

TITLE: THE EFFECTS OF NITROUS OXIDE ON THE VENTILATORY RESPONSE TO SUSTAINED HYPOXIA IN MAN
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Low concentrations of inhalational anesthetics as well as the inhalation of 50% N₂O are known to depress the acute ventilatory response to hypoxia.^{1,2} The effects of 20% N₂O on the ventilatory response to prolonged (> 5 min) hypoxia is addressed in this study. Normally hypoxia causes an initial hyperventilation, followed after 5 min by a decrease in ventilation (V_E).³ In studying the effects of drugs on the hypoxic response it is important to investigate both the hypoxic ventilatory stimulation (HVS) and the hypoxic ventilatory decline (HVD).

Methods: Five healthy male subjects, mean age 24 yr, were studied after informed consent and local ethics committee approval. Each experiment consisted of a control hypoxic test, followed by a 30 min rest period. Then 20% N₂O was inhaled and at least 10 min later the hypoxic test was repeated. The hypoxic test consisted of a 5 min equilibrium period (P_{ET}O₂ 103 mmHg), followed by a rapid decrease in P_{ET}O₂ to 50 mmHg for 20 min. The P_{ET}O₂ was strictly controlled slightly

above resting values (40 to 46 mmHg among subjects) throughout each experiment. Each hypoxic test was followed by a 10 min period of breathing 100% oxygen.

Results. In the control experiments V_E increased from 11.6 ± 4.2 l/min (mean ± SD) to 18.8 ± 8.6 l/min initially with hypoxia and then declined significantly to 14.6 ± 6.4 (P < 0.01, ANOVA). In the N₂O experiments V_E increased from 11.2 ± 3.4 to 21.7 ± 10.0 initially and then decreased to 18.5 ± 7.2 (P < 0.05). Between groups HVS was not significantly different and was caused by an increase in tidal volume and respiratory rate. The HVD was significantly (P < 0.051) lower in the control period than during inhalation of 20% N₂O (P < 0.05). The lower HVD in the N₂O group was caused by a significant increase in respiratory rate against a small decrease in the control group. In both groups tidal volume decreased.

Discussion: Our results show that 20% N₂O inhalation does not change HVS but reduces the magnitude of HVD. The lower concentrations of N₂O that we used may explain why other studies^{1,2} found that N₂O decreased HVS. No data has previously been reported on the effects of N₂O on HVD. The decrease in HVD in our study may be caused by the stimulating effect of 20% N₂O on brain metabolism⁴ or release of catecholamines by N₂O.

1. Anesthesiology 45: 385-389, 1976
2. Can Anaesth Soc J 29: 93-99, 1982
3. J Appl Physiol 52: 1030-1034, 1986
4. Anesth Analg 65: 729-733, 1986

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TITLE: EFFECTS OF IBUPROFEN ON THE ENDOTOXIN-INDUCED INHIBITION OF THE PULMONARY PRESSOR RESPONSE TO HYPOXIA IN DOGS

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Introduction. Loss of hypoxic pulmonary vasoconstriction (HPV) response might be one of the cause of hypoxemia in an acute lung injury such as ARDS. The purpose of this study is to investigate the contribution of cyclooxygenase pathway products to inhibition of HPV response given the low-dose endotoxin in dogs.

Methods. Worm-free 12 mongrel dogs were anesthetized and the left lower lobe (LLL) was separately ventilated from the rest of the lung. Pulmonary artery pressure (PAP) and cardiac output (Qr) were measured by a thermodilution catheter. The blood flow to the LLL (Q_{LLL}) was measured with the electromagnetic flowmeter (Nihon-Kohden Co), and %Q_{LLL} was calculated as Q_{LLL}/Q_r × 100. The vascular pressure flow curve (P-Q curve) of the LLL was recorded by generating occluders placed around the both pulmonary arteries. The intensity of HPV response was evaluated as the changes of %Q_{LLL}, PaO₂ and the shift of P-Q curve when the inspired gas to the LLL was switched from hyperoxic (95%O₂+5%CO₂) to hypoxic (95%N₂+5%CO₂). In the group 1 (n=6), after baseline measurement, 10μg/kg of E.coli endotoxin (Difco) was given and the LLL was intermittently exposed to 30min hyperoxia and 15min hypoxia for 120min. In the group 2 (n=6),

75min after intravenous administration of 20mg/kg of Ibuprofen (Sigma), 10μg/kg of ET was given, and intermittent hypoxic challenges were repeated for 120min. Every data was obtained just before and end of each hypoxic phase and biological measurements; counts of leucocytes, serum 6-keto-PGF_{1α} and TXB₂ were also performed. ANOVA was used for repeated measurements and a p<0.05 indicated statistical significance.

Results. As shown in the table, HPV response in the control group was completely inhibited after ET although the 2nd response slightly recovered, but in the group of ibuprofen pretreatment HPV response was sustained after ET. The shift of P-Q curves indicated the same evidence. ET-induced increase in 6-keto PGF_{1α} from 175.5±27.1 to 332.8±84.1pg/ml was blocked by ibuprofen pretreatment from 204.8±41.0 to 217.1±60.4pg/ml. Decrease in leucocytes counts after ET were observed both in groups of the presence or absence of ibuprofen.

Conclusions. These results suggested that release of prostacyclin was involved with inhibition of HPV response by endotoxin.

	Group	Base line	Ibuprofen	Hypoxic challenges after 1st	Endotoxin 2nd
Changes in %Q _{LLL} (%)	1	76.6	---	5.2*	45.6*
	2	24.5	80.4*	25.6	111.5
		70.0	23.2	80.4*	69.0
Changes in PaO ₂ (%)	1	20.9	---	56.7*	41.8*
	2	22.0	18.1*	23.0	26.2
		29.1	23.8	20.8*	29.9

*: p<0.05 vs baseline