Lung Thermal Volume in Pulmonary Edema:
Effect of Positive End Expiratory Pressure

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Effects of intermittent (IPPB) and positive end-expiratory pressure (PEEP) ventilation on accumulation of pulmonary edema were compared, in dogs, after infusion of oleic acid. Pulmonary extravascular water was approximated as lung thermal volume (LTV), a double indicator method based on differential transit time for simultaneously injected right-to-left conductivity and thermal pulses. LTV was found to be decreased in animals treated with PEEP. The possibility that observed LTV changes reflect only the effect of PEEP on flow distribution, not lung water, was examined by alternating PEEP and IPPB; short-term changes in LTV did not occur. Mean values of other factors influencing pulmonary water transfer, e.g., pulmonary capillary wedge pressure, serum protein, arterial blood gasses, were not significantly different with or without PEEP. It was concluded that, for the oleic acid lesion, PEEP effects a small reduction in the rate of accumulation of pulmonary edema.

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VENTILATION with positive end-expiratory pressure (PEEP) improves gas exchange in experimental pulmonary insufficiency.[13] In man, PEEP is an accepted treatment when intermittent positive pressure ventilation (IPPB) does not achieve satisfactory arterial oxygen saturation at an acceptable inspired oxygen concentration.

Pulmonary insufficiency in surgical patients, while often of mixed or uncertain etiology, is characterized functionally by atelectasis, venous admixture, and edema. PEEP may influence all of these. Its favorable effects include increased functional residual capacity, tending to prevent small airway and alveolar collapse when interfacial forces are abnormal. Its effect on edema is less certain. Pulmonary extravascular water (PEVW) has been found both increased[4] and unchanged[1,8] by PEEP. The question of PEEP's effect on pulmonary extravascular water is clouded by three problems: incomplete understanding of the mechanism of edema formation in the lungs, lack of a completely satisfactory animal model of clinical pulmonary insufficiency, and the difficulties associated with in vivo measurement of PEVW. Measurements by the Chinard double indicator method[3] account for only about 60% of the water that can be found by direct weighing, require large sampling volumes, and are not frequently repeatable. A recently introduced variation employs thermal and conductivity indicators[2,11] to measure lung thermal volume (LTV). Frequent repetition is possible and correlation with weighed lung water reasonably good. The purpose of this study is to compare changes in LTV, with and without PEEP, in dogs with pulmonary insufficiency induced by oleic acid.

Methods

Two sets of experiments were done using 12 dogs. Lung damage was induced by infusion of oleic acid (0.1 ml/kg) into the pulmonary artery. Of the ten dogs used in the first set of studies, five were treated with PEEP, five with intermittent positive pressure breathing (IPPB). Serial measurements of lung thermal volume (LTV) were made in all.

Each animal was anesthetized with pentobarbital (30 mg/kg IV). An esophageal balloon was placed, orotracheal intubation performed with a cuffed side-tap tube,

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a Swan-Ganz catheter floated into the pulmonary artery, and the thermistor-conductivity catheter passed from femoral artery to infradiaphragmatic aorta. Pressure measurements were made with appropriate strain gauges. Dogs in the IPPB group were ventilated with a Harvard respirator set for a 15 ml/kg tidal volume. For the PEEP group the respirator outflow tube was placed under water to maintain end expiratory airway pressure at 10 cm H_2O. The dogs were in the right lateral position except during oleic acid infusion. When the animals were stable on the ventilator, control measurements were made of LTV, esophageal, arterial, pulmonary artery, and pulmonary artery wedge pressures; blood samples were taken for arterial blood gas tension and total plasma protein. Then, with the animals supine, oleic acid (0.1 ml/kg in four minutes) was injectead into the right atrium. After 5 minutes the animal was returned to the lateral position. For the next 2 hours, LTV was measured in triplicate every 20 minutes, pressures every 30, and blood sampling repeated hourly. Supplemental oxygen was given some dogs in the IPPB group (F_IO_2 <50%) to avoid extreme hypoxemia. After two hours the dogs were sacrificed by injecting 20mEq of KCl into the right atrium. The chest was opened, the bronchi clamped, and the lungs removed and drained of blood by gravity. The lungs were weighed, dessicated to constant weight, and the weight difference taken to be weighed lung water (WLW).

In the second experiment, two dogs were used to determine whether rapid changes in LTV occur after end expiratory pressure is increased. It was reasoned that the smaller LTV associated with PEEP in the first group of animals might reflect changes in regional perfusion of the lungs. Experimental conditions were the same except that periods of IPPB and PEEP were alternated; LTV was measured frequently after each transition.

LTV, in all instances, was measured by injection of 10ml of room temperature NaCl solution into the right atrium. Dilution curves for temperature and conductivity were sensed by the thermistor and conductivity cells at the tip of the arterial catheter and recorded on analogue magnetic tape. Mean transit time for each indicator was calculated; their difference, less thermistor time constant, was multiplied by cardiac output obtained from the thermal dilution curve to give lung thermal volume.

Mean LTV in each group was examined for difference using Student's *t*-test. Regression equations were developed for LTV from control to 120 minutes and the slopes evaluated by analysis of covariance.

Results

Gross and microscopic examination of the lungs showed marked hemorrhagic edema. Pulmonary capillary wedge pressure remained low. Mean wedge pressure (± SEM) for IPPB dogs was 6.5 ± 0.6 cm H_2O at two hours; with PEEP, it was 7.6 ± 2.6. These group means were not significantly different by Student's *t*-test and no difference was found by covariance analysis. Significant intergroup differences were not found for serum protein, initially 5.5g% in the IPPB group and 5.4 in the PEEP group, falling to 4.8g% in both at the end of the experiment. Mean arterial PO_2 for the two groups was not significantly different (supplemental oxygen was used with the IPPB group).

Figure 1 shows the observed sequence of changes in cardiac output and LTV. After one hour, cardiac output tended to be lower in PEEP, but the difference was not significant.

Measurements of LTV were at first normal and identical in both groups. Divergence began after 20 minutes (Fig. 1). Mean values at two hours were 18.5 ± 3.2 ml/kg for PEEP and 22.5 ± 2.6 for IPPB. Covariance analysis of the regression of values from control to 120 minutes showed differences both in slope ($P<0.05$) and in mean values ($P<0.001$).

Mean weighed lung water, expressed as g per kg body weight, was 19.2 ± 0.6 for IPPB and 19.9 ± 1.6 for PEEP. No correction was made for intravascular water.

Figure 2 shows results from the second group of experiments where LTV was measured while ventilation was changed from IPPB to PEEP and back to IPPB. The expected pattern of change in LTV was seen: a small decrease early after oleic acid infusion followed by a more or less linear rise to values greater than twice control. However, rapid changes in LTV with changes in ventilator conditions were not seen.

Discussion

Pulmonary extravascular water was the variable of interest in these experiments but lung thermal volume was the variable actually measured. The correlation of LTV with weighted lung water is good ($r = 0.99$) when the two are compared in canine lungs made edematous by Dextran and epinephrine.[2] Direct validation of LTV as a measure of WLW is not as easy for lungs with the hemorrhagic lesion produced by oleic acid infusion. This model of pulmonary insufficiency was used here because it is a closer analogue of the low pressure pulmonary edema commonly treated with PEEP. A problem associated with use of this model is difficulty in correction of wet-dry weight differences for residual intravascular water. The usual method for correction is tissue hemoglobin determination, not reliable when the lung contains extravasated red cells. In the present experiments the mean values of WLW for the PEEP and IPPB groups were not significantly different, but without correction these weights are imprecise and do not of themselves allow any conclusion as to the effects of PEEP on PEVW.

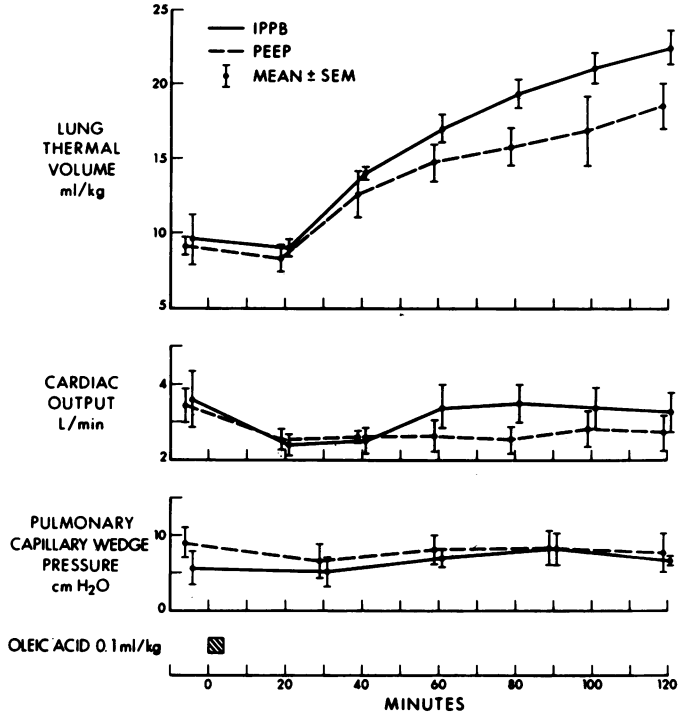

FIG. 1. Mean (± SEM) values for each group. LTV begins to increase 20 minutes after injection; the increase is larger in the IPPB group. Cardiac output tends to be lower in the PEEP group, but the difference not significant.

Interpretation of measurements of LTV depends on the degree to which they approximate PEVW. They are not identical. One source of error is inclusion of nonaqueous tissue in LTV; it is small and should be the same in both groups of dogs.

Another systematic error might be caused by variation in regional flow. No double indicator technique detects water in nonperfused areas of the lung. Although the data of Fig. 1 show LTV to be greater with IPPB than with PEEP, the difference could be only apparent if flow distribution is changed by PEEP. However, if the difference is due to changes in perfusion, alternating PEEP and IPPB should cause rapid reversible changes in LTV. No short time constant changes were seen in the data of Fig. 2, and although it is likely that larger variations in airway pressure or cardiac output might change LTV without real change in lung water, under the conditions of this experiment their effect appears to be small, leading us to conclude that for dogs with the oleic acid lesion, formation of pulmonary edema is retarded by positive end-expiratory pressure.

Several mechanisms can influence movement of water across pulmonary capillaries. The Starling hypothesis states that water transfer follows the balance of osmotic and hydrostatic pressures; it remains a hypothesis because not all forces involved are directly measurable, particularly the osmotic and hydrostatic components of intersitital pressure and the pressure within the pulmonary capillary. Guyton[7] first suggested that interstitial hydrostatic pressure is negative, demonstrating it in dogs with implanted subcutaneous capsules.[6] He further showed that in edematous tissue interstitial pressure increases at least 6-9 mmHg.[5] Levine[10] produced pulmonary engorgement and edema in dogs by changing pulmonary capillary hydrostatic and oncotic pressures, and then calculated normal pericapillary hydrostatic pressure to be -9 mmHg. PEEP increases FRC and hence increases interstitial pressure; this mechanism would favor movement of water out of the lungs.[9] PEEP, however, also increased intrapleural pressure, which may change

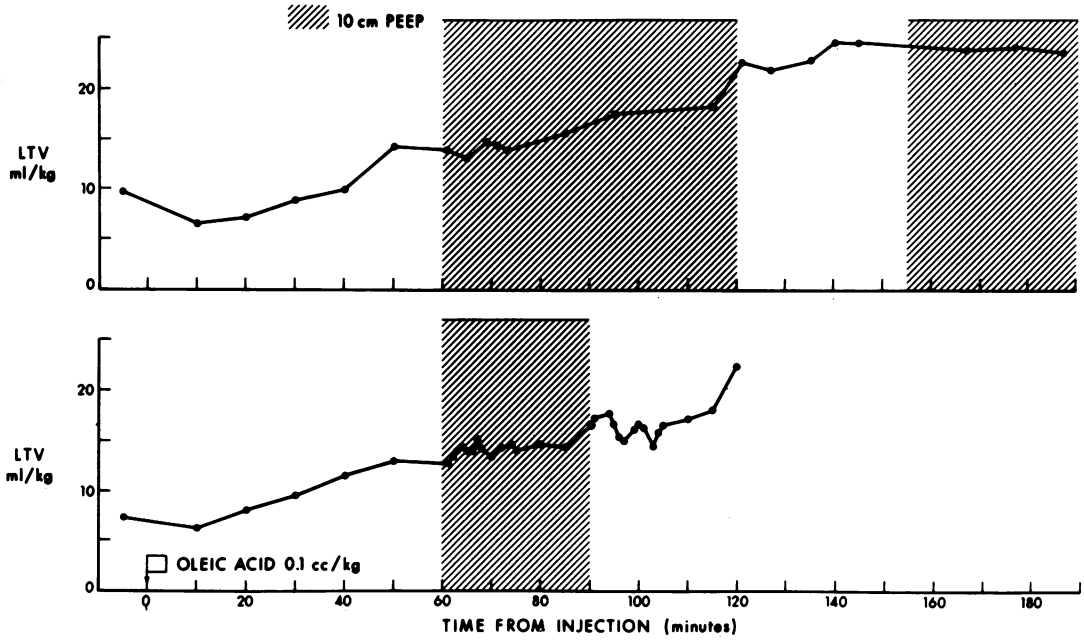

FIG. 2. Sequential measurement of LTV made in 2 dogs, both maintained on IPPB except during intervals shown hatched: here, 10 cm H_2O end-expiratory pressure was added.

the dynamics of pulmonary transfer in several other ways. Permutt[12] observed increased pulmonary capillary pressure with positive breathing; he likened flow from these relatively high pressure vessels to the low pressure left atrium to a waterfall. If respiratory conditions allow transmission of pulmonary venous hypertension to the pulmonary capillary, then pulmonary interstitial pressure should tend to increase. Effects on the right heart, notably reduced right atrial filling, are usually emphasized in explaining the circulatory effects of PEEP, possibly because small pressure changes seem most significant in a low pressure system. Permutt has called attention to an additional mechanism resulting from increased intrapleural pressure effects on the left heart, pointing out that if intrapleural pressure is less negative, transmural pressure is decreased; with reduced left ventricular afterload left atrial pressure falls, and to the extent that left atrial pressure is transmitted to the pulmonary capillary the hydrostatic gradient for water transfer changes toward reduction of lung water. In other words, a rationale can be found for either increased or decreased lung water with PEEP; in the model used here, it appears to effect a small reduction.

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