Low tidal volume ventilation in healthy dogs

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Abstract

Objective – To determine if low tidal volume (VT) ventilation is associated with the development of respiratory acidosis and changes in lung function in healthy dogs.

Design – Randomized prospective experimental cross-over study.

Setting – Pulmonary function laboratory at a university teaching hospital.

Animals – Five healthy Beagle dogs.

Interventions – Dogs were anesthetized and randomly mechanically ventilated with VT of 6, 8, 10, 12, and 15 mL/kg while maintaining a constant minute volume.

Measurements and Main Results – Arterial blood gases and pulmonary mechanics were collected after 15 minutes of equilibration at each VT. Repeated measures ANOVA was used to determine the effect of VT with a P-value of <0.05 considered significant, and a Pearson product moment was used to determine correlation between VT and pH and PaCO2. VT had a significant effect on PaCO2 (P < 0.001) and on pH (P < 0.001) with lower VT being associated with higher PaCO2 and lower pH. There was a strong correlation between VT and PaCO2 (r = -0.87) and VT and pH (r = 0.83). Increased airway pressures and pulmonary compliance were associated with increasing VT.

Conclusions – There is a predictable decrease in the pH, decrease in airway pressure, decrease in compliance, and increase in the PaCO2 associated with lower VT. Low VT ventilation is well tolerated in healthy dogs; the role of low VT ventilation in dogs with acute lung injury/acute respiratory distress syndrome as well as the influence of positive end expiratory pressure requires further evaluation.

(Keywords: acid-base balance, acute respiratory distress syndrome, anesthesia, parenchymal disease)

Introduction

Intermittent positive pressure ventilation (IPPV) is critical to the support of pulmonary failure in dogs, particularly in animals with suspected acute lung injury or acute respiratory distress syndrome (ARDS). It is well recognized, however, that mechanical ventilation may have deleterious consequences, including the effects of volu-trauma and baro-trauma. These complications may occur even in the absence of pre-existing lung disease.1 Resulting ventilator-induced lung injury may induce progressive respiratory failure, with increased morbidity, and even mortality. In human medicine, low tidal volume (VT; ie, 6 mL/kg) ventilation has been demonstrated as the preferred technique in patients with

Abbreviations

ALI acute lung injury
ARDS acute respiratory distress syndrome
IPPV intermittent positive pressure ventilation
MV minute ventilation
PEEP positive end expiratory pressure
PaCO2 end-tidal CO2
TLC total lung capacity
V_A alveolar ventilation
VILI ventilator-induced lung injury
VD_S dead space ventilation
VT tidal volume
ARDS and is the first intervention associated with an improved survival rate.\(^2\) Strategies to minimize lung damage associated with IPPV in dogs, including lower \(V_T\), have not been investigated to date.

The normal \(V_T\) in dogs is reported as 10–15 mL/kg.\(^3\) Predictable effects of lower \(V_T\) ventilation may thus include CO\(_2\) retention with subsequent respiratory acidosis and hypoxemia. Hypoxemia is potentially surmounted with increasing inspired oxygen concentrations, but acidosis will persist and may be the limiting step in promoting low \(V_T\) ventilation. Additionally, a reduction in \(V_T\) will increase the patient’s relative dead space ventilation (\(V_{DS}\)), as \(V_T\) is the sum of alveolar ventilation (\(V_A\)) and \(V_{DS}\). \(V_{DS}\) may be calculated via the Bohr equation and consists of the anatomic dead space (eg, trachea and conducting airways) and alveolar dead space, which includes those alveoli that are ventilated but underperfused. Anatomic dead space is fixed, and is approximately 1/3 the normal \(V_T\).\(^4\) Therefore, with decreasing \(V_T\), even if minute ventilation (MV = Frequency × \(V_T\)) is held constant, there is an increasing proportion of each breath dedicated to \(V_{DS}\) and not available for gas exchange.

The goal of this study was to determine the effect of varying the \(V_T\) on gas exchange in healthy ventilated dogs. We hypothesized that decreasing \(V_T\) will be associated with increased PaCO\(_2\) and the development of respiratory acidosis, even after controlling for MV. MV was controlled by adjusting the respiratory rate.

**Materials and Methods**

Five healthy laboratory beagle dogs of normal body condition with no abnormal history or physical examination findings were included in the study. Dogs were premedicated with hydromorphone\(^\#\) (0.1 mg/kg IM) and diazepamlink \(^\#\) (0.1 mg/kg IM) and general anesthesia was induced using propofol\(^\#\) (4–6 mg/kg IV). Orotracheal intubation was performed. Anesthesia was maintained with a propofol continuous rate infusion (CRI) (100–150 \(\mu\)g/kg/min). Routine anesthetic monitoring, including continuous ECG, pulse oximetry, and end-tidal CO\(_2\) analysis was performed. Intravenous lactated Ringer’s solution\(^\#\) was provided at a rate of 5 mL/kg/h. A 20-G over-the-needle arterial catheter was aseptically placed in the dorsal pedal artery for arterial blood gas analysis.

Dogs were ventilated in a randomized order at \(V_T\) of 6, 8, 10, 12 and 15 mL/kg using a specialized critical care ventilator.\(^\#\) The MV was held constant at 200 mL/kg/min. The inspired oxygen concentration was 25%, with zero end-expiratory pressure. The dogs were ventilated for 15 minutes at each \(V_T\) after which an arterial blood gas was collected from the arterial catheter.

Lung mechanics, including static compliance, and airway pressures were recorded using commercial software contained within the ventilator. Static compliance was given by the formula (\(V_T/P_{plat} - PEEP\); PEEP = positive end expiratory pressure). Oxygen saturation was measured via pulse oximetry and a modified Bohr equation (\(V_{DS}/V_T = PaCO_2 - PeCO_2/PaCO_2\)) was used to calculate the dead space fraction, using end-tidal CO\(_2\) (PeCO\(_2\)) and arterial CO\(_2\) (PaCO\(_2\)).

Following the completion of the study, dogs were recovered from anesthesia and returned to the laboratory animal facility. A single postprocedural dose of carprofen\(^\#\) (2.2 mg/kg SQ) was administered for any potential discomfort associated with endotracheal intubation and catheterization. The dogs were adopted out approximately 3 months after the conclusion of the study.

Repeated measures ANOVA were used to determine the effect of \(V_T\) on PaCO\(_2\), airway pressures, static compliance, and pH with a \(P\)-value of <0.05 considered significant. All data were presented as mean ± SD. The correlation between \(V_T\) and pH and PCO\(_2\) was calculated using the Pearson product moment, with a strong correlation defined as an \(r > 0.8\). The incidence of mild acidosis (defined as <7.351) and severe acidosis (defined as <7.2), as well as hypoxemia (defined as PaO\(_2\) < 80 mm Hg), were recorded using categorical data.\(^\#\)

**Results**

All dogs completed the study successfully. There were no unanticipated anesthetic or ventilatory complications.

As predicted, \(V_T\) had a significant effect on PaCO\(_2\) (\(P < 0.001\)) and on pH (\(P < 0.001\)) (Table 1), with lower \(V_T\) being associated with higher PaCO\(_2\) and lower pH. There was a strong correlation between \(V_T\) and PaCO\(_2\) (\(r = -0.87\)) and \(V_T\) and pH (\(r = 0.83\)).

One dog, while being ventilated with a \(V_T\) of 6 mL/kg, developed mild hypoxemia (PaO\(_2\) = 73 mm Hg, with 92% oxygen saturation). This individual dog has a PaCO\(_2\) of 42 mm Hg with a \(V_T\) of 6 mL/kg. This hypoxemia resolved (PaO\(_2\) = 87 mm Hg 96% saturation) during ventilation with a \(V_T\) of 8 mL/kg. Mild (\(r > 7.2\)) respiratory acidosis was observed in 12/25 arterial blood gases. All 5 dogs had a pH of <7.36 with a \(V_T\) = 6 mL/kg, 4 dogs with a \(V_T\) = 8 mL/kg, 2 dogs with a \(V_T\) = 10 mL/kg, and 1 dog with a pH of 12 mL/kg. No samples had a pH of <7.2.

As predicted, airway pressures significantly increased with higher \(V_T\) (Figure 1). Static compliance increased significantly from 21.3 ± 1.0 mL/cm H\(_2\)O at 6 mL/kg \(V_T\) to 24.5 ± 1.7 mL/cm H\(_2\)O at 15 mL/kg. Neither calculated dead space fraction nor pulse oximetry was significantly affected by changes in \(V_T\).
**Table 1:** The effect of tidal volume on mean ± SD of PCO$_2$ and pH in healthy beagle dogs

<table>
<thead>
<tr>
<th>Tidal volume (mL/kg)</th>
<th>6 mL/kg</th>
<th>8 mL/kg</th>
<th>10 mL/kg</th>
<th>12 mL/kg</th>
<th>15 mL/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCO$_2$ (mm Hg)</td>
<td>40.4 ± 2.2</td>
<td>38.6 ± 2.2</td>
<td>36 ± 2.7</td>
<td>32.8 ± 3.5</td>
<td>29.1 ± 1.7</td>
</tr>
<tr>
<td>pH</td>
<td>7.325 ± 0.02</td>
<td>7.336 ± 0.02</td>
<td>7.368 ± 0.03</td>
<td>7.39 ± 0.04</td>
<td>7.431 ± 0.03</td>
</tr>
</tbody>
</table>

**Discussion**

The results of this study confirmed our hypothesis that decreasing V$_T$ is associated with increased PaCO$_2$ and the development of mild respiratory acidosis, even after controlling for MV. These observations were likely related to greater proportion of fixed anatomic V$_{DS}$. Anatomic dead space is proposed to be 2.2 mL/kg; this assumes greater significance when the V$_T$ is decreased from 15 mL/kg to 6 mL/kg. However, a low V$_T$ (6 mL/kg) was well tolerated in this population of healthy dogs, and there was no evidence of clinically significant acidosis due to CO$_2$ retention or hypoxemia.

As anticipated in this study, increasing V$_T$ was associated with a significant rise in mean, peak, and plateau pressures. Peak pressure is defined as the highest pressure that is reached in the ventilatory circuit, while plateau pressure equivalent to the pressure in the alveoli. Plateau pressure is usually slightly less than peak pressure, although in some cases, such as with very short inspiratory times, the peak pressure is much higher than the plateau pressure. Specific guidelines in human medicine from ARDSnet include trying to limit plateau pressure to less than 30 cm H$_2$O in patients with ARDS although the actual appropriate value as well as method of measurement is still debated. Thirty centimeters of water pressure is considered in a healthy lung to represent total lung capacity and is typically equivalent to an inspiratory volume of approximately 80–90 mL/kg. However, in people with severe ARDS, plateau pressures in excess of 30 cm H$_2$O may be associated with a V$_T$ < 6 mL/kg due to the low lung compliance.

In the normal dogs in this study, compliance increased with increasing V$_T$. The phenomenon is mostly likely associated with recruitment of previously atelectatic lung lobes. Potentially, in dogs with ARDS, increasing V$_T$ to 15 mL/kg may not be associated with recruitment, but rather propagation of lung injury, or the development of pneumothorax. ARDS is a syndrome that accompanies a variety of critical illnesses or injuries in people, and in dogs. ARDS is identified by a variety of clinical parameters, including a pre-existing disease/injury, bilateral pulmonary infiltrates, decreased compliance, and the absence of congestive heart failure. ARDS is associated with a defect in the alveolar-capillary membrane, which permits flooding of the alveolar space with a protein-rich fluid. This results in hypoxemia due to intrapulmonary shunting and V–Q mismatch associated with derecruitment (ie, collapse) of alveoli and an increased work of breathing associated with a low compliance. In people with ARDS, low V$_T$ ventilation has been enthusiastically embraced at medical centers as it results in improved clinical outcome. Hypercarbia is a predictable biochemical change associated with low V$_T$ ventilation in people with ARDS, and is either ignored if possible (eg, permissive hypercapnea), treated by small increases in the V$_T$ if the plateau pressure is low enough, or treated with sodium bicarbonate to increase the pH to a more physiological range.

This study should be repeated in dogs with naturally developing ARDS, as the ability of those critically ill dogs to tolerate low V$_T$ may be markedly different than these healthy beagles.

Of importance, this study did not evaluate the effects of PEEP. PEEP is applied by the ventilator, and prevents the end-expiratory pressure from decreasing below a specific set level. PEEP acts by limiting atelectasis, and by recruiting collapsed alveoli. Moderate-to-high levels of PEEP are considered an essential aspect of ventilatory management of critically ill patients. As such, PEEP would not be anticipated to affect ventilatory values as much as oxygenation, as CO$_2$ is much more diffusible than oxygen. High PEEP in ventilated people may increase V$_{DS}$ (eg, zone 1 ventilation) in people by limiting...
perfusion to specific regions of the lung and this could affect CO₂.

**Conclusion**

This study demonstrates that despite predictable blood gas changes, low \( V_T \) ventilation (6 mL/kg) is well tolerated by healthy dogs, raising the possibility of using low \( V_T \) lung protective ventilation in dogs with ARDS in an effort to reduce ventilator-induced lung injury in these patients. Further work in dogs with ARDS is warranted to assess whether 6 mL/kg \( V_T \) provides adequate ventilation for these patients.

**Footnotes**

\( ^a \) Hydromorphone, Baxter Healthcare Corporation, Deerfield, IL.
\( ^b \) Diazepam, Hospira Inc, Lake Forrest, IL.
\( ^c \) Propofol, Propolco, Abbott Animal Health, North Chicago, IL.
\( ^d \) Lactated Ringer’s Solution, Baxter Healthcare Corporation.
\( ^e \) Puritan Bennett 840 Critical Care Ventilator, Puritan Bennett LLC, Boulder, CO.
\( ^f \) Carprofen, Pfizer Animal Health, Maddison, NJ.

**References**