

Role of renin-angiotensin system in a rat model of neonatal chronic lung disease

Chung-Ming Chen¹, Yaw-Dong Lang², Hsiu-Chu Chou³, Leng-Fang Wang⁴

Department of Pediatrics, Taipei Medical University Hospital¹, Graduate Institute of Medical Sciences², Department of Anatomy³, Department of Biochemistry⁴, Taipei Medical University, Taipei, Taiwan

Objectives: Oxygen toxicity plays an important role in the lung injury that may lead to lung fibrosis. Angiotensin II is a profibrotic mediator which induces human lung fibroblast proliferation. We investigated the effects of hyperoxia on the components of renin-angiotensin system (RAS) and collagen production and the therapeutic effect of angiotensin II type 1 receptor (AT1R) blocker in room air- and hyperoxia-exposed newborn rats.

Methods: Rat pups were exposed to 1 week of > 95% O₂ and a further 2 weeks of 60% O₂. AT1R blocker treated-rats received intraperitoneal injection of losartan 10 mg/kg/day during the first postnatal week and 5 mg/kg/day from postnatal 2-week to 3-week old.

Main Results: Hyperoxia significantly increased total collagen, type I collagen, and α -smooth muscle actin (α -SMA) expression when compared to room air-exposed rats on postnatal days 7 and 21. RAS components including angiotensinogen, angiotensin-converting enzyme, angiotensin II, and AT1R were significantly increased by hyperoxia whereas AT2R was not significantly different when compared to room air-exposed rats on postnatal days 7 and 21. Hyperoxia significantly increased extracellular signal-regulated kinase phosphorylation but did not affect the phosphorylation levels of p38 or c-Jun N-terminal kinase on postnatal days 7 and 21. Losartan significantly reduced total collagen and type I collagen and α -SMA expression when compared to room air-exposed rats on postnatal days 7 and 21.

Conclusion: Hyperoxia induces lung collagen production via the activation of RAS in newborn rats and losartan reduces lung collagen production. AT1R blocker may represent a novel therapeutic strategy for hyperoxia-induced lung fibrosis.