

Increased nitric oxide production accompanies blunted hypoxic pulmonary vasoconstriction in hyperoxic rat lung

高尚志

Yeh DY;Kao SJ;Feng NH;Chen HI;Wang D

摘要

Abstract

Hyperoxia may affect lung physiology in different ways. We investigated the effect of hyperoxia on the protein expression of endothelial nitric oxide synthase (eNOS) and inducible nitric oxide synthase (iNOS), nitric oxide (NO) production, and hypoxic pulmonary vasoconstriction (HPV) in rat lung. Twenty-four male rats were divided into hyperoxic and normoxic groups. Hyperoxic rats were placed in $> 90\%$ FIO₂ for 60 h prior to experiments. After baseline in vitro analysis, the rats underwent isolated, perfused lung experiments. Two consecutive hypoxic challenges (10 min each) were administered with the administration of a non-specific NOS inhibitor, N-nitro-L-arginine methyl ester (L-NAME), in between. We measured intravascular NO production, pulmonary arterial pressure, and protein expression of eNOS and iNOS by immunohistochemistry. We found that hyperoxia rats exhibited increased baseline NO production ($P < 0.001$) and blunted HPV response ($P < 0.001$) during hypoxic challenges compared to normoxia rats. We also detected a temporal association between the attenuation in HPV and increased NO production level with a negative pre-L-NAME correlation between HPV and NO ($R = 0.52$, $P < 0.05$). After L-NAME administration, a second hypoxic challenge restored the HPV response in the hyperoxic group. There were increased protein expression of eNOS (12.6 $\pm$ 3.1-fold, $n = 3$) (X200) and iNOS (8.1 $\pm$ 2.6-fold, $n = 3$) (X200) in the hyperoxia group. We conclude that hyperoxia increases the protein expression of eNOS and iNOS with a subsequent increased release of endogenous NO, which attenuates the HPV response.