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Rosiglitazone attenuates paraquat-induced lung fibrosis in rats by upregulating PTEN and downregulating TGF- β 1 in a PPAR gamma-dependent manner

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Objectives: Rosiglitazone, a PPAR- γ agonist, possesses anti-fibrotic effect; however, its inhibitory effect on paraquat (PQ)-induced pulmonary fibrosis is not completely understood. Here, we investigated the inhibitory effect of rosiglitazone on PQ-induced acute pulmonary fibrosis in rats and its underlying mechanism.

Methods: Male Sprague-Dawley rats were administered a single intraperitoneal injection of 30 mg/kg PQ and euthanised 7, 14, 21, and 28 days after PQ poisoning. Arterial oxygen partial pressure (PaO₂), wet-to-dry (W/D) lung weight ratio, hydroxyproline content, and histopathological changes in the PQ poisoning group were observed. Intraperitoneal injection of 10 mg/kg/d rosiglitazone or 1 mg/kg/d GW9662 (PPAR- γ antagonist) was administered starting at 1 h post-PQ poisoning and continued for 1 week. PaO₂, W/D lung weight ratio, hydroxyproline content, and histopathological changes in each group were observed after 28 days. Western blotting was performed to estimate PPAR- γ , PTEN, TGF- β 1, and α -SMA levels, whereas reverse transcription-polymerase chain reaction was used to determine the mRNA levels of PPAR- γ , PTEN, and TGF- β 1 in the lung tissue of each group.

Results: PQ-induced pulmonary fibrosis was most obvious on day 28. Rosiglitazone reduced PQ-induced decrease in PaO₂, increased the W/D lung tissue weight ratio, and increased lung fibrosis score. Rosiglitazone inhibited the PQ-induced reduction in protein and mRNA levels of PPAR- γ and PTEN and elevation in protein and mRNA levels of TGF- β 1 and α -SMA. GW9662 administration antagonized the effect of rosiglitazone.

Conclusions: These data suggest that rosiglitazone attenuated PQ-induced pulmonary fibrosis by upregulating PTEN and downregulating TGF- β 1 expression in a PPAR- γ dependent manner.