EFFECTS OF PEEP ON DYNAMIC HYPERINFLATION IN
PATIENTS WITH AIRFLOW LIMITATION


SUMMARY
We have studied the effects of extrinsically applied PEEP (PEEPe) and intrinsic PEEP (PEEPi) on lung volume and peak airway pressure (Paw,peak) in 10 patients with airflow limitation during mechanical ventilation. PEEPe was applied in 2-4 cm H2O increments until values greater than PEEPi were reached. Total lung hyperinflation was quantified by measuring the expired volume resulting from deflation (starting at end inspiration) until cessation of expiratory flow. The previous expired tidal volume was subtracted from this volume to obtain the change in functional residual capacity (δFRC), the hyperinflation resulting from PEEPi and PEEPe. PEEPi (0.49-1.66 kPa) was demonstrated in all patients before the application of PEEPe and correlated with δFRC (r = 0.71), with δFRC increasing by 582 ml/kPa PEEPi (P < 0.05). PEEPe at pressures less than PEEPi increased δFRC by (mean) 186 (SEM) 34 ml/kPa PEEPe (P < 0.05) and increased Paw,peak by 0.6 (0.12) kPa/kPa PEEPe (P < 0.05). In contrast, PEEPe at pressures greater than PEEPi increased δFRC by 695 (128) ml/kPa PEEPe (P < 0.05) and Paw,peak by 1.8 (0.26) kPa/kPa PEEPe. We conclude that PEEPe may be applied cautiously at values less than PEEPi when clinically indicated, but the application of PEEPe at values greater than PEEPi may substantially aggravate lung hyperinflation. (Br. J. Anaesth. 1993; 70: 267-272)

KEY WORDS

Patients with an exacerbation of obstructive lung disease occupy a significant portion of the resources of an intensive care unit. It has been shown that, despite mechanical ventilatory support, many patients still perform significant work of breathing during assisted ventilation [1]. In the presence of airflow limitation, if minute volumes are increased by the disease process or through attempts by the physician to achieve normocapnia, residual expiratory flows and positive alveolar pressures with dynamic hyperinflation may exist at end-expiration. Part of the work of breathing is a consequence of this hyperinflation and positive end-expiratory alveolar pressures [2].

The presence of an alveolar pressure greater than airway pressure at end-expiration has been termed occult, auto-, or intrinsic PEEP (PEEPi) [3]. This is in contrast with ventilator-applied or extrinsic positive end-expiratory pressure (PEEPe). PEEPi cannot be detected on routine inspection of the airway pressure waveform, but is associated with adverse effects similar to those of PEEPe, such as hypotension and barotrauma. Strategies that minimize PEEPi and dynamic hyperinflation, such as the use of small minute volumes without seeking to achieve normocapnia, are accepted modes of therapy in some centres, with reported improved outcomes [4].

In addition, PEEPi represents the residual pressure that has to be overcome by inspiratory muscle effort in order to initiate airflow [5]. It has been shown that PEEPi in the presence of dynamic flow limitation helps to reduce excessive and potentially fatiguing work of breathing during assisted or spontaneous ventilation [5,6]. Small PEEPe has therefore been suggested to be beneficial in the assisted ventilation and weaning of these patients. The assumption is that, when flow limitation exists, PEEPe does not diminish the driving pressure for expiratory flow and therefore dynamic hyperinflation is not further aggravated. As previous studies on the effect of PEEPe on dynamic hyperinflation have produced variable results, we re-examined the effect of PEEPe on dynamic hyperinflation in patients with airflow obstruction.

PATIENTS AND METHODS
The study was approved by the Research Ethics Committee of the Chinese University of Hong Kong. We studied 10 patients with an exacerbation of chronic obstructive pulmonary disease or asthma, who required mechanical ventilation. Tracheal intubation with size 8-9 mm i.d. tracheal tubes (Portex Ltd, Kent, England) was performed on all patients. The patients were sedated and paralysed with i.v. infusions of midazolam and atracurium, and studied...
in the supine position within 24 h of admission to the intensive care unit. Conventional mechanical ventilation with a square wave inspiratory flow pattern was provided by a Servo 900C ventilator (Siemens–Elema, Solna, Sweden) in which minute volume, ventilatory frequency and inspiratory time settings were determined previously by an intensivist independent of the investigators and remained unchanged for the duration of the study. None of the patients was receiving PEEPe. The airway and breathing systems were visibly devoid of secretions and no air leak was detectable. These patients were haemodynamically stable and were monitored by pulse oximetry, intra-arterial pressure, central venous pressure and continuous ECG monitors.

Flow was measured at the proximal end of the tracheal tube with a heated pneumotachograph (Fleisch No. 2, Fleisch, Lausanne, Switzerland) coupled to a sensitive differential pressure transducer (Validyne MP45-1,±2 cm H₂O, Validyne Engineering, Northridge, CA, U.S.A.). Airway pressure was measured with a pressure transducer (Gaeltec 8T 50, Medical Measurements Inc., NJ, U.S.A.) between the tracheal tube and the pneumotachograph. The flow and pressure transducers were calibrated in vitro before the patient measurements, using an RT 200 calibration analyser (Timetometer Corp, PA, U.S.A.). Flows were calibrated for values up to 100 litre min⁻¹ and pressures up to 8 kPa, immediately downstream from a size 9 mm Portex tracheal tube. The flow and pressure signals were captured at 24–124 Hz, balanced and amplified (Gould 13 U615-35, Gould Inc., OH, U.S.A.), and displayed and stored on a Gould 1624 digital storage Oscilloscope (Gould Electronics Ltd, Essex, U.K.). Polynomial regression was used to plot a "best fit" curve of the transducer signals against their respective calibration flow or pressure values. The equation expressing flow or pressure as a function of the respective transducer signals was applied to the subsequent in vivo measurements. These recorded patient signals were similarly stored in the Gould oscilloscope and transferred later to an IBM computer. A data and waveform analysis of each patient’s digitized signals was performed using a computer program written by one of the authors (Y.H.T.). Volume displacement was determined by electronic integration of the flow signal. Calibration of the transducers was performed for each set of patient measurements in order to avoid baseline drift. The methodology and apparatus have been described previously [7].

PEEPi was determined by two previously described methods: occlusion of the expiratory port of the ventilator at end-expiration (Poc) [3], and by noting the airway pressure at the beginning of passive inspiratory flow (Paw,0) [8]. Measurements of Paw,0 were repeated at least three times and the arithmetic mean obtained. Poc was accepted if the time of occlusion of the expiratory hold button of the ventilator was within 0.3 s from the beginning of the next mechanical breath. Peak airway pressures (Paw,peak) were measured also. PEEPe was applied in 2–4 cm H₂O increments until pressures greater than PEEPi were obtained. At each new PEEPe, a 5-min interval was allowed for equilibration before measurements were obtained. The "end-inspiratory volume" [9] at each PEEP was determined by measuring the expired volume obtained from disconnecting the patient from the ventilator at end-inspiration, and allowing complete exhalation to functional residual capacity (FRC) where no further expiratory flow was measurable. This end-inspiratory volume has been found previously to be a reproducible index of hyperinflation [9]. The expired tidal volume of the previous breath was subtracted from the end-inspiratory volume to obtain δFRC, the hyperinflation resulting from the presence of PEEPe and PEEPi. A sample recording of the methodology is shown in figures 1 and 2.

Linear regression analysis was performed on the data using a packaged statistical software program (Statview II, Abacus Concepts, CA, U.S.A.). Analysis of variance and Student’s t tests were performed on the results. Data are expressed as mean (SEM). P < 0.05 was considered significant.
FIG. 2. Calculation of δFRC. Top: Flow signal obtained during disconnection of the patient from the ventilator at end-inspiration, and allowing complete expiration until zero expiratory flow. Bottom: Electronic integration of the flow signal in the top panel. The final height of the left shaded area is the expired tidal volume, and the final height of the right shaded area is the "end-inspiratory volume" obtained from the above deflation manoeuvre. δFRC is the difference between these two volumes.

TABLE I. Patient characteristics and ventilatory settings at the commencement of the study. COPD = Chronic obstructive pulmonary disease; f = ventilatory frequency; Insp. time = duration of inspiration as a fraction of the ventilatory cycle; PEEPi = intrinsic PEEP; SFRC = hyperinflation volume

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Minute volume (litre)</th>
<th>f (b.p.m.)</th>
<th>Insp. time (%)</th>
<th>PEEPi (kPa)</th>
<th>SFRC (ml)</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>83</td>
<td>M</td>
<td>COPD</td>
<td>9.00</td>
<td>16</td>
<td>0.43</td>
<td>0.98</td>
<td>344</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>M</td>
<td>COPD</td>
<td>7.20</td>
<td>12</td>
<td>0.38</td>
<td>0.85</td>
<td>364</td>
</tr>
<tr>
<td>3</td>
<td>81</td>
<td>M</td>
<td>COPD</td>
<td>8.00</td>
<td>12</td>
<td>0.35</td>
<td>0.49</td>
<td>260</td>
</tr>
<tr>
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<td>M</td>
<td>COPD, pneumonia</td>
<td>7.70</td>
<td>14</td>
<td>0.43</td>
<td>0.85</td>
<td>273</td>
</tr>
<tr>
<td>5</td>
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<td>M</td>
<td>Bronchiectasis</td>
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<td>20</td>
<td>0.35</td>
<td>0.54</td>
<td>220</td>
</tr>
<tr>
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<td>F</td>
<td>COPD, pneumonia</td>
<td>7.20</td>
<td>12</td>
<td>0.35</td>
<td>0.89</td>
<td>249</td>
</tr>
<tr>
<td>7</td>
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<td>M</td>
<td>COPD</td>
<td>9.00</td>
<td>15</td>
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<td>593</td>
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<tr>
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<td>M</td>
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<td>1.43</td>
<td>1206</td>
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<tr>
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</tr>
<tr>
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<td>M</td>
<td>Asthma</td>
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<td>12</td>
<td>0.35</td>
<td>0.89</td>
<td>425</td>
</tr>
</tbody>
</table>

RESULTS

The flow and pressure responses from each calibration were found to be linear over the range of values recorded from the patients. No patient complications occurred during the study. Patient characteristics are shown in table I. PEEPi (range 0.49–1.66 kPa) and δFRC (220–1206 ml) were demonstrated in all patients even before any PEEPe was applied (table I). The PEEPi measurements by the two methods described above were in reasonable agreement (r = 0.87) (fig. 3) and henceforth, in this paper, PEEPi refers only to that obtained by expiratory port occlusion at end-expiration.
Before the application of PEEP, δFRC correlated with initial PEEPi values ($r = 0.71, P < 0.05$); δFRC increased by 582 ml/kPa PEEPi ($P < 0.05$). The increase in lung volume is comparable with published compliance values for the ventilatory system of sedated and paralysed patients undergoing mechanical ventilation.

When PEEP was applied in increments, δFRC increased progressively (fig. 4). Linear regression analysis of all 10 patients revealed that, with PEEP at pressures less than PEEPi, PEEP increased δFRC by a mean of only 186 (34) ml/kPa of PEEP ($P < 0.05$). However, when PEEP values were greater than PEEPi, PEEP increased δFRC by a much larger mean of 695 (128) ml/kPa of PEEP ($P < 0.05$). A similar analysis was performed on the relationship between PEEP, PEEPi and Paw,peak (fig. 5). The application of PEEP at pressures less than PEEPi increased peak airway pressure by a mean of 0.61 (0.12) kPa/kPa of PEEP ($P < 0.05$). The increase in Paw,peak was much larger when PEEP was greater than PEEPi, increasing by 1.78 (0.26) kPa/kPa of PEEP ($P < 0.05$).

**DISCUSSION**

Airflow limitation results from flow through compliant airways. Two models have been postulated to explain flow limitation: the wave-speed mechanism and the dissipative mechanism [10]. In the wave-speed mechanism, the pressure change required to accelerate gas from alveoli determines both flow and transmural pressure. With accelerating flow from a region of larger to smaller cross-sectional area, the intramural pressure decreases cephalad, as does the transmural pressure, until a maximal flow is reached at “choke” points. In the dissipative mechanism, the pressure change results from laminar or turbulent energy dissipation. With both models, mouth pressures less than a “critical” pressure downstream of the choke point do not affect driving pressures upstream of the choke point. Analogy with a waterfall has been made [11]. If there is airway constriction at any level, impedance of expiratory driving pressures (e.g. by PEEP), or when inspiration occurs before expiration is complete, dynamic hyperinflation and PEEPi result.

PEEPi refers to an alveolar pressure greater than PEEP at end-expiration [3]. Three forms of PEEPi have been described, reflecting their mechanisms of production [12]. In the absence of flow limitation, PEEPi may arise from expiratory muscle activity at end exhalation, or from the use of minute volumes too great for the time constant properties of the patient’s ventilatory system. The existence of these forms of PEEPi is unlikely in the present study as the patients were paralysed and the lungs ventilated mechanically with moderate minute volumes of 6-10 litre min$^{-1}$. Dynamic hyperinflation can arise also from the short expiratory times of large ventilatory frequencies, but this is unlikely in the present study as moderate rates were used with low inspiratory:expiratory ratios [13].

Airway flow limitation was demonstrated by the presence of transient increased flows after the opening of the ventilator expiratory valve (fig. 1) [14] and marked downward convexities in the patient’s flow–volume curve which remained unchanged when small PEEP was applied [15]. The latter observation was exemplified best by the flat flow–volume curve of patient No. 8, who had the most severe flow limitation (fig. 6).

The present study found PEEPi in all the patients examined. This is not surprising, as the subjects were those with obstructive lung disorders severe enough to require mechanical ventilation of the lungs. A previous study on PEEPi found a 60% incidence in patients with various disorders who were older than 60 yr and undergoing mechanical ventilation with minute volumes greater than 10 litre min$^{-1}$ [16]. None of our patients received mechanical ventilation with minute volumes in excess of 10 litre min$^{-1}$, yet all had PEEPi, ranging up to 1.66 kPa, with δFRC ranging up to 1206 ml. Thus the dangers of attempting to achieve normocapnia during ventilation in patients who have severe obstructive airways disease are obvious.
PEEP AND HYPERINFLATION

PEEPi, in common with PEEPe, is known to cause a reduction in cardiac output and predispose to barotrauma [3]. If dynamic hyperinflation is induced by PEEPi or by airflow limitation, the shortened inspiratory muscles generate a smaller contractile force. The resultant larger radius of curvature of the diaphragm is associated with diminished pressure generation as a consequence of LaPlace’s law [17]. Furthermore, PEEPi represents the threshold load that has to be overcome by inspiratory muscle effort in order to initiate airflow, or for triggering the machine-assisted breath. Impaired ability to generate work thus coexists with increased respiratory load resulting from overdistension, and patients with airflow limitation thus become difficult to wean from mechanical ventilation. In this context, it has been suggested that PEEPe may be used to mitigate some of the adverse effects of PEEPi [5]. PEEPe would reduce the difference between PEEPi and airway pressure, thus decreasing the inspiratory threshold load and the work of breathing [6]. Central to this argument is the assumption that PEEPe does not diminish the driving pressure for expiratory flow to occur and thus cause further hyperinflation. Although Tuxen noted progressive hyperinflation with the use of PEEPe [18], other workers reported no worsening of hyperinflation by PEEPe applied at values less than PEEPi [5, 19, 20].

We found that, despite values of PEEPe less than PEEPi, increases in hyperinflation and Paw,peak did occur. This contradicts the findings of other workers [5, 19, 20]. Although the increase in δFRC with PEEPe less than PEEPi in the present study is significant statistically, it is small. The increase in hyperinflation in our patients, despite reduced PEEPe, may have been caused by regional inhomogeneities in their lungs, possibly with the existence of non-flow-limited pathways. Gay, Rodarte and Hubmayr [21] showed that hyperinflation with PEEP occurred in patients who were not flow-limited while, in patients who were flow-limited, the value of PEEPe that resulted in the reduction of isovolume expiratory flow was unrelated to the initial value of PEEPi. In their analysis of isovolume pressure-flow curves, they described Pcrit, the driving expiratory pressure less than which flow becomes submaximal and greater than which no further increase in flow occurs. Pcrit is less than PEEPi at end expiratory lung volumes, so that if PEEPe equal to PEEPi is applied, isovolume flows must decrease and hyperinflation would occur [22].

Increases in hyperinflation and airway pressure in the present study were considerably greater with values of PEEPe greater than PEEPi. Tuxen reported progressive hyperinflation with the application of PEEPe [18]. However, in that study PEEPi was not measured directly, and it is possible that the smallest PEEPe used (5 cm H$_2$O) may have exceeded the PEEPi of his patients. Also, all patients in that study received mechanical ventilation with minute volumes in excess of 10 litre min$^{-1}$, from which further hyperinflation may have resulted with PEEPe independent of flow limitation. The absence of flow limitation or the presence of regional inhomogeneities in his patients may also explain his results.

Isolated case reports [23–25] of reductions in lung volume with PEEPe in patients with asthma or chronic obstructive airways disease were based essentially on clinical impressions and make comparison with the present study or other reports difficult.

Our findings were derived from sedated and paralysed patients, and may not be applicable to patients with obstructive airway disease undergoing assisted or spontaneous ventilation, for whom PEEPe is proposed to reduce work of breathing [5, 6]. These patients may have frequent variations in ventilatory requirement, breathing pattern, recruitment of respiratory muscles during expiration and degrees of bronchospasm. These factors complicate the resultant effects of PEEPe on the dynamics of breathing and lung volume, even in the absence of regional inhomogeneities or non-flow-limiting segments in the lung. Large regional increases in lung volume and alveolar pressures may occur transiently with adverse effects. Nonetheless, Petroff and co-workers [6] did not find large increases in overall lung volume at smaller values of PEEPe.

It is not clear if PEEPe may ultimately affect weaning outcome by reducing inspiratory work. Factors leading to gas trapping, PEEPi and unnecessary work of breathing should be minimized. Use of bronchodilators, treatment of the underlying disease, reduction of pain, anxiety, fever and other causes of increased ventilatory requirements, and minimizing imposed loads from small tracheal tubes, secretions and humidifiers, are all important. Furthermore, in the presence of regional inhomogeneities in airway resistance and lung compliance, the use of PEEPe might cause serious local over-distension not detectable by changes in PEEPi, which averages gas trapping over the whole lung. Safe values of PEEPe in the patient with both flow-limited and non-flow-limited pathways would thus be one of clinical judgement, while PEEPe at pressures greater than PEEPi would be unwise. We conclude that PEEPe may be applied cautiously at pressures less than PEEPi as the increases in lung volume and airway pressure are relatively small.

REFERENCES


