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The Protective Effects of Rho Kinase Inhibitor on Paraquat-Induced Acute Lung Injury in Rats

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OBJECTIVE: Fasudil, rock Kinase inhibitors, may also inhibit systemic inflammation and prevent PQ-induced acute lung injury in rats, although the mechanisms remain elusive. This study is aimed to investigate the role of Rho/ROCK signaling pathway in the protective effects of fasudil on acute lung injury in PQ rats.

METHODS: 120 Wistar rats were pretreated with fasudil (10 and 30mg/kg) through intraperitoneal injections 1 hour before PQ administration. Levels of TNF-α, IL-1β and IL-6 and the number of polymorphonuclear neutrophils (PMN) in bronchoalveolar lavage fluid (BALF) were determined. Lung tissues were collected to measure the wet-to-dry (W/D) ratios, oxidative stress index, and lung injury scores. Expression levels of Rho, ROCK1 and ZO-1 proteins were determined by western blotting; expression of Bcl-2, bax and activated caspase-3 mRNA was determined by RT-PCR.

RESULTS: Treatment with fasudil demonstrated significant decreases in PMN count, TNF-α, IL-1β and IL-6 in BALF in rats with PQ-induced acute lung injury. In addition, fasudil also effectively reduced the wet-to-dry weight ratio, the lung injury score and the levels malondialdehyde, conversely increasing the activity of superoxide dismutase in lung tissue. Furthermore, the expression of Rho, ROCK1 was significantly down-regulated, whereas the protein expression levels of ZO-1 were increased in fasudil-treated rats ($P<0.05$). It was found that the mRNA expression of bax and activated caspase-3 decreased, and the mRNA expression of Bcl-2 up-regulated by fasudil.

CONCLUSION: Fasudil could improve endothelial permeability and inhibit inflammation, oxidative stress and cell apoptosis to alleviate acute lung injury in PQ rats through inhibition of Rho/ROCK signaling pathway.