Effects of inspiratory pause on CO₂ elimination and arterial Pco₂ in acute lung injury

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Devæquet J, Jonson B, Niklason L, Si Larbi A-G, Uttman L, Aboab J, Brochard L. Effects of inspiratory pause on CO₂ elimination and arterial Pco₂ in acute lung injury. J Appl Physiol 105: 1944–1949, 2008. First published 18 September 2008; doi:10.1152/japplphysiol.90682.2008.—A high respiratory rate associated with the use of small tidal volumes, recommended for acute lung injury (ALI), shortens time for gas diffusion in the alveoli. This may decrease CO₂ elimination. We hypothesized that a postinspiratory pause could enhance CO₂ elimination and reduce PacCO₂ by reducing dead space in ALI. In 15 mechanically ventilated patients with ALI and hypercapnia, a 20% postinspiratory pause (Tp20) was applied during a period of 30 min between two ventilation periods without postinspiratory pause (Tp0). Other parameters were kept unchanged. The single breath test for CO₂ was recorded every 5 min during Tp20, VtCO₂ increased immediately by 28% and slope of the alveolar plateau fell to 65% of the initial value and continued to decrease. Tp20 induced a 10% decrease in PaCO₂ at 30 min (from 55 ± 10 to 49 ± 9 mmHg, P < 0.001) with no significant variation in Pao₂. Postinspiratory pause has a significant influence on CO₂ elimination when small tidal volumes are used during mechanical ventilation for ALI.

AFTER TRANSPORT of inspired gas through conducting airways, gas mixing in the respiratory zone by diffusion is time dependent. Therefore, a pause following gas insufflation may enhance gas exchange. Mechanical ventilators allow setting of a postinspiratory pause time (Tp), often in percent of the breathing cycle. During mechanical ventilation, prolonged Tp has been shown to enhance CO₂ elimination (8, 10–12, 14, 21). In healthy pigs, a prolonged Tp increases CO₂ elimination per tidal breath (VtCO₂) by decreasing airway dead space (V_Daw) (20). It was suggested that a prolonged Tp increased the mean distribution time (MDT) of inspired gas, so as to allow more time for diffusion of CO₂ towards more central airways (7). MDT, further explained below, expresses the time available for enhanced diffusion between inhaled tidal volume and resident alveolar gas (2).

In pigs at health and with acute lung injury (ALI), Aström et al. recently found that a certain prolongation of MDT achieved with a longer Tp or with a longer inspiratory insufflation time had similar positive effects on CO₂ exchange (4). They noted that a prolonged Tp had a larger effect on MDT than a similar prolongation of inspiratory insufflation time.

Recently Aboab et al. showed that a longer Tp enhances CO₂ exchange evaluated from volumetric capnography in ALI and acute respiratory distress syndrome (ARDS) (2). Positive effects were observed both with regards to a reduced V_Daw and an elevated alveolar plateau. In their study Tp was only changed for one breath at a time, and PacCO₂ was not measured.

The question was left open if the beneficial effect of Tp was of temporary nature. In pigs, Aström et al. showed that a shortened MDT led to an increase in PacCO₂, that was nearly stable after 30 min. The study by Lessard et al. assessing CO₂ elimination in patients with ARDS was not controlled for the eventual increase in auto-positive end-expiratory pressure (PEEP) and hemodynamic effects induced by the extension of inspiratory time (12). Mercat et al. did so and found that in ARDS, an extended end-inspiratory pause led to lower PacCO₂ by reducing physiological dead space but did not lead to improved Pao₂ (14).

In this study, we hypothesized that in patients with ALI or ARDS ventilated with small tidal volume, a postinspiratory pause applied over a sufficient period of time would enhance CO₂ elimination and reduce PacCO₂ by reducing airway dead space and ventilation/perfusion nonhomogeneity at the alveolar level. By applying volumetric capnography during the whole study, we aimed at increased understanding about mechanisms behind effects of a prolonged Tp and dynamics of CO₂ exchange in ARDS.

PATIENTS AND METHODS

Material. Fifteen consecutive hypercapnic mechanically ventilated patients (Paco₂ ≥ 45 mmHg, Table 1), were studied within 48 h after they fulfilled criteria for ALI or ARDS (5).

Sedation was achieved by continuous infusion. Neuromuscular blockade was used in three patients. The level of sedation (modified Ramsay score ≥ 5) and the absence of respiratory effort on the flow-time curve during an end-expiratory pause of 6 s were checked before the beginning of the study. The patients were studied in semirecumbent position when stable with respect to ventilation, he-
During the last period Tp was reset to 0%. The periods were denoted Tp was set to 0%. Tp was changed to 20% for the second period. Constant throughout the study.

A postinspiratory pause was thereby introduced already for the first breaths during Tp20 and Tp0late were recorded. Ten breaths were performed during this period every 5 min. At 35 and 70 min, the very first breaths during Tp20 and Tp0late were recorded. Ten breaths were analyzed during each recording. Blood gas analysis was performed with GEM Premier 3000 (Instrumentation Laboratory, Barcelona, Spain). Measurements during Tp0init are denoted baseline values.

If needed, endotracheal suction was performed well before the study and was not repeated during data collection. Clinically applied humidification/warming of inspired gas was maintained (heat/moisture exchanger in 10 patients, heated humidifier in 5). All patients had an arterial line.

Exclusion criteria were: age < 18 years, presence of a chest tube, intracranial disease, PaO2/FIO2 < 18 mmol/l, known severe Chronic Obstructive Pulmonary Disease (FEV1 < 50% predicted) or chronic respiratory insufficiency with long-term oxygen therapy. High age of the patients and, as will be shown, high physiological dead space (VTphys) indicate a group of patients with a poor prognosis, in accordance with a 53% mortality rate (15). Patients were ventilated in volume-controlled mode with a constant flow (ServoVentilator 900C with a mainstream CO2 Analyzer 930, Siemens-Elema, Solna, Sweden). Tidal volume (VT) was 7 ± 1 ml/kg of predicted body wt. At baseline, set inspiratory time (Ti) was 20% and Tp 0%. Applied positive end expiratory pressure (PEEP) varied from 5 to 14 cmH2O (Table 2). The ventilator/computer system used for data recording has previously been described (16, 19). Signals representing airway flow, pressure, and CO2 were fed to the A/D converter of a personal computer and sampled at 100 Hz. Compliance of the ventilator tubing was 1.7 ml/cmH2O. Tracheal tube, CO2 analyzer, and heat and moisture exchanger dead space were measured in vitro (apparatus dead space volume was 86 ml if a heat and moisture exchanger was used, 41 ml for a humidified humidifier). The Ethics Committee of French Intensive Care Society approved the protocol. Patients' next of kin were informed of the study protocol and gave their consent.

Procedure. Before the study, it was ensured that the extended Tp from 0% to 20% of total breathing cycle duration did not increase intrinsic PEEP by more than 1 cmH2O. Insufflation time (20%), inspiratory flow, respiratory rate, VT, Fio2, and PEEP were kept constant throughout the study.

Three periods were recorded. During the initial period of 30 min, Tp was set to 0%. Tp was changed to 20% for the second period. During the last period Tp was reset to 0%. The periods were denoted Tp0init, Tp20, and Tp0late respectively. Referring to Fig. 3, at 35 min, the knob on the ventilator panel for setting Tp was reset from 0 to 20%. A postinspiratory pause was thereby introduced already for the ensuing inspiration. At 70 min the knob was turned back to 0% for recording of data for a further 30 min. Signal recordings were performed during this period every 5 min. At 35 and 70 min, the very first breaths during Tp20 and Tp0late were recorded. Ten breaths were analyzed during each recording. Blood gas analysis was performed with GEM Premier 3000 (Instrumentation Laboratory, Barcelona, Spain). Measurements during Tp0init are denoted baseline values.

Data analysis. Data for airway flow, pressure, and CO2 were transferred to a spreadsheet for Excel 2002 (Microsoft, Redmond, WA, USA) and analyzed according to Utman and Jonson (19). The expiratory flow signal was normalized by a correction factor so that expired tidal volume equaled the inspired measured at normal breaths.

Table 1. Characteristics of patients with acute lung injury/acute respiratory distress syndrome

<table>
<thead>
<tr>
<th>No</th>
<th>Age, y</th>
<th>SAPS II</th>
<th>Cause of ALI/ARDS</th>
<th>Underlying Disease</th>
<th>PaO2/FIO2, mmHg</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>78</td>
<td>37</td>
<td>Pneumonia</td>
<td>Ischemic cardiopathy</td>
<td>160</td>
<td>alive</td>
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<tr>
<td>2</td>
<td>78</td>
<td>74</td>
<td>Pneumonia</td>
<td>Ischemic cardiopathy</td>
<td>147</td>
<td>alive</td>
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<tr>
<td>3</td>
<td>38</td>
<td>22</td>
<td>Septic shock</td>
<td>Cirrhosis</td>
<td>121</td>
<td>alive</td>
</tr>
<tr>
<td>4</td>
<td>57</td>
<td>40</td>
<td>Septic shock</td>
<td>Alcoholism</td>
<td>146</td>
<td>dead</td>
</tr>
<tr>
<td>5</td>
<td>76</td>
<td>47</td>
<td>Pneumonia</td>
<td>Cachexy</td>
<td>174</td>
<td>dead</td>
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<td>6</td>
<td>58</td>
<td>52</td>
<td>Pneumonia</td>
<td>Ischemic cardiopathy</td>
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<td>alive</td>
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<tr>
<td>7</td>
<td>91</td>
<td>95</td>
<td>Pneumonia</td>
<td>Epilepsy</td>
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<td>8</td>
<td>81</td>
<td>57</td>
<td>Pneumonia</td>
<td>Hypertension</td>
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<td>9</td>
<td>82</td>
<td>99</td>
<td>Septic shock</td>
<td>Hypertension</td>
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<tr>
<td>10</td>
<td>39</td>
<td>55</td>
<td>Inhalation</td>
<td>Cachexy</td>
<td>193</td>
<td>dead</td>
</tr>
<tr>
<td>11</td>
<td>50</td>
<td>57</td>
<td>Inhalation</td>
<td>Cirrhosis</td>
<td>92</td>
<td>dead</td>
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<tr>
<td>12</td>
<td>71</td>
<td>41</td>
<td>Pneumonia</td>
<td>Leukemia</td>
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<td>dead</td>
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<td>13</td>
<td>44</td>
<td>40</td>
<td>Pneumonia</td>
<td>Aortic dissection</td>
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</tr>
<tr>
<td>14</td>
<td>75</td>
<td>60</td>
<td>Tumor infiltration</td>
<td>Lymphoma</td>
<td>170</td>
<td>alive</td>
</tr>
<tr>
<td>15</td>
<td>86</td>
<td>33</td>
<td>Pneumonia</td>
<td>Atrial fibrillation</td>
<td>196</td>
<td>dead</td>
</tr>
</tbody>
</table>

Mean ± SD 67±18 51±18 — 148±2.5

SAPS, simplified acute physiology score; ALI, acute lung injury; ARDS, acute respiratory distress syndrome.

modynamics, and metabolism (constant temperature). Hemodynamic stability was defined as <15% variation of heart rate and mean arterial pressure between two sets of measurements performed 60 and 10 min before the beginning of the study. During the study, 10 patients were receiving vasoactive drugs (dobutamine and/or epinephrine) at constant infusion rates. No fluid administration was made during the measurements. Values are mean ± SD. Vr, tidal volume; RR, respiratory rate; Ti, inspiratory time including postinspiratory pause; Te, expiratory time; (Ti/T)tot, in-

Table 2. Experimental parameters

<table>
<thead>
<tr>
<th>No</th>
<th>Tp0init</th>
<th>Tp20</th>
<th>Tp0late</th>
<th>Friedman Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT, ml</td>
<td>489±63</td>
<td>502±63*</td>
<td>489±63</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RR, min⁻¹</td>
<td>18±4</td>
<td>18±4</td>
<td>18±4</td>
<td></td>
</tr>
<tr>
<td>Ti, s</td>
<td>0.7±0.2</td>
<td>1.4±0.3</td>
<td>0.7±0.2</td>
<td></td>
</tr>
<tr>
<td>Te, s</td>
<td>3.0±0.6</td>
<td>2.3±0.5</td>
<td>3.0±0.6</td>
<td></td>
</tr>
<tr>
<td>Ppeak, cmH2O</td>
<td>31.5±5.7</td>
<td>31.3±5.4</td>
<td>31.3±5.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Pplat, cmH2O</td>
<td>21.7±4.5</td>
<td>21.7±4.5</td>
<td>21.7±4.5</td>
<td></td>
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<tr>
<td>PEEP, cmH2O</td>
<td>8.5±2.5</td>
<td>8.8±2.5</td>
<td>8.8±2.5</td>
<td></td>
</tr>
<tr>
<td>PEEPtot, cmH2O</td>
<td>9.1±2.5</td>
<td>9.5±2.6 *</td>
<td>9.1±2.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vphys/%, %Vr</td>
<td>68.2±7.4</td>
<td>60.8±8.8*</td>
<td>67.6±7.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VEmax, %, %Vr</td>
<td>40.3±8.8</td>
<td>33.4±8.8*</td>
<td>40.4±8.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VEmax, ml</td>
<td>194±40</td>
<td>166±41*</td>
<td>195±39</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VEmax, %, %Vr</td>
<td>23.8±9.1</td>
<td>22.8±10.1</td>
<td>22.9±8.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Fio2</td>
<td>0.8±0.2</td>
<td>0.8±0.2</td>
<td>0.8±0.2</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.27±0.07</td>
<td>7.31±0.08*</td>
<td>7.27±0.08</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PaCO2, mmHg</td>
<td>55±10</td>
<td>48±9*</td>
<td>55±10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PaO2, mmHg</td>
<td>113±32</td>
<td>110±32</td>
<td>116±34</td>
<td>0.2</td>
</tr>
<tr>
<td>Pao2/Fio2, ratio, mmHg</td>
<td>148±45</td>
<td>145±45</td>
<td>151±45</td>
<td>0.2</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>69±7</td>
<td>73±11</td>
<td>70±6</td>
<td>0.6</td>
</tr>
<tr>
<td>HR, min⁻¹</td>
<td>85±20</td>
<td>87±18</td>
<td>89±18</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Ventilatory and respiratory mechanical parameters, dead spaces, blood gases and hemodynamic parameters were taken at the end of each study period. Values are mean ± SD. VT, tidal volume; RR, respiratory rate; Ti, inspiratory time including postinspiratory pause; Te, expiratory time; (Ti/T)tot, insufflation and postinspiratory pause as percent of the breathing cycle; PEEP, external positive end expiratory pressure; PEEPtot, external positive end expiratory pressure + intrinsic positive end expiratory pressure; Vphys, physiological dead space in percent of VT; VEmax, %, alveolar dead space in percent of VT; Fio2, fraction of inspired oxygen; MAP, mean arterial pressure; HR, heart rate. * P = 0.001 Tp20 vs. Tp0init or Tp0late.
Flow rate and its integral volume were then corrected for gas compression in tubing and adjusted to body temperature and pressure, saturated with water vapor (BTPS). Accordingly, tidal volume was measured as the volume really delivered to the patient, corrected for gas compression in tubing. An unforeseen problem, further discussed below, was that during Tp20, the pressure drop at the end of inspiration caused redistribution from tubing to the lung. Thereby, VT increased by about 13 ml or 2.6%. Partial pressure of CO2 at airway opening was calculated at actual barometric pressure.

Distribution and diffusion of tidal gas in the lung periphery starts at the moment when the interface between “fresh” inspired gas and “used” alveolar gas reaches the respiratory zone of the lung. It ends abruptly when the interface is pushed back into the airways at the start of expiration. Therefore, MDT is the interval from mean time of arrival of partitions of tidal volume in the respiratory zone until start of expiration. It expresses the time available for enhanced diffusion between inhaled tidal volume and resident alveolar gas, as mathematically described by Aboab et al. (2).

Further analysis was based upon the complete single breath test for CO2 (SBT-CO2), which is a loop comprising an inspiratory and an expiratory limb (6). VTphys corresponds to the area within the loop (Fig. 1).

Different parameters related to dead space (VD) were calculated from the SBT-CO2. Mean values of 10 breaths were used. Physiologic dead space (Vphys) was calculated as follows:

\[
V_{\text{phys}} = \left(\frac{\text{PaCO}_2 \cdot V_T - \text{area A}}{\text{PaCO}_2 \cdot V_T}\right) \cdot 100
\]

Vphys was calculated from signal recordings at the end of each period and simultaneous blood gas tests. Airway dead space distal to the CO2 sensor (Vaw) was calculated as the volume at which maximum slope of the SBT-CO2 was measured. Carbon dioxide reinspired from airway dead space proximal to the CO2 sensor (Vaw,prox) corresponds to area A (Fig. 1).

\[
V_{\text{aw,prox}} = \text{area C}/(\text{PaCO}_2 \cdot V_T) \cdot 100
\]

Alveolar dead space, Vaw, was calculated as follows:

\[
V_{\text{aw}} = V_{\text{phys}} - (V_{\text{aw,prox}} + V_{\text{aw}})
\]

The slope of the alveolar plateau (Slope) was determined at the midpoint of the alveolar plateau from a logarithmic equation describing PCO2 over volume (Fig. 1) (3).

Upon adding the postinspiratory pause, the change during the very first eight breaths in VtCO2, Slope, MDT, and Vaw were denoted in ∆VtCO2, ∆Slope, ∆MDT, and ∆Vaw, respectively. The change of PaCO2 between the ends of Tp0init and Tp20 periods is denoted ∆PaCO2.

**Statistical methods.** Data are presented as mean and SD or SE as specified. Friedman’s nonparametric test was used to study the relationship between the quantitative variables at different periods. Differences at the level of P < 0.05 were considered statistically significant. For statistically significant differences, a Wilcoxon matched pairs signed-rank test was done to compare variables at Tp0init or Tp0late and Tp20. Spearman correlation coefficient was used to compare ∆VtCO2, ∆Slope, ∆MDT, ∆Vaw, and ∆PaCO2. Correlation coefficients were considered statistically significant at the 0.05 level, and linear regression was used to establish the relationship between ∆Vaw and ∆PaCO2.

**RESULTS**

**Ventilation and hemodynamics.** VT was 489 ± 63 ml, corresponding to 7 ± 1 ml/kg of predicted body weight. Peak inspiratory flow rate was 0.7 ± 0.2 l/s. During Tp20, airway pressure fell by 9.6 cmH2O during the pause (Table 2). Then tube decompression led to an increase of VT, on average by 13 ± 6 ml (2.6%) (Table 2). MDT changed from 0.21 ± 0.07 s during Tp0init and Tp0late to 0.88 ± 0.24 s during Tp20.

Mean airway pressure was 12.4 ± 2.7 cmH2O at Tp0 and 15.1 ± 2.9 cmH2O at Tp20 (P < 0.01). Total PEEP increased by 0.4 cmH2O on average during Tp20 because of a slight but significant increase in intrinsic PEEP (Table 2). Resistance and compliance of the respiratory system at Tp20 was 13.5 ± 2.8 cmH2O·l⁻¹·s⁻¹ and 44.0 ± 11.4 ml/cmH2O, respectively, yielding an average time constant of 0.59 s. The expiratory time for those 7 subjects who had a respiratory rate above 18 was 1.8 ± 0.2 s at Tp20, i.e., about three time constants. Accordingly, expiration was long enough to allow near-cessation of expiratory flow and low values of auto-PEEP also during Tp20 (Fig. 2). Hemodynamics remained constant during all periods (Table 2).

**CO2 elimination and dead space.** During Tp20, VTCO2 increased immediately by 28% (14 ± 5 ml) compared with baseline during Tp0init, and then decreased without reaching baseline within the Tp20 period (Fig. 3). At the end of Tp20, Vawphys was 11 ± 4% lower than at Tp0, while Vawphys was unchanged (Table 2).

During the whole Tp20, Vawphys was reduced by 28 ml (P < 0.0001, Table 2, Fig. 3). The decrease was 2.2 times higher than the increase in VT. During Tp0late, Vawphys equaled that during Tp0init (Fig. 3). At the end of Tp20, Vawphys was 11 ± 4% lower than at Tp0, while Vawphys was unchanged (Table 2).

During Tp20, the slope of the alveolar plateau fell immediately to 65 ± 10% of baseline value (35 ± 19 vs. 53 ± 23 mmHg/l) and then slowly decreased further to 32 ± 17 mmHg/l (Figs. 3 and 4). During Tp0late the slope returned to baseline.

**Arterial blood gases.** During Tp20, PaCO2 fell by 10 ± 3% (from 55 ± 10 to 49 ± 9 mmHg; P < 0.0001) (Fig. 5, Table 2). During Tp0late, it returned to baseline. No significant change in PaO2 was observed.

The change in PaCO2 from baseline until end of Tp20 (ΔPaCO2, mmHg) correlated with the immediate change in Vaw when the pause was instituted (∆Vaw, ml) (ρ = 0.60, P < 0.02).
No correlations were found between \( \Delta PaCO_2 \) and \( \Delta V_{Daw} \), \( \Delta TcCO_2 \), or \( \Delta MDT \).

A comparison was made between 8 patients with respiratory rate \( \leq 18 \) and 7 patients with rates \( > 18 \). During Tp20, in both groups, total PEEP increased by 0.4 cmH\(_2\)O, PaCO\(_2\) decreased by 6 mmHg and VDaw by 28 ml.

DISCUSSION

During volume-controlled ventilation with small tidal volume and constant inspiratory flow in hypercapnic patients with ALI or ARDS, this study shows that a 20% postinspiratory pause time leads to a 10% decrease in PaCO\(_2\) after 30 min, secondary to enhanced CO\(_2\) elimination. The main explanation of increased CO\(_2\) elimination is lower VDaw.

Our results agree with previous findings that a postinspiratory pause enhances CO\(_2\) elimination in healthy or surfactant-depleted animals (4, 10, 11, 20) and with those obtained in surfactant-depleted pigs in which inspiration at pressure-controlled ventilation was prolonged (13). They also agree with results in patients with ALI/ARDS (2, 8, 12, 14).

The main effect of the postinspiratory pause on CO\(_2\) elimination reflects an instantaneous and continuous reduction of VDaw that was immediately abolished during Tp0late. According to the MDT concept, this reflects enhanced diffusion of CO\(_2\) from alveoli towards airways during the pause. As the decrease of VDaw was more than two times larger than the small increase in VT, the effect on PaCO\(_2\) was about two-thirds caused by the change in VDaw. As further discussed below, the ultimate changes in PaCO\(_2\) could not be estimated during the test periods of 30 min. During Tp20, decompression of gas in the tubing during the pause reflects the product between (Ppeak – Pplat) and tube compliance and was calculated to 16 ml. The increase in VT during Tp20 can accordingly be fully explained by gas decompression. The lower slope of the alveolar plateau during Tp20 indicates that a more even alveolar ventilation-perfusion relationship may have contributed to enhanced CO\(_2\) elimination. The slope of the alveolar plateau mainly reflects nonsynchronous emptying of lung compartments with different ventilation/perfusion ratios (7). The immediate and nearly stable drop in slope during Tp20 (Fig. 3) suggests more even alveolar ventilation due to diffusion within

\[
\Delta PaCO_2 = 0.15\Delta V_{Daw} - 1.49
\]

Fig. 2. Representative tracings from single breaths of airway flow, pressure (Paw), and partial pressure of CO\(_2\) at y-piece in mainstream CO\(_2\) analyzer, PCO\(_2\). Thin black lines represent postinspiratory pause time of 0% (Tp0), and thicker grey lines postinspiratory pause time of 20% (Tp20).

Fig. 3. Diamonds represent mean values for 15 patients at 5-min intervals throughout study. At 35 min the knob on the ventilator panel for setting Tp was reset from 0 to 20% to start Tp20. At 70 min Tp0late was started by turning knob back to 0%. Times for resetting are indicated with vertical interrupted lines. Data at 35 and 70 min represent first breaths during Tp20 and Tp0late. A: Tidal elimination of CO\(_2\) (VtCO\(_2\)) against time. For 15 patients, diamonds and thin lines represent percent of mean value during Tp0init ± 2 SE. B: Airway dead space (V_{Daw}) against time in each subject, patients ventilated with heated humidifiers (continuous lines) or heat and moisture exchangers (broken lines). Diamonds show mean V_{Daw}. C: Slope of alveolar plateau against time. For 15 patients diamonds and thin lines represent percent of mean value during Tp0late ± 2 SE.
At completely steady state, the change in PaCO₂ should equal the change in initial effect on rate of CO₂ elimination, in this reasonable explanation is that CO₂ stores in the body of this reasonable explanation is that CO₂ stores in the body of this period VtCO₂ should, after the initial increase, return towards baseline as a sign of constant metabolic rate. Then, during Tp20, VtCO₂ should, after the initial increase, return towards the baseline that represents metabolic rate. In patients without significant cardiopulmonary disease, when ventilation was decreased by 10%, a new steady state was established along a mono-exponential path with a time constant of ~35 min (17). In the present study, the return towards baseline during Tp20 was far from complete (Fig. 3). Initially during that period VtCO₂ fell rapidly and then very slowly. The reasonable explanation is that CO₂ stores in the body of this group of patients are large and distributed among compartments with very different time constants for equilibration of CO₂. Severe cardiopulmonary disease, increased extravasal liquid space, and poor circulation in peripheral edematous regions are likely causes of slow equilibration of CO₂. Similar conclusions have previously been drawn by Henneberg et al. (9).

During Tp20, the fall in PaCO₂ of 10% is the result of enhanced CO₂ elimination as expressed by enhanced VtCO₂. However, the full effect on PaCO₂ of a change in efficient alveolar ventilation cannot be observed until CO₂ stores in the body have been equilibrated, as discussed by Taskar et al. (17). At completely steady state, the change in PaCO₂ should equal the change in initial effect on rate of CO₂ elimination, in this study represented by change in VtCO₂ by 28%. That VtCO₂ did not return to baseline indicates that a steady state was not achieved during Tp20, as discussed. Accordingly, the observed change in PaCO₂ probably understimates the full effect of a postinspiratory pause of 20%. To limit confounding factors due to spontaneous changes of metabolism and hemodynamic and other physiological parameters, the study periods were limited to 30 min as a compromise against a desirable steady state during each period. Aström et al. observed in pigs at health and with a model of ALI that after 30 min of ventilation with a different MDT, PaCO₂ changed by 0.75 of what was expected on the basis of immediate change in VtCO₂ (4). In the present study this fraction was only 10/28, i.e., 0.36. The difference may represent a much slower equilibration time in the gravely sick patient population. In the study of Mercat et al. PaCO₂ changed by only 5% when the pause was prolonged, although an equilibration time of 1 h left more time available for equilibration of CO₂ stores in the body (14). In their study we estimate that MDT doubled from about 0.6 s to 1.3 s at prolonged Tp, while MDT in ours increased more than four-fold, from 0.21 to 0.88. The lower change in PaCO₂ in Mercat’s study can be explained by the lower relative change in MDT, considering that the effect of variable MDT according to Aström et al. is nonlinear, i.e., more important towards lower MDT values.

At Tp20, shortening of expiration time from 80% to 60% led to a small but significant increase in intrinsic PEEP (<0.5 cmH₂O), PEEP tends to increase VDaw and may hamper CO₂ elimination through hemodynamic effects. Increased PEEP increases in itself VDaw due to airway distension (6, 18). Accordingly, the small increase in total PEEP might have attenuated the observed decrease in VDaw and enhanced CO₂ elimination at Tp20. In spite of higher total PEEP at Tp20, peak pressure remained unchanged. This might indicate that some recruitment took place during Tp20. However, PaO₂ did not increase as was also observed in the study of Mercat et al. (14). One may speculate that positive effects of recruitment were balanced by negative effects caused by diversion of blood flow to collapsed lung, thereby increasing shunt. The two groups with respiratory rate (RR) ≤ 18 and RR > 18 showed equal response to a prolonged pause, which finding may reflect a low variation in RR in the present material.

In this experimental study, we aimed at unchanged tidal volume and used CO₂ turnover PaCO₂ as indicators of more efficient ventilation caused by a postinspiratory pause. In clinical practice, the utility of more efficient gas exchange would rather be to decrease tidal volume for enhanced lung protection. This could, depending on circumstances, be applied so as to either reduce peak pressure to limit barotrauma or to increase PEEP to stabilize lung recruitment. Notably, a postinspiratory pause is one of several options to lower Vₜ. Another is an increase in respiratory rate. At high rates, MDT becomes shorter. Aström showed a steep decline in CO₂ exchange at
low MDT values (4). At high respiratory rates, it may therefore be important to use a pause to adequately prolong MDT.

Conclusion. Postinspiratory pause has a great influence on CO₂ exchange not only for breaths immediately following resetting. A prolongation of Tp leads to a decrease of PaCO₂, as hypothesized. The effects of Tp are mostly due to diffusion of CO₂ into airways but also to a more homogenous ventilation/puffusion at the alveolar level. The mode of inspiratory gas delivery should be taken into account, e.g., in the context of low tidal volume ventilation (1). The ancillary observation of a long equilibrium time for PaCO₂ in ALI, indicating that 30 min is too short for full appreciation of the effect on PaCO₂ of a change in ventilation, merits further studies.

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REFERENCES


