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Does PEEP facilitate the resolution of extravascular lung water after experimental hydrostatic pulmonary oedema?

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Does PEEP facilitate the resolution of extravascular lung water after experimental hydrostatic pulmonary oedema? H. Blomqvist, C-J. Wickerts, B. Berg, C. Frostell, Å. Jolin, G. Hedenstierna.

ABSTRACT: The effect of mechanical ventilation with positive end-expiratory pressure on the resolution of hydrostatic pulmonary oedema created by temporary left atrial balloon inflation was studied in mechanically ventilated dogs. Immediately after the hydrostatic process was terminated, by deflating the left atrial balloon, the animals were ventilated for 4 h with zero end-expiratory pressure (ZEEP, n=6) or with a positive end-expiratory pressure (PEEP, n=6) of 1.0 kPa (10 cmH_2O). Gas exchange and extravascular lung water content (EVLW) with the double indicator dilution technique (dye/cold) were studied and gravimetric determination of lung water was made postmortem.

EVLW decreased from 31.6±7.3 mean±SD $ml \cdot kg^{-1}$ during maximal oedema to 14.5±2.1 $ml \cdot kg^{-1}$ ($p<0.001$) 4 h after deflation of the left atrial balloon in dogs ventilated with ZEEP. The corresponding values in dogs ventilated with PEEP were a reduction in EVLW from 28.0±4.1 to 20.7±4.0 $ml \cdot kg^{-1}$ ($p<0.01$) (mean decrease 7.3±4.0 $ml \cdot kg^{-1}$). EVLW was significantly higher after 4 h on PEEP than after ZEEP ($p<0.01$). Gravimetric values at the end of the experiment were 12.4±2.8 $ml \cdot kg^{-1}$ (ZEEP) and 14.7±4.5 $ml \cdot kg^{-1}$ (PEEP) (NS). Oxygenation improved in both groups during the resolution of oedema with a more evident and early effect in the PEEP group.

It is concluded that mechanical ventilation with PEEP of 1.0 kPa (10 cmH_2O) in the resolution phase after experimental hydrostatic oedema improves oxygenation but retards the resolution of oedema.

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Mechanical ventilation with positive end-expiratory pressure (PEEP) has proved beneficial in treating hypoxaemia in experimental and clinical pulmonary oedema. The effect of PEEP on the concomitant pulmonary oedema, assessed as extravascular lung water (EVLW) has become a controversial issue [1–9]. Some authors consider PEEP to have a protective effect on the development of pulmonary oedema, or at least to have no harmful effects [1–5]. On the other hand, others propose that EVLW is increased with PEEP [6–9]. Possibly, some of the conflicting results in the studies cited might be due to the fact that PEEP was applied at different phases of pulmonary oedema (before, during or after oedema formation), the level of PEEP applied and whether the oedema had been of the hydrostatic or the permeability type. This study has been undertaken to analyse the effect of mechanical ventilation with PEEP of 1.0 kPa (10 cmH_2O) on EVLW and gas exchange during the resolution phase after experimental hydrostatic pulmonary oedema.

Materials and methods

Twelve mongrel dogs, mean (±SD) body weight 21.9±4.2 kg were used in the study, approved by the regional Animal Ethics Committee. The dogs were premedicated with ketamine 200–300 mg and anaesthetized with pentobarbitone 300–600 mg *i.v.* Anaesthesia was maintained with additional doses of pentobarbitone, 50–100 mg or diazepam, 5–10 mg and fentanyl 0.1–0.2 mg *i.v.* Muscle paralysis was achieved with pancuronium 1–2 mg *i.v.*, when necessary. The animals were intubated and placed in the supine position throughout the experiment and mechanically ventilated with an Erica ventilator (Gambro-Engström AB, Stockholm, Sweden). The tidal volume was 15–20 $ml \cdot kg^{-1}$ and ventilatory frequency 12–18 $breaths \cdot min^{-1}$. The inspiratory oxygen fraction was 0.5. The ventilator displayed peak and mean airway pressures (Pmax, Pmean) continuously. A computer built into the ventilator calculated total

thoracic compliance (Ct) by dividing expiratory tidal volume by end-inspiratory pressure minus end-expiratory pressure. Normocapnia, defined as arterial carbon dioxide tension ($PaCo_2$) of 4.5–6.0 kPa, was maintained by adjusting ventilatory frequency and was checked intermittently by blood gas analysis and continuously by monitoring end-tidal carbon dioxide tension ($Etco_2$) with a CO_2 analyser (Eliza, Gambro-Engström AB, Stockholm, Sweden). The CO_2 analyser was checked and calibrated intermittently throughout the study.

A thermistor-tipped pulmonary artery balloon catheter (Swan-Ganz, Edwards Lab., Anasco, Puerto Rico) was introduced into a femoral vein and advanced to pulmonary artery position for pressure recordings, cardiac output measurements and blood sampling. Cardiac output (CO) was measured by standard thermodilution technique. A bolus of 10 ml ice-cold glucose 5% was injected automatically by a temperature controlled syringe in the right atrium or inferior vena cava and the dilution curve for temperature was recorded and CO calculated by a CO-computer (Model 9520A Edwards Lab., Santa Ana, USA). A short arterial cannula was introduced into a femoral artery for pressure recordings and blood sampling. A 5F fibreoptic thermistor-tipped catheter (Pulsion, Münich, Germany) was introduced into the same artery and advanced to the proximal aorta (35–45 cm) for measurement of extravascular lung water (EVLW) using the double-indicator dilution technique (see below).

Mean arterial pressure (MAP), central venous pressure (CVP), pulmonary artery mean (PAP) and wedge pressures (PCWP) were recorded with capacitive transducers (P23, Gould, Bilthoven, Netherlands) positioned at the mid-thoracic level. All recordings were made with an ink-jet writer (Mingograph 4, Siemens-Elema, Solna, Sweden). Arterial blood was taken for blood gas analyses using standard electrode technique (ABL2, Radiometer, Copenhagen, Denmark). The blood samples were stored on ice until analysed. The shunt fraction (Qs/Qt) was calculated by standard formula according to BERGGREN [10] from inspiratory oxygen fraction, arterial and venous blood gases. Arterial to end-tidal carbon dioxide difference ($a\text{-}Etco_2$) was calculated as the difference between simultaneously measured arterial carbon dioxide tension and $Etco_2$. The bladder was catheterized for measurement of urine production. The dogs were hydrated intravenously with isotonic saline and glucose 5% at a rate of 6–10 $ml \cdot kg^{-1} \cdot h$, except when creating pulmonary oedema. Severe metabolic acidosis (pH <7.25) was corrected by 0.6 M sodium bicarbonate in an amount corresponding to half the calculated deficit. During pulmonary oedema formation all animals were given 30–50 ml sodium bicarbonate. Body temperature was maintained at 36–38°C by electric heating pads.

The same bolus used for CO-measurements (10 ml ice-cold indocyanine green dissolved in glucose 5% and injected into the inferior vena cava or right atrium) was used for measurement of EVLW. The dilution curves for dye and temperature were recorded intravascularly from the aorta with the thermistor-tipped fibreoptic catheter and were analysed as functions of time by a "lung water computer" (Pulsion, System Cold, Münich, Germany). The computer calculated the mean transit time (MTT) for the indicators (dye/temp) and calculated the total thermal volume (TTV), the central blood volume (CBV) and the extravascular lung water (EVLW) according to the formulae;

$$\begin{aligned} TTV &= CO \cdot MTT\text{-thermo} \\ CBV &= CO \cdot MTT\text{-dye} \\ EVLW &= TTV - CBV \end{aligned}$$

The temperature of the injectate was corrected for catheter deadspace, taking into consideration the different sections of the catheter that lay intravascularly and in room air. For further details see [11]. All measurements, including CO, were made with random distribution of the injection over the respiratory cycle. The mean of three to five measurements was used for statistical analysis. Postmortem gravimetric analysis of EVLW was carried out in five dogs in each group with a correction for pulmonary residual blood as described by PEARCE *et al.* [12] and with modification in ultracentrifugation according to SELINGER *et al.* [13]. Immediately before the dogs were sacrificed, blood was withdrawn for analysis of water content, haemoglobin content and haematocrit. The animals were sacrificed with an overdose of pentobarbitone and potassium chloride and the lungs were clamped and removed within 5 min. The lungs were weighed and homogenized in an equal weight of distilled water in a mixer. The well-stirred homogenate was centrifuged at 30,000 G at +5°C for 60 min (Dupont-Sorvall RCB, Wilmington, USA) to obtain a clear supernatant. The water contents of lung homogenate, supernatant and whole blood was determined by drying weighed samples at +85°C to constant weight (>72 h).

Total serum protein concentration (TSP) in blood was measured according to a modified Biuret method [14]. Albumin (alb) concentration in blood was measured using the Bromcresol-green binding method [15].

A transverse thoracotomy was performed in the TH5–TH6 intercostal space. A balloon-tipped 20 CH urinary catheter (Escman, Lancing, UK) was placed in the left atrium and secured by sutures. The lungs were hyperinflated to reopen collapsed tissue, the chest was closed and intrapleural air and blood were evacuated by suction drainage.

Experimental protocol

After induction of anaesthesia, catherization and thoracotomy the dogs were held at rest for 30 min. Hydrostatic oedema was then created by inflating the left atrial balloon (12–25 ml) simultaneously with an intravenous infusion of prewarmed isotonic saline,

600–2,500 ml. When EVLW, assessed by the double-indicator dilution technique, had increased 200–300%, the hydrostatic process was terminated by deflating the left atrial balloon and the saline infusion rate was reduced to basal infusion rate (5 ml·kg^{-1}·h). When the hydrostatic process was terminated the dogs were allocated to be ventilated with zero positive end-expiratory pressure (ZEEP, group 1, n=6) (*i.e.* the same ventilatory technique as during oedema formation) or with a positive end-expiratory pressure of 1.0 kPa (10 cmH_2O) (PEEP, group 2, n=6). Measurements of pulmonary mechanics, central haemodynamics, gas exchange and EVLW were performed before induction of pulmonary oedema, and during pulmonary oedema immediately prior to termination of the hydrostatic process. The same measurements were carried out 1–4 h after terminating the hydrostatic process.

Statistics

Results are presented as mean ±SD. Comparison between experimental conditions within a group were made by means of analysis of variance (ANOVA). If significant, paired data were analysed with Fisher's least significant difference method (PLSD). Comparisons between groups were made by means of the Mann Whitney U-test, $p<0.05$ was considered significant.

Results

The two groups (ZEEP and PEEP) did not differ regarding the volume used for inflating the left atrial balloon (ZEEP-group: 16.6±5.6 ml; PEEP-group: 18.0±4.5 ml) or volume of saline infused during formation of pulmonary oedema (ZEEP-group: 1350±690 ml; PEEP-group: 1180±370 ml). Urinary output during the resolution phase (4 h) was not significantly different in the two groups (4.0±2.1 ml·kg^{-1}·h in the ZEEP-group, 3.7±3.9 ml·kg^{-1}·h in the PEEP-group).

Total serum protein and albumin concentrations in blood did not differ between the two groups at baseline, during maximal oedema or at the end of the experiment. On the other hand, TSP as well as alb decreased significantly from baseline values during maximal oedema (TSP: 46.6±4.3 to 37.6±7.8, ($p<0.001$) (ZEEP) and 45.2±5.3 to 38.3±3.9, $p<0.01$ (PEEP); alb: 16.1±1.1 to 12.4±2.3, $p<0.01$ (ZEEP) and 16.3±2.6 to 13.3±1.2, $p<0.05$ (PEEP)). TSP and alb did not change further in either group at the end of the experiment as compared to values during maximal oedema.

Effects of hydrostatic oedema

Pooled data on pulmonary mechanics, central haemodynamics, gas exchange, and EVLW before and during pulmonary oedema before terminating the hydrostatic process and before allocating the dogs to the ZEEP or PEEP groups, are given in table 1. No reliable recordings of PCWP could be obtained during pulmonary oedema while the left atrial balloon was inflated. Hydrostatic oedema significantly increased Pmax, Pmean, PAP, CVP, a-$Etco_2$ difference, Qs/Qt, CBV and EVLW increased from baseline value 10.7 to 29.8 ml·kg^{-1} ($p<0.001$). There were also significant reductions in Ct and Pao_2, the latter fell from baseline 37.4 to 8.0 kPa ($p<0.001$) during maximal oedema.

Table 1. – Pooled data on pulmonary mechanics, haemodynamics, gas exchange and extravascular lung water content during baseline conditions and after experimental hydrostatic oedema in mechanically ventilated dogs (n=12)

		Baseline	Maximal oedema
Ct	ml·kPa^{-1} (ml·cmH_2O^{-1})	373±61 (37.3±6.1)	203±38*** (20.3±3.8)
Pmean	kPa (cmH_2O)	0.7±0.1 (7.1±1.3)	1.0±0.1*** (9.9±1.3)
Pmax	kPa (cmH_2O)	2.3±0.2 (23.4±2.2)	3.2±0.5*** (32.1±5.3)
CO	*l*·min^{-1}	2.72±0.45	2.45±0.64
MAP	kPa (mmHg)	12.1±1.3 (90.7±9.7)	10.3±2.6* (77.3±19.2)
PAP	kPa (mmHg)	2.0±0.6 (14.8±4.1)	5.1±1.0*** (38.3±7.2)
PCWP	kPa (mmHg)	1.2±0.5 (9.2±0.5)	-
CVP	kPa (mmHg)	0.6±0.4 (4.3±2.7)	1.1±0.4*** (8.1±2.8)
Pao_2	kPa	37.4±3.3	8.0±1.4***
a-$Etco_2$	kPa	0.48±0.39	1.50±0.67***
Qs/Qt	%	3.1±1.9	35±16.2***
EVLW	ml·kg^{-1}	10.7±2.0	29.8±5.9***
CBV	ml·kg^{-1}	19.1±2.6	25.5±6.0**

Analysis of variance (ANOVA). Fisher's least significant difference method (PLSD) for paired data. Significantly different from preceding value: *: $p<0.05$; **: $p<0.01$; ***: $p<0.001$. Ct: compliance; Pmean: mean airway pressure; Pmax: maximum airway pressure; CO: cardiac output; MAP: mean arterial pressure; PAP: mean pulmonary artery pressure; PCWP: mean pulmonary artery wedge pressure; Pao_2: arterial oxygen tension; a-$Etco_2$: arterial to end tidal carbon dioxide difference; Qs/Qt: shunt fraction; EVLW: extravascular lung water content; CBV: central blood volume. Data are given as mean±SD.

Table 2. – Data on pulmonary mechanics, haemodynamics, and gas exchange during hydrostatic oedema and 1, 2 and 4 h after terminating the hydrostatic process in mechanically ventilated dogs with an end-expiratory pressure of 1.0 kPa (10 cmH_2O) or without (ZEEP, n=6)

	CT $ml \cdot kPa^{-1}$ ($ml \cdot cmH_2O^{-1}$)	Pmax kPa (cmH_2O)	Pmean kPa (cmH_2O)	CO $l \cdot min^{-1}$	MAP kPa (mmHg)	PAP kPa (mmHg)	PCWP kPa (mmHg)	CVP kPa (mmHg)	Pao_2 kPa	a-$Etco_2$ kPa	Qs/Qt %	CBV $ml \cdot kg^{-1}$
ZEEP (n=6)												
Max. oedema	207±45 (20.7±4.5)	3.2±0.7 (31.5±6.5)	1.0±0.2 (9.8±1.6)	2.46±0.49	10.8±2.8 (81±21)	4.9±1.0 (36.7±7.7)	-	1.1±0.4 (8.3±2.6)	7.7±1.7	1.9±0.7	39.7±17.8	24.4±5.3
1 h	223±35 (22.3±3.5)	3.0±0.5 (29.8±5.1)	0.9±0.2 (9.2±1.5)	2.26±0.49	14.8±2.1** (111±17)	3.4±0.6** (25.7±4.1)	1.6±0.4 (12.2±2.7)	1.0±0.3 (7.2±2.1)	12.6±2.3*	1.2±0.5*	12.3±4.5***	20.2±4.8
2 h	225±33 (22.5±3.3)	3.0±0.5 (29.7±4.8)	0.9±0.1 (9.0±1.4)	2.03±0.53	14.1±2.1 (106±16)	3.6±0.6 (27.0±4.6)	1.5±03 (11.5±1.9)	1.0±0.2 (7.2±1.8)	16.8±5.7	0.9±0.3	8.6±2.1	19.9±1.7
4 h	223±39 (22.3±3.9)	3.0±0.3 (29.8±3.4)	0.9±0.1 (9.0±0.9)	2.30±0.68	13.8±1.9 (104±14)	3.4±0.6 (25.5±4.4	1.5±0.2 (11.2±1.7)	0.9±0.2 (6.7±1.8)	21.2±12.9	1.0±0.6	10.3±10.6	17.1±4.3
PEEP (n=6)												
Max. oedema	198±32 (19.8±3.2)	3.3±0.4 (32.7±4.1)	1.0±0.1 (10.0±1.1)	2.43+0.81	9.8±2.5 (74±19)	5.3±0.9 (39.8±7.0)	-	1.0±0.4 (7.8±3.3)	8.2±1.2	1.2±0.5	31.3±14.7	26.6±6.9
1 h	235±70 (23.5±7.0)	4.4±0.8** (43.8±8.0)†	1.9±0.2*** (18.8±2.0)††	2.03±0.60	13.7±1.7*** (103±13)	3.1±0.3*** (23.0±2.3)	1.6±0.3 (12.0±2.3)	1.2±0.3 (9.3±2.1)	29.9±8.7***††	0.5±0.4*†	3.3±1.6***††	15.5±2.4***
2 h	243±80 (24.3±8.0)	4.2±0.6† (42.3±6.0)	1.9±0.2†† (18.7±1.9)	2.04±0.45	13.8±1.5 (104±11)	3.2±0.3 (23.8±2.0)	1.8±0.2 (13.5±1.8)	1.3±0.3 (10.0±2.4)	31.5±8.6†	0.6±0.6	2.5±1.5††	15.4±2.9†
4 h	242±70 (24.2±7.0)	4.2±0.6† (41.8±6.3)	1.9±0.2†† (18.5±2.1)	1.89±0.54	12.8±1.6 (96±12)	3.5±0.6 (26.2±4.3)	1.7±0.3 (13.0±2.1)	1.4±0.3†† (10.5±2.2)	29.2±9.9	0.7±0.5	2.8±1.6	15.5±1.7

Analysis of variance (ANOVA). Fisher's least significant difference method (PLSD) for paired data. Significantly different from preceding value: *: $p<0.05$; **: $p<0.01$; ***: $p<0.001$. Mann-Whitney U-test. Significantly different from ZEEP value: †: $p<0.05$; ††: $p<0.01$. For abbreviations, see legend to table 1. Data are given as mean±SD.

Effects after left atrial balloon deflation

Effects on pulmonary mechanics, central haemodynamics and gas exchange before the termination of the hydrostatic process (left atrial balloon deflation) and in the subsequent 1–4 h after left atrial balloon deflation in the ZEEP- and PEEP-group are given in table 2. After deflating the left atrial balloon, significant reductions in PAP, a-$Etco_2$ and Qs/Qt were seen in both groups. There were also significant increases in MAP, Pao_2 (fig. 1) and an increase in compliance of borderline significance in both groups. Extravascular lung water fell successively in both groups (table 3 and fig 2).

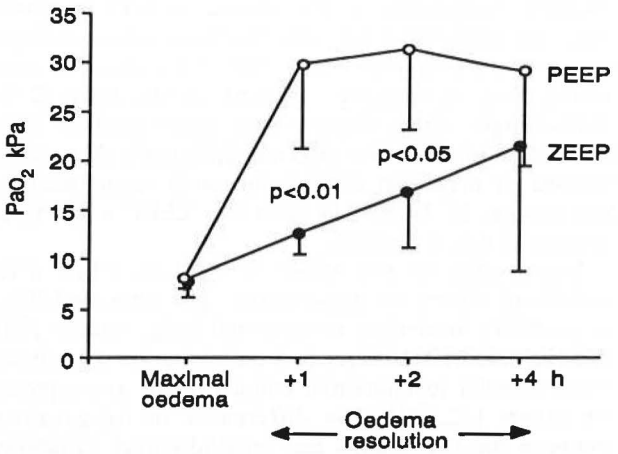

Fig. 1. – Oxygenation in dogs mechanically ventilated with a positive end-expiratory pressure of 1.0 kPa (10 cmH_2O) (PEEP) or with zero end-expiratory pressure (ZEEP) during 4 h period after terminating the hydrostatic process. Data are given as mean±SD. Pao_2: arterial oxygen tension.

Table 3. – Data on extravascular lung water content in dogs ventilated with a positive end-expiratory pressure of 1.0 kPa (10 cmH_2O) (PEEP, n=6) or with zero end-expiratory pressure (ZEEP, n=6) during a 4 h period after experimental hydrostatic oedema

	EVLW $ml \cdot kg^{-1}$	ΔEVLW (max. oedema - actual) $ml \cdot kg^{-1}$
ZEEP (n=6)		
Max. oedema	31.6±7.3	0
1 h	24.2±7.1*	-7.4±1.8*
2 h	20.2±5.7	-11.3±3.9
4 h	14.5±2.1	-17.1±7.7
PEEP (n=6)		
Max. oedema	28.0±4.1	0
1 h	27.9±6.0	-0.2±5.2
2 h	22.4±4.4*	-5.6±3.9*
4 h	20.7±4.0††	-7.3±4.0††

*: analysis of variance (ANOVA). Fisher's least significant difference method (PLSD) for paired data. Significantly different from preceding value, p<0.05. ††: Mann Whitney U-test for unpaired data. Significantly different from ZEEP value, p<0.01. Extravascular lung water content (EVLW) and difference in extravascular lung water content between two measurement occasions (ΔEVLW). Data are given as mean±SD.

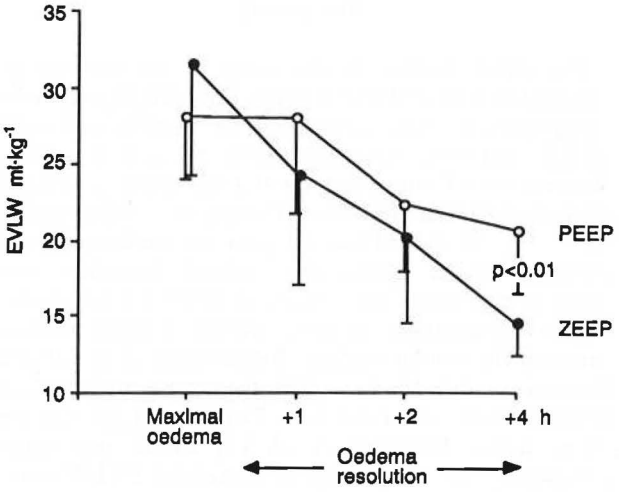

Fig. 2. – Extravascular lung water content (EVLW) during maximal hydrostatic oedema and during 4 h period after terminating the hydrostatic process in dogs ventilated with an end-expiratory pressure of 1.0 kPa (10 cmH_2O (PEEP) or zero end-expiratory pressure (ZEEP). Data are given as mean±SD.

Effects of ZEEP vs *PEEP (tables 1 and 2)*

Airway pressures (Pmax, Pmean) were significantly increased (p<0.01) when PEEP was applied and were both increased compared to the ZEEP group (p<0.05) during the 4 h period after deflation of the left atrial balloon.

Central venous pressure increased when PEEP was applied (NS) but the PEEP group as a whole was significantly different from the ZEEP group only at 4 h. Central blood volume was reduced (p<0.001) when PEEP was applied but the PEEP group as a whole was significantly different from the ZEEP group only at 2 h. Oxygenation was increased in both groups after left atrial balloon deflation, with a significantly higher Pao_2 with PEEP compared to ZEEP after 1 h (29.9 kPa compared to 12.6 kPa, p<0.01) The higher Pao_2 with PEEP was less obvious in the succeeding period and was no longer significant compared to ZEEP after 4 h (29.2 kPa (PEEP) and 21.5 kPa (ZEEP)). The a-$Etco_2$ and Qs/Qt decreased in both groups after atrial balloon deflation, with a significantly lower $Etco_2$ and Qs/Qt in the PEEP group compared to the ZEEP group after 1 h (p<0.01).

EVLW and rate of change in EVLW during the 4 h resolution period are presented in table 3 and figure 2. EVLW was successively and significantly reduced in both groups after terminating the hydrostatic process. EVLW was reduced by 17.1 $ml \cdot kg^{-1}$ (from 31.6 to 14.5 $ml \cdot kg^{-1}$) in the ZEEP group (p<0.001) and by 7.3 $ml \cdot kg^{-1}$ (from 28.0 to 20.7 $ml \cdot kg^{-1}$) in the PEEP group (p<0.01) 4 h after deflation of the left atrial balloon. The more pronounced decrease in EVLW with ZEEP compared to PEEP was significant after 4 h (p<0.01). Gravimetric values of EVLW in the two groups were 12.4±2.8 $ml \cdot kg^{-1}$ in the ZEEP group (n=5) and 14.7±4.5 $ml \cdot kg^{-1}$ in the PEEP group (n=5) (NS).

Discussion

The major finding in this study is that mechanical ventilation with PEEP of 1.0 kPa (10 cmH_2O) improves oxygenation, but, compared to ventilation with ZEEP, retards the resolution of oedema after termination of the experimental hydrostatic process (left atrial balloon deflation). Compared to other studies [2, 3, 7] on the effect of positive end-expiratory pressure during hydrostatic oedema formation, this study demonstrates the effects of PEEP on the resolution of hydrostatic oedema during normal cardiac function. In similar studies, BREDENBERG *et al.* [2] and HOPEWELL and MURRAY [3] found no differences between dogs ventilated with PEEP or ZEEP. On the other hand, DEMLING *et al.* [7] found that dogs ventilated with PEEP had an increased EVLW compared to dogs ventilated with ZEEP. In all of these studies PEEP was applied before the hydrostatic pulmonary oedema was established and the animals were studied over a shorter period (less than 4 h) compared to the conditions in this study. The protocol in this study should, therefore, more distinctly simulate a situation with established pulmonary oedema without interference with its formation.

This study also shows that a spontaneous clearance of severe hydrostatic oedema takes many hours despite a normal cardiac function. We suppose the cardiac function to be normal as no cardiac damage had been incurred by us and the PCWPs during the resolution phase were all within normal limits. The EVLW was still high 4 h after termination of the hydrostatic process even in the dogs ventilated with zero end-expiratory pressure.

The effects of PEEP on EVLW have yielded conflicting results, irrespective of measurement with the double indicator dilution technique or by gravimetry. In healthy lungs, EVLW may be increased when PEEP is applied [6, 9]. In conditions with lung injury, there are studies reporting EVLW to be reduced [4–5], or to remain unchanged [1–3, 16] when PEEP is applied. In other studies however, EVLW has been increased by the application of PEEP [7, 8]. This discrepancy found in the various studies can probably be related to differences in experimental protocol. Thus, the application of PEEP in normal or in damaged lungs, type of pulmonary damage, and the initiation of ventilation with PEEP before or after inducing lung damage may yield different results. The level of intrathoracic pressure and the duration of PEEP may also differ in various studies.

In this study, EVLW was measured by means of the double indicator dilution technique (dye/cold) and gravimetry. The double indicator dilution technique for measuring EVLW has been shown to be reliable under most conditions [17–20] and correlates well with the gravimetric technique in various types and degrees of pulmonary oedema [17–19]. This has also been confirmed, by means of correlation analysis between the double-indicator dilution technique and gravimetry (r=0.90) [20] in this laboratory using the same equipment for measuring EVLW as used in this study. Even if no clearly significant difference was obtained in this study between the two groups with the gravimetric technique there was a tendency for a correspondingly greater EVLW in the PEEP group.

Possible effects of PEEP on EVLW that have been discussed involve the following: 1) the rate of fluid filtration or absorption [21]; 2) the available surface area for fluid filtration [22]; 3) the effect of lung volume on interstitial capacity for fluid [23, 24]; and 4) the effect of reduced lymphatic drainage [25, 26]. It is conceivable that the mechanisms cited are operating in a different manner and are of varying importance during different phases of pulmonary oedema. Variations in the change in EVLW could also be explained by non-uniform relationships between airway pressures, vascular pressures and blood flow in different regions of the lung [27]. Accordingly, these factors may again explain why EVLW is found to be affected differently in various studies. It may also explain the wide range seen in the change in EVLW in both the ZEEP and PEEP groups in this 4 h study.

Irrespective of the effect on EVLW, PEEP had beneficial effects on oxygenation. The improved Pao_2 is probably secondary to recruited lung volume [28] but can also be secondary to a redistribution of oedema from alveolar to interstitial compartments as proposed by others [22, 23]. The differences in oxygenation between the two groups and interindividual variations also confirm that gas exchange is not related only to the amount of EVLW [19, 29].

In summary, the present study shows that during the resolution phase after experimental hydrostatic pulmonary oedema and with normal cardiac function, ventilation with PEEP of 1.0 kPa (10 cmH_2O) improves oxygenation but with a reduced rate of oedema clearance compared to ventilation with ZEEP.

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La PEEP facilite-t-elle la résorption de l'eau pulmonaire extra-vasculaire après oedème pulmonaire hydrostatique expérimental? H. Blomqvist, C-J. Wickerts, B. Berg, C. Frostell, Å. Jolin, G. Hedenstierna.

RÉSUMÉ: L'effet de la ventilation mécanique sous pression positive en fin d'expiration sur la résorption de l'oedème pulmonaire hydrostatique créé par le gonflement temporaire d'un ballonnet auriculaire gauche, a été étudié chez des chiens ventilés mécaniquement. Immédiatement après que le processus hydrostatique soit terminé par dégonflement du ballonnet auriculaire gauche, les animaux ont été ventilés pendant 4 heures, soit sans pression en fin d'expiration (ZEEP, n=6), soit avec pression positive en fin d'expiration (PEEP, n=6) de 1.0 kPa (10 cmH_2O). Les échanges gazeux et le contenu en eau extra-vasculaire pulmonaire (EVLW) mesurés par la technique de dilution au double indicateur (colorant/froid) ont été étudiés, et des déterminations gravimétriques de l'eau pulmonaire ont été faites en post mortem.

EVLW a diminué de 37.6±7.3 (moyenne±SD) $ml \cdot kg^{-1}$ au cours de l'oedème maximal, jusqu'à 14.5±2.1 $ml \cdot kg^{-1}$ ($p<0.001$) 4 heures après le dégonflement du ballonnet auriculaire gauche chez les chiens ventilés sous ZEEP. Les valeurs correspondantes chez les chiens ventilés sous PEEP ont été une réduction de EVLW de 28.0±4.1 à 20.7±4.0 $ml \cdot kg^{-1}$ ($p<0.01$). EVLW était significativement plus élevé après 4 heures de PEEP qu'après ZEEP ($p<0.01$). Les valeurs gravimétriques obtenues à la fin de l'expérience furent de 12.4±2.8 $ml \cdot kg^{1}$ (ZEEP) et de 14.7±4.5 $ml \cdot kg^{-1}$ (PEEP) (non significatif). L'oxygénation s'est améliorée dans les deux groupes pendant la période de résorption de l'oedème, avec toutefois un effet plus évident et plus précoce dans le groupe PEEP.

L'on conclut que la ventilation mécanique avec une PEEP de 1.0 kPa (10 cmH_2O) dans la phase de résorption après l'oedème hydrostatique expérimental améliore l'oxygénation, mais retarde la résorption de l'oedème.

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