Title: EFFECTS OF FLOW ON HYPOXIC PULMONARY VASOCONSTRICTION (HPV)

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Introduction: It is believed that increasing pulmonary artery flow and/or pressure result in a reduction of hypoxic pulmonary vasoconstriction (HPV) (1,2). This concept is based on experiments undertaken in vivo where changes in cardiac output were accompanied by changes in both pulmonary artery and pulmonary venous pressures. The purpose of this experiment was to determine the effect of increasing lung blood flow on HPV when pulmonary venous pressure (PVP) was maintained constant.

Method: Isolated rat lungs, ventilated at the rate of 180 ml/min with 21% O_2, 5% CO_2, balance N_2, were perfused with a blood-PSS solution (oncotic pressure = 19.2 ± 4 cmH_2O) for 30 min, subsequently the lungs were intermittently stimulated for 5 min with an hypoxic gas mixture containing 3% Oxygen, 5% carbon dioxide. When two equal pulmonary pressor responses to hypoxia were obtained the baseline pressure was increased by increasing the flow. PVP was maintained at zero by lowering the level of the venous return. The lungs were again stimulated with 3% hypoxic gas mixture for 5 min. This procedure was continued until HPV responses were abolished. Pulmonary artery pressure (PAP), PVP, airway pressure, PO_2 PCO_2 were recorded on an 8-channel Grass recorder. Blood-PSS PO_2, PCO_2, pH, Hcrit, Hb, oncotic pressure and wet/dry weight of the lung were measured.

The hypoxic pressor responses were subjected to analyses of variance and the Neuman-Keul test.

Results: The mean general conditions of the animals were: weight 260 ± 21.02 gm, PCO_2 40.8 ± 1.4, pH 7.33 ± 0.02, Hcrit 19 ± 0.99, and the results in Table 1 are means ± S.E. for six rats.

As the flow increased the baseline, PAP increased but there were no significant differences in the pressor responses to hypoxia until the flow was increased six fold and the PAP was 57.2 ± 7.5 cmH_2O. At this point the response to hypoxia decreased significantly (Table 1). With any further increment of flow the airway pressures increased to over 30 cmH_2O and the lungs became visibly edematous and further stimulation with 3% hypoxic gas elicited no pressor responses. The water content of the lungs at 9.5 ± 1.6 ml/gm dry lung and were significantly greater than the water content of normal rat lungs (3.0 ± 0.02 ml/gm dry lung).

Table 1

Flow ml/Kg/min		57.6	103.6	203.5	280
PAP Normoxia cmH_2O	$\bar{X}$ ± SE	18.2 1.1	24.8 2.2	41.7 2.1	57.2 2.4
PAP Δ Hypoxia cmH_2O	$\bar{X}$ ± SE	10.5 1.1	14.3 2.2	12.0 2.1	7.0* 2.4
Pc cmH_2O	$\bar{X}$ ± SE	7.3 0.6	9.9 0.6	16.7 1.6	22.4 0.8

(*significantly different $p < 0.05$)

Discussion: This study has shown that the magnitude of the HPV response is not altered by flow or PAP changes until pulmonary edema occurs. The capillary hydrostatic pressure (Pc) calculated from Pc = 0.4 (PAP) was 22.4 ± 0.83 cmH_2O when the HPV response became reduced. The perfusate oncotic pressure was 19.2 cmH_2O and therefore the edema was of hydrostatic origin. Depression of HPV responses observed in previous studies were always associated with increased venous pressures and possibly pulmonary edema.

Conclusion: Increasing pulmonary artery flow and pressure do not impair HPV until flow is so increased as to induce hydrostatic pulmonary edema.

References:

1) Benumof JL, Wahrenbrock EA: J. Appl. Physiol. 38:846-850, 1975.
2) Marshall BE, Marshall C: J. Appl. Physiol. 49:189-196, 1980.

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