Atrial Natriuretic Factor May Mediate the Renal Effects of PEEP Ventilation

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Mechanical ventilation with PEEP decreases urine output and urinary sodium excretion. Observed changes in cardiac output, renal blood flow, renin release, and antidiuretic hormone (ADH) secretion do not adequately explain the renal effects of PEEP. Altered release of atrial natriuretic factor (ANF), which is natriuretic and diuretic, may complete this explanation. The following hypothesis was tested: a PEEP-induced decrease in transmural right atrial pressure decreases ANF release, and this mechanism mediates subsequent alterations in renal function. Seven female mongrel dogs were anesthetized with halothane and their lungs ventilated mechanically for three consecutive 40 min periods of 0 PEEP, 10 cmH₂O PEEP, and 20 PEEP. Addition of 10 cmH₂O PEEP during mechanical ventilation decreased right atrial dimension and transmural right atrial pressure, while intracavitory right atrial pressure was increased. Urine output was significantly decreased during PEEP, as were absolute and fractional excretion of sodium and osmolar clearance. PEEP ventilation resulted in a consistent and significant decline in plasma ANF concentration (82 ± 11 to 62 ± 11 pg/ml, P < 0.05). Hemodynamic parameters, renal function, and ANF concentration returned to control values after cessation of PEEP. A second series of experiments in five dogs demonstrated a close temporal relationship between changes in atrial dimension or atrial transmural pressure, plasma ANF concentration, and urine output or sodium excretion. The results of this study demonstrate that PEEP-induced decreases in atrial distension resulted in decreased ANF release, which may mediate, in part, the antinatriuretic and antidiuretic effects of PEEP.

(Key words: Heart, atria: stretch receptors. Hormones: atrial natriuretic factor. Kidneys: function. Ventilation: positive end-expiratory pressure.)

MECHANICAL VENTILATION with positive end-expiratory pressure (PEEP) acutely decreases urine output and urinary electrolyte excretion by as much as 30–50%. Despite numerous investigations, the mechanism(s) responsible for the renal response to PEEP remain incompletely understood. Known factors contributing to PEEP antidiuresis and antinatriuresis include altered renal hemodynamics and the release of neurohumoral effectors.

PEEP acutely decreases cardiac output as a result of increased intrathoracic pressure, decreased venous return, and diminished ventricular preload. Decreased cardiac output and neural or humorally mediated reflex vasoconstriction may result in diminished renal blood flow. However, maintenance of cardiac output during PEEP does not prevent antidiuresis, suggesting that depression of renal hemodynamics alone is not sufficient to explain renal function changes. Increased antidiuretic hormone (ADH) levels during PEEP have been reported; however, there is a poor correlation between plasma ADH concentration and changes in renal function. Furthermore, recent evidence suggests that plasma ADH concentration is not altered during PEEP ventilation in humans. PEEP ventilation does stimulate the renin–angiotensin system, increasing plasma renin and aldosterone levels. However, these changes have not been confirmed by all observers, and the contribution of renin–aldosterone stimulation to the short-term antinatriuretic effects of PEEP is unclear. Together, these findings suggest the existence of previously unrecognized mechanisms responsible for the renal effects of PEEP.

Atrial natriuretic factor (ANF) is a peptide hormone synthesized, stored, and secreted by cardiac atria. ANF acts on the kidney to increase urine flow and sodium excretion and may also enhance renal blood flow and glomerular filtration rate. In addition, ANF antagonizes both the release and end-organ effects of renin, aldosterone, and ADH. Inhibition of endogenous ANF has been shown to diminish urine output and urinary sodium excretion while increasing plasma renin activity. The stimulus for ANF release is atrial distension, specifically atrial pressure and atrial stretch. Circulating peptide concentrations are linearly related to right and left atrial pressure, and are also proportional to atrial diameter.

PEEP ventilation has been shown to decrease both atrial diameter and atrial transmural pressure. Because atrial diameter and atrial pressure are the stimuli for ANF release, we tested the hypothesis that a PEEP-induced decrease in atrial distension decreases tonic ANF release, and this mechanism may mediate subsequent alterations in renal function.

Materials and Methods

The surgical and experimental protocols conformed to the standards of the AAALAC and were approved by the
Animal Care and Use Committee of the University of Washington.

**Surgical Preparation**

Female mongrel dogs (20–52 kg) were anesthetized with sodium thiamylal and halothane and underwent a sterile right thoracotomy. Lensed 2–3 mm piezoelectric crystals were sewn to the posterior surface of the right atrium near the aortic root and to the anterolateral surface of the right atrium. The sonomicrometer crystal pairs were used to measure right atrial dimension. A Tygon catheter was inserted in the right atrium via the superior vena cava for measurement of right atrial pressure, and then the pericardium was closed. Mediastinal pressure adjacent to the right heart (juxta cardiac pressure) was determined using a thin silicon rubber wafer as described by Marini et al. The wafer (35 × 35 × 1.5 mm) was sutured at its edges to the lateral aspect of the pericardium, with the central pressure-sensing portion (15 mm diameter disk) overlying the right atrium. Care was taken to avoid distortion of vascular structures by wafer placement. The optimal chamber volume for each wafer, linearity of response, and accuracy (±1 cmH₂O over the range 0–20 cmH₂O) were determined prior to implantation as described previously. A Tygon catheter was inserted into the internal mammary artery for blood sampling and determination of arterial pressure. Pressure catheters and sonomicrometer wires were externalized and the chest was closed in layers. Animals received morphine sulphate (15 mg) for postoperative pain relief and were allowed to recover for at least one week. Implanted devices are depicted in figure 1.

**Experimental Protocol**

Dogs were studied after they were fasted overnight. They were anesthetized with sodium thiamylal (15 mg/kg, iv) and placed supine on a warming blanket. Following tracheal intubation with a large bore cuffed endotracheal tube equipped with an inner catheter to allow continuous monitoring of airway pressure, their lungs were ventilated mechanically (Harvard Respirator, 15 ml/kg) at a rate adjusted to maintain normocapnia (PaCO₂, 35–45 mmHg, Instrumentation Laboratories Model 813). Anesthesia was maintained with halothane (1–1.5%) in oxygen. Lactated Ringer's solution (50 ml/kg) was administered for rehydration following the overnight fast. Creatinine (50 mg/kg) was administered by a peripheral iv bolus, followed by an infusion of ringers solution (5 ml·kg⁻¹·h⁻¹) containing succinylcholine (0.5 mg·kg⁻¹·h⁻¹; 0.1 mg/ml) and creatinine (60 mg·kg⁻¹·h⁻¹; 12 mg/ml). A catheter modified to allow continuous, low-pressure aspiration was placed in the bladder for quantitative urine collection. Mean arterial pressure (MAP), intracavitary right atrial pressure (RAP), and juxta cardiac pressure were determined with calibrated transducers placed at mid-heart level and referenced to atmosphere. Atrial transmural pressure (RAP – PEEP) was obtained by subtracting juxta cardiac pressure from intracavitary right atrial pressure by use of an analog circuit. Pressures are reported as the mean (determined electronically) averaged over several cardiac cycles at end-expiration. Heart rate was determined from the arterial pressure signal by a cardiotachometer. Right atrial dimension (RAD) is reported as the maximum dimension over the cardiac cycle. Data were recorded on an oscillograph (Gould Brush Model 260). Animals were allowed to stabilize for 45 min after bolus creatinine administration before timed urine collections were begun.

In the first experiment seven dogs were used to determine the influence of PEEP ventilation on renal function, hemodynamic variables, and plasma ANF concentration. There were three consecutive 40 min periods consisting of 0 PEEP, 10 cmH₂O PEEP, and 0 PEEP. Each period allowed two 20 min timed urine collections. The experiment began when urinary flow remained relatively stable (within 20%) for two 20 min periods. Blood was obtained at the midpoint of each 20 min collection interval for determination of plasma electrolytes, osmolality, and creatinine concentration. At the end of each 20 min collection interval blood was obtained for ANF quantitation, urine was collected for electrolyte, osmolality, and creatinine
quantitation, and hemodynamic variables were recorded. Blood was replaced with an equal volume of 5% dextran in normal saline. Data (mean ± SEM) from the second timed urine collection in each experimental period are presented. Results were compared by Friedman's repeated measures analysis of variance and the Newman-Keuls test, with a value of $P < 0.05$ considered significant.

The second experiment was designed to compare the time course of changes in atrial distension, plasma ANF concentration, and renal function in five animals. A control period (0 PEEP) defined as two consecutive 20 min periods of relatively stable urine output was followed by two consecutive 60 min periods of 10 cmH$_2$O PEEP and 0 PEEP. Blood and urine were obtained at the midpoint and end of each collection period for determination of electrolyte, osmolar, and creatinine clearance as described above. In addition, blood and urine samples were obtained 5, 10, 15, 20, 30, 40, and 60 min after initiation and cessation of PEEP for determination of plasma ANF concentration, urine output, and urine sodium excretion.

Glomerular filtration rate (GFR) was determined from the clearance of creatinine, determined colorimetrically (Kit 555, Sigma) in serum and urine. Serum and urine electrolytes were determined by flame photometry (Instrumentation Laboratories Model 443) and osmolality determined by vapor pressure osmometry (Wescor Model 5100B). Urine output (UV), urinary absolute ($U_{Na}V$) and fractional ($FE_{Na}$) sodium excretion, osmolar clearance ($C_{osm}$), and free water clearance ($C_{H_2O}$) were calculated according to standard formulas.

Blood for ANF quantitation was collected into chilled polypropylene tubes containing aprotinin (500 KIU/ml) and disodium EDTA (1 mg/ml) and centrifuged at 4°C. Plasma was immediately frozen in dry ice and stored at
**TABLE 1. Influence of PEEP Ventilation on Hemodynamic Variables, Renal Function, and Plasma ANF Concentration**

<table>
<thead>
<tr>
<th>Variable</th>
<th>PEEP 0</th>
<th>PEEP 10 cmH₂O</th>
<th>PEEP 0</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mmHg)</td>
<td>110 ± 3</td>
<td>100 ± 7</td>
<td>106 ± 4</td>
<td>7</td>
</tr>
<tr>
<td>HR (min⁻¹)</td>
<td>119 ± 3</td>
<td>126 ± 3</td>
<td>118 ± 5</td>
<td>7</td>
</tr>
<tr>
<td>RAP (cmH₂O)</td>
<td>4.3 ± 0.8</td>
<td>8.5 ± 0.8*</td>
<td>4.8 ± 0.6</td>
<td>6</td>
</tr>
<tr>
<td>RAPm (cmH₂O)</td>
<td>-0.5 ± 0.5</td>
<td>-1.9 ± 0.5*</td>
<td>-1.0 ± 0.5</td>
<td>5</td>
</tr>
<tr>
<td>RAD (mm)</td>
<td>15 ± 0.8</td>
<td>13 ± 0.4*</td>
<td>15.6 ± 0.7</td>
<td>5</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>74 ± 4</td>
<td>73 ± 5</td>
<td>94 ± 6†</td>
<td>7</td>
</tr>
<tr>
<td>UV (ml/min)</td>
<td>1.4 ± 0.4</td>
<td>0.5 ± 0.1†</td>
<td>1.4 ± 0.4</td>
<td>7</td>
</tr>
<tr>
<td>UNa,V (µEq/min)</td>
<td>193 ± 78</td>
<td>45 ± 23†</td>
<td>145 ± 47</td>
<td>7</td>
</tr>
<tr>
<td>FEso₂ (%)</td>
<td>1.7 ± 0.7</td>
<td>0.4 ± 0.2†</td>
<td>1.0 ± 0.3</td>
<td>7</td>
</tr>
<tr>
<td>Cₘₐₙ (ml/min)</td>
<td>3.0 ± 0.7</td>
<td>1.6 ± 0.3†</td>
<td>2.8 ± 0.4</td>
<td>7</td>
</tr>
<tr>
<td>Cₙₐₕ (ml/min)</td>
<td>-1.6 ± 0.4</td>
<td>-1.1 ± 0.2</td>
<td>-1.4 ± 0.3</td>
<td>7</td>
</tr>
<tr>
<td>ANF (pg/ml)</td>
<td>82 ± 41</td>
<td>62 ± 11*</td>
<td>83 ± 11</td>
<td>7</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SEM.
* P < 0.05 compared to control 0 PEEP.
† P < 0.01 compared to control 0 PEEP.

-70° C until analyzed. Plasma ANF concentrations were determined in duplicate within two weeks by radioimmunoassay (RAS-8798, Peninsula Laboratories, Belmont, California) following Sep-Pak (Millipore, Medford, Massachusetts) extraction. The assay used radiolabeled human ANF and rabbit anti-human ANF antibody because the primary structures of human and dog ANF are identical. The validity of this technique has been established previously. Results were corrected for extraction efficiency, which averaged 66%. Interassay and intraassay coefficients of variation were 19% and 9%, respectively.

**Results**

The influence of PEEP on systemic and right atrial hemodynamics are shown in figure 2, which presents the results of a typical experiment. Table 1 summarizes the results obtained in seven animals. Addition of 10 cmH₂O PEEP during mechanical ventilation resulted in a significant decrease in maximum RAD, from 15.6 ± 0.8 to 13.3 ± 0.4 mm (P < 0.05). Right atrial excision (the difference between maximum and minimum right atrial dimension at end-expiration) also declined during PEEP, from 2.6 ± 0.2 to 2.0 ± 0.2 mm (P < 0.05). Intracavitary RAP increased following addition of PEEP from 4.3 ± 0.8 to 8.5 ± 0.8 cmH₂O (P < 0.05). Because the increase in intracardiac pressure exceeded that of intracavitary RAP during PEEP, transmural RAP was significantly decreased during PEEP, from -0.5 ± 0.6 to -1.9 ± 0.5 cmH₂O (P < 0.05). These changes were abolished following cessation of PEEP. MAP and heart rate were unchanged during PEEP ventilation.

Table 1 summarizes the influence of PEEP ventilation on renal function. Urine flow rate was significantly decreased following addition of PEEP during mechanical ventilation, as were absolute and fractional excretion of sodium. Osmolar clearance was also significantly diminished during PEEP. Glomerular filtration rate and free water clearance were not significantly affected by PEEP ventilation. Indicators of renal function rapidly returned to control values following cessation of PEEP, with the exception of GFR, which was moderately increased.

Mechanical ventilation with 10 cmH₂O PEEP resulted in a consistent and significant decrease in plasma ANF concentration. Mean plasma peptide levels were diminished from 82 ± 11 to 62 ± 11 pg/ml (P < 0.05) 40 min after initiation of PEEP (table 1). Peptide concentrations returned to control values after PEEP was discontinued. Changes in individual plasma ANF levels from experiments with seven dogs are presented in figure 3.

Figure 3 also depicts the relationship between renal function and ANF concentration before and during PEEP. In six animals there was a PEEP-induced reduction in plasma ANF concentration, which was consistently associated with a decrease in urine output and urinary sodium excretion. In one dog there was no change in plasma ANF during PEEP, and no change in either urine output or sodium excretion was observed.

The second experiment was designed to compare the temporal relationship between changes in atrial distension, ANF release, and renal function following initiation and cessation of PEEP ventilation. Figure 4 depicts the time course of changes in RAD, transmural RAP, plasma ANF concentration, urine output, and urinary sodium excretion after initiation and cessation of 10 cmH₂O PEEP during mechanical ventilation. Initiation of PEEP was followed immediately by decreases in RAD and transmural RAP, which reached their nadir within five minutes. This was associated with an immediate decline in plasma ANF concentration, which continued for approximately 40 min. Urine output and sodium excretion were also diminished within five minutes of PEEP onset. Cessation of PEEP was associated with an immediate increase in atrial distension, followed by a rise in circulating ANF concentration and urine output and sodium excretion. Thus, there was excellent temporal correlation between changes
in atrial distension, plasma ANF concentration, and urine output and sodium excretion.

Discussion

The results of this investigation demonstrate that mechanical ventilation with 10 cmH₂O PEEP resulted in a consistent, rapid, and reversible 25% decline in plasma concentrations of atrial natriuretic factor following a decrease in right atrial size and transmural right atrial pressure. The decline in plasma ANF levels was associated with a significant decline in urine output, urine sodium excretion, and urinary osmolar clearance, which were decreased approximately 60% during PEEP. Cessation of PEEP was followed by return of mean plasma peptide concentration, urine output, and urinary sodium excretion to control values. There was a close temporal correlation between changes in plasma ANF concentration and changes in urine output and sodium excretion following initiation and cessation of PEEP. These data suggest that a reduction in circulating ANF concentration during PEEP ventilation may explain, in part, the antidiuretic and antinatriuretic effects of PEEP. Increased plasma ANF concentration may likewise explain, in part, the relative diuresis following cessation of PEEP.

PEEP AND ATRIAL DISTENSION

Marini et al.5,25 have extensively characterized the influence of PEEP on cardiac dynamics. Elevated intracavitary RAP due to external juxta cardiac compression by distended lungs diminishes the driving force for venous return. Extrinsic compression and decreased venous return together diminish right atrial distension and transmural RAP. In agreement, we observed elevated intracavitary RAP and diminished transmural RAP during PEEP. Although others have reported greater reductions in transmural RAP during PEEP,6,26 the intrapleural balloons and transducer-tipped catheters used in those studies are known to underestimate juxta cardiac pressure,5 leading to an overestimate of transmural RAP. Our sonomicrometer measure of RAP provided only a single axis measurement of atrial size from which we inferred atrial distension; however, Toma et al.54 have shown an excellent correlation between a single axis echocardiographic atrial dimension and angiographic atrial volume. Thus, diminished RAP during PEEP observed herein and in patients19 does reflect reduced right atrial distension.

PEEP AND ANF RELEASE

Atrial distension is recognized as the major stimulus for ANF secretion. Distension of either atrium elicits peptide release,14,16,17,25,26 although some evidence suggests a greater contribution from the right atrium.27 Atrial pressure is one component of the stimulus for ANF release. A linear relationship between basal plasma ANF concentration and both right atrial and pulmonary capillary wedge pressure has been shown.16,17,26 In addition, changes in atrial pressure are followed rapidly by corresponding modulation of ANF release15 and plasma ANF concentration.26 Atrial size is a second major component of atrial distension promoting ANF release. Echocardiographic studies have shown that plasma ANF concentrations are proportional to atrial dimension.16,26

In the present investigation diminished plasma ANF concentrations following PEEP-induced reductions in RAD and transmural RAP, and increased ANF levels following normalization of RAD and transmural RAP, are consistent with these prior studies. In dogs Edwards et al.55 found a significant linear relationship between plasma ANF levels and transmural RAP, with a slope of 16 pg·ml⁻¹·cmH₂O⁻¹. We found an average ANF decline of 21 pg/ml with a mean transmural RAP decrease of 1.4 cmH₂O, in excellent agreement. Circulating ANF
concentrations represent a balance between peptide release and elimination. Because ANF is eliminated primarily by the kidney and renal function declines during PEEP, enhanced ANF excretion is unlikely to occur during PEEP. Rather, diminished plasma ANF levels during PEEP represent decreased atrial ANF release. Thus, increased intrathoracic pressure during PEEP resulted in decreased venous return and atrial compression, with decreased atrial distension and a consequent decline in the release of ANF.

The time course of change in circulating ANF concentration following initiation and cessation of PEEP is consistent with the known kinetics of ANF release and elimination. ANF levels fell within five minutes after PEEP initiation and declined thereafter over approximately 40 min. In isolated perfused hearts a decrease in RAP was followed within two minutes by a corresponding change in the rate of ANF release into the perfusate. In anesthetized dogs Ledsome et al. found that an immediate decrease in atrial pressure was followed by a gradual decline in circulating ANF concentration, which reached baseline levels over 20–30 min. This was consistent with a plasma half-life of 4–5 min.

The exact nature of the pressure stimulus for ANF secretion is unknown. In the present investigation PEEP ventilation increased intracavitary RAP while decreasing transmural RAP, and these changes resulted in diminished secretion of ANF. These results suggest that transmural RAP, rather than intracavitary RAP, is the stimulus for ANF secretion. A similar conclusion was reached using a model of cardiac tamponade in dogs. The influence of pericardial tamponade on ANF release has also been observed clinically.

ANF AND RENAL FUNCTION

Endogenous circulating ANF exerts a tonic, minute-to-minute influence on renal function. Basal urinary sodium excretion has been shown to be linearly related to resting plasma ANF concentration. In addition, inhibition of endogenous circulating ANF activity with a specific peptide antibody resulted in a rapid 40–60% decrease in urine output and urinary sodium excretion. Dynamic alterations in ANF levels also influence renal function. A linear relationship has been demonstrated between the fall in plasma ANF concentration and the decline in urinary sodium excretion. Similarly, increases in plasma ANF concentration produced a proportional increase in urinary sodium excretion following peptide infusion. ANF-induced increases in urine output, urine absolute and fractional sodium excretion, and osmolar clearance have been well described.

In the present investigation a 25% decrease in ANF levels during PEEP was associated with a rapid 60% decline in urine output, sodium excretion, and osmolar clearance. Can the small PEEP-induced decline in ANF levels explain the magnitude of renal function changes? Zimmerman et al., using dogs recently demonstrated that manipulation of ANF concentration within the physiologic range does influence renal function. An increase in plasma ANF from 68 ± 8 to 100 ± 8 pg/ml resulted in a twofold increase in single kidney urine output (0.16 ± 0.02 to 0.38 ± 0.08 ml/min) and threefold increases in absolute (22 ± 6 to 66 ± 15 μEq/min) and fractional (0.41 ± 0.11 to 1.30 ± 0.33%) excretion of sodium.
ANF can influence urine flow and sodium excretion without changes in free water clearance, consistent with the renal effects of PEEP observed herein and elsewhere. Can the time course of PEEP-induced reductions in ANF levels explain the rapidity of renal function changes? In dogs urine flow responded within one minute of starting or stopping a physiologic ANF infusion. Thus, changes in ANF levels similar to those observed herein can produce renal changes of comparable magnitude and speed to those occurring during PEEP ventilation.

Alterations in plasma ANF levels during PEEP may influence urine output and urinary sodium excretion directly by specifically altering glomerulotubular function. Depending on the dose employed, postulated mechanisms of ANF action include transient increases in renal blood flow, enhanced GFR and glomerular capillary permeability, and inhibition of tubular sodium reabsorption. We observed diminished urine output and sodium excretion during PEEP in the absence of altered GFR. Although ANF in pharmacologic concentrations may increase GFR, smaller physiologic concentrations elicit natriuresis and diuresis without altering GFR. Loss of tonic ANF influence during PEEP may therefore result directly in antidiuresis and antinatriuresis.

Alterations in plasma ANF levels during PEEP may also influence urine output and sodium excretion indirectly by modulation of neurohumoral effectors. PEEP increases plasma renin activity and aldosterone concentrations. ANF inhibits renin release, decreases plasma renin activity, antagonizes renal vasoconstriction to angiotensin II, and inhibits the adrenal release and renal effects of aldosterone. Plasma renin activity and aldosterone levels are inversely proportional to plasma ANF levels, and inhibition of endogenous ANF enhances plasma renin activity. PEEP-induced alterations in ANF release may therefore influence renin–aldosterone concentrations, thereby indirectly altering renal function. PEEP ventilation in dogs has been associated with elevated plasma ADH levels, although PEEP may have little effect on plasma ADH levels in humans. ANF inhibits the release of ADH, decreases circulating ADH concentration, and antagonizes the renal effects of ADH. Thus, alterations in ANF release during PEEP may also alter ADH release, and thereby indirectly influence renal function. The modulation by ANF of ADH and renin–angiotensin systems during PEEP requires further investigation.

Control of renal function during PEEP is clearly multifactorial. We do not attribute the renal effects of PEEP exclusively to diminished ANF release. Rather, PEEP inhibition of ANF release more likely participates in concert with the other known hemodynamic and neurohumoral determinants of renal function. Thus changes in cardiac output, renal blood flow, glomerular filtration rate, renal nerve activity, renin release, and ADH secretion, as well as ANF release, may influence renal function during PEEP. We have provided evidence for a strong association between PEEP-induced changes in atrial distension, plasma ANF levels, urine output, and sodium excretion. Further investigations are needed to establish a definite causal relationship between the PEEP-induced physiologic reductions in plasma ANF and the renal response to PEEP. We measured only ANF levels during PEEP. Therefore, the fractional contribution of diminished ANF release to the renal effects of PEEP, relative to that of other renal hemodynamic and neurohumoral effectors, must also be assessed. These experiments await the development of a specific antagonist of the ANF peptide or ANF receptor.

The present studies used normal dogs and must be interpreted prudently with respect to patients with lung disease, who may have altered pulmonary compliance and diminished juxtaocular pressure transmission during PEEP. Nevertheless, our results correspond closely to clinical observations that PEEP decreases right and left atrial transmural pressures and cross-sectional dimensions. In hydrated patients with acute respiratory failure, 15 cmH2O PEEP resulted in a 20% decrease in arterial ANF levels along with a 50% decrease in urine output.

In summary, we have used chronically instrumented dogs to show that mechanical ventilation with PEEP decreased right atrial size and transmural right atrial pressure, resulting in a consistent, rapid, and reversible decline in plasma atrial natriuretic factor concentration. These data suggest that a reduction in ANF release may explain, in part, the antidiuretic and antinatriuretic effects of PEEP. The ANF-mediated reduction in urine output and sodium excretion during PEEP represents a physiologic mechanism for attempted restoration of intravascular volume, which atrial stretch receptors perceive to be decreased.

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References


