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Cardiorespiratory and Sympathoadrenal Responses to Weaning with Synchronized Intermittent Mandatory Ventilation from Mechanical Ventilatory Support

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Abstract The author studied the cardiopulmonary effects of synchronized intermittent mandatory ventilation (SIMV) used for weaning in the patients with acute respiratory failure. Weaning from assisted ventilation by means of SIMV was attempted in 22 patients, who had been ventilated with a Servo 900 C ventilator for at least 48 hours before entering the trial. Fourteen of the 22 patients were weaned successfully, but eight were not weaned. The non-weaners had a significantly higher $PaCO_2$ and cardiac index both before and during SIMV than the weaners. Non-weaners showed significantly higher right ventricular stroke work index before weanig, and significantly lower mean arterial pressure during SIMV in comparison with weaners. Hence, the changes in systemic vascular resistance were opposite in the two groups. There was no significant difference in arterial oxygenation and oxygen delivery between weaners and non-weaners. Blood epinephrine and norepinephrine showed no significant changes between weaners and non-weaners before and during weaning. These results suggest that SIMV may be better than conventional methods for weaning patients with acute respiratory failure from the point of view of the cardiorespiratory and sympathoadrenal responses.

Key Words : Respiration; synchronized IMV, weaning, acute respiratory failure, Circulation; sympathoadrenal system, catecholamine.

Introduction

Although intermittent mandatory ventilation (IMV) is most frequently used to facilitate the weaning of patients from mechanical ventilatory support because of its simplicity and patient acceptance, there is no real consensus as to the best means of weaning from mechanical ventilation[1]. The issue remains controversial because the superiority of IMV over other forms of mechanical ventilatory support has not been scientifically established[2]. Accordingly, we performed a prospective randomized trial to assess the effects of synchronized intermittent mandatory ventilation (SIMV) on cardiorespiratory and sympathoadrenal function in 22 patients with acute respiratory failure due to diverse causes. Blood epinephrine and norepinephrine were measured as an index of the sympathoadrenal response to SIMV.

Subjects and Methods

Twenty-two patients (Table 1) with acute respiratory failure due to diverse causes who underwent mechanical ventilation in the Intensive Care Unit (ICU) of Kurashiki Cen-

tral Hospital were included in this trial. Permission for the investigation was obtained from the Ethical Committee of the hospital and informed consent was obtained from each patient's relatives.

Patient Selection

Patients were chosen for this trial among those patients deemed by the ICU medical staff to be suitable candidates for a trial of weaning from mechanical ventilation. All had been mechanically ventilated by a Servo 900 C (Siemens-Elema, Solna) for at least 48 hours before entering the trial. All decisions were made independently of the investigators, including the decision to remove the endotracheal tube. Patients were considered candidates for weaning from assisted ventilation on the basis of the following criteria: (1) stable circulatory hemodynamics; (2) alert conscious state; (3) vigorous voluntary breathing; (4) PaO_2 above 80 mmHg at an F_IO_2 of 0.4; and (5) $PaCO_2$ below 55 mmHg. During weaning these criteria were rigidly adhered to and in cases which did not satisfy all the criteria, the trial was terminated and the patients were not extubated.

Study Protocol

Determination of systemic and pulmonary hemodynamics, blood gases, oxygen consumption, oxygen delivery, oxygen content, and the catecholamine levels (epinephrine and norepinephrine) in arterial and mixed venous blood was performed during assisted mechanical ventilation (AMV) immediately before weaning (stage I), during weaning by SIMV (stage II), and during spontaneous breathing 30 minutes after endotracheal extubation (stage III). No measurements were made in stage III if weaning was failed. Weaning was attempted first in each patient by using SIMV at a rate of 10 or 12 breaths/min. The SIMV rate was lowered to four or

Table 1 Clinical characteristics of 22 patients with acute respiratory failure

No.	Age	Sex	Diagnosis	Weaning*
1	50	F	Pulmonary edema, Cushing's syndrome	W
2	63	M	Acute pneumonia, postabdominal surgery	W
3	49	F	Sepsis, postabdominal surgery	W
4	48	M	Pulmonary edema, postthoracic surgery	W
5	80	F	Broncheal asthma, postabdominal surgery	W
6	50	F	Congestive heart failure, chronic renal failure	W
7	64	M	Acute pneumonia	W
8	62	M	Sepsis, postabdominal surgery	W
9	72	M	Congestive heart failure	W
10	66	M	Hemorrhagic shock, posthepatectomy	W
11	53	M	Congestive heart failure	W
12	55	M	Congestive heart failure, chronic renal failure	W
13	74	M	Sepsis, postabdominal surgery	W
14	45	F	Acute pneumonia	W
15	51	M	Exacerbation of COPD	N
16	66	M	Sepsis, postabdominal surgery	N
17	74	M	Organophosphate poisoning	N
18	75	F	Exacerbation of COPD	N
19	80	M	Sepsis, postabdominal surgery	N
20	57	M	Sepsis, postesophageal surgery	N
21	60	M	Pulmonary edema, liver cirrhosis	N
22	77	F	Exacerbation of COPD	N

Abbreviations ; COPD=chronic obstructive pulmonary disease, W ; weaner, N ; non-weaner

*Results of attempted weaning

five breaths/min and measurements were made 30 min. later.

Measurement

The radial artery was cannulated for measurement of arterial pressure. A Swan-Ganz triple-lumen balloon-tipped flow-directed thermodilution catheter (#7, American Edwards Laboratories, Cal) was positioned in the pulmonary artery percutaneously via the right internal jugular vein to measure pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP), and cardiac output (CO). Catheter position was confirmed by a portable chest radiograph and by visualization of the appropriate wave form before and after wedging. Vascular pressures were measured with a Hewlett Packard 1290A transducer (Hewlett Packard, Mass) at end-expiration. The transducers were positioned at the mid-axillary line of the patients in the supine position, and at mospheric pressure was used as the zero reference point. The following parameters were determined: mean arterial pressure (MAP), heart rate (HR), mean PAP, PCWP, central venous pressure (CVP), CO, arterial and mixed venous oxygen tension (PaO_2 and $P\bar{v}O_2$), hemoglobin (Hb), oxygen saturation (SO_2), and epinephrine (Epi) and norepinephrine (Nepi) levels.

The CO was determined by the thermodilution technique, using 10 ml of 5% dextrose in water at 0℃ (coefficient of variation=0.1). Measurements of CO were performed in triplicate and averaged. Pulmonary vascular resistance (PVR) was calculated from the ratio of the difference between the mean PAP and PCWP to the CO. Arterial and mixed venous blood samples were drawn anaerobically into heparinized syringes at the same time that the pressure was recorded. The PO_2, PCO_2 and pH of arterial and mixed venous blood were measured with a Corning 178 pH/Blood Gas Analyzer (Corning Medical and Scientific, Mass). Pulmonary oxygenation was evaluated to calculate the alveolar-arterial oxygen tension difference ($A-aDO_2$) with alveolar equation[3]. Arterial and mixed venous oxygen saturation (SaO_2 and $S\bar{v}O_2$) and Hb were measured with a Hemoximeter (OSM2, Radiometer, Copenhagen). Arterial and mixed venous oxygen content (CaO_2 and $C\bar{v}O_2$) were calculated from the hemoglobin oxygen-carrying capacity and the amount of dissolved oxygen, as estimated from the PaO_2 and the oxygen solubility. The intrapulmonary shunt ($\dot{Q}s/\dot{Q}t$) was calculated using the standard shunt equation[4]: $\dot{Q}s/\dot{Q}t = C\acute{c}O_2 - CaO_2/C\acute{c}O_2 - C\bar{v}O_2$, where $C\acute{c}O_2$ is the pulmonary capillary oxygen content. The oxygen delivery ($\dot{D}O_2$) was calculated as the product of CaO_2 and CO. Oxygen consumption ($\dot{V}O_2$) was determined using the Fick principle as follows: $\dot{V}O_2 = CO\ (CaO_2 - C\bar{v}O_2)$.

Stroke volume (SV), stroke volume index (SVI), cardiac index (CI), systemic vascular resistance (SVR), PVR, left ventricular stroke work index (LVSWI), and right ventricular stroke work index (RVSWI) were calculated as follows: CI=CO/body surface area (BSA); SV=CO/HR×1000; SVI=SV/BSA; SVR=(MAP-CVP)/CO×80; PVR=(PAP-PCWP)/CO×80; LVSWI=1.36(MAP-PCWP)/100×SVI and RVSWI=1.36(PAP-CVP)/100×SVI. Blood epinephrine and norepinephrine were measured by high-performance liquid-chromatography[5].

Data analysis

Derived variables were calculated using a programmable calculator (HC-20, Epson, Shinshu Seiki, Tokyo). All values were expressed as the mean ± standard deviation (SD). Student's *t* test was used for statistical analysis of results. P value of <0.05 was considered statistically significant.

Results

Of the 22 patients (mean age; 61 years; range; 45 to 80 years), fourteen (mean age; 59 years; range; 45 to 80 years) were weaned successfully. Eight patients (mean age; 68 years; range; 51 to 80 years) were not weaned and required the reinstitution of mechanical ventilation. Weaners were ventilated for a mean duration of 5±2 days and non-weaners for a mean duration of 10±7 days. Non-weaners developed hypotension and/or hypercarbia within 30 min. when the ventilator mode was switched to SIMV and repeated weanings were unsuccessful. Circulatory

hemodynamics, blood gases, and catecholamine levels are shown in Tables 2, 3, and 4, respectively.

Blood gas data

At the transition from AMV to SIMV, the $PaCO_2$ increased significantly from 36±4 to 41±6 mmHg in weaners ($p<0.05$), and from 43±6 to 52±13 mmHg in non-weaners ($p<0.05$). Moreover, non-weaners already had a significantly higher $PaCO_2$ before weaning ($p<0.05$). There were no significant differences in arterial oxygenation between weaners and non-weaners.

Hemodynamic data

During SIMV, the MAP (76 ± 20 mmHg) in non-weaners was significantly lower than that in weaners (90 ± 11 mmHg) ($p<0.05$). At the transition from AMV to SIMV, CI increased significantly from 3.3 ± 0.5 to 4.0 ± 0.6 l/min/m² in weaners and from 4.4 ± 1.0 to 4.8 ± 1.1 l/min/m² ($p<0.05$) in non-weaners. Weaners had a significantly lower CI before and during weaning than non-weaners ($p<0.05$). A rough positive linear correlation was observed between CO(y) and $PaCO_2$(x) in all patients who underwent weaning trial ($y=0.0664x + 3.4602$, $r=0.3666$, $p<0.05$) (Fig.1). Hence, in weaners the SVR was significantly higher than that of non-weaners ($p<0.05$). Only before weaning was the RVSWI of non-weaners (9±3 g·m/m²) significantly higher than that of weaners (4±2 g·m/m²). In both groups, the mean PAP and PCWP were within normal limits, being below 20 mmHg for PAP and 14 mmHg for PCWP, respectively. No significant changes in either $\dot{V}O_2$ or $\dot{D}O_2$ were observed.

Catecholamine data

There were no significant differences in epinephrine and norepinephrine levels between weaners and non-weaners, and also between the two stages of ventilation and spontaneous breathing.

Discussion

The major findings of this trial were the following: 1) Transition from AMV to SIMV resulted in a significant increase in both the CI and $PaCO_2$ in weaners, but only $PaCO_2$ increased in non-weaners. 2) Both CI and $PaCO_2$ in non-weaners were significantly higher before and during SIMV than those in

Table 2 Hemodynamic data during respiratory management (mean ± SD)

Group		Weaner (n=14)			Non-weaner (n=8)	
Stage		I	II	III	I	II
MAP	mmHg	85±13	90±11*	99±22	75±15	76±20
HR	bpm	83±18	87±21	87±22	91±14	103±29
CO	l/min	5.2±1.1**	6.3±1.9**	6.0±1.0	6.8±1.7	7.4±1.6
CI	l/min/m²	3.3±0.5**	4.0±0.6**	3.8±0.4	4.4±1.0	4.8±1.1
SV	ml	64±12	75±16	70±17	76±18	72±24
SVI	ml/m²	44±13	49±10	45±10	49±12	50±16
PAP	mmHg	16±4	16±7	18±7	18±6	18±7
PCWP	mmHg	6±4	6±6	7±5	7±4	7±4
SVR	dyn·s/cm⁵	1316±347*	1152±278*	1270±354	867±146	850±296
PVR	dyn·s/cm⁵	165±65	125±56	125±23	160±79	129±46
LVSWI	g·m/m²	44±11	55±16	51±18	48±19	49±21
RVSWI	g·m/m²	4±2*	6±2	6±2	9±3	8±4
$\dot{V}O_2$	ml/min/m²	128±39	137±34	138±30	150±28	148±24
$\dot{D}O_2$	ml/min/m²	772±238	830±269	821±217	950±338	1061±343

I = AMV, II = SIMV, III = spontaneous breathing
*significant difference from the non-weaner goup ($p<0.05$)
**significant difference between stages I and II and significant from the non-weaner group ($p<0.05$)

Table 3 Blood gas data during respiratory management (mean ± SD)

Group		Weaner (n=14)			Non-weaner (n=8)	
Stage		I	II	III	I	II
F_IO_2		0.4±0.1	0.4±0	0.5±0.1	0.4±0.1	0.4±0.1
PaO_2	mmHg	100±26	107±17	90±21	92±12	111±9
$PaCO_2$	mmHg	36±4**	41±6**	39±4	43±6*	52±13*
$A\text{-}aDO_2$	mmHg	154±58	137±32	214±85	144±33	133±51
$\dot{Q}s/\dot{Q}t$	%	12±4	11±3	15±6	12±3	11±3
CaO_2	vol%	14±3	13±3	14±3	14±3	14±3
$C\bar{v}O_2$	vol%	10±3	10±3	10±2	10±3	11±3
$C(a\text{-}\bar{v})O_2$	vol%	4±1	3±1	4±1	4±1	3±1

*significant difference between stages I and II ($p<0.05$)
**significant difference between stages I and II, and significant from the non-weaner group ($p<0.05$)

Table 4 Blood epinephrine and norepinephrine levels during respiratory management (mean ± SD)

Group		Weaner (n=14)			Non-weaner (n=8)	
Stage		I	II	III	I	II
Arterial blood						
Epinephrine	ng/ml	.06±.05	.07±.07	.07±.08	.05±.04	.05±.02
Norepinephrine	ng/ml	.36±.21	.42±.30	.41±.32	.41±.26	.60±.52
Venous blood						
Epinephrine	ng/ml	.05±.05	.07±.09	.08±.12	.05±.05	.06±.03
Norepinephrine	ng/ml	.36±.23	.41±.25	.42±.34	.42±.25	.62±.56

weaners, with a simultaneous decrease in SVR. 3) Non-weaners showed a significantly higher RVSWI before SIMV and a significantly lower MAP during SIMV. 4) No significant changes in catecholamines were observed in either group. These findings suggested that SIMV was a favorable technique to wean patients with acute respiratory failure from prolonged mechanical ventilatory support.

Although many studies have found that IMV may hinder weaning[6-8], IMV remains the most frequently used weaning technique in many hospitals[1], and also in our ICU weaning with SIMV is commonly performed.

When the ventilatory mode was switched from assisted ventilation to SIMV, CO was increased in successfully weaned patients. This increase in CO has been explained by an increase in the work of breathing[9], a rise in $PaCO_2$[10], or an increase in cardiac filling pressure caused by a fall in intrathoracic

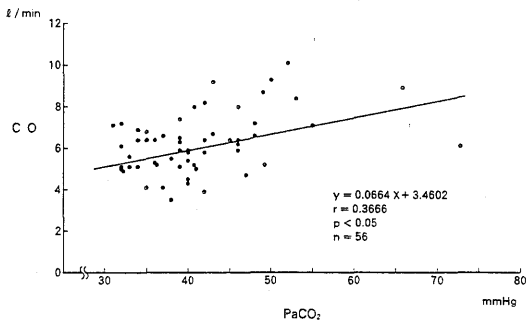

Fig.1 Relationship between $PaCO_2$ (x) and cardiac output (CO) (y).
A rough positive linear correlation was observed between the two measurements in all patients who underwent weaning trial ($y=0.0664x+3.4602$, $r=0.3666$, $p<0.05$).

pressure[11]. The positive correlation between $PaCO_2$ and CO (Fig.1), with VO_2 remaining unchanged, suggested that an increase in CO at the transition from AMV to SIMV may be explained by $PaCO_2$ stimulation, and not by an increase in the work of breathing. Kennedy and co-workers[10] also described a positive linear relationship between $PaCO_2$ and CO and stated that $PaCO_2$ was the stimulus causing an increase in CO. The $PaCO_2$ increased significantly with IMV, not because alveolar ventilation was decreased, but because the body's production of CO_2 increased. This very likely occured because of an increase in the work of breathing[12]. The study by Christopher et al.[8] has clearly demonstrated that the demand-valve configuration of several IMV devices is associated with considerable inspiratory loading and increased work of breathing.

Non-weaners initially had both higher $PaCO_2$ and CI than weaners. Clowes et al.[13] found an increase rather than a decrease in CO during controlled ventilation in a group of very sick patients. Our non-weaners were already in a hyperdynamic state during AMV and did not respond to the increase in $PaCO_2$ during SIMV because of already exhausted compensation mechanisms. In non-weaners, the significantly higher RVSWI during AMV in comparison with weaners may be related to unsuccessful weaning. In some patients with acute respiratory failure, a marked increase in right ventricular (RV) afterload resulted in increased RVSWI and increased RV O_2 requirements. Thus, right ventricular dysfunction may limit survival in acutely ill patients[14]. The high CI associated with a reduction in SVR caused a lower MAP in non-weaners than in weaners, especially during SIMV. The MAP during weaning may be another important factor in determining success.

Smith and Hanning[15] concluded by saying that recent reviews have challenged many of the assumptions regarding IMV[16], but that it remains a popular method of respiratory supports and weaning. Several of the negative reports have dealt only with patients following cardiac bypass surgery[17,18], a different and less heterogenous population compared with that seen in the general ICU where the clinical impression of IMV is more favorable. Controlled mechanical ventilation should be withdrawn in stable patients after surgery following a short trial of spontaneous ventilation, unless they are severely ill. However, IMV probably is preferable in patients who need prolonged mechanical ventilation. Kennedy et al.[10] observed that urinary norepinephrine excretion increased during weaning by T-piece technique in both weaners and non-weaners, and that the mean value in weaners was higher than non-weaners during both before and during weaning periods. These results suggested that sympathoadrenal stimulation is more intense in weaners. This may be due to an emotional response or may be due to a more normal response to increases in $PaCO_2$ and CO during weaning in patients who can be weaned successfully. We also measured the blood catecholamine levels of our patients before and during weaning by SIMV. However, we found no significant differences in catecholamine levels between weaners and non-weaners, or between before and during SIMV. The mean blood norepinephrine and epinephrine levels were increased during weaning, but since considerable scatter was observed no significant differences between before and during SIMV were detected. This discrepancy between trials may reflect differences in the patient population; Postoperative patients were studied by Kennedy et al., while we measured in patients with acute respiratory failure due to diverse causes. In addition, the technique used for weaning was different; they used their T-piece technique under spontaneous breathing while we used SIMV. Finally, there may be differences in the catecholamine levels between urine and blood. Our results suggested that the sympathoadrenal stimulation was not so great as judged by blood catecholamine levels when weaning was accomplished by SIMV.

In conclusion, we recommend SIMV for weaning of patients who have undergone prolonged mechanical ventilation, because SIMV seems to cause less stimulation to the sympathoadrenal system in comparison to methods previously reported[10]. The increase in RVSWI may be an aid in predicting which patients will be successfully weaned, but the

author did not measure the transmural pressure and therefore cannot comment on the mechanism of the beneficial hemodynamic effects of SIMV in greater detail.

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