

Title: RITODRINE DOES NOT INCREASE LUNG CAPILLARY PERMEABILITY IN SHEEP

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**Introduction.** Ritodrine given for premature labor may precipitate pulmonary edema. The mechanism is unknown, but may be due to increased lung capillary permeability. To identify the cause, Hauth and Hankins et al (1,2) studied pregnant baboons, and found that ritodrine did not increase lung water. However, their technique (the indicator dilution method) is indirect, and may be inaccurate.(3) They also used anesthetized animals. Therefore, we studied the effect of ritodrine on lung capillary permeability, using the more direct extravascular fluid to blood free dry weight (EVF) method, using unanesthetized sheep.(4)

**Methods.** Twenty-four non-pregnant sheep were prepared with left atrial balloons (LAB) and catheters in the pulmonary artery, left atrium, and femoral artery and vein. Pulmonary capillary pressure (Pc) was estimated as the average of left atrial and pulmonary artery pressures. In 12 controls, either baseline (BL) was studied, or the LAB was used to raise Pc to +5 or +10 mm Hg above plasma oncotic pressure ( $\pi_c$ ). After three hours, we estimated the lung EVF. The same experiment was done in six sheep two hours after 1 mg/kg of E. coli endotoxin, and also in seven sheep during ritodrine infusion (15 mcg/kg/min). Difference of EVF's from control at each Pc- $\pi_c$  was compared by the t-test.

**Results.** The relationship of EVFs vs Pc- $\pi_c$  was as follows (mean  $\pm$  S.D.):

	Pc- $\pi_c$ (mm Hg)		
	BL(-10)	+5	+10
Control	4.0 $\pm$ .2	4.3 $\pm$ .1	4.5 $\pm$ .1
Endotoxin	4.0 $\pm$ .2	5.0 $\pm$ .2*	
Ritodrine	4.0 $\pm$ .1	4.3 $\pm$ .4	4.3 $\pm$ .2

\* Significant difference from control at the indicated Pc- $\pi_c$

Endotoxin EVF was greater than control at Pc- $\pi_c$  = 5 mm Hg ( $p < 0.05$ ), but not at baseline. Ritodrine EVFs were not greater than controls at each Pc- $\pi_c$ .

**Discussion.** The major determinants of lung extravascular water are Pc (forcing fluid into the lungs), and  $\pi_c$  (drawing fluid out of the lungs). The relationship of EVF to Pc- $\pi_c$  (Table 1) provides a good index of lung capillary permeability; thus, in controls, the capillary membrane is impermeable enough that  $\pi_c$  prevents excess fluid accumulation. After endotoxin, lung EVF increases at a lower Pc- $\pi_c$  because of greater lung capillary permeability. After ritodrine, EVF's were not greater than controls at each Pc- $\pi_c$ , indicating that in our experiments, there is no evidence that ritodrine increased lung capillary permeability. Further studies to determine the mechanism of ritodrine-induced pulmonary edema are indicated, especially in pregnant sheep, because optimal therapy would depend on the mechanism.

**References.**

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