Title : EFFECT OF LUNG INJURY ON PULMONARY OXYGEN TOXICITY

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Introduction. Exposure to high inspired concentrations of oxygen is known to cause diffuse pulmonary injury. The injury is characterized by an early exudative phase in which fluid accumulates in the lung,[1] followed by fibrosis and healing. It has previously been shown[2] that pre-existing diffuse lung injury caused by oleic acid prevents or retards the development of pulmonary oxygen toxicity in animals breathing 100% oxygen. The following experiments were done to determine if 80% oxygen caused an exudative type of pulmonary injury, and whether pre-existing injury by oleic acid would modify the response to 80% oxygen. The methods were designed to measure extravascular, extracellular lung water (EVECW) and the concentration of ^{131}I-albumin (RISA) in EVECW as a measure of pulmonary vascular permeability.

Methods. Experiments were performed in rabbits, 2.5-3.5 kg of both sexes. Group 1 animals with normal lungs were maintained in an atmosphere of 80% O_2:20% N_2, and then sacrificed after 1 (n=4), 2 (n=4), 3 (n=4), and 5 days (n=5). Group 2 animals received oleic acid, 0.12 ml/kg intravenously, and then were maintained in 80% O_2:20% N_2 until sacrificed at 4 (n=7), 5 (n=4, or 7 days (n=8). Group 3 animals received oleic acid, 0.9-0.12 ml/kg intravenously, then breathed room air until sacrificed at 1 (n=7), 2 (n=6), 3 (n=7) or 5 days (n=9). ^{24}Na-NaCl and ^{131}I-albumin (RISA) were injected intravenously two and five hours respectively prior to sacrifice. Previous studies had shown steady-state levels of isotopes in plasma and lung one and four hours respectively, after injection. Animals were sacrificed with pentobarbital, 60 mg intravenously. The amount of water, blood and isotope was determined in excised lungs from each animal. EVECW (ml/gm dry lung) was calculated from the [^{24}Na cpm/gm dry lung]/[^{24}Na cpm/ml plasma]. The apparent concentration of RISA in EVECW compared to plasma ($[RISA]_L/[RISA]_{Pl}$) was obtained from [RISA cpm/gm dry lung/ ^{24}Na cpm/gm dry lung]/[RISA cpm/ml plasma/ ^{24}Na cpm/ ml plasma].

Results. The results are shown in Fig. 1 and 2.

Discussion. The effects of breathing 80% O_2:20% N_2 alone, manifested as an increase in EVECW, and RISA concentration in EVECW, are significant by 5 days. Oleic acid injury alone, breathing room air, caused an acute vascular injury with high concentrations of RISA in EVECW which appeared to have healed after three days. When animals were exposed to 80% O_2 following oleic acid injury, there was no significant additional effect of 80% O_2 compared to oleic acid treated animals breathing room air at five days, or at seven days when compared to normal control values previously obtained in our laboratory. These experiments demonstrate that an 80% O_2 environment may cause a significant increase in EVECW in normal rabbits. This acute exudative response may be prevented by pre-existing diffuse vascular injury and may partially account for the protective effect of pre-existing lung injury in delaying or preventing the onset of pulmonary oxygen toxicity.

Supported by NIH Young Investigators Award #HL/GM21050 & NIH #HL20612-02.

References.

1. Kapanci Y et al.: Pathogenesis of reversibility of pulmonary lesions of O_2 toxicity in monkeys. Lab Invest 20:101, 1969

2. Smith G, Winter PM, Wheelis RF: Increased normobaric oxygen tolerance of rabbits following oleic acid induced lung damage. J Appl Physiol 35:395, 1973

FIGURE 1

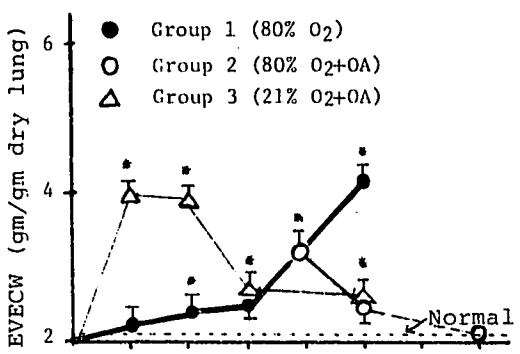
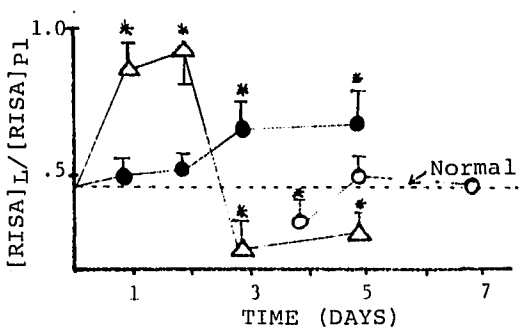


FIGURE 2



*p<.05 compared to "normal" values established in our laboratory