Metabonomics Followed of the Evolution of Bleomycin-Induced Pulmonary Fibrosis in the Rat

Anouar Abidi1*, Alexandre Robbe2, Nadia Kourda3, Alexandre Legrand2 and Saloua Ben Khamsa1

1Research Unit 03/UR/08-05 Pulmonary Fibrosis Prevention and Treatment, Faculty of Medicine of Tunis, University Tunis Al Manar, Tunis, Tunisia
2Laboratory of Animal Physiology and Pharmacology, Faculty of Medicine of Mons, University of Mons-Hainaut, Belgium
3Service of Anatomo-Pathology, Hospital Charles Nicolle, Tunis, Tunisia

Corresponding author: Anouar Abidi, Research Unit 03/UR/08-05 Pulmonary Fibrosis: Prevention and Treatment, Faculty of Medicine of Tunis-University Tunis Al Manar, Tunis, Tunisia, Tel: +2167187225; E-mail: abidi_anouar3@yahoo.fr

Introduction

The objective of this work is to look for biomarkers scalability of pulmonary fibrosis by metabonomics, genetics and immunohistochemical approaches in an animal model of pulmonary fibrosis induced by bleomycin in the Wistar rat.

Methods

Twenty Wistar rats, weighing 220 g to 240 g, were randomly divided into two groups: a control group (G1, n=10) and treated group (G2, n=10). The rats in group G2 were investigated at various times after instillation of Bleomycin (4 mg/kg) intra-tracheally (in days 3, 7, 14 and 21). The rats in the G1 group underwent the same treatment by replacing bleomycin with saline. During the experimental period, the rats were placed in metabolic cages for urine collection until the 21st day. Samples of urine, blood and bronchoalveolar lavage liquid were analyzed by proton nuclear magnetic resonance (1H NMR) and the spectra, showed an increase in the rate of β-hydroxybutyrate, lactate dehydrogenase, α-ketoglutarate, creatine and taurine in days 3 and 7.

Results

In the treated group (G2), a significant increase in inflammation and fibrosis score compared to the control group (G1) on days 3 and 7. For results obtained from NMR spectra, chemical shifts in the samples of urine showed an increase in the secretion of acetate, succinate dehydrogenase, α-ketoglutarate, creatine and taurine in days 3 and 7 corresponding to the inflammatory phase of fibrotic processes. For fibrosis phase (day 14 and 21), it is marked essentially by an increase in secretion of α-ketoglutarate and citrate. Bronchoalveolar lavage spectra, showed an increase in the rate of β-hydroxybutyrate, lactate and dimethylamine during the inflammatory phase, and a decrease of the choline secretion, trimethylamine, glycine and glucose during the fibrosis phase. These results provide an indication of the inflammatory component (days 3 and 7) by increasing taurine and creatinine and the difficulties of oxygenation via the general increase in the Krebs cycle intermediates secreted by the liver. The fibrotic component (days 14 and 21) is marked by significant activity of mitochondrial oxidative phosphorylation and the development of fibrotic tissue.

Conclusion

The pathological, metabonomic, patterns of H3K9/27me and DNA methylation results, in normal group compared to Bleomycin-induced pulmonary fibrosis could facilitate the understanding towards with mechanisms that involved in the initiation and development processes of pulmonary and other organ fibrosis and consequently could contribute to possible better target to find the appropriate treatment for pulmonary fibrosis.

References