Therapeutic potential of amitriptyline for paraquat-induced pulmonary fibrosis: involvement of caveolin-1-mediated anti-epithelial-mesenchymal transition and inhibition of apoptosis

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Abstract

The present study was performed to investigate the anti-fibrotic effect of Amitriptyline (AMT) on paraquat (PQ)-induced pulmonary fibrosis and its possible mechanism. A total of 32 C57BL/6 mice were randomly divided into control, PQ, PQ + AMT and AMT groups. Lung histopathology, blood gas analysis, hydroxyproline (HYP), TGF-β1 and IL-17 were measured. E-cadherin, N-cadherin, α-SMA and caveolin-1 were studied by immunohistochemistry and Western-blot analysis in mice and A549 cells. As we found that, compared with the PQ group, the PQ + AMT group displayed mild pathological changes in pulmonary fibrosis, lower HYP, IL-17 and TGF- β1 levels in lung, and levels of N-cadherin and α-SMA in the lungs were significantly decreased, but caveolin-1 was increased ($p < 0.01$). While SaO2 and PaO2 levels were higher. Compared with the PQ group, the apoptosis rate, N-cadherin and α-SMA levels in the A549 cells were significantly decreased after PQ treatment and high-dose AMT intervention ($p < 0.01$). The expressions of E-cadherin, N-cadherin and -SMA in the PQ-induced cells transfected with caveolin-1 siRNA or siControl RNA were significantly different ($p < 0.01$). Our results suggested that AMT inhibits PQ-induced EMT in A549 cells and improves lung histopathology and oxygenation in mice by up-regulating caveolin-1.

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