TITLE: THE EFFECTS OF DIFFERENTIAL LUNG PEEP ON HYPOXIC PULMONARY VASOCONSTRICTION IN OPEN-CHESTED DOGS

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Introduction. Hypoxic pulmonary vasoconstriction (HPV) regulates the pulmonary circulation to improve matching of ventilation and perfusion in regional lung disease, by diverting blood flow from hypoxic to normoxic regions (1). Unilateral lung PEEP increases blood flow to the contralateral lung (2). This change in pulmonary blood flow increases hypoxic lobe blood flow when PEEP is administered to normoxic lung regions and to the entire lung (3). The purpose of this study was to assess if the changes in hypoxic lung blood flow with regional and whole-lung PEEP are due to an alteration of HPV per se or to superimposed changes in pulmonary blood flow.

Methods. Six male dogs were anesthetized with pentobarbital and paralyzed with pancuronium. Each lung was ventilated separately through a Kottmier double lumen endobronchial tube to achieve normocapnia. Airway pressures were determined by the experimental sequence below. Left lung blood flow ($\dot{Q}_L$) and total cardiac output ($\dot{Q}_T$) were measured by electromagnetic flow probes placed around the left pulmonary artery and aorta. An hydraulic vascular occluder positioned around the inferior vena cava (IVC) and an arteriovenous (AV) fistula were used to alter cardiac output. Systemic and pulmonary arterial, right atrial, left atrial, and airway pressures; inspired, mixed expired, and end-tidal O_2 and CO_2 tensions; and arterial and mixed venous blood gas tensions were measured. The right lung was ventilated with 100% O_2 throughout the experiment. The left lung was alternately ventilated with 100% O_2 (normoxia phases) or with an hypoxic gas mixture (4% O_2, 3% CO_2, balance N_2) (hypoxia phases). Following demonstration of a stable HPV response, each animal was exposed to all experimental conditions. The study sequence began and ended with "No PEEP" control phases (5 cm H_2O bilaterally). 15 cm H_2O of PEEP was applied to right, left, or both lungs in a counterbalanced order in the middle of the sequence. The HPV response was tested in each phase with measurements obtained at the baseline cardiac output (CO) when the AV fistula was closed. The CO was then altered by occluding the IVC and opening the AV fistula in counterbalanced order; left pulmonary and aortic flows, pulmonary arterial and left atrial pressures were measured after 15 seconds. $PaCO_2$, pH, and temperature were controlled. Data were analyzed by a within-subjects two-way ANOVA (ventilation by PEEP) and Duncan post-hoc test. The slopes of the pressure-flow ($\dot{P}$-$\dot{Q}$) curves were determined by linear regression analysis and were compared by an ANCOVA. $P<.05$ was deemed significant. Means ± SE are shown.

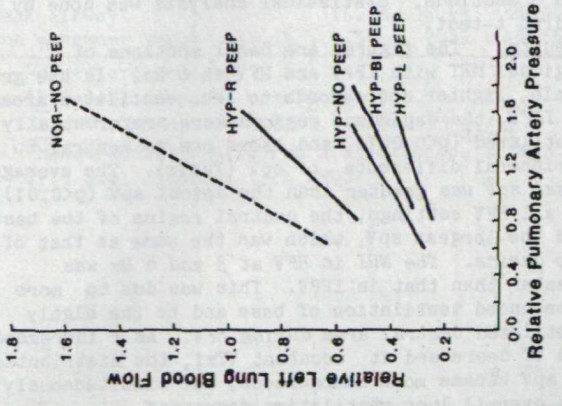
Results. Ventilation of the left lung with the hypoxic gas significantly reduced $\dot{Q}_L\%$ (expressed as percent of total cardiac output) from 40.8 ± 1.9% to 18.7 ± 2.6% during the No PEEP phase. PAP increased from 16.6 ± 1.2 to 19.3 ± 1.1 mm Hg. Ipsilateral lung PEEP increased contralateral lung blood flow (see Table). Hypoxic ventilation of the left lung reduced $\dot{Q}_L\%$, independent of PEEP. The two-way interaction of ventilation by PEEP was not significant. The ANCOVA revealed that hypoxic ventilation of the left lung significantly ($p<.001$) reduced the slopes of the P-Q curves independent of PEEP (see Figure: relative $\dot{Q}_L$ versus relative $\overline{PAP}$, compared to No PEEP normoxia controls).

Discussion. This study demonstrates that both PEEP and hypoxia independently alter pulmonary blood flow and that their effects are additive. The HPV response per se is not affected by unilateral or whole-lung PEEP in open-chested dogs. The study confirms that hypoxic lung blood flow is increased when PEEP is administered bilaterally and to the contralateral lung (3), and oxygenation is impaired. Hypoxia, independent of PEEP, reduces $\dot{Q}_L$ by an increase in pulmonary vascular resistance, as defined by a decreased slope on the $\dot{P}$-$\dot{Q}$ curves. This suggests that under the experimental conditions of this study, hypoxia reduces $\dot{Q}_L$ by increasing both Ohmic and Starling resistances (4).

References. 1) Marshall, Marshall: J Appl Physiol 49:189-196, 1980. 2) Fuhrman et al: J Appl Physiol 56:1439-1448, 1984. 3) Benumof et al: Anesthesiology 51:503-507, 1979. 4) Rock et al: J Appl Physiol 59:1891-1901, 1985.

	NO PEEP	RIGHT PEEP	LEFT PEEP	BILATERAL PEEP
$\dot{Q}_L\%$ Normoxia	40.8 ± 1.9	66.6 ± 4.6*	26.0 ± 2.9*	51.1 ± 3.1*
$\dot{Q}_L\%$ Hypoxia	18.7 ± 2.6	43.2 ± 5.7*	14.5 ± 2.2	28.6 ± 5.5*
$\overline{PAP}$ Hypoxia (mm Hg)	19.3 ± 1.1	23.6 ± 1.1*	19.8 ± 0.8	24.9 ± 1.1*
LAP Hypoxia (mm Hg)	8.6 ± 1.1	9.2 ± 0.5	10.0 ± 1.2	10.4 ± 0.6
$P\bar{v}O_2$ Hypoxia (mm Hg)	44 ± 1	39 ± 3*	43 ± 2	39 ± 2*
PaO_2 Hypoxia (mm Hg)	242 ± 35	147 ± 54*	279 ± 41	126 ± 20*
$\dot{Q}_T$ Hypoxia (ml/min)	1690 ± 160	1440 ± 100	1690 ± 17	1340 ± 130

*means $p < .05$ from respective NO PEEP controls



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