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Inverse ratio ventilation compared with PEEP in adult respiratory failure

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Abstract. We have compared the cardiorespiratory effects of an inspiratory: expiratory (I:E) ratio of 4:1 with a ratio of 1:2 in 10 adult patients requiring intermittent positive pressure ventilation (IPPV) for acute respiratory insufficiency. Further comparisons were made with IPPV with positive end-expiratory pressure (PEEP) which was adjusted to achieve an equal external end-expiratory volume (EEEV) to that produced by the 4:1 ratio, as determined by respiratory inductive plethysmography, and with an I:E ratio that only changed the EEEV minimally (IRV-min). Percentage pulmonary shunt ($\dot{Q}s/\dot{Q}t$) was reduced equally with PEEP and with the 4:1 I:E ratio but both patterns reduced cardiac output and oxygen delivery. IRV-min also reduced $\dot{Q}s/\dot{Q}t$ significantly but had no effect on cardiac output so that oxygen delivery was increased. The dead space to tidal volume ratio (V_D/V_T) during IPPV-4:1 and IRV-min was reduced significantly when compared with that during IPPV-1:2. The clinical implications of the findings suggest that for some ITU patients, a modest increase in I:E ratio to between 1.1:1 and 1.7:1 may produce better gas exchange without significantly effecting the cardiac output.

Key words: Inverse ratio ventilation – PEEP – Respiratory failure

The most commonly used method of improving oxygenation in ventilated patients with acute respiratory insufficiency is the application of positive end expiratory pressure. However, it has been reported that a similar improvement occurs when the inspiratory: expiratory time ratio is inverted to 2:1 or even 3:1 or 4:1 [1, 10, 13]. It has been suggested that the use of inverse ratio ventilation may be preferable to the use of PEEP because CO_2 elimination is more efficient and peak pressure is less thus diminishing the risk of barotrauma. The beneficial effects of PEEP are thought to be associated with an increase in functional residual capacity (FRC) which recruits previously collapsed alveoli for useful gas exchange. However, inverse ratio ventilation may also increase FRC because the shortened expiratory time may prevent full expiration. The change in FRC has not been measured in previous studies on inverse ratio ventilation and it has therefore not been possible to establish whether the improved gas exchange is solely a function of the increased FRC or whether it is secondary to a special characteristic of the prolonged inspiratory period. The development of the respiratory inductive plethysmograph has provided a practical method of measuring external respiratory volume changes in the clinical situation. We have therefore used this device to compare the effects of inverse ratio ventilation with a level of PEEP which produced the same increase in external end-expiratory volume (EEEV).

Methods

The 10 adult patients who were selected for the study required IPPV for the treatment of the adult respiratory distress syndrome, pulmonary infection or cardiogenic pulmonary oedema. All the patients had bilateral pulmonary disease. Patients with cardiovascular instability or an increase in airway resistance were excluded. Two patients were receiving an infusion of an inotropic agent and in both, the infusion rate remained unchanged during the study. Mechanical ventilation was provided by a Siemens-Elema 900 B Servo ventilator using a constant inspired

oxygen concentration (39% – 76%) which was initially adjusted to produce an arterial PO_2 above 8 KPa without PEEP. Respiratory frequency was set at 10 breaths per min and the minute volume initially adjusted to produce a $PaCO_2$ of 4.5 KPa ± 0.5 KPa and then maintained constant throughout the rest of the study. Muscle paralysis and sedation were maintained throughout the study and the cuff of the endotracheal tube repeatedly checked to ensure that it was leakproof. Intravenous fluid therapy was kept at a constant rate during the study and was designed to replace losses.

The study was divided into five periods of 30 min each. The first and fourth were control periods of IPPV without PEEP. An inspiratory time of 25% and an inspiratory hold of 10% gave an I:E ratio of 1:1.9 during these periods. The second and third periods were randomly allocated to either a period of IPPV with an inspiratory time (IT) of 50% and an inspiratory hold (IH) of 30% giving an I:E ratio of 4:1 or to a period of PEEP with an I:E ratio of 1:1.9. The level of PEEP required to produce the same increase in EEEV as that produced by the 4:1 ratio was determined by the use of the respiratory inductive plethysmograph, in a short test period between the first and second study periods. During the fifth period IPPV was used with an I:E ratio of either 1.1:1 (IT = 33%; IH = 20%) or 1.7:1 (IT = 33%; IH = 30%). The inspiratory time chosen was the longest compatible with an increase in EEEV, equivalent to the application of less than 1.5 cm H_2O PEEP (IRV-min). The first 20 min of each period was allowed for stabilisation, all measurements being made during the last 10 min.

Ventilatory measurements

The expired gas from the ventilator was directed through a gas mixing box into a dry gas meter (Parkinson Cowan) that was calibrated against a wet spirometer at flow rates up to 60 l min^{-1}. 80 ml min^{-1} of mixed expired gas was pumped through a Beckman LB2 infrared CO_2 analyser and a Servomex OA 570 paramagnetic oxygen analyser placed in series and then returned to the circuit before the gas meter. Both analysers were calibrated using known gas mixtures. Inspired oxygen concentration was measured by directing a sample of gas from the inspiratory limb of the ventilator continuously through the oxygen analyser. Dynamic airway pressures were measured by a transducer connected to the patient end of the ventilator tubing and mean pressures were obtained by both mechanical and electronic damping.

Patient measurements

During the last 10 min of each period arterial and venous blood samples were taken and analysed for PaO_2, $PaCO_2$, and pH on an ABL2 acid-base laboratory (Radiometer-Copenhagen). The electrodes were checked daily with quality control solutions. The venous sample was taken from the pulmonary artery (PA) in five patients who had PA catheters already in place. In the others, the sample was taken from the central venous pressure (CVP) line which had been shown to be located close to the right atrium by X-ray. At least three blood samples were taken during the study period for haemoglobin estimation. These were analysed in the hospital haematology laboratory, the maximum discrepancy between samples being 0.4 g dl^{-1}. In the five patients who had a PA catheter, cardiac output was estimated by thermodilution using an Edwards cardiac output computer (model 9520A). Measurements were made on three consecutive occasions during each study period, using 10 ml 5% Dextrose solution at 0 °C, the injection being timed at the beginning of inspiration. A rectal thermistor probe was used to record patient temperature during each period and ambient pressure and temperature were noted.

Changes in EEEV were measured using a digital, automatically calibrated modification of the respiratory inductive plethysmograph [17] originally described by Cohn et al. [4]. The contributions of the rib cage and abdomen to ventilation could be measured by the change in inductance in two coils, one placed at the level of the 5th rib anteriorly and the other at the level of the umbilicus. The inductance of the coils is proportional to the enclosed cross-sectional area and both long term and rapid changes in EEEV can be recorded. Calibration was performed against the Servo 900B expiratory flow transducer during IPPV without PEEP by multiple linear regression using an online computer. Following calibration tidal volume and change in EEEV have been shown to be within 4% (40 ml) of the integrated pneumotachograph value [17].

Calculations

Minute volume and tidal volume were calculated from timed expired volume measurements. A correction was made for the gas compressed in the ventilator circuit. "Ideal alveolar" pO_2 was calculated from the simplified alveolar gas equation. $\dot{Q}s/\dot{Q}t$ was calculated using oxygen contents derived from the modified Kelman equation [8] and the haemoglobin measurement. Five patients had true mixed venous blood samples taken from the PA. The CVP blood samples in the other five patients were used as mixed venous samples because in this study the change in venous ad-

mixture was under investigation rather than the absolute values. V_D/V_T was calculated from the Enghoff modification of the Bohr equation. In all cases the cardiac output was calculated by the Fick principle using oxyen consumption calculated from the inspired and expired concentrations and the minute volume. In those patients in whom thermodilution measurements were also made, linear regression analysis between cardiac output (Fick) and cardiac output (thermodilution), showed $r^2 = 0.831$. The cardiac output value used to calculate the oxygen delivery ($\dot{Q}O_2$) was either that determined by the Fick principle, in those without a thermodilution catheter, or a mean value of both the Fick and the thermodilution measurement. Dynamic total thoracic compliance was calculated from the tidal volume and the end-inspiratory pressure during the control periods.

Statistical analysis

A comparison of the two control periods was made using a paired Student's t-test. The other results were analysed by a two-way analysis of variance, followed by Duncan's multiple range tests as appropriate.

Results

The mean increase in EEEV during the period of IPPV-4:1 was 1200 ml with a range of 465 – 2110 ml. The PEEP level required to produce similar EEEV changes varied between 9 and 19 cm H_2O with a mean value of 12.8 cm H_2O. No statistical difference was found in the $\dot{Q}s/\dot{Q}t$, V_D/V_T, mean airway pressure, cardiac output or compliance between the control periods (1 and 4). The mean results of these two periods were therefore compared with the mean results of $\dot{Q}s/\dot{Q}t$ (Fig. 1), V_D/V_T (Fig. 2), mean airway pressure (Fig. 3) and cardiac output (Fig. 4) during the other three periods. The reduction in $\dot{Q}s/\dot{Q}t$ and cardiac output during the periods of IPPV-4:1 and CPPV resulted in a net reduction in oxygen delivery in all cases. However the reduction in $\dot{Q}s/\dot{Q}t$ ($p < 0.05$) without change in cardiac output during period 5 (where there was minimal change in EEEV) resulted in a significant mean increase in oxygen delivery ($p < 0.05$) (Fig. 5).

Figure 6 shows individual patient $\dot{Q}s/\dot{Q}t$ response to both IPPV-4:1 and CPPV. It can be seen that in three patients (2, 3 and 7) there was little or no change in $\dot{Q}s/\dot{Q}t$, when compared with the changes in the other patients. Also shown at the bottom of Fig. 6 is the difference between the change in EEEV and the FRC change expected with the application of PEEP, if compliance remained constant (PEEP × Compliance). No pattern between clinical condition and response to IPPV-4:1 and CPPV could be found.

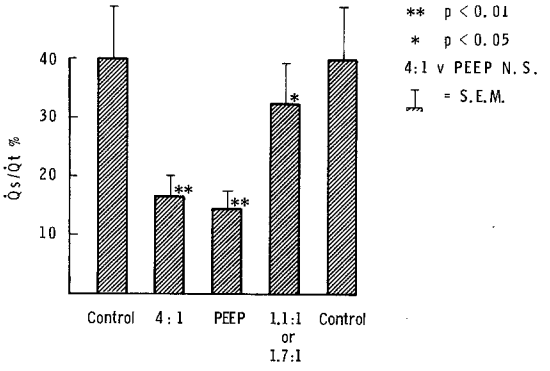

Fig. 1. Comparison of mean Qs/Qt during the different periods of the study

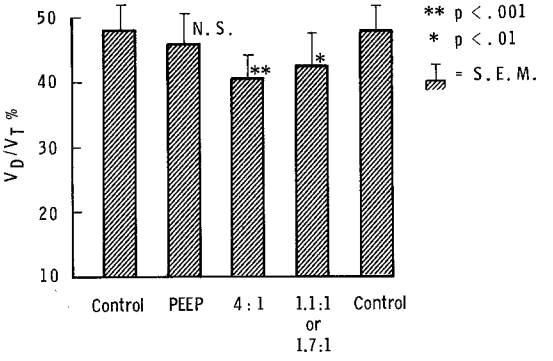

Fig. 2. Comparison of mean V_D/V_T during the different periods of the study

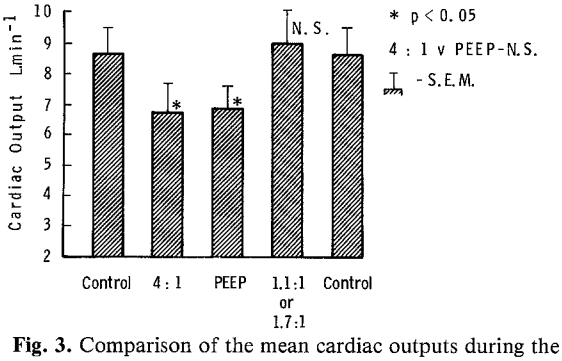

Fig. 3. Comparison of the mean cardiac outputs during the different periods of the study

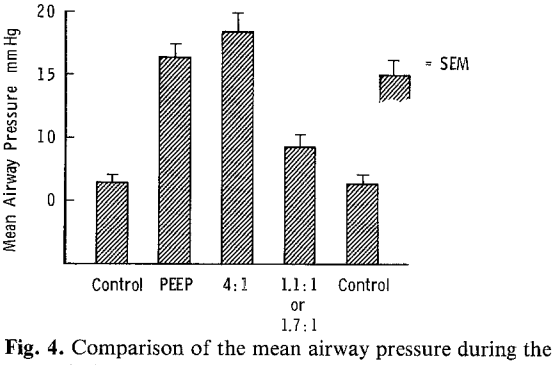

Fig. 4. Comparison of the mean airway pressure during the different periods of the study

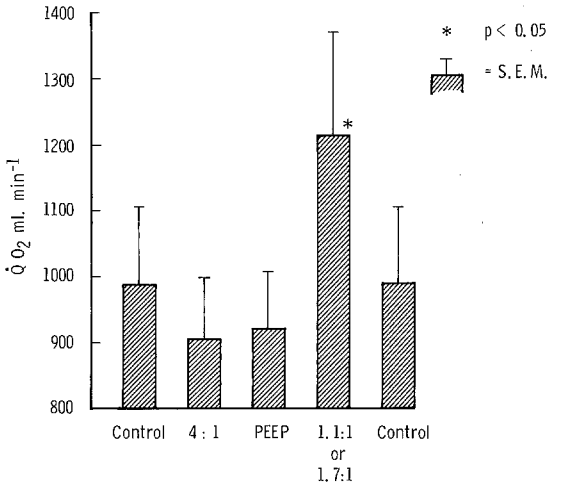

Fig. 5. Comparison of mean oxygen delivery ($\dot{Q}O_2$) during the different periods of the study

The mean airway pressure during IPPV-4:1 was approximately 2 mmHg higher than that during PEEP. However the peak airway pressure was always less during IPPV-4:1 than during PEEP, the mean difference being 6 cm H_2O.

Discussion

The respiratory inductive plethysmograph measures change in volume externally and, in addition to gas volume change, may reflect changes in blood or other fluid volume in the chest or abdomen. The limited width of the two induction coils may not detect abnormal chest expansion outside the straps. However, the linearity of the relationship between the plethysmograph measurements and the tidal volume measured by pneumotachograph suggests that most of the change in respiratory inductive plethysmograph volume is due to change in gas volume. Thus change in EEEV probably closely approximates to the change in FRC.

In this study the prolongation of the inspiratory time was achieved by both reducing the flow rate and adding an inspiratory hold. Previous work in this field has suggested that an increased flow rate can increase both $\dot{Q}s/\dot{Q}t$ [6] and V_D/V_T [5, 16] but this has only occurred at flow rates in excess of those used during this study. Other investigators have found a change in gas exchange characteristics solely related to an inspiratory hold [7, 9, 11, 14]. It seems likely that the most important factor in changing the ventilation/perfusion relationship is the duration of the inspiratory period whether this is achieved by reducing the flow rate or adding an inspiratory hold.

The reduction in pulmonary shunt was the same for both IPPV-4:1 and PEEP when the EEEV change was the same. This implies that the improved oxygen transfer that has been reported before with a prolonged I:E ratio [1, 9, 10, 13] is due to FRC change rather than the change in inspiratory pattern. However, when a less prolonged I:E ratio was used (1.1:1 or 1.7:1) which changed the FRC only minimally there was a smaller but significant reduction in $\dot{Q}s/\dot{Q}t$. This may suggest that FRC change is not the sole determinant of the change in pulmonary shunt.

In the present studies mean airway pressure was significantly higher during IPPV-4:1 than during PEEP with the same EEEV. In previous work on animals [3, 12] the mean airway pressures instead of FRC were used to match PEEP with IRV. This would have produced a higher FRC during PEEP and might have explained the greater improvement in $\dot{Q}s/\dot{Q}t$ with PEEP which was observed. However peak air-

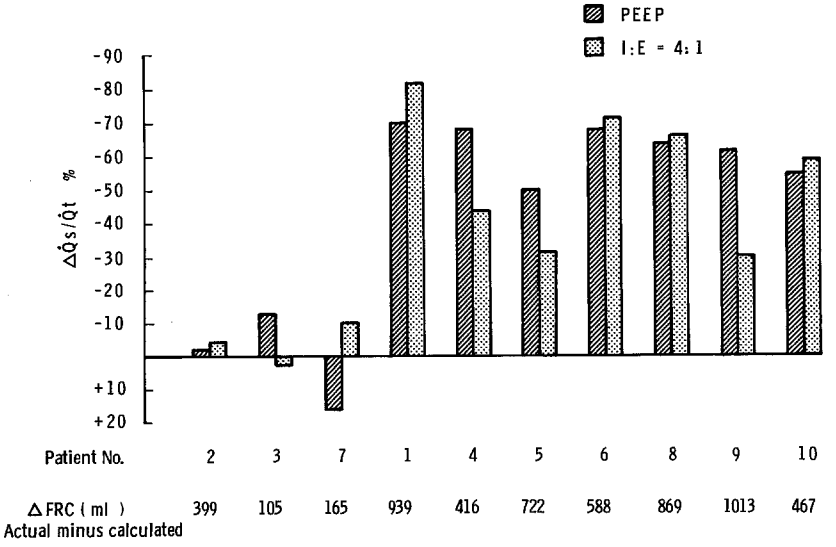

Fig. 6. Changes in $\dot{Q}s/\dot{Q}t$ in individual patients with IPPV-4:1 and CPPV and the change in FRC as measured by respiratory inductive plethysmograph

way pressures were significantly lower with IPPV-4:1 and this should cause less barotrauma. Cardiac output was significantly and equally reduced by both IPPV-4:1 and PEEP to such an extent that oxygen delivery was significantly reduced thus negating the effects of the reduced $\dot{Q}s/\dot{Q}t$. IRV-min, however, did not reduce the cardiac output so that the advantage gained by the reduction in $\dot{Q}s/\dot{Q}t$ with this pattern led to an overall increase in oxygen delivery. The mean airway pressure during IRV-min was significantly higher than during the control periods and may confirm the suggestion that arterial oxygenation in pulmonary insufficiency is a function of mean airway pressure [2].

A reduction in physiological dead space when using a prolonged I:E ratio, has been widely reported before [3, 7, 9, 12, 15, 16]. This occurred with IPPV-4:1 and to a lesser, but still highly significant extent ($p < 0.01$) with IRV-min. This improved CO_2 elimination reduces the tidal volume requirement and thus helps to reduce barotrauma. Possible explanations for this effect have been discussed previously [12]. However, because of the decrease in V_D/V_T found with IRV-min when there was only a small change in EEEV it seems unlikely that the increased CO_2 elimination is due to increased recruitment of collapsed alveoli.

It can be shown that an increase in FRC will occur if the tidal volume (TV) or the time constant (Tc) is increased or the expiratory time (t) is decreased:

$$\Delta FRC = \frac{TV}{e^{(t/Tc)} - 1}.$$

In diseased lungs an increase in FRC increases compliance and decreases resistance and so modifies the time constant which is the product of compliance and resistance. If the increase in compliance predominates, there will be an increase in time constant which will further increase the FRC. In this study the FRC changes were marked, particularly in those cases which responded with a reduction of $\dot{Q}s/\dot{Q}t$. This suggests that an alveolar recruitment may have lengthened the time constant and so augmented the increase in FRC caused by shortening the inspiratory period.

Measurements of compliance in this study were crude and only performed during the control periods. However it is interesting to compare the actual FRC change with that that could be predicted if the compliance had remained the same when PEEP was applied. The difference in these volumes is shown in Fig. 6. It can be seen that in the non-responders the difference was always less than 400 ml but that it was always greater than 400 ml in the responders. This again implies an increase in compliance in the responders.

This study suggests that the use of a 4:1 I:E ratio reduces the venous admixture in proportion to the FRC change and is therefore analogous to the use of PEEP. When similar increases in EEEV are produced by the two techniques there is a similar reduction in $\dot{Q}s/\dot{Q}t$ and although peak pressures are reduced, mean airway pressure is slightly increased with the 4:1 ratio. The main advantage of the technique is that CO_2 clearance is increased. However the change in time constant induced by the increase in compliance and decrease in airway resistance makes the change in FRC very unpredictable with the 4:1 ratio. On the other hand an I:E ratio which only increases the FRC minimally does appear to reduce $\dot{Q}s/\dot{Q}t$ without affecting cardiac output. A significant reduction in V_D/V_T also occurs which may help to reduce barotrauma. This suggests that the use of ratios in the region of 1:1 or 2:1 may be worth exploring in the future.

References

1. Baum M, Benzer H, Mutz N, Pauser G, Toncsar L (1980) Inversed ratio ventilation (IRV). Die Rolle des Atemzeitverhältnisses in der Beatmung beim ARDS. Anaesthesist 29:592
2. Berman LS, Downs JB, Van Eeden A, Delhagen D (1981) Inspiration: expiration ratio. Crit Care Med 9:775
3. Cheney F, Burnham C (1971) Effect of ventilatory pattern on oxygenation on pulmonary edema. J Appl Physiol 31:909
4. Cohn MA, Watson H, Weisshault R, Stott F, Sackner MA (1977) A transducer for non-invasive monitoring of respiration. In: Stott FD, Raftery EB, Sleight P, Goulding L (eds) Proceedings of the Second International Symposium on Ambulatory Monitoring. Academic Press, London, p 119
5. Fairley H, Blenkarn G (1966) Effect on pulmonary gas exchange of variations in inspiratory flow rate during intermittent positive pressure ventilation. Br J Anaesth 38:320
6. Finlay WEI, Wightman AE, Adams AP, Sykes MK (1970) The effects of variations in inspiratory: expiratory ratio on cardiorespiratory function during controlled ventilation in normo-, hypo- and hypervolaemic dogs. Br J Anaesth 42:935
7. Fulheihan S, Wilson R, Pontoppidan H (1976) Effect of mechanical ventilation with end-inspiratory pause on blood-gas exchange. Anesth Analg 55:122
8. Keiman GR (1966) Digital computer subroutine for the conversion of oxygen tension into saturation. J Appl Physiol 21:1375
9. Knelson J, Howatt W, De Muth G (1970) Effects of respiratory pattern on alveolar gas exchange. J Appl Physiol 29:328
10. Lachmann B, Haendly H, Schultz H, Jonson B (1980) Improved arterial oxygenation, CO_2 elimination, compliance and decreased barotrauma following changes of volume-generated PEEP ventilation with inspiratory/expiratory (I/E) ratio of 1:2 to pressure-generated ventilation with I/E ratio of 4:1 in patients with severe adult respiratory distress syndrome (ARDS). Intensive Care Med 6:64
11. Lyager S (1970) Ventilation-perfusion ratio during intermittent positive pressure ventilation. Importance of a no-flow interval during the insuflation (1970). Acta Anaesthesiol Scand 14:211

12. Perez-Chada RD, Gardaz J-P, Madgwick RG, Sykes MK (1983) Cardiorespiratory effects of an inspiratory hold and continuous positive pressure ventilation in goats. Intensive Care Med 9:263
13. Reynolds EOR (1971) Effect of alterations in mechanical ventilator settings on pulmonary gas exchange for hyaline membrane disease. Arch Dis Child 49:505
14. Suter P, Brigljevic M, Hemmer M, Gemperle M (1977) Effets de la pause en d'inspiration sur l'échange gazeux et l'hémodynamique chez des patients en ventilation mechanique. Can Anaesth Soc J 24:550
15. Sykes MK, Lumley J (1969) The effect of varying inspiratory: expiratory ratios on gas exchange during anaesthesia for open-heart surgery. Br J Anaesth 41:374
16. Watson WE (1962) Observations on physiological dead space during intermittent positive pressure ventilation. Br J Anaesth 34:502
17. Weller SF (1983) Modelling and estimation of respiratory variables. MSc Thesis, University of Oxford

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