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Inhaled Nitric Oxide Selectively Reverses Human Hypoxic Pulmonary Vasoconstriction without Causing Systemic Vasodilation

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Background: **Nitric oxide (NO), an endothelium-derived relaxing factor, acts as a local vasodilator. The authors examined the effects of NO on pulmonary and systemic circulation in human volunteers.**

Methods: **Nine healthy adults were studied awake while breathing 1) air, 2) 12% O_2 in N_2, 3) followed by the same mixture of O_2 and N_2 containing 40 ppm of NO. Pulmonary artery and radial artery pressures were monitored.**

Results: **The Pa_{O_2} decreased from 106 ± 4 (mean ± standard error of the mean) while breathing air (21% O_2) to 47 ± 2 mmHg after 6 min of breathing 12% O_2. Concomitantly, the pulmonary artery mean pressure (PAP) increased from 14.7 ± 0.8 mmHg to 19.8 ± 0.9 mmHg, and the cardiac output (CO) increased from 6.1 ± 0.4 to 7.7 ± 0.6 L/min. After adding 40 ppm NO to the inspired gas while maintaining the $F_{I_{O_2}}$ at 0.12, the PAP decreased ($P < 0.01$, by analysis of variance) to the level when breathing air while the Pa_{O_2} and Pa_{CO_2} were unchanged. The dilation (or recruitment) of pulmonary vessels produced by inhaling NO during hypoxia was not accompanied by any alteration in the systemic vascular resistance or mean arterial pressure (MAP). The authors also examined the effects of inhaling NO while breathing air. Breathing 40 ppm NO in 21% O_2 for 6 min produced no significant changes of PAP, CO, Pa_{O_2}, MAP, or central venous pressure. Plasma endothelinlike immunoreactivity concentrations did not change either during hypoxia or hypoxia with NO inhalation.**

Conclusions: **Inhalation of 40 ppm NO selectively induced pulmonary vasodilation and reversed hypoxic pulmonary vasoconstriction in healthy humans without causing systemic vasodilation. (Key words: Anesthetics: nitric oxide. Heart: vascular pressures. Hormones: endothelin. Lung: vascular resistance, hypoxia. Muscle, smooth: endothelium-derived relaxing factor.)**

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IN 1987, it was reported that nitric oxide (NO) is an important endothelium-derived relaxing factor.[1–3] It is produced by the endothelium from arginine and acts as a local vasodilator, diffusing into subjacent vascular smooth muscle and combining intracellularly with the heme present in guanylate cyclase.[4,5] This activates the guanylate cyclase, resulting in an increased synthesis of the second messenger, cyclic guanosine 3′,5′ monophosphate and consequent relaxation of the smooth muscle cells.[5–7] It has been established that clinically used vasodilators, such as sodium nitroprusside and nitroglycerin, exert their effects by releasing NO intracellularly.[6–8]

We recently reported that inhalation of 5–80 ppm NO causes pulmonary vasodilation (*i.e.*, vascular relaxation with dilation and, possibly, recruitment) during pulmonary vasoconstriction caused by severe hypoxia (HPV) or an infusion with a thromboxane analogue in awake lambs.[9] In other awake lambs provoked to protamine-induced pulmonary hypertension after endogenous thromboxane release, pulmonary vasodilation was achieved when inhaling 180 ppm NO.[10] No systemic vasodilation occurred at these levels of inhaled

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