Differential Ventilation and Selective Positive End-expiratory Pressure: Effects on Patients with Acute Bilateral Lung Disease

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Eleven patients with acute respiratory failure due to diffuse, bilateral lung disease were treated according to a new ventilation concept. The patients were intubated with a double-lumen catheter and positioned in the lateral decubital posture. With two synchronized ventilators, each lung received half of the tidal volume (VT), in accordance with its presumed perfusion (differential ventilation—DV), and the end-expiratory pressure was increased locally in the dependent lung (selective PEEP). DV with and without selective PEEP was compared with conventional ventilation with free distribution of VT, with and without PEEP applied to both lungs. The major findings were that DV with a selective PEEP of 12 cmH₂O to the dependent lung decreased venous admixture by 38% (P < 0.01) in comparison with conventional ventilation with no PEEP. Furthermore, it was found that selective PEEP, in contrast to general PEEP, had no deleterious effect on cardiac output. Consequently, DV with selective PEEP increased arterial oxygen tension by 23% (P < 0.05) compared with general PEEP and by 46% (P < 0.001) in comparison with conventional ventilation with no PEEP. (Key words: Lung; perfusion; respiratory distress syndrome. Ventilation: differential; positive end-expiratory pressure.)

ACUTE RESPIRATORY FAILURE (ARF) is, by definition, accompanied by an increased alveolo-arterial oxygen tension gradient, leading to hypoxemia, unless, and sometimes even when, supplementary oxygen is added to the inspired gas.1-5 Reduced functional residual capacity (FRC), decreased pulmonary compliance and mismatching of ventilation, and perfusion (V̇/Q̇) are considered hallmarks of ARF.1

The institution of artificial ventilation is frequently obligatory for counteraction of life-threatening hypoxemia. Paradoxically, though, conventional ventilation might further deteriorate V̇/Q̇. The mechanically administered breath is distributed preferentially to the more compliant, nondependent regions of the lung.4,5

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while dependent lung ventilation is reduced owing to airway closure (AC)6-8 and alveolar collapse. Perfusion, on the other hand, still being gravity dependent, is diverted mainly toward dependent lung regions.9 Application of positive end-expiratory pressure (PEEP) partly can restore the distribution of ventilation by increasing FRC and reducing AC in dependent lung regions.10 However, general PEEP increases the alveolar pressure, which further impedes nondependent lung perfusion.9 Moreover, PEEP increases the mean intrathoracic pressure and frequently has a major negative impact on overall cardiac output.11,12

Since V̇/Q̇ mismatching seems to be a major contributor to hypoxemia, methods for restoring matching should be beneficial for the pulmonary gas exchange.

A ventilation distribution technique recently has been suggested by Hedenstierna et al.,13 aimed toward improving the vertical matching of ventilation and perfusion. The prerequisites for such a ventilation method (differential ventilation) are as follows: 1) double-lumen intubation, 2) patient positioned in the lateral decubital posture, and 3) two separate gas-delivering sources.

Differential ventilation with even distribution of tidal volumes between the dependent and the nondependent lung has been shown to result in an improved gas exchange in patients with diffuse bilateral lung disease treated in the lateral decubital posture.14 Double-lumen intubation and the lateral posture also make it possible to apply PEEP solely to the lung regions where AC and alveolar collapse are most extensive, i.e., the dependent lung (selective PEEP). In a recent investigation it was demonstrated that selective PEEP could increase FRC locally in dependent lung regions and reduce venous admixture without concomitant decrease in cardiac output.15 The aim of the present study was to evaluate the combined effect of differential ventilation in the lateral posture and selective application of PEEP to the dependent lung.

Materials and Methods

The study comprised data from 11 patients (nine men and two women), all of whom were in ARF because of diffuse, bilateral lung disease. Relevant patient data are presented in table 1. All patients were in need of
TABLE I. Clinical Patient Data

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Age, Years</th>
<th>Sex</th>
<th>Clinical Diagnosis</th>
<th>FIO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67</td>
<td>M</td>
<td>Diffuse lung fibrosis, bilateral pneumonia</td>
<td>0.55</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>M</td>
<td>Bilateral bronchopneumonia</td>
<td>0.43</td>
</tr>
<tr>
<td>3</td>
<td>76</td>
<td>M</td>
<td>Acute myocardial infarction, circulatory arrest, bilateral aspiration pneumonia</td>
<td>0.40</td>
</tr>
<tr>
<td>4</td>
<td>72</td>
<td>F</td>
<td>Acute myocardial infarction, pulmonary congestion, bilateral pneumonia</td>
<td>0.46</td>
</tr>
<tr>
<td>5</td>
<td>46</td>
<td>M</td>
<td>Hypnotic drug poisoning, bilateral aspiration pneumonia</td>
<td>0.39</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>M</td>
<td>Brain stem infarction, bilateral pneumonia</td>
<td>0.45</td>
</tr>
<tr>
<td>7</td>
<td>51</td>
<td>M</td>
<td>Hypnotic drug poisoning, bilateral aspiration pneumonia</td>
<td>0.53</td>
</tr>
<tr>
<td>8</td>
<td>49</td>
<td>M</td>
<td>Bilateral bronchopneumonia</td>
<td>0.40</td>
</tr>
<tr>
<td>9</td>
<td>50</td>
<td>M</td>
<td>Bilateral bronchopneumonia</td>
<td>0.48</td>
</tr>
<tr>
<td>10</td>
<td>40</td>
<td>F</td>
<td>Poststatus epilepticus condition, bilateral aspiration pneumonia</td>
<td>0.60</td>
</tr>
<tr>
<td>11</td>
<td>39</td>
<td>M</td>
<td>Bilateral bronchopneumonia</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Artificial ventilator support. The mean inspired oxygen fraction (FIO2) was 0.48 (range 0.39–0.60). The FIO2 was set at the lowest possible level, which during conventional ventilation without PEEP resulted in acceptable arterial oxygen tension. It was kept constant during the course of the study. The patients were unconscious or sedated so as to tolerate the ventilator treatment. The patients were not paralyzed. Informed consent was obtained from a close relative of the patient. The study was approved by the local Ethical Committee. There were no complications attributable to the study.

Hemodynamic Analysis

A pulmonary arterial thermodilution catheter (Swan-Ganz®, Edwards Laboratories) was positioned with its tip in a branch of the pulmonary artery under pressure-tracing guidance and during simultaneous electrocardiogram (ECG) monitoring. A catheter was inserted in the radial artery. Cardiac output (QT) was determined by thermodilution (Cardiac Output Computer Model 9529A®, Edwards Laboratories), as described by Ganz et al.16 Under each experimental condition, a minimum of three determinations of QT were made and the mean value computed.

Systemic arterial (SAP) and pulmonary arterial (PAP) pressures were recorded with pressure transducers (AE 840®, Micro Electronics AS), calibrated with a water manometer. The signal was fed into an amplifier (XV 1505/20®, Philips Medical Systems) and recorded (UV Oscilograph®, EMI) (fig. 1).

The diaphragms of the pressure transducers were positioned horizontally and at midthoracic level, with the patient in the supine position. This level corresponded approximately to 10 cm above the lowermost lung regions when the patient was in the lateral decubitus posture. The location of the tip of the pulmonary artery catheter was not determined in each patient, and a representative left atrial pressure thus could not be taken for granted with the catheter in wedge position. Pulmonary vascular resistance therefore was not calculated.

Blood Analysis

Arterial oxygen and carbon dioxide tensions (Pao2 and Paco2) were measured with conventional electrode techniques (ABL 2, Radiometer). The mean body temperature was 37.3 ± 0.9°C. All blood–gas measurements were made at a standard temperature of 37.0°C. Hemoglobin concentration (Hb) and oxygen saturation (SO2) were determined spectrophotometrically (CO Oximeter 282®, Instrumentation Laboratories). Arterial and mixed venous oxygen contents (CaO2 and CVO2) were calculated from the formula:

\[ C_{O2} \text{ (ml/l)} = \text{Hb (g/l)} \times 1.39 \times S_O2 + P_O2 \text{ (mmHg)} \times 0.03 \]

Venous admixture (QS/QT) was calculated as follows:

\[ \frac{Qs}{Qt} = \frac{CcO2 - CaO2}{CcO2 - CVO2} \]

Pulmonary end-capillary oxygen content (CcO2) was derived from alveolar oxygen tension (Pao2), using the nomogram of Kelman and Nunn.17 Pulmonary end-capillary oxygen tension (PFO2), which was assumed to equal Pao2, was calculated from the alveolar gas equation:

\[ P_{ao2} = FIO2 \times (P_b - P_{H2O}) - PacO2 \times \left( FIO2 + \frac{1 - FIO2}{RQ} \right) \]

where Pb and P H2O stand for barometric and water vapor pressures, respectively, and RQ for respiratory quotient. The latter was assumed to be 0.8.

Volume Measurement

Expired volume (VE) from each lung was measured continuously by argon dilution as described by Davies and Denison,18 using a mass spectrometer (MGA 200®, Centronic (fig. 1)).

Functional Residual Capacity

The increase in functional residual capacity (AFRC) brought about by PEEP was measured by discontinuing PEEP after full expiration, collecting the released gas.
in a bag and measuring its volume by a vortex flow meter (Bourns Medical Systems Inc). The procedure was repeated three to four times for each experimental condition and the mean value was calculated. It was found that gas was released from the nondependent lung when selective PEEP was applied to the dependent lung. This gas (ΔFRC) also was collected in a bag and its volume was measured by the vortex meter.

Airway Pressure

The pressure signals from each of the two channels in the double-lumen tube were recorded continuously using air-filled pressure transducers. Mean airway pressure (Paw) was obtained by electrical damping of the signal (pressure transducer, amplifier and recorder, see “Hemodynamic Analysis” above).

Differential Ventilation

In order to permit differential ventilation, the conventional single-lumen orotracheal tube was exchanged for a double-lumen orobronchial tube (fig. 1). A disposable plastic tube with high-volume, low-pressure cuffs (Broncho-Cath®, National Catheter Co.) was used. Lidocaine was applied topically before insertion of the tube. The position of the double-lumen tube was checked by inflating each lung separately while auscultating the breath sounds. This procedure gave a rough indication of the tube’s position and ensured that both lungs were ventilated. The position was established further by fitting a small balloon to each of the two openings of the tube and ventilating only through the other. The inflation–deflation of the balloon, in phase with the ventilation of the contralateral lung, with no successive increase in
residual balloon volume, indicated a tight airway system. The procedure was repeated whenever the patient was moved or his position altered. To allow sampling of expired gas from each lung during ventilation with one ventilator, a pair of pneumatic valves were fitted to the double-lumen tube.

One or two ventilators (Servoventilator 900B®, Siemens–Elema) were used in the study. They were synchronized electronically in such a way that the start of inspiration was simultaneous for the two lungs. One of the ventilators (master) controlled the other (slave). Apart from the individual tidal volumes and the various forms of PEEP, all ventilatory features were kept constant and equal for the two lungs. A square wave flow mode was used with an inspiratory/expiratory ratio of 1:2 and an end-inspiratory pause corresponding to 10% of the respiratory cycle.

The following modes of ventilation were examined: A) Supine posture, conventional ventilation, ZEEP: Conventional ventilation with zero end-expiratory pressure (ZEEP), in the supine posture. A double-lumen tube and one ventilator were used. B) Supine posture, conventional ventilation, general PEEP: Conventional ventilation with a PEEP of 12 cmH₂O applied to both lungs. A single-lumen tube and one ventilator were used. C) Left lateral posture, conventional ventilation, ZEEP: Conventional ventilation with ZEEP, in the left lateral posture. A double-lumen tube and one ventilator were used. D) Left lateral posture, differential ventilation, ZEEP: Differential ventilation with 50% of the tidal volume distributed to each lung and ZEEP, in the left lateral posture. A double-lumen tube and two ventilators were used (fig. 1). E) Left lateral posture, differential ventilation, selective PEEP: Differential ventilation with 50% of the tidal volume distributed to each lung in the left lateral posture and with a PEEP of 12 cmH₂O applied to the dependent lung only. A double-lumen tube and two ventilators were used (fig. 1).

The sequence of the different ventilator settings was randomized, with the exception of general PEEP (B), which, for practical reasons, was used as the first or the last experimental condition.

STATISTICS

The statistical analysis consisted of calculation of mean values (x), standard deviations (SD), and standard errors of the means (SEM). A two-sided ANOVA test was used to assess the significance of differences. P < 0.05 was considered significant.

Results

The results are summarized in table 2 and figure 2.

CONVENTIONAL VENTILATION

In the supine posture with ZEEP, 54% of the average total tidal volume (VT) of 0.67 l (9.6 ml/kg) was distributed to the right lung and 46% to the left lung. Peak and mean airway pressures (Paw and P̄aw) averaged 26 and 8 cmH₂O, respectively. The pulmonary arterial mean pressure (P̄AP) averaged 21 mmHg, and cardiac output (QT) was 6.8 ± 1.8 l/min. Systemic arterial mean pressure (SAP) was, on an average, 87 mmHg. Fractional venous admixture (QS/QT) was 0.39 ± 0.16 and PaO₂ was 64 ± 15 mmHg. The mean PaCO₂ was(1156,737) mmHg.

When a general PEEP of 12 cmH₂O was applied to both lungs, the distribution of total VT (0.71 l) was not measured for technical reasons. P̄aw increased by 8 cmH₂O and P̄aw by 10 cmH₂O. Both thus were increased to a smaller extent than the amount of PEEP applied. The average ∆FRC was 0.33 l. PAP was increased to 25 ± 12 mmHg. Cardiac output decreased to 4.9 l/min and SAP to 72 ± 11 mmHg. QS/QT was reduced by 36% to a mean of 0.25. PaO₂ was reduced to 77 ± 16 mmHg. PaCO₂ was not affected significantly.

PEEP then was discontinued, and the patients were positioned in the left lateral decubital posture. Of the total VT (0.66 l), 70% was distributed to the nondependent (right) lung and 30% to the dependent (left) lung. All other variables returned to essentially the same level as with ZEEP in the supine posture.

DIFFERENTIAL VENTILATION (DV)

During DV with ZEEP, 50% of the total VT was distributed to each lung in the lateral posture. This resulted in an increase in P̄aw to 30 ± 6 cmH₂O in P̄aw to 9 ± 2 cmH₂O in the dependent lung in comparison with conventional ventilation in the lateral posture. In the nondependent lung, P̄aw and P̄aw were decreased to 19 ± 5 and 5 ± 1 cmH₂O, respectively. PAP was 21 ± 12 mmHg, which was less than with general PEEP but not different from conventional ventilation with ZEEP in either posture. QT was, on average, 7.3 l/min, which was greater than at all other ventilator settings studied. SAP was 85 ± 12 mmHg and not different from that during conventional ventilation with ZEEP. QS/QT was decreased by 27% compared with ZEEP ventilation in either posture but did not differ significantly from that during general PEEP. The mean PaO₂ was 85 mmHg, which was 28% greater than during conventional ventilation with ZEEP and not significantly different from that with general PEEP. PaCO₂ was much the same as with the other ventilator settings.
| Table 2. Comparison of Data from 11 Patients Given Differential Ventilation with Even Tidal Volume Distribution with and without Selective PEEP to the Dependent Lung in the Lateral Posture, in Comparison with Conventional Ventilation with ZEEP in the Supine and Lateral Postures and with General PEEP in the Supine Posture (Mean ± SD) |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                  | Supine Posture                  | Supine Posture                  | Lateral Posture                 | Lateral Posture                 |
|                                  | Conventional                    | Ventilation                     | Conventional                    | Ventilation                     |
|                                  | ZEEP                            | General PEEP                    | ZEEP                            | General PEEP                    |
| QT (l/min)                       | 6.8 ± 1.8                       | 4.9 ± 1.4*                      | 6.7 ± 1.6*                      | 7.3 ± 1.8*                      |
| SAP (mmHg)                       | 87 ± 18                         | 72 ± 11‡                       | 90 ± 17‡                        | 85 ± 12                         |
| PAP (mmHg)                       | 21 ± 11                         | 25 ± 12‡                       | 22 ± 12‡                        | 21 ± 12                         |
| Q/S/QT                           | 0.39 ± 0.16                     | 0.25 ± 0.12‡                   | 0.39 ± 0.13*                    | 0.29 ± 0.11*                    |
| PacO2 (mmHg)                     | 64 ± 15                         | 77 ± 16‡                       | 66 ± 14‡                        | 83 ± 15‡                        |
| PacO2 (mmHg)                     | 34 ± 4                          | 31 ± 4                          | 36 ± 5                          | 34 ± 4                          |
| VT (l)                           | 0.67 ± 0.10                     | 0.71 ± 0.11                     | 0.66 ± 0.12                     | 0.68 ± 0.11                     |
| VT (l)                           | 0.36 ± 0.07                     | —                               | 0.46 ± 0.06                     | 0.34 ± 0.06                     |
| VT (l)                           | 0.31 ± 0.07                     | —                               | 0.19 ± 0.08                     | 0.34 ± 0.06                     |
| PAW (cmH2O)                      | 26 ± 6                          | 34 ± 7*                         | 26 ± 5*                         | 19 ± 5*                         |
| PAW (cmH2O)                      | 26 ± 6                          | 34 ± 7*                         | 26 ± 5*                         | 30 ± 6*                         |
| PAW (cmH2O)                      | 8 ± 1                           | 18 ± 6‡                        | 7 ± 1‡                          | 5 ± 1‡                          |
| PAW (cmH2O)                      | 8 ± 1                           | 18 ± 6‡                        | 7 ± 2‡                          | 9 ± 2‡                          |
| PAW (cmH2O)                      | 26 ± 5                          | 30 ± 5                          | 30 ± 7                          | 30 ± 7                          |
| PAW (cmH2O)                      | 22 ± 7                          | 18 ± 4                          | 23 ± 4                          | —                               |

Abbreviations: QT = cardiac output; SAP = systemic arterial mean pressure; PAP = pulmonary arterial mean pressure; Q/S/QT = venous admixture; PacO2 and PacO2 = arterial oxygen and carbon dioxide tensions; VT = tidal volume; PAW and PAW = peak and mean airway pressures; CT = total (lung and chestwall) compliance; nd and d = non-dependent and dependent lung; ZEEP = zero end-expiratory pressure; and PEEP = positive end-expiratory pressure.

With maintained distribution of VT and an average selective PEEP of 12 cmH2O to the dependent lung, PAW and PAW in the dependent lung both were increased by 9 and 11 cmH2O, respectively. The corresponding pressures in the nondependent lung were not altered significantly. The FRC of the dependent lung increased by 0.23 l, while that of the nondependent lung decreased by 0.09 l. The net increase in FRC (ΔFRC) thus amounted to as little as 0.14 l, which was less than half of that brought about by general PEEP. The average PAP was 22 mmHg, which was less than with general PEEP but not different from any other ventilator setting. QT was 6.9 ± 1.4 l/min and thus less than that during DV with ZEEP but not different from that during conventional ventilation with ZEEP. The average SAP was 88 mmHg and thus similar to the value during DV with ZEEP. Q/S/QT was decreased to 0.24 ± 0.11, which was the lowest fractional venous admixture recorded in the study. PacO2 was increased further (P < 0.05) to an average of 95 mmHg, i.e., 46% greater (P < 0.01) than during conventional ventilation with ZEEP and 23% greater (P < 0.05) than during general PEEP. PacO2 was much the same throughout the study.

Discussion

The major findings in this study were that differential ventilation substantially could decrease venous admixture and increase arterial oxygenation (fig. 2), in comparison with conventional ventilation with ZEEP. The application of selective PEEP further augmented oxygenation. Moreover, selective PEEP had no negative impact on cardiac output (fig. 2).

CONVENTIONAL VERSUS DIFFERENTIAL VENTILATION

During anesthesia and artificial ventilation, the lung volume is decreased, causing dependent lung regions to attain their residual volume. If the lung is in a diseased state, as in ARF, a similar and even more marked decrease in FRC may occur. This is accompanied by an impaired dependent lung ventilation as shown during anesthesia and in ARF. In the present study, 70% of the total lung ventilation was distributed to the nondependent lung during conventional ventilation with ZEEP in the lateral posture. This hardly could have resulted in an optimal gas exchange. When differential ventilation with equal tidal volume distribution was instituted, ventilation of the well-perfused dependent lung was improved. At the same time, ventilation of the nondependent less perfused lung was decreased. This could be expected to improve the V/Q ratios of the two lungs, an assumption that is supported by the observed decrease in venous admixture and the increased arterial oxygen tension.
tance of the larger extraalveolar vessels.\textsuperscript{23} Nondependent already-expanded lung regions were less inflated, a fact that, on the other hand, should have decreased the resistance of the intraalveolar vessels.\textsuperscript{24} Pulmonary vascular resistance was not measured in the present study, since a true pulmonary capillary wedge pressure could not be ascertained. However, cardiac output was increased and pulmonary arterial mean pressure was unchanged, which indicate that a reduction of overall pulmonary vascular resistance actually took place.

**General versus Selective PEEP**

The beneficial effect of PEEP seems to lie in the counteraction of airway closure and recruitment of collapsed alveoli, through an increase in FRC.\textsuperscript{25,26} But while PEEP in most studies decreases venous admixture,\textsuperscript{27,28} it also impairs cardiac output.\textsuperscript{11,12} It has been postulated that the mechanism underlying shunt reduction by PEEP actually is brought about by decreased cardiac output.\textsuperscript{28} Airway closure and alveolar collapse are most extensive in dependent regions of the lung,\textsuperscript{29,30} owing to the lesser transmural pressure there.\textsuperscript{31} It has been shown previously that general PEEP increases the lung volume much more in nondependent than in dependent lung regions.\textsuperscript{10} This is obviously unfavorable if the desired effect is counteraction of airway closure and recruitment of collapsed alveoli. In addition, the further increase in nondependent lung volume enhances the danger of barotrauma,\textsuperscript{32} and it also causes the blood flow to be squeezed further toward dependent lung regions as a result of the greater alveolar pressure.\textsuperscript{9}

Ideally, PEEP should be “aimed” at dependent lung regions, where it could be allowed to increase FRC locally, with less or no increase in overall intrathoracic pressure. Selective application of PEEP to the dependent lung has been shown to decrease venous admixture as efficiently as general PEEP and with no concomitant decrease in cardiac output.\textsuperscript{15}

The findings in the present study corresponded well with our previous ones. On application of selective PEEP, the increase in dependent lung FRC was 0.23 l. The FRC of the nondependent lung was concomitantly decreased by 0.09 l. The net increase in total FRC was thus as little as 0.14 l (c.f. 0.33 l with general PEEP). It is reasonable to assume that the smaller increase in total lung volume led to a lesser increase in intrathoracic mean pressure (which was not measured in the present study) and, hence, had less impact on the central hemodynamics than had general PEEP. This assumption also is supported by the greater cardiac output with selective than with general PEEP ($P < 0.01$), being no longer different from that during conventional ventilation without PEEP. However, venous admixture was
essentially the same as with general PEEP. As a result of the maintenance of the lesser fractional venous admixture as with general PEEP, and the preserved cardiac output as with no PEEP, selective PEEP gave the largest arterial oxygen tension in the study.

It is concluded that differential ventilation and selective PEEP to the dependent lung can decrease the venous admixture and improve the arterial oxygen tension without a concomitant deleterious effect on the cardiac output.

References

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