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Title: Effect of fasudil on the bleomycin-induced pulmonary fibrosis and hypertension in mice

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Body: Background: RhoA/Rho kinase (ROCK) pathway is important in regulating vascular tone and vascular remodelling in pulmonary hypertension (PH). It has been shown to be altered in the bleomycin-induced pulmonary fibrosis (PF) and PH in mice. However, the exact mechanism by which it leads to PF and PH remains to be clarified. Objectives: The present study aimed to assess whether fasudil, a ROCK inhibitor, is able to inhibit PF and PH induced by bleomycin in mice. Methods: Male C57BL/6 mice were randomized into 3 groups: G1 (saline), G2 (bleomycin) and G3 (bleomycin + fasudil). Bleomycin (3.3U/kg) was given intratracheally (day 0) and fasudil (30mg/kg/d) intraperitoneally from day -1 during 21 days. Right ventricular systolic pressure (RVSP) was measured by RV puncture at 7, 14, and 21 days, followed by sacrifice and lung and heart samplings for collagen analysis. Results: Pulmonary fibrosis was present at 7 days, and became more apparent at 14 days. RVSP increased at 14 days, accompanied by right ventricular hypertrophy. Fasudil improved survival, reversed PF and attenuated PH. Conclusions:The efficacy of the ROCK inhibitor, Fasudil, suggests that RhoA/ROCK is involved in causing PF and PH induced by bleomycin in mice.