Ameliorative Potential of Biguanides on Experimentally-induced Lung Fibrosis

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Abstract

Lung fibrosis is a disease that carries poor prognosis and high mortality rate. The mechanisms of fibrosis may include disordered wound healing, infiltration with inflammatory cells and fibroblasts and release of reactive oxygen species and growth factors. The aim of this study was to assess the effect of metformin (Biguanide) on lung fibrosis induced by bleomycin and to clarify the molecular mechanisms of this effect. Sixty male Wistar rats were divided into 6 equal groups as follows: control group; bleomycin for 4 weeks group; metformin prophylactic group; bleomycin for 6 weeks group; metformin therapeutic group and metformin alone group. The weight of rats was recorded. Bronchoalveolar lavage (BAL) was analyzed for total and differential leukocyte count, tumor necrosis factor alpha (TNF-α) and transforming growth factor beta 1 (TGF-β1). Lung tissue hydroxyproline, malondialdehyde and superoxide dismutase were measured. Also, parts of the lungs were subjected to histopathological and immunohistochemical examination for nuclear factor kappa B (NF-κB). Metformin used prophylactically improved the histopathological picture and NF-κB immunostaining and decreased the oxidative stress, TGF-β1, TNF-α and BAL cellularity. When used therapeutically, metformin decreased oxidative stress and TGF-β1 but didn’t improve TNF-α, the histopathological picture and NF-κB immunostaining. In conclusion, metformin has ameliorative effect on bleomycin-induced lung fibrosis when used prophylactically better than when used therapeutically.

Keywords
- Biguanides
- Lung
- Fibrosis
- Bleomycin
- Rats

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