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Title: Prevention of hyperoxia-induced lung injury: Counterbalancing the deleterious effects of endothelin-1 in rat lungs

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Body: RATIONALE: Endothelin (ET-1) plays a major role in the hyperoxia-induced pulmonary hypertension leading to lung damage. We determined the role of the nitric oxide NO/ET-1 pathway in the lung function decline changes following hyperoxia exposure in rats. METHODS: Airway resistance (Raw), respiratory tissue damping (G) and elastance (H) were obtained by forced oscillations at baseline condition and following incremental doses of iv methacholine (MCh) in 4 groups of 28-day-old rats. Animals were exposed for 3 days to: room air (Group C, n=6), hyperoxia (> 95% O₂, Group HC, n=5), hyperoxia with concomitant administration of vasoactive intestinal peptide (VIP 150 µg/kg/day ip, Group HV, n=4) or oral sildenafil citrate (20 mg/day, Group HS, n=4). RESULTS: Hyperoxia led to significant increases in G (38.66%, 62.63%, 38.41% in groups HC, HV, HS respectively, p<0.05) and in H (58.91%, 67.3%. 70.85%, p<0.05) in all groups, while Raw did not change. Airway hyperresponsiveness to MCh was observed in rats of Group HC, which was prevented by treatments with VIP or sildenafil.

CONCLUSIONS: These findings evidence the beneficial role of NO and VIP pathways in preventing the lung inflammatory response to hyperoxia and indicating their protective potentials against the subsequent development of airway hyperresponsiveness. Grant support: OTKA K81179. The first author is a laureate of the long-term ERS fellowship.