

TITLE: HYDRALAZINE DOES NOT INHIBIT HYPOKIC PULMONARY VASOCONSTRICTION

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Introduction. Constriction of pulmonary vessels in areas of alveolar hypoxia constitutes an important protective mechanism by which blood flow is diverted from unventilated and poorly ventilated lung units towards well ventilated lung units. Inhibition of this response by drugs such as nitroprusside and nitroglycerine has been shown to worsen hypoxemia in patients with abnormal lungs. Because of this inhibition, patients receiving vasodilators in the postoperative period because of hypertension and/or a need for afterload reduction may develop a worsening of their gas exchange. In an attempt to identify a drug which would produce systemic vasodilation with a minimum of pulmonary vasodilation, we investigated the effects of hydralazine on hypoxic pulmonary vasoconstriction (HPV) in the dog.

Methods. Seven mongrel dogs were anesthetized with intravenous pentobarbital 30 mg/kg, intubated, paralyzed with pancuronium .2 mg/kg and ventilated with an $F_{I}O_2$ of .30 to a $PaCO_2$ of 30-35. Each dog then underwent three 10 minute hypoxic challenges with an $F_{I}O_2 = .1$ with a return to an $F_{I}O_2 = .30$ for 10 minutes between challenges. Following this, the dogs received 1 mg/kg of hydralazine intravenously followed by a continuous infusion of .1 mg/kg/hour. Thirty minutes after the intravenous bolus dose, the 3 hypoxic challenges were again repeated. Systemic pressures were measured directly via a forepaw arterial line. Pulmonary artery and pulmonary artery wedge pressures were measured via Swan-Ganz catheter. Cardiac output was measured by thermodilution. Simultaneous mixed venous and arterial gases were drawn and temperature corrected and venous admixture was calculated by computer program.

Results. During the control period, hypoxia produced a significant rise in pulmonary vascular resistance (PVR) (Figure 1) with a mean rise from 235 ± 28 dyne \cdot sec \cdot cm $^{-5}$ to 482 ± 73 dyne \cdot sec \cdot cm $^{-5}$ ($p < .001$). After hydralazine was given, we noted the predicted cardiovascular effects of the agent during the normoxic periods; cardiac output increased from $3.18 \pm .12$ to $5.35 \pm .30$ liters/min ($p < .01$) while systemic vascular resistance declined from 3366 ± 140 to 1835 ± 97 dyne \cdot sec \cdot cm $^{-5}$. In the presence of hydralazine, the normoxic PVR showed a small decline (Figure 1). During hypoxic challenge in the presence of hydralazine, there continued to be a brisk response to hypoxia with a rise in PVR just as great as during the control period (Figure 1). After hydralazine, arterial oxygen tension remained unchanged despite a small increase in venous admixture. Mixed venous oxygen tension showed a marked rise after hydralazine, presumably due to the large increase in cardiac output.

Discussion. Hydralazine produces a marked peripheral vasodilation, as we have again documented, resulting in a significant increase in the cardiac output. Such increases in cardiac output may cause a decrease in calculated pulmonary vascular resistance on a passive basis in addition to any direct vasodilating

effects. However, this vasodilation did not prevent a brisk response to hypoxia, the rise in pulmonary vascular resistance during hypoxia remaining just as great after hydralazine as during the control period. These results are in marked contrast to our findings with another vasodilator, minoxidil, which produced a very marked inhibition of HPV when used in doses which produced a reduction in systemic vascular resistance comparable to that produced by hydralazine.

The vasodilation resulting from increased cardiac output may well have produced the small increase in venous admixture which we noted, and suggests that one runs some risk of increasing venous admixture with any pharmacologic intervention used to increase the cardiac output. Again, however, the effect is much less marked than has been found with comparable systemic vasodilation with other agents. Indeed, arterial oxygenation was well preserved despite the small rise in venous admixture because of the marked rise in mixed venous PO_2 after hydralazine.

This study suggests that hydralazine may be a useful drug to reduce systemic vascular resistance in patients at risk for hypoxemia.

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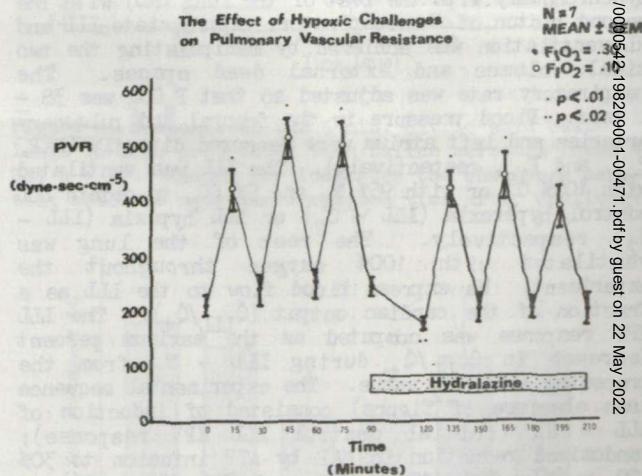


Figure 1: Response of PVR to hypoxia in the absence and present of hydralazine. Asterisks represent significant differences from value during immediate previous period of normoxia.

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