

Title: EFFECTS OF CYCLOOXYGENASE INHIBITION WITH INDOMETHACIN ON SURFACTANT-DEFICIENT LUNG INJURY.

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INTRODUCTION: Ventilation of a surfactant deficient lung created by repetitive lung lavage produces poor gas exchange, pulmonary hypertension and a large protein leak into the lung. Pathologically there is atelectasis, hyaline membrane formation and marked neutrophil infiltration. Prior neutrophil depletion protects the lung from these injuries - but the protection can be lost by re-infusion of small numbers of neutrophils ¹. This study shows that part of the adverse effect of neutrophils may be mediated by cyclooxygenase products.

METHODS: Ten adult rabbits were anesthetized and ventilated. Femoral and pulmonary arterial lines were inserted. Five rabbits were given 1 mg/kg i.v. Indomethacin (Indo.) All rabbits were lung lavaged x 5. ¹²⁵I-Albumin was given i.v. All rabbits were ventilated for 4 hrs in an identical manner. PaO₂, PvO₂, mean pulmonary arterial pressure (PAP) and peripheral neutrophil count were measured serially. After sacrifice the lungs were again lavaged and ¹²⁵I-Albumin and neutrophils measured.

RESULTS: Indo. prior to lavage abolished pulmonary hypertension ($p < 0.05$) (Fig 1). It also reduced the shunt ($p < 0.05$) (Fig 2). ¹²⁵I-Albumin leak was high in both groups. There was no neutropenia after Indo. and significantly fewer neutrophils recovered from the lavage fluid. (Control: $62 \times 10^6 \pm 4 \times 10^6$ /dl; Indo. $41 \times 10^6 \pm 5 \times 10^6$ /dl).

DISCUSSION: Increases in PAP following lavage can be prevented by Indo. implicating prostanoids as mediators of pulmonary hypertension. Indo. pre-treatment improves shunt, reflecting either diminished edema due to abolition of pulmonary hypertension or direct effects of prostanoids on gas exchange. Prostanoids do not seem to mediate increased permeability since Indo. pre-treatment does not affect protein leak. Finally, lack of neutropenia and diminished neutrophils recovered in the final lavage fluid in Indo. rabbits suggest that decreased neutrophil margination and activation may be responsible for the beneficial effects of Indo.

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REFERENCE:

1. Kawano T. et al. The effect of granulocyte depletion in a ventilated surfactant depleted lung. J. Appl. Physiol. 62:27-33, 1987

Fig.1: Indo. prevents increases in pulmonary artery pressure (PAP) after lavage (AL).

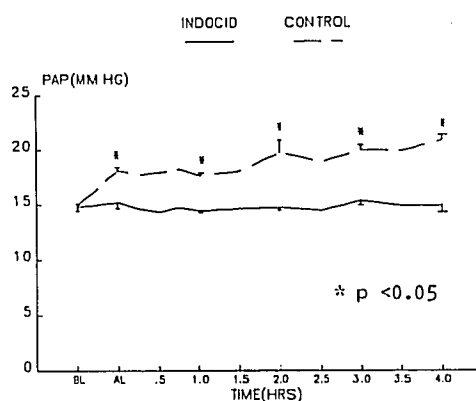


Fig.2: Shunt (Q_s/Q_t) is lower in Indo. animals after lung lavage (AL).

