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Under Open Lung Conditions Inverse Ratio Ventilation Causes Intrinsic Peep and Hemodynamic Impairment

Agneta M. Markström,[1,2] Michael Lichtwarck-Aschoff,[1,3] Anders J. Hedlund,[4] K. Anders Nordgren[1] and Ulf H. Sjöstrand[1]

[1]*Department of Anesthesiology, University Hospital, Uppsala, Sweden,* [2]*Department of Otorhinolaryngology, University Hospital, Uppsala, Sweden,* [3]*Institute of Anesthesiology and Surgical Intensive Care Medicine, Zentralklinikum Augsburg, Augsburg, FRG and* [4]*Department of Plastic Surgery–Burn Unit, University Hospital, Uppsala, Sweden*

ABSTRACT

Inverse ratio ventilation (IRV) is commonly used in clinical practice. Several studies have used IRV in order to recruit collapsed alveoli. In a randomised trial in twelve surfactant depleted piglets, the lungs were ventilated with sufficient positive end-expiratory pressure (PEEP) to prevent end-expiratory collapse, and the effects of increased inspiration-to-expiration (I:E ratio) were evaluated. Pressure regulated ventilation (with I:E of 1:1, constant tidal volume and decelerating inspiratory flow) was used at 30 breaths per minute (bpm). I:E ratios of 1.5:1, 2.3:1 and 4:1 were applied sequentially. When the I:E ratio was increased, external PEEP had to be reduced in order to keep total PEEP constant. Functional residual capacity, airway pressures, gas exchange, extrathermal volume and hemodynamics were measured. With I:E ratios above 2:1 intrinsic PEEP was generated and with concomitant decrease in cardiac index. PaO_2 was not affected, but oxygen delivery was reduced. It is concluded that I:E ratios of 2:1, or above, generate increased intrinsic PEEP with compromised hemodynamics.

INTRODUCTION

Interest in ventilation of patients with acute respiratory failure but without further impairment of the lungs has made it important to identify characteristics of different ventilatory patterns and strategies that affect airway pressures, volumes, pulmonary gas exchange and hemodynamics.

Pressure-controlled ventilation with prolonged inspiratory time (PC-IRV) has been used in an attempt to reduce ventilation-related lung injury and to improve oxygenation (3, 6, 8, 24). The mechanism responsible for the increased PaO_2 with the PC-IRV pattern is believed to be the occurrence of intrinsic PEEP and its attendant increase in functional residual capacity (FRC) (2, 7). Increased FRC by increased PEEP is, however, known to reduce cardiac output and oxygen delivery (DO_2) (13, 20, 23). For similar reasons, intrinsic PEEP, caused by shortened expiratory time, could also have detrimental effects on cardiac function in the same way as does external PEEP.

In a previous experimental study (12) on inverse ratio ventilation we maintained constant mean airway pressure. In that study with an increased I:E ratio, oxygenation remained unaffected, whereas hemodynamics were impaired. The aim of the present investigation was to study prolonged inspiration-to-expiration when the lung was ventilated with sufficient total PEEP to prevent end-expiratory collapse. Our hypothesis was that an increased inspiration-to-expiration ratio ought not to affect hemodynamics when total PEEP was maintained constant.

MATERIALS AND METHODS

Twelve piglets of Swedish Landrace, with a mean body mass of 25.4 kg (±1.9 SD), were subjected to lavage. Two papers describing the methods in detail have been published previously (11, 16).

Premedication: Pentobarbital 15 $mg \cdot kg^{-1}$ + 0.5 mg atropine was given intraperitoneally 15 min before induction. Induction: 500 mg ketamine and 0.5 mg atropine were given i.v. followed by a ketamine (Ketalar®, Parke-Davis) infusion at 20 $mg \cdot kg^{-1} \cdot h^{-1}$. In addition a bolus of 20 mg morphine i.v. was given before the initial tracheotomy, preparation and introduction of intravascular catheters. Relaxant: Pancuronium bromide was given as a continuous infusion at 0.26 $mg \cdot kg^{-1} \cdot h^{-1}$. The animals were ventilated through an 8 mm diameter endotracheal tube (Mallinckrodt Inc., Glens Falls, NY, USA) with a Servo 300 (Servo Ventilator 300, Siemens-Elema AB, Solna, Sweden). A thermostatically controlled heating pad was used to keep the animal's body temperature at 37.6 C (± 0.6).

The investigations were performed at the Experimental Laboratories of the Department of Anesthesiology and Intensive Care at University Hospital, Uppsala. The local Ethics Committee for animal experimentation reviewed and approved the protocol.

Monitoring

Intravascular catheters were surgically placed for the measurement of central venous, pulmonary arterial (via the external jugular vein) and aortic pressures (via the carotid artery). The exact position of catheters was confirmed by pressure tracings. ECG and heart rate and all pressures were displayed on a bedside monitor (Siemens Sirecust), and recorded with reference to the mid-thorax and at end-expiration level. Arterial and mixed venous blood gases were measured (ABL 300/OSM III®, Radiometer A/S, Denmark). Carbon dioxide production was recorded by a metabolic monitor (Datex Deltatrac®, Datex Instrumentation Corp., Finland).

The estimation of cardiac output was performed using the COLD® System (Pulsion Medizintechnik KG, Germany); details of the method have been published elsewhere (17). A 4-F fiberoptic catheter with a thermistor was introduced via the femoral artery, and advanced to the descending aorta. The thermistor in the femoral artery catheter connected to the COLD system detects the temperature signal in the descending aorta from which cardiac output is calculated.

Extrathermal volume (ETV) and intrathoracic blood volume (ITBV) were measured using the technique of double indicator dilution described in detail elsewhere (18). The double indicator, consisting of 5 mg indocyanine green mixed in 10 mL dextrose 5% in water at a temperature of 5-7°C, was injected in a bolus into the superior vena cava. The dilution curves for dye and temperature were recorded simultaneously in the descending aorta with the thermistor-tipped fiberoptic catheter. ETV was calculated as the difference between the volume accessible to the intravascular indicator, indocyanine green and the extra thermal volume measured by thermodilution. ITBV was calculated as the product of cardiac output and the mean transit time of indocyanine green between the points of injection in the superior caval vein and its detection in the descending aorta at the level of the diaphragm.

Airway pressures were obtained from the digital displays of the ventilator. Before starting the study, the pressure and flow transducers of the ventilator had been calibrated with independent devices. Every morning a pre-use functional check was performed according to the procedure recommended in the operating manual for the ventilator. Mean airway pressure as measured by the ventilator was accepted to represent pressures which could be measured during cyclic ventilation.

The static chest-lung compliance (Clt) was calculated according to the formula

$$Clt = \text{Tidal volume} \times (\text{end-inspiratory pressure} - \text{end-expiratory pressure})^{-1},$$

but with appropriate modifications to account for the compressible volume (21).

When the end-inspiratory occlusion pressure (n =12), and the total end-expiratory pressure (n = 6) were measured, the ventilators hold function was applied for 5 s before the equilibrium values were noted.

During cyclic ventilation, total PEEP was measured as the sum of external PEEP set by the PEEP valve of the ventilator, and the intrinsic PEEP resulting from the incomplete emptying of the lungs at end-expiration, and, for technical reasons, only measured as end-expiratory occlusion pressure in 6 animals. In the ventilator this measurement was representative of the conditions 61 msec prior to the next inspiratory cycle during cyclic ventilation.

To measure the functional residual capacity (FRC), serial dead space (SDS) and alveolar mixing efficiency, the SF_6 tracer gas washing-washout method (for details of the method, see (9, 10). was used. The SF_6 equipment was only available in 10 animals, i.e. all data for FRC presented in this study comprise measurements where n =10. In our laboratory the coefficient of variation for three sequential measurements in 9 animals for FRC, under a broad range of tidal volumes and different flow conditions, was 1± 0.8%.

Recruitment procedure

Immediately after lavage the surfactant deficient-lungs were recruited with I:E 1:1 and the external PEEP set to produce a peak inspiratory pressure (PIP) of 50 cmH_2O for 5 min.

Inflection point (P_{infl})

The static pressure-volume (PV) loop of the inspiratory limb of the respiratory system was generated with the ventilator, using a total volume of 1200 mL delivered by a constant inspiratory flow of 0.15 L/min during 8 seconds, FIO_2 1.0. From this PV-loop, P_{infl} was determined by inspection (15).

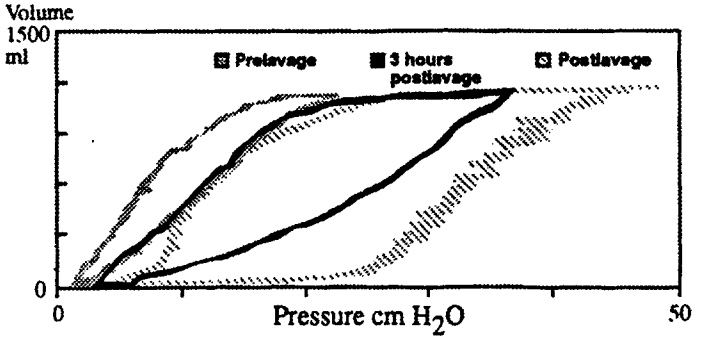

Figure 1
Pressure-volume (PV-) loops before, immediately after, and 3 hours after lavage in one of the piglets.

Inspiratory flow pattern

(see Figure 3)

Servo Ventilator 300 provides pressure-controlled ventilation as a modality called pressure-regulated volume-controlled ventilation (Siemens-Elema AB, Solna, Sweden). This provides the set tidal volume by regulating the inspiratory pressure to a value based on the pressure/volume conditions for the previous breath. By allowing the drive gas pressure to be adjusted between each breath, the set tidal volume is maintained within limits that are given by the set upper pressure limit, and the fact that pressure differences between breaths are not allowed to exceed 3 cmH_2O. Decelerating inspiratory flow (see Figure 3) was therefore delivered together with a constant tidal volume for all settings.

Experimental procedure

Following anesthesia and preparation the animals were placed in the prone position. Prelavage pulmonary function parameters were measured using I:E 1:1 and zero PEEP with a ventilatory frequency of 30 bpm as baseline conditions. For this baseline condition an intrinsic PEEP was already present, of 1.4 (±1.1) cmH_2O . Lavage was performed as described previously (11, 16). With zero PEEP ventilation, lavage increased Qs/Qt from 9 to 32.5%. Thereafter the (P_{infl}) was determined by inspection, followed by a second recruitment procedure. Ventilation was resumed with decelerating inspiratory flow and the external PEEP set to 75% (17 cmH_2O) of the inflection point value, which in a previous study was shown to maintain open lung conditions (22). With

this PEEP level, Qs/Qt was in a range of 10%. This latter setting was then used as a reference setting with I:E ratio 1:1, FIO_2 0.5 and the tidal volume (TV) adjusted to 11±1 $mL \cdot kg^{-1}$ to achieve a $PaCO_2$ of 5.5±0.3 kPa. Three different I:E ratios (1.5:1, 2.3:1 and 4:1) were sequentially applied to each animal, i.e. four possible combinations. All measurements were obtained in ventilatory, metabolic and hemodynamic steady state, i.e. during stable CO_2 production. Each setting was applied for at least half an hour to achieve ventilatory and hemodynamics steady state. As prolonged inspiratory times generated increasing intrinsic PEEP, external PEEP had to be reduced in order to keep total PEEP constant (see Fig 2).

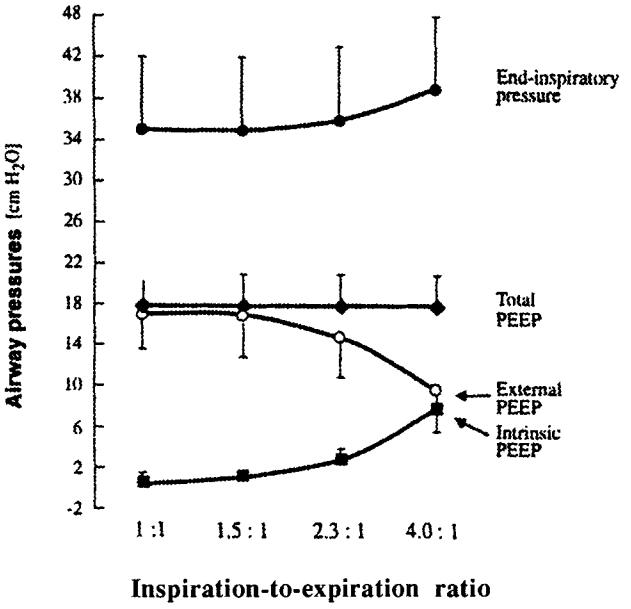

Figure 2
End-inspiratory and mean airway pressures, and the relationship between external and intrinsic PEEP, and the resulting total PEEP, with stepwise inverse I:E ratio while total PEEP was kept constant. Regarding PEEP values, see *Discussion.*

Calculations and statistics

Values are as mean ±1 standard deviation (SD). A standard statistics package was used (STAT-VIEW)™. Differences between the ventilatory settings were evaluated with a t-test for all paired differences within each variable. Statistical significance is indicated as $p \leq 0.01$ (=**).

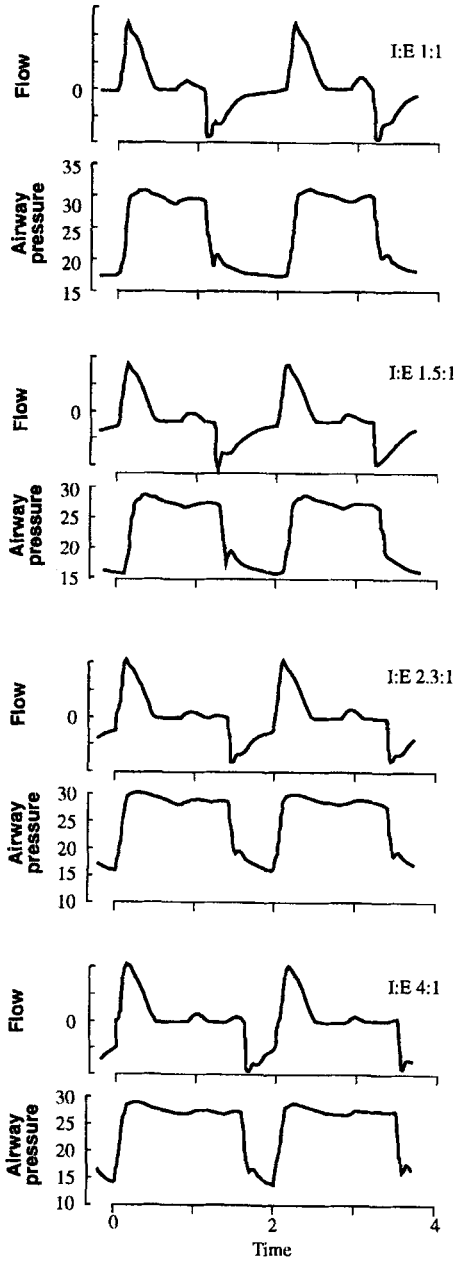

Figure 3
Original experimental record (from top to bottom) of gas flow and airway pressure for two breaths at 30 bpm and with increasing I:E ratios. The pressure-regulated volume-controlled mode provided the set tidal volume (by regulating the inspiratory pressure to a value based on the pressure/volume conditions for the previous breath). By allowing the drive gas pressure to be adjusted between each breath, decelerating inspiratory flow was, therefore, delivered together with a constant tidal volume for all settings. Time is given in seconds, airway pressures in cm H_2O, and flow in a relative scale. Paper speed is 12.5 $mm \cdot s^{-1}$.

RESULTS

The results are presented in Tables 1-3, and Figures 1-4. Immediately postlavage, ventilation with zero PEEP increased Qs/Qt from 9 to 32.5%. External PEEP was set at 17 cmH_2O and with the reference setting I:E of 1:1, there was an intrinsic PEEP of 1 cmH_2O, i. e. total PEEP was 18 cmH_2O. This reduced Qs/Qt to about 10%.

Airway pressures

(See Table 1 and Fig 3)

In order to maintain a total PEEP of 18 cmH_2O with prolonged inspiratory time, and when intrinsic PEEP increased, external PEEP had to be reduced to 15 cmH_2O (I:E 2.3:1) and to 10 cmH_2O (I:E 4:1), respectively. End-inspiratory occlusion pressure and peak inspiratory pressure increased to 36±7 cmH_2O with I:E ratio 4:1.

With prolonged inspiratory time, mean airway pressure as measured by the ventilator increased to 26±6 cmH_2O (I:E 1.5:1), to 28±6 cm H_2O (I:E 2.3:1) and to 31±7 cmH_2O for I:E 4:1.

Ventilation, gas exchange, lung volumes and compliance

(See Table 1 and Figs 1 and 2)

PaO_2 only increased with I:E ratio 1.5:1, and no further improvement was seen with prolonged inspiration time. No change was seen in $PaCO_2$ from the reference level with inverse I:E ventilation Compliance decreased to 13±2 $mL \cdot cmH_2O^{-1}$, and FRC increased to 1703±319 mL with I:E 4:1.

Hemodynamics and oxygen delivery

(See Table 2 and Fig 4)

Stroke index (SI) decreased to 30±8 $mL \cdot (m^2)^{-1}$ with prolonged inspiratory time. Cardiac index was 5175±1059 (I:E 1:1), 4467±1170 (I:E 1.5:1), 4742±1077 (I:E 2.3:1), and 4008±889 (I:E 4:1). With I:E ratio 2.3:1 and 4:1, oxygen delivery index (DO_2I) decreased to 547±127 and 464 ±85 $mL \cdot min^{-1} \cdot (m^2)^{-1}$ despite PaO_2 was unaffected.

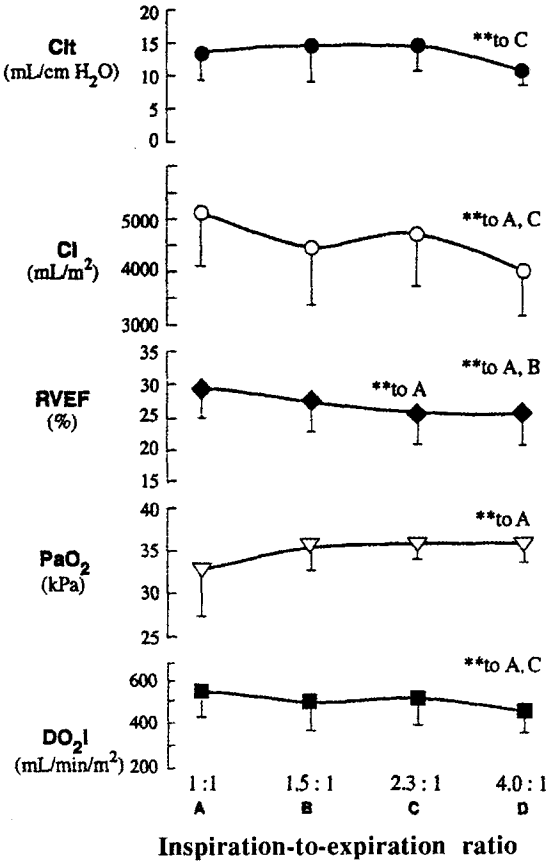

Figure 4
The effects on compliance (Clt), cardiac index (CI), right ventricular ejection fraction (RVEF), PaO_2 and oxygen delivery (DO_2I) with stepwise inverse I:E ratios.

Table 1

Pulmonary function parameters with stepwise inverse inspiration-to-expiration ratio.

Inspiration time (s)	1.00	1.00	1.20	1.40	1.60
I:E ratio	1:1	1 : 1	1.5 : 1	2.3 : 1	4 : 1
	Pre 0	A	B	C	D
End-inspiratory pressure [cmH_2O]	18 ±1	32 ±7	32 ±7	33 ±7 B	36 ±7 A, B, C
Peak inspiratory pressure [cmH_2O]	18 ±1	32 ±7	32 ±7	34 ±7 B	36 ±7 A, B, C
Mean airway pressure [cmH_2O] displayed by the ventilator	4 ±0	24 ±5	26 ±6 A	28 ±6 A, B	31 ±7 A, B, C
Total PEEP[cmH_2O](n=12)	1 ±1	18 ±3	18 ±3	18 ±3	18 ±3
External PEEP [cmH_2O] (n=12)	0	17 ±4	17 ±4	15 ±4 A, B	10 ±4 A, B, C
Intrinsic PEEP [cmH_2O] (n=12)	1.2 ±0.7	0.9 ±0.7	1.4 ±0.5 A	3.2 ±1.1 A, B	8.3 ±1.8 A, B, C
Intrinsic PEEP measured with expiratory hold [cmH_2O] (n=6)	1.4±1.1	1.7±0.5	3.1±0.8 A	5.1±1.0 A	12.0±2.8 A, B, C
Compliance [$mL \cdot cmH_2O^{-1}$]	32 ±5	18 ±4	17 ±4	16 ±3	13 ±2 C
Functional residual capacity [mL]	763 ±205	1620 ±371	1721 ±395	1667 ±383	1703 ±319 A
$PaCO_2$ [kPa]	5.52 ±0.24	5.67 ±0.31	5.35 ±0.25	5.25 ±0.39 A	5.21 ±0.26 A
PaO_2 [kPa]	37 ±2	33 ±5	36 ±3 A	36 ±2 A	36 ±2 A
CO_2 production [$mL \cdot min^{-1} \cdot (m^2)^{-1}$]	209 ±23	268 ±35	193 ±18	193 ±17	191 ±22 A

Table 1

Pulmonary function parameters with stepwise inverse inspiration-to-expiration ratio. Values are means ±1 SD; n=12 (for FRC: n=10). Pre 0 are values obtained before lavage, A, B, C and D are values after lavage. "A" denotes significant ($p \leq 0.01$) difference to I:E 1:1, "B" to I:E 1.5:1, "C" to I:E 2.3:1. Airway pressures in cm H_2O and partial pressures in kPa.

Table 2

Hemodynamic function parameters with stepwise inverse inspiration to expiration ratio.

Inspiration time (s)	1.00	1.00	1.20	1.40	1.60
I:E ratio	1 : 1	1 : 1	1.5 : 1	2.3 : 1	4 : 1
	Pre 0	A	B	C	D
SvO_2 [%]		62 ±9	60 ±8	55 ±14	55 ±8 B
Pulmonary arterial pressure [mmHg]	18 ±3	28 ±4	30 ±7	34 ±7 A	36 ±7 A, B
Cardiac index [mL·min^{-1}·(m2)$^{-1}$]	7092 ±1173	5175 ±1059	4467 ±1170	4742 ±1077	4008 ±889 A, C
Stroke index [mL·(m2)$^{-1}$]	46 ±7	40 ±10	32 ±7	37 ±7 A	30 ±8 A
Venous admixture [%]	9 ±1	10 ±1	10 ±1	11 ±1	11 ±1
Intrathoracic blood volume [mL·kg^{-1}]	27 ±4	23 ±6	20 ±4	21 ±5	19 ±4
Extravascular lung water [mL·kg^{-1}]	5 ±1	19 ±3	18 ±3	17 ±4 A	17 ±3
RV end- diastolic volume [mL·(m2)$^{-1}$]	145 ±9	120 ±23	116 ±24	115 ±23	106 ±20 A
RV ejection fraction [%]	32 ±4	31 ±5	29 ±5	27 ±5 A	27 ±5 A, B
Oxygen delivery [mL·min^{-1}·(m2)$^{-1}$]	820 ±171	571 ±125	509 ±132	547 ±127	464 ±85 A, C

Table 2
Hemodynamic function parameters with stepwise inverse inspiration-to-expiration ratio. Values are mean ±1 SD; n=12." A" denotes significant difference to I:E 1:1, "B" to I:E 1.5:1, "C" to I:E 2.3:1.

Table 3

Hemodynamic function parameters with stepwise increased PEEP (0, 8 and 15 cm H_2O) before lavage.

Inspiration time (s)	1.00	1.00	1.00
I:E ratio	1 : 1	1 : 1	1 : 1
	Pre 0	Pre 8	Pre 15
SvO_2 [%]	77 ±5	75 ±5	68 ±8 Pre 0, 8
Pulmonary arterial pressure [mmHg]	18 ±3	30 ±5 Pre 0	36 ±5 Pre 0, 8
Cardiac index $[mL \cdot min^{-1} \cdot (m^2)^{-1}]$	7092 ±1173	6525 ±898	5200 ±933 Pre 0, 8
Stroke index $[mL \cdot (m^2)^{-1}]$	46 ±7	47 ±5	37 ±4 Pre 0, 8
Venous admixture [%]	9 ±1	9 ±1	10 ±1
Intrathoracic blood volume $[mL \cdot kg^{-1}]$	27 ±4	24 ±3	22 ±3
Extravascular lung water $[mL \cdot kg^{-1}]$	5 ±1	6 ±2	7 ±2
RV end- diastolic volume $[mL \cdot (m^2)^{-1}]$	145 ±9	141 ±21	128 ±19
RV ejection fraction [%]	32 ±4	33 ±3	29 ±5
Oxygen delivery $[mL \cdot min^{-1} \cdot (m^2)^{-1}]$	820 ±171	740 ±147	593 ±139 Pre 0, 8

Table 3

Hemodynamic function parameters with stepwise increased PEEP (0, 8 and 15 cm H_2O) before lavage. (values are mean ±1 SD). Pre 0 = are values obtained before lavage with no PEEP, Pre 8 and Pre 15 with PEEP of 8 and 15 cm H_2O, respectively. "Pre 0" and "Pre 8" denote significant ($p \leq 0.01$) difference to measurements under Pre 0 and/or Pre 8 PEEP conditions. Airway pressures in cm H_2O, and partial pressures in kPa.

DISCUSSION

In a previous experimental study (12) using inverse ratio ventilation we maintained constant mean airway pressure. In the present investigation, total PEEP was kept constant in order to isolate the effect of prolonged inspiratory time on airway pressures and hemodynamics. As arterial oxygen tension was in the normal range even during ventilation with the reference setting I:E 1:1, no improvement in oxygenation could be expected, either at mean airway pressure (12) or with total PEEP kept constant.

Our hypothesis was that, if inverse ratio ventilation was to be proved efficient, an increased inspiration-to-expiration ratio should not influence hemodynamics when total PEEP was kept constant. Above an I:E ratio of 2.3:1 there was a decrease in cardiac output with prolonged inspiration time.

These findings are discussed in the following paragraphs after a comment on the surfactant-depleted lung model.

Methodological considerations

With decelerating inspiratory flow, the major part of the tidal volume is delivered during early inspiration. End-expiratory occlusion airway pressure reflects the end-expiratory elastic recoil of the respiratory system under static conditions, i. e. during equilibration of lung units with different time constants, which is not equivalent to the total PEEP during cyclic ventilation.

Mean airway pressure is defined as the pressure in the ventilator circuit connected to the subject averaged over the entire ventilatory cycle, but it does not include intrinsic PEEP. With the ventilator used, mean airway pressure was calculated as in most modern ventilators by using the set external PEEP added to a time-weighted value of the peak inspiratory pressure during cyclic ventilation. During cyclic ventilation intrinsic PEEP is a pressure which actually could not be measured. The implication of this is that measurements of true total PEEP (being the sum of external and intrinsic PEEP) are not taken into account in the calculated (displayed) mean airway pressure during cyclic ventilation. Consequently, during cyclic ventilation, total PEEP could in effect not be set identical with different I:E ratios, and the disparity increased with increasing inspiration-to-expiration ratios.

Before lavage, baseline ventilation was performed with zero PEEP and I:E 1:1. Cardiac output was about 7 litres. At 8 cmH_2O of PEEP there was a decrease in cardiac output and at 15 cmH_2O the cardiovascular depression was in the same range as for the postlavage mode with an I:E ratio of 1:1. With I:E ratio 4:1 postlavage and an external PEEP of 10 cmH_2O, the shortened expiratory time generated a substantially increased intrinsic PEEP of 12 cmH_2O, which compromised cardiac output still further. Even when we tried to keep total PEEP constant, we found a higher than expected intrinsic PEEP (see Table 1).

The inflection point of the inspiratory limb of the pressure volume loop was determined by inspection. The projection on the airway pressure axis of the vertex of the lower curved section

was defined as the inflection point pressure. As such a procedure implies a low accuracy of estimation, ventilation was performed within the high volume segment of the PV-curve (Fig 1).

In order to ensure open lung conditions, we chose a rather high PEEP level. In the present study, the period of ventilation was 30 minutes, which may be too short to demonstrate the benefits of prolonged inspiratory time on lung mechanics. Several studies (14, 24) have found a substantial lag between the point at which inverse ratio ventilation was instituted and the maximal observed benefit for lung mechanics.

Hemodynamics and oxygen delivery

During inverse ratio ventilation, the effects of shortened expiratory time lead to increased intrinsic PEEP. As shown in Fig 1, prolonged inspiration-to-expiration and constant inspiratory pressure will increase mean airway pressure considerably.

It is a well known fact that the cardiovascular effects of mechanical ventilation are closely related to mean airway pressure (MPAW) and its effects on transpulmonary pressure (15). In the present study, this is illustrated by the increased MPAW which reduced cardiac output and stroke index (SI) as inspiration time of I:E 2.3:1 was extended. In a previous study (12) with MPAW kept constant, hemodynamics were also impaired due to the increase in intrinsic PEEP. Moreover, MPAW is known to be an important determinant of oxygenation (4). In this study PaO_2 was unaffected, but due to cardiovascular compromise, oxygen delivery was decreased at I:E 4:1.

When compared with other findings (19) the venous admixture in this study was low even during reference mode due to the high PEEP level. With inverse ratio ventilation above I:E ratio 1.5:1, no further reduction was to be expected.

Airway pressure

Even though PEEP and tidal volume were set constant, peak inspiratory pressure (PIP) and end-inspiratory occlusion pressure ($PAW_{endinsp}$) increased as inspiratory time was prolonged.

Prolonged inspiration time reduces expiratory time, which results in intrinsic PEEP with concomitant adverse effects on lung mechanics. This impairment of lung mechanics is in contrast to other studies reporting no change (2) or even improved (19) lung mechanics with IRV. - It is conceivable that in those studies in which an improvement was found, the measurements were started under conditions of collapse of the alveoli which was then recruited by IRV.

During IRV intrinsic PEEP is present due to incomplete pulmonary evacuation. Short expiratory time or airway obstruction could account for this. In the present study we suggest that intrinsic PEEP was related mainly to the short expiratory time, as airway obstruction could be reasonably rejected.

Speculations

Inverse ratio ventilation is commonly used in clinical practice. Several studies have used IRV to recruit alveolar collapse. To eliminate this we attemted to ventilate the lung with sufficient PEEP to prevent end-expiratory collapse (open lung conditions). To elucidate the underlying mechanism of prolonged inspiration-to-expiration, mean airway pressure was kept constant in the first study (12) while total PEEP was kept constant in the present study. When an I:E ratio of 2:1, or above, was used, both investigations showed impaired hemodynamics. This led us to speculate that the impairment was due to effects of shortened expiratory time. If the lung is ventilated with sufficient total PEEP to prevent end-expiratory collapse, then IRV will not provide any additional advantage. In order to prevent lung damage due to high shear forces between open and closed lung units, ventilation which results in the smallest possible pressure amplitude (peak inspiratory pressure - total PEEP) should be used.

We conclude therefore that, under open lung conditions, inspiration-to-expiration ratios of 2.3:1, or above, generate increased intrinsic PEEP with compromised hemodynamics.

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REFERENCES

1. Boros, S., Matalon, S., Ewald, R., Leonard, A. & Hunt, C.: The effect of independent variations in inspiratory-expiratory ratio and end-expiratory pressure during mechanical ventilation in hyaline membrane disease: The significance of mean airway pressure. J Pediat 91: 794-798, 1977.
2. Brandolese, R., Brogseghini, C., Polese, G., Bernasconi, M., Brandi, G. & Milic-Emili, J.: Effects of intrinsic PEEP on pulmonary gas exchange in mechanically ventilated patients. Eur Respir J 6: 358-363, 1993.
3. Chan, K. & Abraham, E.: Effects of inverse ratio ventilation on cardiorespiratory parameters in severe respiratory failure. Chest 102: 1556-1561, 1992.
4. Cole, A.G.H., Weller, S.F. & Sykes, M.K.: Inverse ratio ventilation compared with PEEP in adult respiratory failure. Intensive Care Med 10: 227-232, 1984.
5. Dantzker, D., Lynch, J.P. & Weg, J.G.: The influence of cardiovascular function on gas exchange. Clin Chest Med 4: 149-159, 1979.
6. Gurevitch, M., Dyke, J.V., Young, E. & Jackson, K.: Improved oxygenation and lower peak airway pressures in severe adult respiratory distress syndrome: Treatment with inverse ratio ventilation. Chest 89: 211-213, 1986.
7. Kacmarek, R. & Hoss, D.: Pressure-controlled inverse-ratio ventilation: Panacea or auto-PEEP? Respir Care 35: 945-948, 1990.
8. Lain, D., Benedetto, R., Morris, S., Nguyen, A.V., Saulters, R. & Causey, D.: Pressure controlled inverse ratio ventilation as a method to reduce peak inspiratory pressure and provide adequate ventilation and oxygenation. Chest 95: 1081-1088, 1989.
9. Larsson, A., Jonmarker, C. & Werner, O.: Ventilation inhomogeneity during controlled ventilation. Which index should be used? J Appl Physiol 65: 2030-2039, 1988.
10. Larsson, A., Linnarsson, D., Jonmarker, C., Jonson, B., Larsson, H. & Werner, O.: Measurement of lung volume by sulphur hexafluoride washout during spontaneous and controlled ventilation. Further development of a method. Anesthesiology 67: 543-550, 1987.

11. Lichtwarck-Aschoff, M., Nielsen, J.B., Sjöstrand, U.H. & Edgren, E.L.: An experimental randomised study of five different ventilatory modes in a piglet model of severe respiratory distress. Intensive Care Med 18: 339-347, 1992.
12. Lichtwarck-Aschoff, M., Markström, A.M., Hedlund, A.J., Nielsen, J.B. & Nordgren, K.A. & Sjöstrand, U.H.: Oxygenation remains unaffected by increased inspiration-to-expiration ratio but impairs hemodynamics in surfactant depleted piglets. Intensive Care Med 22: 192-198, 1996.
13. Lutch, J. & Murray, J.: Continuous positive-pressure ventilation effect on systemic oxygen transport and oxygenation. Ann Intern Med 76: 193-202, 1972.
14. Marcy, T. & Marini, J.: Inverse ratio ventilation in ARDS: Rationale and implementation. Chest 100: 494-504, 1991.
15. Matamis, D., Lemaire, F., Harf, A., Brun-Buisson, C., Ansquer, J. & Atlan, G.: Total respiratory pressure-volume curves in the adult respiratory distress syndrome. Chest 86: 58-66, 1984.
16. Nielsen, J.B., Sjöstrand, U.H., Edgren, E.L., Lichtwarck-Aschoff, M. & Svensson, B.A.: An experimental study of different ventilatory modes in piglets in severe respiratory distress induced by surfactant depletion. Intensive Care Med 17: 225-233, 1991.
17. Pfeiffer, U.J., Backus, G., Blümel, G., Eckart, J., Müller, P. & Winkler, P.: A fiberoptics based system for integrated monitoring of cardiac output, intrathoracic blood volume, extravascular lung water, O_2-saturation, and a-v differences. In: Lewis, F.R., Pfeiffer, U.J (eds) Fiberoptics in Critical Care Monitoring. Springer Verlag, Heidelberg, 114 - 125, 1990.
18. Pfeiffer, U., Zeravik, J., Lichtwarck-Aschoff, M. & Obermaier, J.: Intrathoracic blood volume reflects circulating volume status in critically ill patients. In: New aspects on respiratory failure (Rügheimer, E., ed.). Springer Verlag, Berlin, Heidelberg, 294-306, 1992.
19. Poelaert, J.I., Visser, C.A., Everaert, J.A., Koolen, J.I. & Colardyn, F.A.: Acute hemodynamic changes of pressure-controlled inverse ratio ventilation in the adult respiratory distress syndrome. Chest 104: 214-219, 1993.
20. Qvist, J., Pontoppidan, H., Wilson, R., Lowenstein, E. & Laver, M.: Hemodynamic response to mechanical ventilation with PEEP: The effects of hypervolemia. Anesthesiology 42: 45-55, 1975.
21. Scott, L.R., Benson, M.S. & Pierson, D.J.: Effect of inspiratory flow rate and circuit compressible volume on auto-PEEP during mechanical ventilation. Respir Care 31: 1075-1079, 1986.
22. Sjöstrand, U.H., Lichtwarck-Aschoff, M., Nielsen, J.B., Markström, A.M., Larsson, A. & Svensson, B.A.: Different ventilatory approaches to keep the lung open. Intensive Care Med 21: 310-318, 1995.
23. Suter, P., Fairley, H. & Isenberg, M.: Optimum end-expiratory pressure in patients with acute pulmonary failure. N Engl J Med 292: 284-289, 1975.
24. Tharatt, R., Allen, R. & Albertson, T.: Pressure controlled inverse ratio ventilation in severe adult respiratory failure. Chest 94: 755-762, 1988.

Correspondence address: Agneta M. Markström, Department of Anesthesiology,
University Hospital, S-751 85 UPPSALA, Sweden.
Fax: +46 18 55 93 57