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Effects of Inversed Ratio Ventilation and Positive End-expiratory Pressure Ventilation on Cardiorespiratory Functions in Acute Respiratory Failure

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Abstract The effects of inversed ratio ventilation (IRV) or those of positive end-expiratory pressure (PEEP) on hemodynamics, pulmonary oxygenation and oxygen delivery were examined in 12 patients each who needed prolonged mechanical ventilation because of acute respiratory failure. Patients were divided into two groups: IRV group and PEEP group. No significant change in hemodynamics and oxygen delivery was observed during the study in either IRV or PEEP group. Inversed ratio ventilation and PEEP increased significantly in PaO_2/FIO_2, which was taken for 6 hours by IRV (I:E=2:1) and for 2 hours by PEEP (5 cm H_2O), respectively. Further improvement of oxygenation was not observed in IRV even if inspiratory time was prolonged above 2:1. Inversed ratio ventilation showed a linear correlation between PaO_2/FIO_2 (y) and mean airway pressure (MAWP;x) ($y=7.71x + 67.49$, $r=0.37$, $p<0.05$), but PEEP did not. These results suggest that there is a difference in the mechanism by which IRV and PEEP improve arterial oxygenation, but the present data are not sufficiently conclusive to be certain.

Key Words : Respiration; mechanical ventilation, IRV,I:E ratio, PEEP, Circulation; cardiac output, oxygen delivery

Introduction

Positive end-expiratory pressure (PEEP) has been applied frequently during mechanical ventilation in acute respiratory failure (ARF) (1). However, PEEP is associated with a few adverse effects i.e.; reduction of cardiac output (CO) (2), redistribution of blood flow from well-ventilated to poorly ventilated regions of the lung (3), and barotrauma due to high peak airway pressure (4). Reynolds and co-worker (5-6) first suggested the use of prolonged inspiration in neonates with distress syndrome. Subsequently, it was observed that a similar or better improvement occured when the inspiratory (I) to expiratory (E) ratio was increased (inversed ratio ventilation; IRV). It was then suggested that IRV was preferable to high PEEP because the more efficient elimination of CO_2 and a lower peak pressure diminished barotrauma (7).

In the present study, the effects of IRV with different I:E ratio or those of PEEP at an I:E ratio of 1:2 on pulmonary oxygenation, hemodynamics, and tissue oxygenation were examined in 12 patients each with acute respiratory failure.

Method

Twenty-four patients (table 1) were studied

who had acute respiratory failure from divese causes receiving mechanical ventilation in the Intensive Care Unit (ICU) of Kurashiki Central Hospital. Sanction for the investigation was obtained from the Ethical Committee of the hospital and a written informed consent was obtained from each patient's relatives. All patients were mechanically ventilated by a Servo 900 C Ventilator (Siemens-Elema, Sweden). They were sedated with intravenous injection of diazepam or buprenorphine and were palalyzed with pancuronium bromide for facilitating mechanical ventilation. The twelve patients were selected for IRV group, when PaO_2 could not be maintained above 80 mmHg or the peak inspiratory pressure (PIP) exceeded 40 cm H_2O with PEEP at 6 cm H_2O. Inversed ratio ventilation was superimposed with PEEP. The other twelve patients were selected for PEEP group, when PaO_2 could not be maintained above 100 mmHg while breathing oxygen ($FIO_2=1.0$). They were otherwise treated similarly to the IRV group.

Study Protocol

Systemic and pulmonary hemodynamics, blood gases, oxygen consumption ($\dot{V}O_2$), oxygen delivery ($\dot{D}O_2$), and oxygen content in arterial and mixed venous blood (CaO_2 and $C\bar{v}O_2$) were measured with different I:E ratios and different PEEPs. In the IRV group, when patients could not maintain PaO_2 above 80 mmHg in spite of PEEP up tp 6 cm H_2O, the I:E ratio was increased stepwisely from 1:2 to 2:1 and to 2.6-4:1 with the same level of PEEP. Prolonged inspiratory time was achieved according to the Servo 900 C operating manual (published by Siemens Co.). In the PEEP group, when PaO_2 could not be maintained above 100 mmHg on an FIO_2 of 1.0, PEEP was increased stepwisely from 0 to 5, and to 10 cm H_2O following confirmation of improved arterial oxygenation.

Following reduction of FIO_2 to 0.5, when the PaO_2 remained above 80 mmHg and the patient's chest x-ray film began to reveal clear. The I:E ratio was gradually decreased to 1:2 in the IRV group and the PEEP value was reduced to 4 cm H_2O at which time paralysis was terminated. Weaning from ventilator was initiated by synchronized intermittent mandatory ventilation to achieve normocarbia, and PaO_2 above 80 mmHg on an FIO_2 of 0.4 without PEEP.

Measurement

The radial artery was cannulated for the measurement of arterial pressure and blood sampling. A Swan-Ganz triple-lumen balloon tipped flow-directed thermodilution catheter (Edward Laboratories MA, U.S.A) was positioned in the pulmonary artery percutaneously through the right internal jugular vein to measure the right atrial pressure as central venous pressure (CVP), mean pulmonary arterial pressure (MPAP), pulmonary capillary wedge pressure (PCWP) and CO. The catheter's position was confirmed by a portable chest radiograph and visualization of the appropriate pressure wave forms in the pulmonary artery. Vascular pressure was measured with a Hewelett 1290A transducer at end-expiration. The transducers were zero-refered at the mid-axillary line of the patient lying supine. Cardiac output was determined by thermodilution technique using 10 ml of 5 % dextrose in water at 0 ℃. Pulnonary vascular resistance (PVR) was calculated from the ratio of the difference between MPAP and PCWP, and CO. All measurements of pressure, including peak inspiratory pressure (PIP), mean airway pressure (MAWP) and of CO were taken on the day of admission to the ICU and then at intervals as needed. Values were the means of triplicated measurements. Arterial and mixed venous samples were drawn anaerobically into heparinized syringes simultaneously when pressures were recorded. Arterial and mixed venous PO_2, PCO_2, and pH were measured with a blood gas analyzer (178 pH/Blood Gas Analyzer, Corning Medical and Scientific, MA, U.S.A.). Oxygen saturation (SaO_2, $S\bar{v}O_2$) and hemoglobin (Hb) were measured with a Hemoximeter (OSM2, Radiometer, Copenhagen). Oxygen content was calculated from hemoglobin oxygen-carrying capacity and the amount of dissolved oxygen, as estimated from PaO_2 and oxygen solubility. The intrapulmonary shunt ($\dot{Q}s/\dot{Q}t$) was calculated using the standard equation (8): $\dot{Q}s/\dot{Q}t = Cc'O_2-CaO_2/Cc'O_2-C\bar{v}O_2$, where $Cc'O_2$ is pulmonary capillary oxygen content, and $C\bar{v}O_2$ is the mixed venous oxygen content. To calculate $\dot{Q}s/\dot{Q}t$, we assumed that pulmonary capillary oxygen tension was the same as alveolar oxygen tension. A ratio of PaO_2/FIO_2 was calculated as an index of pulmonary oxygenation.

The $\dot{D}O_2$ was calculated as the product of

CaO_2 and CO. Oxygen consumption ($\dot{V}O_2$) was calculated using the Fick principle as follows: $\dot{V}O_2 = CO \times (CaO_2 - C\bar{v}O_2)$.

Data analysis

All variables were calculated with a programable calculator (HC-20, Epson, Shinshu Seiki, Tokyo). All values are expressed as mean ± standard deviation (SD). Student's t test for paired data was used in statistical treatment of results. P value of <0.05 was considered statistically significant.

Results

Patients' characteristics are shown in table 1.

1) IRV group

Patients had no complication related to IRV except for two cases with interstitial pneumonia, who developed a pneumothorax on the 2 nd and 3rd day following IRV with an I:E ratio of 2:1. A chest tube was effectively placed immediately after the episode. Seven patients died from multiple organ failure while on the ventilator in the ICU. Table 2 shows the changes of respiratory variables in the IRV group. Table 3 shows systemic and pulmonary hemodynamics, and oxygen delivery and consumption. PaO_2, $\dot{Q}s/\dot{Q}t$ and PaO_2/FIO_2 were significantly improved by prolonging inspiratory time at 2:1 but not at 2.6:1 or 4:1. These changes in pulmonary oxygenation corresponded to changes in MAWP. A direct linear relationship was observed between PaO_2/FIO_2 (y) and MAWP (x) ($y=7.71x + 67.49$, $r=0.37$, $n=39$, $p<0.05$, Fig. 1). The improvements of PaO_2 and PaO_2/FIO_2 were observed just over six hours after intiation of IRV (Fig.2). A linear correlation existed between PaO_2/FIO_2 (y) and time (x), the regression equation being $y=11.29x + 76.17$ ($r=0.75$, $n=33$, $p<0.01$). There were no significant changes in parameters of pulmonary and systemic hemodynamics, tissue oxygenation or oxygen delivery. No signigicant changes in $PaCO_2$ were observed at any I:E ratio.

2) PEEP group

There was no complication related to PEEP in this group. Eight patients died from multiple organ failure. Table 4 shows the effects of PEEP on the respiratory parameters, and table 5 shows systemic and pulmonary hemodynamics, and oxygen delivery and consumption. There was no significant improvement of pulmonary oxygenation parameters when PEEP was elevated to 5 cm

Table 1. Patients' characteristics

Mode of ventilation	IRV	PEEP
No. of patients	12	12
Age (yr)	66±17	58±18
Sex		
female	7	7
male	5	5
Case of ARF		
pulmonary infection	5	4
sepsis	3	3
cardiogenic ARF	3	3
aspiration	1	2
Days of mechanical ventilation	17±19	13±12
Complications	2	0
Outcome		
survived	5	4
died	7	8

Mean ± SD

IRV ; inversed ratio ventilation, PEEP ; positive end-expiratory pressure, ARF ; acute respiratory failure

Table 2 Effects of IRV on the values related to respiration

I : E ratio		1 : 2 (n=12)	2 : 1 (n=12)	2.6−4 : 1 (n=12)
FIO_2		1.0	1.0	1.0
PaO_2	mmHg	65±15	115±42*	136±4*
$PaCO_2$	mmHg	51±15	52±13	51±15
pH		7.41±0.13	7.41±0.12	7.38±0.04
Base Excess	mEq/L	8±8	7±4	5±7
$\dot{A}$-$a\dot{D}O_2$	mmHg	581±65	452±130	461±143
$\dot{Q}s/\dot{Q}t$	%	42±11	30±10*	27±5*
PaO_2/FIO_2		65±15	115±42*	136±46*
PIP	cm H_2O	25±5	26±7	33±9
MAWP	cm H_2O	10±4	13±5	17±7

*significantly different from the value of an I : E ratio of 1 : 2, mean±SD ($p<0.05$)

Table3 Effects of IRV on hemodynamics, oxygen delivery and consumption

I : E ratio		1 : 2 (n=12)	2 : 1 (n=12)	2.6−4 : 1 (n=12)
CI	ml/min/m²	3.7±1.7	4.2±1.7	3.0±0.7
SVI	ml/b/m²	32±14	32±13	30±11
MAP	mmHg	78±15	84±17	67±16
HR	b/min	116±29	113±20	107±18
CVP	mmHg	8±4	8±3	11±3
SVR	dyn·sec/cm⁵	1163±553	1227±497	995±243
PCWP	mmHg	11±6	10±4	11±3
LVSWI	gm·m/m²/b	30±16	31±18	32±12
RVSWI	gm·m/m²/b	9±8	10±7	9±6
MPA	mmHg	23±8	24±8	24±9
PVR	dyn·sec/cm⁵	195±121	223±113	225±84
$P\bar{v}O_2$	mmHg	35±6	38±5	39±7
CaO_2	vol%	12±3	13±4	12±1
$C\bar{v}O_2$	vol%	8±3	9±3	7±2
$\dot{D}O_2$	ml/min/m²	507±253	591±273	378±164
$\dot{V}O_2$	ml/min/m²	164±79	175±81	146±25

mean ± SD

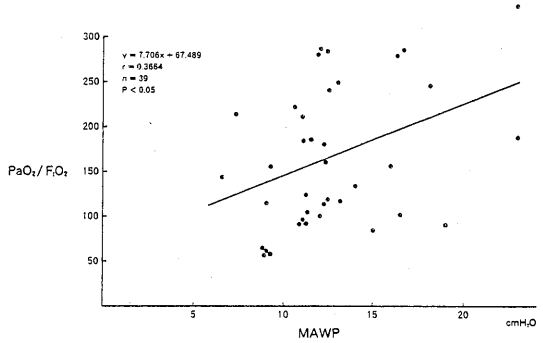

Fig. 1 Correlation between PaO_2/FIO_2(y) and MAWP(x) in the IRV group. Regression equation is $y=7.71x+67.49$ ($r=0.37$, $n=39$, $p<0.05$)

H_2O in spite of a significant increase in MAWP. However, when PEEP was elavated to 10 cm H_2O, both PaO_2 and PaO_2/FIO_2 ratio significantly increased in association with a significant increase in MAWP. The ratio of PaO_2/FIO_2 had increased significantly 2 hours after initiation of PEEP (Fig.2). There was a linear relationship between PaO_2/FIO_2 (y) and time (x), the regression equation being $y=33.11x + 91.11$ ($r=0.59$, $n=18$, $p<0.01$). There was a significant difference between the slopes of the two regression equation of IRV and PEEP ($p<0.01$). There was no correlation between PaO_2 and MAWP. No significant change in hemodynamics, or oxygen delivery and consumption was observed. Elavation of PEEP values increased MAWP signicantly but it did not increase PIP.

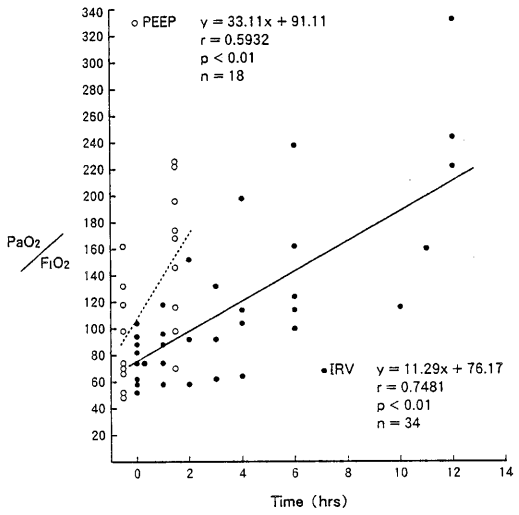

Fig. 2 Time course of PaO_2/FIO_2 in the IRV and PEEP groups. A lineal correlation existed between PaO_2/FIO_2(y) and time(x) and the equations were $y=11.29x + 76.17$ ($r=0.75$, $n=33$, $p<0.01$) and $y=33.11x + 91.11$ ($r=0.59$, $n=18$, $p<0.01$), in the IRV and PEEP groups respectively. There was a significant difference between the two equations ($p<0.01$).

Discussion

The major finding of this study was that both IRV and PEEP significantly improved arterial oxygenation without any adverse effects on pulmonary and systemic hemodynamics in patients with ARF. There was a time difference in the mainfestation of PaO_2 improvements, i.e.; 6 hours and 2 hours after initiation of IRV and PEEP respectively.

It is widely accepted that the improvement of arterial oxygenation by PEEP is cased by restoring the functional residual capacity (FRC) towards normal, recruiting unventilated alveoli and improving compliance. In the IRV group, prolonged inspiratory time appears to have similar effects on arterial oxygenation to that of PEEP, particularly if a plateau phase is used to inflate lungs. The

Table 4 Effects of PEEP on the values related to respiration

PEEP (cmH20)		0 (n=12)	5 (n=12)	10 (n=12)
FIO_2		0.9±0.1	0.8±0.2	0.9±0.1
PaO_2	mmHg	80±27	102±49	110±25*
$PaCO_2$	mmHg	44±9	49±13	51±11
pH		7.36±0.10	7.36±0.06	7.35±0.05
Base Excess	mEq/L	5±4	7±4	7±7
$A\text{-}aDO_2$	mmHg	542±76	440±140	432±117
Qs/Qt	%	43±15	38±16	36±11
PaO_2/FIO_2		87±32	127±59	132±30*
PIP	cm H_2O	23±5	27±9	28±5
MAWP	cm H_2O	7±2	9±3*	15±4##

*significantly different from the value of 0 cm H_2O PEEP ($p<0.05$) mean ± SD
significantly different between 5 and 10 cm H_2O of PEEP ($p<0.01$)

Table 5 Effects of PEEP on hemodynamics, oxygen delivery and consumption

PEEP (cm H_2O)		0 (n=12)	5 (n=12)	10 (n=12)
CI	ml/min/m²	4.3±0,4	4.6±0.5	4.9±1.7
SVI	ml/b/m²	40±13	40±15	47±13
MAP	mmHg	74±11	79±13	80±16
HR	b/min	111±28	117±21	106±23
CVP	mmHg	10±5	10±4	11±5
SVR	dyn·sec/cm⁵	916±489	931±465	788±348
PCWP	mmHg	13±8	12±5	13±7
LVSWI	gm·m/m²/b	32±12	36±17	43±17
RVSWI	gm·m/m²/b	14±6	15±8	18±10
MPA	mmHg	28±8	32±20	26±9
PVR	dyn·sec/cm⁵	240±242	303±358	146±81
$P\bar{v}O_2$	mmHg	39±6	41±5	43±8
CaO_2	vol%	13±5	13±4	14±5
$C\bar{v}O_2$	vol%	10±4	10±4	11±4
$\dot{D}O_2$	ml/min/m²	492±117	560±220	654±315
$\dot{V}O_2$	ml/min/m²	118±40	124±35	130±60

mean ± SD

effects of IRV on arterial oxygenation were not achieved immediately after applying IRV but the improvements grew increasingly significant with continued IRV (9). In the present study it took more than 6 hours to provide a signigicant increase in PaO_2 (Fig. 2). This may explain why some investigators have reported no improvement of PaO_2 after IRV, since results were registered from 15 min to 60 min after initiation (10-13). However, PEEP was much faster in improving arterial oxygenation than IRV. Increases in FRC and MAWP account for the improvement of oxygenation by IRV and PEEP. An increase in FRC will occur if the tidal volume (TV) or time constant (Tc) is increased : $FRC = TV/e(t/Tc)-1$ (Fig.3) (14). Theoretically, the shorter expiratory time and the longer inspiratory time will give larger FRC and Tc values, which means that the harder alveoli will be expanded. These results indicate that IRV improves gas exchange by progressive alveolar recruitment. The role of MAWP in improving an arterial oxygenation have been debated (11, 15-17). However, our data supports the studies by Boros (11) and Stewart et al (16) demonsrating that increases in oxygenation appeared to be directly related to an increase in MAWP. Prolonging inspiration will produce an increase in MAWP while allowing constant and/or low PIP. The present study suggests that PaO_2/FIO_2 in the IRV group is a function of MAWP (Fig.1).

In the PEEP group, an improvement of arterial oxygenation did not parallel to an increase in MAWP. With a PEEP of 5 cm H_2O, PaO_2/FIO_2 ratio did not increase significantly inspite of a significant increase in MAWP, but when PEEP was raised to 10 cm H_2O the PaO_2/FIO_2 increased significantly, according to the significant increase in MAWP. MAWP produced by 5 cm H_2O may be too low to restore FRC in severe ARF in our patients. Since there was no significant difference in MAWP between IRV and PEEP, the factor may not be the sole determining parameter to improve pulmonary oxygenation.

Cole and colleagues (14) suggested that the use of IRV reduces Qs/Qt in proportion to changes in FRC, so that it is analogous to the use of PEEP. Although, PEEP improves gas exchange by preventing terminal airway collapse and increasing the FRC, it increase PIP (18). Accordingly, high levels of PEEP are reported to increase the incidence of pulmonary barotrauma (PBT) and a safe upper limit of PEEP has not yet been established (4). Since, PIP did not increase with IRV in the present study, it should cause less PBT. However, we had two cases of pneumothorax

out of 12 patients (17%) during IRV. Petersen and Baier (4) reported that the incidence of PBT was 8 per cent (14 of 171 patients) and no PBT occured with a PIP of less than 50 cm H_2O. The PIP of our patients with pneumothorax was less than 40 cm H_2O, so that higher level of PIP did not seem to be the sole cause. Two patients' primary diseases were chronic myeloblastic leukemia and systemic lupus erythematosus, respectiverly, complicated with interstitial pneumonia, which may have made lungs vulnerable to PBT.

Inversed ratio ventilation and PEEP, producing an increase in FRC, may reduce cardiac output and impair oxygen delivery to the tissue, despite an increase in PaO_2 (19). In the present study, we determined the optimum IRV and PEEP for producing optimum ÇO, so that there was no reduction in overall DO2 to the tissue. Our results suggests that the optimum IRV is 2:1 and optimal PEEP ranges from 5 to 10 cm H_2O, to provide better gas exchange without affecting CO in the patients with ARF. It was reported that no evidence of tissue hypoxemia was observed, If $\dot{V}O_2$ and $\dot{D}O_2$ were stable and $P\bar{v}O_2$ was above 31 mmHg (20). In the present study, all patients were maintained under these circumstances.

In conclusion, there are some mechanical differences by which IRV and PEEP improve arterial oxygenation, and the effects were appeared much faster by PEEP than by IRV.

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