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The Effect of Unilateral PEEP on Gas Exchange and Pulmonary Perfusion in Canine Lobar Pneumonia

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Positive end-expiratory pressure (PEEP) has little beneficial effect in improving gas exchange in canine left lower lobe (LLL) pneumonia. This is true because while PEEP improves lobar gas exchange, it also increases relative perfusion (Q_L) to the diseased lobe. The authors hypothesized that PEEP administered to only the diseased lung would avoid the increased Q_{LLL}. Six dogs with LLL pneumonia in which PEEP was applied only to the left lung were observed. The dogs were studied supine and each lung was ventilated separately with 100 per cent O_2. Measurements of arterial oxygen tension (Pa_{O_2}), shunt ($\dot{Q}_s/\dot{Q}_t$) and lobar distribution of pulmonary perfusion were made before, during, and after 12 cm H_2O PEEP. Changes in Q_{LLL} expressed as per cent of cardiac output were determined using radiolabeled microspheres. PEEP improved Pa_{O_2} from 310 ± 86 to 532 ± 58 torr and $\dot{Q}_s/\dot{Q}_t$ from 29 ± 5 per cent to 12 ± 5 per cent, returning after PEEP to 337 ± 84 torr and 26 ± 5 per cent, respectively. Q_{LLL} per cent did not increase during PEEP. These results suggest that unilateral PEEP improves regional gas exchange within the pneumonia lobe, probably by ventilating units which were previously perfused but not ventilated. Further, this improvement in regional gas exchange occurred without the diversion of blood flow towards consolidated lung that occurs with whole-lung PEEP, and so resulted in a substantial net improvement in overall gas exchange. (Key words: Lung: pneumonia; shunting. Measurement techniques: microspheres. Oxygen: blood levels. Ventilation: positive end-expiratory pressure.)

POSITIVE END-EXPIRATORY PRESSURE (PEEP) improves arterial oxygenation in diffuse lung diseases such as the adult respiratory distress syndrome.[1,2] It is less effective in localized lung diseases like pneumonia. Kanarek and Shannon[3] noted a deterioration in overall gas exchange when PEEP was used to treat refractory hypoxemia in a case of unilateral pneumonia. An angiographic study of this case suggested that this was due to diversion of pulmonary blood flow towards the diseased lung. In a study of the effects of PEEP in a canine model of lobar pneumococcal pneumonia, we also observed an increase in perfusion to diseased lung with PEEP.[4] Although the pneumonia lobe had a reduced shunt with PEEP, there was no improvement in overall gas exchange because blood flow increased to the pneumonia region. The increased perfusion of the pneumonia lobe on PEEP could result from reduced pulmonary vasoconstriction in this region or to a greater mechanical compression of the vessels in the normal lung.

Several case reports[5–8] suggest that PEEP applied only to the abnormal lung might improve gas exchange when the lung disease is worse on one side. Based on our earlier study, we hypothesized that unilateral PEEP would improve gas exchange in the pneumonia lobe but would not divert blood flow from the normal to abnormal lung. Such effects would improve oxygenation and would also imply that the diversion of blood flow seen in our previous dog study was due to differential mechanical compression of blood vessels in normal and abnormal lung, rather than to a vasoactive mechanism related to improved local oxygenation. The present study was designed to describe and explain the effects of differential PEEP on overall gas exchange and on pulmonary perfusion distribution in a canine model of lobar pneumococcal pneumonia.

Methods

Animal Preparation

Six mongrel dogs weighing 25–30 kg were anesthetized with pentobarbital (30 mg/kg), ventilated with air via an endotracheal tube using a constant volume respirator (Harvard® 607) at a tidal volume of 20 ml/kg and a respiratory rate of about 15/min. A chest roentgenogram was obtained and esophageal temperature was taken to ensure absence of significant lung disease. We then passed a fiberoptic bronchoscope into the left lower lobe bronchus and injected an inoculum of *Streptococcus pneumoniae* Type III, prepared as previously described.[9] The dogs were then extubated and returned to their cages where they awakened 6–8 h later.

Forty-eight hours later, the dogs were brought back

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to the laboratory and anesthetized and ventilated as before. Lobar pneumonia was then confirmed by chest roentgenogram. A tracheostomy was performed and a double-lumen Kottmeier endotracheal tube (Roesch Co.) passed into the trachea, wedged at the carina and the balloon inflated. Each lung was ventilated with a tidal volume of 10 ml/kg using two volume-cycled ventilators. Separate ventilation of the two lungs was demonstrated by recording no pressure change in the expiratory line of each lung during ventilation of the other and absence of bubbles when one lung was ventilated while the tube to the other was placed under water.

A catheter placed in a femoral artery and connected to a pressure transducer (Statham® P23 AC) provided samples of arterial blood and continuous measurement of systemic arterial pressure. ($P_{\overline{sa}}$). Another catheter was placed in the femoral vein and used for phlebotomy or fluid infusion as necessary and for injecting additional pentobarbital to maintain anesthesia. A thermistor-tipped Swan-Ganz catheter connected to a pressure transducer (Statham® P23 BB) was introduced into an exposed jugular vein, advanced with continuous pressure monitoring and manipulated until both mean pulmonary artery pressure ($\overline{PAP}$) and mean pulmonary wedge pressure ($\overline{PWP}$) could be obtained. In addition to providing pressure measurements and samples of mixed venous blood, this catheter was connected to a cardiac output computer (Columbus Cardio Therm 500®) for measurement of cardiac output (CO).

A second Swan-Ganz catheter was advanced through the same vein into the right atrium and used to inject 3-ml boluses of room temperature saline for measurement of CO and to inject radiolabeled microspheres for determination of relative lobar perfusion. Airway opening pressure (P_{ao}) in each lung was measured with a pressure transducer (Statham PM5) connected to both sides of the endotracheal tube. All pressure signals were displayed on an 8-channel recorder (Beckman).

Before the initial series of measurements, respiratory rate was adjusted to bring arterial *p*H to 7.35–7.45. Body temperature was maintained within 1°C of the initial measurement throughout the study using heating pads applied to the abdomen.

Experimental Protocol

After all measurement devices were in place, approximately one liter of 6 per cent Dextran 75 was infused into the femoral vein catheter and after a brief equilibration period, a phlebotomy of about 0.6–0.8 l was performed. This blood was heparinized and saved for later infusion. Thirty minutes later, baseline measurements (C_1) were made of $\overline{PAP}$, $\overline{PWP}$, $P_{\overline{sa}}$, CO, arterial P_{O_2}, intrapulmonary shunt ($\dot{Q}_s/\dot{Q}_t$), and distribution of pulmonary perfusion. PEEP (12 cm H_2O) was then added to the expiratory line of the left lung ventilator. This usually produced a prompt reduction in CO. Over the next 15 min, CO was measured repeatedly while the saved blood was reinfused until triplicate CO measurements approximately matched the value obtained before PEEP. After another 30-min equilibration period, the measurements of central hemodynamics, gas exchange, and perfusion distribution were repeated. PEEP was then removed from the left lung ventilator, CO again adjusted to baseline levels by phlebotomy, and a third set of measurements made (C_2). After the final set of measurements the dogs were heparinized and exsanguinated, and the lungs were excised. The lobes were separated, placed in beakers, and weighed. Pneumonia was confirmed histologically and by culture as previously described.[9]

Gas Exchange Measurements

All measurements were made during ventilation of both lungs with 100 per cent oxygen. Samples of arterial and mixed venous blood were drawn simultaneously in each condition and analyzed for P_{O_2}, P_{CO_2}, and *p*H using a Corning® 165-2 blood-gas analyzer. The blood-gas analyzer electrodes were maintained at 37°C and appropriate corrections made when the animal's temperature was different from this value.[10] Blood oxygen contents (Ca_{O_2} and $C\bar{v}_{O_2}$) were measured using a carbon monoxide displacement technique.[11] Shunt ($\dot{Q}_s/\dot{Q}_t$) was then calculated from the equation:

$$\dot{Q}_s/\dot{Q}_t = \frac{Cc'_{O_2} - Ca_{O_2}}{Cc'_{O_2} - C\bar{v}_{O_2}}$$

The oxygen content of blood equilibrated with ideal alveolar gas (Cc'_{O_2}) was calculated as

$$Cc'_{O_2} = (PA_{O_2})(0.003) + \frac{Ca_{O_2} - (0.003)Pa_{O_2}}{Sa_{O_2}}$$

The oxygen saturation of arterial blood (SaO_2) was estimated from a nomogram[12] using measured values of Pa_{CO_2}, Pa_{O_2}, and temperature and the oxygen tension of ideal alveolar gas (PA_{O_2}) was calculated from the alveolar gas equation $PA_{O_2} = P_{bar} - P_{H_2O} - Pa_{CO_2}$.

Distribution of Pulmonary Perfusion

For each of the three measurements of the distribution of pulmonary perfusion, 1–2 ml of dextrose solution containing 150,000–500,000 15-μm radiolabeled

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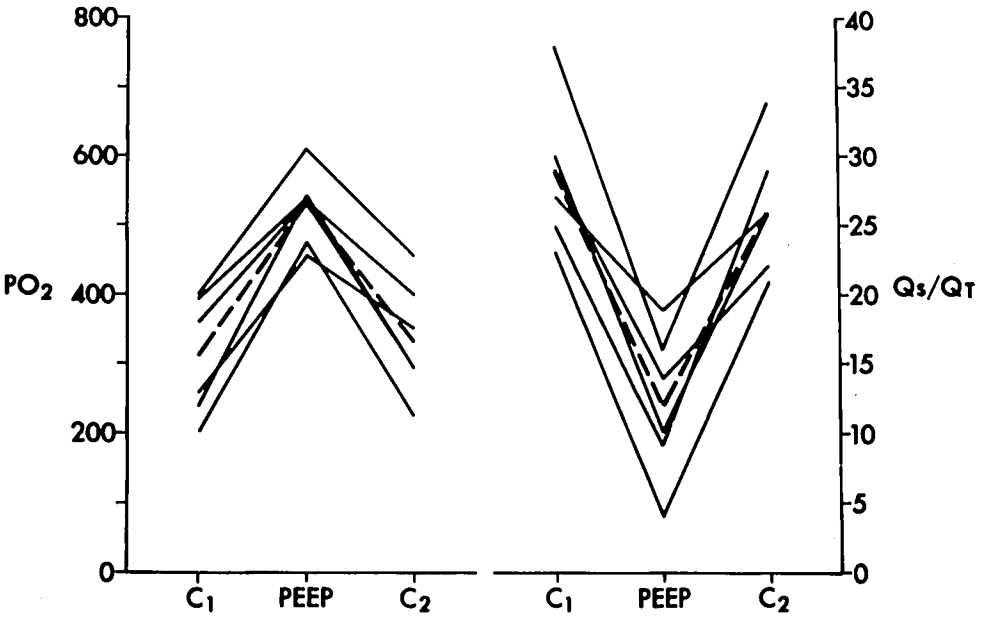

FIG. 1. Arterial oxygen tension (P_{O_2}) before (C_1), after (C_2), and during PEEP is shown in the left-hand panel and intrapulmonary shunt ($\dot{Q}_s/\dot{Q}_t$ per cent) in the right-hand panel. Solid lines show data from individual dogs. Interrupted lines are mean values.

microspheres were injected into the right atrial catheter and flushed with saline. The spheres were labeled with one of the radionuclides ^{51}Cr, ^{141}Ce, or ^{85}Sr and were administered in random order. The dose, size, and specific gravity were chosen to be within the range that has been shown to mix well with blood down to sublobar regions and to cause no alterations in subsequent measurements.[13]

The weighed excised lobes were homogenized in 150–200 ml of water at the end of the experiment. Three 10-ml aliquots were transferred into test tubes (Amersham/Searle #003328®), centrifuged, and counted in a gamma well counter (Nuclear Chicago 1185®) set for energy channels appropriate for the three isotopes used. The raw counts for each isotope were corrected for background and for spillover from the other isotopes using counts obtained from reference samples. Aliquot volume (V_A), the mean counts from the three aliquots (C_A), and the total volume of the homogenate (V_H) for each lobe were used to calculate the counts (C_L) for each isotope present in the lobe

$$C_L = C_A \times \frac{V_H}{V_A}$$

The sum of C_L for all lobes gave the total counts from both lungs (C_T) representing 100 per cent of pulmonary blood flow. The perfusion to each lobe (Q_L, expressed as per cent CO) at the time each isotope was injected was then calculated as

$$\text{per cent CO} = C_L/C_T \times 100$$

The mean results of all parameters were compared by one-way analysis of variance and the differences between conditions tested for significance using Tukey's multiple range comparison test.

Results

The six dogs in this study all had radiologic, histologic, and bacteriologic lobar pneumococcal pneumonia confined to the left lower lobe (LLL). The LLL wet weight (±SD) averaged 312 ± 100 g, while the grossly normal right lower lobe (RLL) weighed 97 ± 36 g.

Overall baseline gas exchange (fig. 1) was substantially abnormal in all six dogs. The average Pa_{O_2} was 310 ± 86 torr, and the mean shunt was 29 ± 5 per cent. The addition of 12 cm H_2O PEEP to the left lung ventilator improved the Pa_{O_2} to 532 ± 58 torr and decreased shunt to 12 ± 5 per cent. Both differences were statistically significant ($P < 0.01$). After PEEP was removed from the left lung ventilator, both Pa_{O_2} and $\dot{Q}_s/\dot{Q}_t$ returned to baseline values of 337 ± 84 torr and 26 ± 5 per cent, respectively.

Figure 2 depicts the perfusion of the LLL, RLL, and left upper lobe (LUL) expressed as per cent CO (±SD). There was no significant change in flow to either the LLL or the RLL during PEEP, while flow to the LUL decreased ($P < 0.05$). No other lung lobe evidenced any change in perfusion. CO was not significantly different during either control condition or PEEP (table 1). It can also be seen in table 1 that $\overline{PWP}$ increased with PEEP from 5 ± 4 torr to 10 ± 5 torr ($P < 0.05$), returning to 8 ± 4 torr in the second

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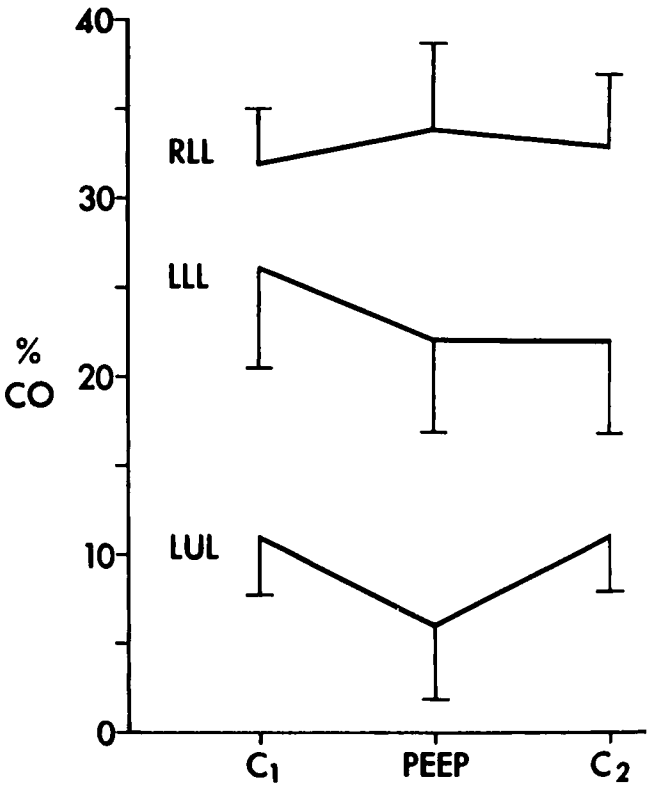

FIG. 2. Perfusion to the right lower lobe (RLL), pneumonic left lower lobe (LLL), and left upper lobe (LUL) are shown before (C_1), after (C_2), and during PEEP. Perfusion is expressed as percentage of cardiac output (per cent CO) to the lobe and shown as mean ± SD.

control condition. There were no significant changes in either $\overline{PAP}$ or $P_{\bar{s}\bar{a}}$.

Peak P_{ao} in the left lung was 26 ± 3 cm H_2O compared to 12 ± 2 cm H_2O in the right lung (table 1). Since the tidal volume was the same for each lung, this means that the inflation tidal compliance of the left lung and chest wall was about one-half that of the right. When 12 cm H_2O PEEP was added to the left lung ventilator, peak P_{ao} increased to 39 ± 5 cm H_2O ($P < 0.01$) while there was no change on the right. The pressure cost of tidal inflation (39 − 12 = 27 cm H_2O) was not different from control values, indicating no change in the inflation tidal compliance of the left lung and chest wall with PEEP.

Discussion

Other studies in dogs from our laboratory[4] and anecdotal evidence in patients[3,6,7] have indicated that whole lung PEEP is not effective in improving gas exchange in localized lung disease such as pneumonia. On the other hand, there are several case reports suggesting that gas exchange can be improved when disease is much worse in one lung than the other by applying PEEP only to the diseased lung using a Carlens tube.[5–8] The present study of unilateral PEEP in canine lobar pneumococcal pneumonia clearly demonstrates that this is indeed the case; unilateral PEEP produced dramatic improvements in both Pa_{O_2} and $\dot{Q}_s/\dot{Q}_t$.

Although overall gas exchange in canine lobar pneumonia is not much improved by whole lung PEEP, gas exchange in the pneumonia lobe does improve substantially.[4] Clearly, if the beneficial effect of PEEP on gas exchange in diseased lung could be realized without the associated marked increase in local blood flow, overall gas exchange would be improved. This appeared to be what was achieved in the present study, since unilateral PEEP produced an improvement in overall gas exchange and did not exhibit any significant increase in blood flow to consolidated lung.

In our previous study of whole lung PEEP, the shunt fraction within the pneumonia lobe fell from 94 per cent to 64 per cent.[4] Since virtually all units with abnormally increased shunt are contained within the pneumonia lobe[9] and there was no interlobar flow redistribution in the present experiment, the large improvement in $\dot{Q}_s/\dot{Q}_t$ with unilateral PEEP must be due to a decrease in shunt within the pneumonia lobe similar to that which occurred with whole lung PEEP.

The mechanism by which PEEP improves gas exchange is probably recruitment of alveoli that were previously nonventilated but which were perfused at normal or near-normal levels.[9] It is clear that interlobar flow redistribution cannot account for the reduced shunt since there was no significant change in the perfusion to the LLL. PEEP usually produces a decrease in cardiac output, and reduced pulmonary blood flow has been reported to reduce shunt,[14] but in the present study care was taken to keep total flow constant and thus eliminated that possibility. One additional possibility that has not been excluded is PEEP-induced redistribution of blood flow away from more diseased units and towards healthier units within the pneumonia lobe without a change in interlobar flow distribution; however, this seems to us an unlikely and unnecessarily complex explanation.

TABLE 1. Central Hemodynamics and Peak Airway Pressures*

	C_1	PEEP	C_2
$\overline{CO}$ (l/min)	8.1 ± 1.5	7.6 ± 1.4	8.1 ± 1.6
$\overline{PWP}$ (torr)	5 ± 4	10 ± 5	8 ± 4
$\overline{PAP}$ (torr)	13 ± 4	15 ± 6	15 ± 3
$P_{\bar{s}\bar{a}}$ (torr)	134 ± 18	124 ± 27	135 ± 22
P_{ao} right lung (cm H_2O)	12 ± 2	12 ± 2	12 ± 2
P_{ao} left lung (cm H_2O)	26 ± 3	39 ± 4	26 ± 2

* Values are means ± SD.

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Because no lung or lobar gas volumes were measured in this study, we have no direct evidence to support the contention that PEEP recruited previously nonventilated units. However, it did appear to us, in open-chested dogs in previous experiments, that PEEP produced substantial increases in gas volume of the pneumonia lobe.[4] Further, though one might have expected a decrease in compliance as the lung was ventilated from a higher point on its pressure-volume curve, the inflation compliance of the left lung in this experiment did not change with the addition of PEEP. One explanation might be that, because of recruitment, more units were participating in tidal inflation, obscuring the expected decrease in compliance.

The reason that whole lung PEEP does not improve gas exchange in pneumonia is that pulmonary blood flow is redistributed away from normal lung towards consolidated lung. In our previous study, the perfusion of the pneumonia lobe increased from 22 ± 7 to 37 ± 5 per cent with whole lung PEEP.[4] This increase could conceivably have resulted from either mechanical effects of PEEP such as compression of alveolar blood vessels in normal lung, or to a vasoactive mechanism such as relief of hypoxic vasoconstriction due to improved ventilation of the pneumonia lobe. With unilateral PEEP, the substantial improvement in whole lung gas exchange without significant redistribution of perfusion indicates that unilateral PEEP improved gas exchange within the pneumonia lobe by an amount similar to that achieved with whole lung PEEP. Since perfusion to the LLL did not increase with this improved gas exchange, it is unlikely that improved regional gas exchange with reduced hypoxic vasoconstriction is the major factor in producing the increased LLL perfusion with whole lung PEEP. More probably, PEEP redistributes blood flow by direct mechanical effects which increase resistance to blood flow more in normal lung than in consolidated lung. This concept receives support from the observation that left-sided PEEP reduced relative perfusion to the normal left upper lobe (see fig. 2), while the left lower lobe did not change. One way this may occur is from compression of the alveolar vessels in normal lung to a greater extent than in consolidated lung due to protection of alveolar vessels from airway pressure by the relatively solid exudate in the pneumonia lobe. Another possibility is that because the pneumonia lobe has reduced volume and is less compliant,[15] similar levels of PEEP produce less inflation than in normal lobes. At lung volumes above the functional residual capacity the vascular resistance of the lung increases with inflation[16], so the lesser inflation would result in a lesser increase in vascular resistance. This tendency of PEEP to direct blood flow away from normal lung led to a marked increase in flow to consolidated lung and negated the beneficial effect of PEEP on gas exchange. With unilateral PEEP the only normal lung exposed to PEEP was the left upper lobe, and its 5 per cent fall in perfusion led to a small increase shared by all other lung lobes without a significant increase in flow to the consolidated left lower lobe.

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