by means of a MicroSprayer® aerosolizer.
- Control group: vehicle-treated (saline).

Lung function:
- Invasive, repetitive lung function measurements in anesthetized, orotracheally intubated, but spontaneously breathing animals [1, 2] on Day 14 + 21 (Notocord HEM)
- Dynamic compliance (Cdyn) and lung resistance (Rdyn)
- Recruitment maneuver by deep inspiration up to 30 cm H2O on Day 14

Bronchoalveolar lavage and histology:
- Bronchoalveolar lavage (BAL) followed by cell differentiation
- Left lungs inflated with formalin under a pressure of 20 cm water column for histopathology
- Right lung frozen for biochemical investigations incl. hydroxyproline content of lung tissue

Results

Histology and collagen concentration (Fig. 2+3):
- A pronounced alveolar/interstitial fibrosis in the lungs of both bleomycin groups detected by histology
- Increased collagen concentrations in lungs indicated by hydroxyproline measurement in lung homogenate and BAL

Lung function (Fig. 4+5):
- Decrease in Cdyn on Day 14 and 21 indicates loss of distensibility of the lungs
- Increase in Rdyn indicates elevated tissue and/or airway resistance
- Recruitment maneuver on Day 14 showed lower Cdyn in both bleomycin groups indicating that the bleomycin rats recruit much less alveoli than the control

References


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