Title: DOES HYPOTHERMIA IMPROVE OXYGEN DELIVERY IN CANINE ASYMMETRIC PULMONARY EDEMA TREATED WITH PEEP?

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Introduction Although positive end-expiratory pressure (PEEP) is commonly used to manage patients with acute respiratory failure, systemic cooling to 32-34°C has also been found to be useful (1,2). However, there have been no studies on the effects of hypothermia on tissue oxygen delivery ($\dot{D}O2$) in experimental pulmonary edema. We studied those effects in a canine model of asymmetric pulmonary edema ventilated with 10 cm H2O PEEP. The study was approved by the Institutional Research and Animal Care Committees.

Methods To date, 12 mongrel dogs have been studied. Each was anesthetized with pentobarbital and succinylcholine, intubated, and ventilated with 40% inspired oxygen concentration. Catheters were placed in the femoral artery and vein, the left ventricle, and the pulmonary artery. Thermodilution was used to measure cardiac output (Qt), and arterial and mixed venous O2 tensions (PaO2, P$\bar{v}$O2) and saturations were measured. Intrapulmonary blood flow distribution was quantitated by radioactive microspheres; standard formulas were used to calculate $\dot{D}O2$, venous admixture (Qva/Qt), and tissue oxygen consumption ($\dot{V}O2$).

With the right lung dependent, the left main pulmonary artery was occluded for six minutes while oleic acid, 0.06 ml/kg, was administered through a central catheter. Two hours later, the dog was turned supine and 10 cm H2O PEEP was added to the expiratory circuit of the ventilator. Measurements were taken 30 minutes later, and the dog was then randomized for normothermia (n = 5; 37±1°C) or hypothermia (n = 7; 32±1°C). Hypothermia was induced by systemic cooling with topical and intraabdominal ice packs. All measurements were repeated 30 minutes later.

Intrapulmonary blood flow distribution and the degree of edema (by percent water content) were quantitated in four lung regions (left high, left low, right high, and right low) using the mid-left atrium as a horizontal dividing line. Data were analyzed by analysis of variance.

Results Our model produced asymmetric injury, with the right lung having greater water content than the left lung (normothermia: 87.5±0.4% vs 82.9±0.9%; $p < 0.001$) (hypothermia: 87.1±0.8% vs 82.4±0.8%; $p < 0.001$). Water content did not differ between the high and low regions on each side.

With hypothermia, there was a 15% reduction in Qt ($p < 0.01$), and a 16% commensurate decrease in $\dot{D}O2$ ($p < 0.02$) (Table 1). $\dot{V}O2$ was reduced by 32% ($p < 0.01$), and PaO2 and P$\bar{v}$O2 were increased slightly. The ratio of $\dot{D}O2$ relative to $\dot{V}O2$ increased from 1.96±0.05 to 2.49±0.20 ($p = 0.026$). With normothermia, there were no significant changes among these variables. Mean pulmonary artery pressure remained unchanged in normothermic (16±2 vs 17±1 mmHg) and hypothermic animals (17±2 vs 16±2 mmHg); Qva/Qt and intrapulmonary distribution of blood flow did not change in either group. There was no detrimental effect of hypothermia per se on lung water content.

Table 1. Response to Temperature Variation (mean ± SEM)

	Normothermia		Hypothermia	
	before	after	before	after
PaO2 (mmHg)	121±9	126±14	120±13	154±22
P$\bar{v}$O2 (mmHg)	31±1	34±1	31±1	35±2
Qt (L/min)	1.4±0.2	1.5±0.3	1.3±0.1	1.1±0.1*
$\dot{D}O2$ (ml/min)	291±25	283±21	223±11	188±14*
$\dot{V}O2$ (ml/min)	145±13	134±13	114±6	77±7*
Qva/Qt (%)	8.6±3.8	10.1±3.1	13.4±3.9	15.7±6.9

* $p < 0.02$ compared with preceding value

Discussion By the Fick equation, any beneficial effect of hypothermia on $\dot{D}O2$ assumes that $\dot{V}O2$ decreases more than Qt so that P$\bar{v}$O2 and PaO2 increase. However, hypothermia increases vascular resistance in normal pulmonary vessels (3) and attenuates hypoxic pulmonary vasoconstriction (4). In addition, any therapy that augments PvO2 may increase Qva/Qt. Therefore, the risks of increasing hypoxemia from increasing Qva/Qt may exceed any benefit derived from reduced metabolic demands.

In our model of asymmetric pulmonary edema treated with PEEP, hypothermia significantly decreased Qt and $\dot{D}O2$ by similar amounts, with an even greater reduction in $\dot{V}O2$. We conclude that hypothermia does not increase Qva/Qt or lung water in injured or noninjured lung regions, and that hypothermia decreases $\dot{D}O2$ to a lesser extent than $\dot{V}O2$, so that the oxygen supply:demand ratio is improved.

This study was funded in part by the American Lung Association, North Carolina Affiliate.

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