Monitoring Paraquat-induced Pulmonary Fibrosis in Rats with Micro-CT Finding and Histological Examination

Kai-Sung Wang[1] Shih-Hsien Chang[1] Chi-Yuan Lu[1]

Chung-Hsin Yeh[1] Ming-Wei Lee[2,*]

[1]Department of Public Health, Chung Shan Medical University, Taichung 402, Taiwan, ROC
[2]School of Medical Laboratory and Biotechnology, Chung Shan Medical University, Taichung 402, Taiwan, ROC

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Abstract

The aim of this study is to monitor paraquat-induced pulmonary fibrosis in rats with micro-computed tomography (micro-CT) findings. Adult rats were divided into four groups and given a single oral dosage of aqueous solution of paraquat at 0 mg/kg, 40 mg/kg, 60 mg/kg, and 80 mg/kg, respectively. In the control group, the color and luster of the lung samples appeared normal and no petechia was observed. In the experimental groups, some petechia was observed in lung samples, and fibroblast and fibrinogen were found in histological sections, and the ground-glass predominance and reticulation in micro-CT findings increased during the period from the 1st week to the 3rd week, and decreased in the 4th week after the administration. In the experimental groups, the lung weight of adult rats increased when the dosage of paraquat was increased, but the body weight increments of adult rats decreased, therefore the ratios of lung weight over body weight increased with increased dosage. From the analysis of 3D micro-CT images, the results show that the effective capacity volume of the lungs gradually decreased with increased dosage, therefore micro-CT is seen as a powerful tool for fast diagnosis and longitudinal monitoring of pulmonary fibrosis.

Keywords: Micro-CT, Paraquat, Pulmonary fibrosis, Histological sections, 3D reconstruction

1. Introduction

Micro-CT is a powerful instrument used in animal molecular image systems for construction of animal models for human disease and drug research. It uses a non-invasive method and provides 3D structure and in vivo information, including perspectives on minute structures inside the object, and also facilitates comprehension of the structures of organs and tissue in experimental animals [1-4].

A normal lung is divided into the respiratory passage for air transportation, alveoli for gas-exchange, and pulmonary interstitial tissue composed of elastin, glycoprotein, and collagen for distribution. Collagen is excreted by fibroblasts, which are located in the interstitial tissue. When fibroblast cells are injured by various chemical and physical stimuli, they will be activated to excrete collagen to repair the pulmonary interstitial tissue, resulting in pulmonary fibrosis. Briefly, pulmonary fibrosis, manifesting as scars, is the result of tissue repair after the lung has been injured [5]. The lung is the organ most sensitive to paraquat in terms of reflecting symptoms and syndromes. Human and mouse histological sections both show the same type of pulmonary injury [6]. Because previous animal experiments all used invasive methods, animals needed to be sacrificed to obtain experimental data, and individual differences could not be determined. In addition, the interpretation of results of diagnosis on humans is very subjective and lacks evaluation references, so the outcomes are easily affected for the different readers [7-12].

There are many causes of pulmonary fibrosis, including asbestos, silicon, coal ash, harmful chemical gases, SARS, careless ingestion of some pesticides such as paraquat, administration of certain drugs, radiotherapy, immuno-chemotherapy, hyperbaric oxygen-therapy, sarcoidosis, autoimmune disease, many pulmonary infections (especially pulmonary tuberculosis), and other unclear reasons. Most reasons have been unknown until recently [13]. Progressive interstitial fibrosis disease, which widely infringes on the pulmonary alveoli wall, septa, blood vessels, lymph, and connective tissue around the trachea, leads to pulmonary fibrosis, which is a chronic inflammation; gases can't exchange, and this leads to respiratory failure and functional disability. The symptoms include dry cough, heavy breathing and body weight loss. Prognosis is poor, patients may lose their ability to work, and they usually die in five to six years after

* Corresponding author: Ming-Wei Lee
Tel: +886-4-24730022 ext. 11767; Fax: +886-4-23248171
E-mail: d880430@csmu.edu.tw