TITLE: ATRIAL NATRIURETIC PEPTIDE AND THE RENAL EFFECTS OF PEEP VENTILATION

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Introduction: Mechanical ventilation with positive end-expiratory pressure (PEEP) decreases urine output and urinary electrolyte excretion. Several factors may account for these changes, including decreased cardiac output and renal blood flow, enhanced plasma renin activity and increased ADH release.[1] However, the hemodynamic and neurohumoral changes following PEEP do not fully explain the observed alterations in renal function. Atrial natriuretic peptide (ANP) is a hormone that is synthesized and stored in cardiac atria and secreted in response to atrial distension. ANP increases glomerular filtration rate (GFR), sodium excretion and urine output. ANP also inhibits the release and action of renin, aldosterone and ADH. We tested the hypothesis that a PEEP-induced decrease in transmural right atrial pressure decreases ANP release, and this mechanism mediates subsequent alterations in renal function.

Methods: Seven female mongrel dogs (20-32 kg) were instrumented with the following: paired sonomicrometer crystals for measurement of right atrial diameter (RAD), right atrial catheter for measurement of atrial pressure (RAP), and an arterial catheter for measurement of blood pressure and heart rate. An intrathoracic silicon rubber wafer was sutured to the external surface of the pericardium near the atrial portion of the heart for determination of juxtacardiac pressure (JCP).

For experiments, dogs were anesthetized with halothane (1-1.5%), given lactated Ringers (50 cc/kg), and ventilated mechanically (15 cc/kg) during a 45 min equilibration period. This was followed by three consecutive 40 min experimental periods: 0 PEEP, 10 cm $H_2O$ PEEP and 0 PEEP. Urine and blood samples were obtained for determination of GFR (creatinine clearance), urine output, urinary absolute ($U_{Na}V$) and fractional (FeNa) sodium excretion, osmolar clearance ($C_{osm}$), and free water clearance ($C_{H_2O}$). ANP in arterial blood samples was determined by radioimmunoassay (Peninsula Labs). Transmural right atrial pressure ($RAP_{tm}$) was calculated as RAP-JCP. Data were analyzed by paired t-test.

Results: Table 1 summarizes the results of this study. Addition of PEEP during mechanical ventilation resulted in decreased RAD and $RAP_{tm}$ while absolute RAP was increased. Mean arterial pressure and heart rate were unchanged. Urine output was significantly decreased during PEEP, as were absolute and fractional excretion of sodium. Osmolar clearance was also significantly diminished during PEEP. Free water clearance and glomerular filtration rate were not affected by PEEP ventilation. Mechanical ventilation with 10 cm $H_2O$ PEEP resulted in a consistent and significant decrease in plasma ANP concentration. Hemodynamic variables, renal function values, and ANP levels returned to control after cessation of PEEP.

Discussion: Addition of PEEP (10 cm $H_2O$) during mechanical ventilation resulted in a 25% decrease in plasma ANP concentrations and a 60% decrease in urine output and sodium excretion. Diminished ANP levels were associated with decreased atrial transmural pressure and atrial size. These observations suggest that PEEP-induced decreases in atrial distension result in decreased ANP release, which mediates in part, the antidiuretic and antinatriuretic effects of PEEP. Furthermore, these results demonstrate that transmural right atrial pressure rather than intracavitary right atrial pressure is the stimulus for ANP release.

Table 1. Influence of PEEP Ventilation on Atrial Dynamics, Renal Function and Plasma ANP Concentration

| | 0 PEEP | 10 cm $H_2O$ PEEP | 0 PEEP | n |
|---|---|---|---|---|
| MAP mm Hg | 110 ± 3 | 100 ± 7 | 106 ± 4 | 7 |
| HR $min^{-1}$ | 119 ± 3 | 126 ± 3 | 118 ± 5 | 7 |
| RAP cm $H_2O$ | 4.3 ± 0.8 | 8.5 ± 0.8* | 4.8 ± 0.6 | 6 |
| $RAP_{tm}$ cm $H_2O$ | -0.5 ± 0.6 | -1.9 ± 0.5+ | -1.2 ± 0.6 | 5 |
| RAD mm | 15.6 ± 0.8 | 13.3 ± 0.4* | 15.6 ± 0.7 | 5 |
| GFR $ml \cdot min^{-1}$ | 73 ± 4 | 71 ± 6 | 93 ± 7 | 7 |
| UV $ml \cdot min^{-1}$ | 1.4 ± 0.4 | 0.5 ± 0.1* | 1.4 ± 0.4 | 7 |
| $U_{Na}V$ $\mu Eq \cdot min^{-1}$ | 193 ± 78 | 45 ± 23* | 146 ± 47 | 7 |
| FeNa % | 1.7 ± 0.7 | 0.4 ± 0.2* | 1.0 ± 0.3 | 7 |
| $C_{osm}$ $ml \cdot min^{-1}$ | 3.0 ± 0.3 | 1.6 ± 0.3* | 2.8 ± 0.4 | 7 |
| $CH_2O$ $ml \cdot min^{-1}$ | -1.6 ± 0.4 | -1.1 ± 0.2* | -1.4 ± 0.3 | 7 |
| ANP $pg \cdot ml^{-1}$ | 82 ± 11 | 62 ± 10+ | 79 ± 9 | 7 |

Data are presented as mean ± SEM
* $p < 0.05$ compared to 0 PEEP
+ $p < 0.005$ compared to 0 PEEP

Reference:

1. Berry AJ: Respiratory Support and Renal Function. Anesthesiology 55:655-667, 1981.