대한마취과학회지 2007; 52: S 66～71
Korean J Anesthesiol Vol. 52, No. 6, June, 2007

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The Effects of Repetitive Alveolar Recruitment on Oxygenation and Compliance in ARDS Patients

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Background: If the effects of alveolar recruitment are beneficial, but of short duration, repetitive recruitment maneuvers (RMs) will be necessary to maintain oxygenation. This study was performed to assess the effect of repetitive alveolar recruitment, with high-sustained inflation pressure on oxygenation and compliance of the respiratory system, in patients with acute respiratory distress syndrome.

Methods: Ten adult patients on ventilator support, with controlled mechanical ventilation, received three repetitive RMs with a high-sustained inflation pressure. The time intervals from the first to second RM and from the second to third RM were 8.42 ± 0.56 hours and 12.43 ± 1.45 hours, respectively. Recruitment was conducted by setting the ventilator mode to a continuous positive airway pressure of 40 cmH_2O for 40 seconds. After each alveolar recruitment, the previous ventilator settings in the pressure control mode were re-established with a high positive end expiratory pressure. The F_IO_2, PaO_2/F_IO_2 and lung compliance (tidal volume/[plateau pressure - PEEP]) were recorded with reference to the arterial blood gas analysis at both 30 minutes pre and post recruitment.

Results: The F_IO_2 was able to be decreased from 0.9 to 0.5 while maintaining the PaO_2 at higher than 80 mmHg after three recruitments. The PaO_2/F_IO_2 improved from 98 to 288 and the compliance of the respiratory system improved from 26 to 41 ml/cmH_2O after three recruitments.

Conclusions: Our results suggest that repetitive recruitment can be used to maintain the beneficial effects of alveolar recruitment in patients with acute respiratory distress syndrome when supported using a lung protective mechanical ventilation strategy.

(Korean J Anesthesiol 2007; 52: S 66～71)

Key Words: acute respiratory distress syndrome, lung compliance, oxygenation, positive end-expiratory pressure, repetitive alveolar recruitment.

INTRODUCTION

Pressure limited lung protective mechanical ventilation strategies have been proposed for patients with acute respiratory distress syndrome (ARDS).[1] This emphasizes the need to open the lung and keep it open[2] while avoiding alveolar overdistention. ARDS patients would be recommended to ventilate with a high level of positive end expiratory pressure (PEEP) to achieve lung protective effects of alveolar recruitment.[3,4] Lung recruitment also may be achieved by periodic and brief increases in transpulmonary pressure to higher levels than are achieved during tidal ventilation (recruitment maneuvers, RMs).[3,5-8]

Amato et al.[3] showed reduced mortality in ARDS patients who were managed with a lung protective strategy of relatively higher PEEP and small tidal volume combined with RMs. RMs consisting of sustained inflation (SI) have been advocated as an adjunct to mechanical ventilation in ARDS.

The lung protective ventilation strategy used by Amato et al.[3] resulted in better survival, but it was not clear if the RMs contributed substantially to lung recruitment, reduced ventilation-associated lung injury, or improved outcomes. If RM effects were beneficial but short duration, frequent RMs would be necessary to maintain their effects. The effects of repetitive RMs must be better defined. We hypothesized that arterial oxygenation and lung compliance would be improved

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Received : November 1, 2006

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by following short, repetitive RMs, while avoiding the adverse effects of recruitment. We performed this study to assess the effects of single and repetitive RMs on oxygenation and compliance in ARDS patients receiving protective lung ventilation strategy with relatively high level of PEEP and lower tidal volume.

MATERIALS AND METHODS

Informed consent was obtained from all patients or their next of kin. Ten patients eligible for the recruitment protocol were those with hypoxemic respiratory failure and bilateral pulmonary infiltrates. Those who had obstructive airway disease, pulmonary barotraumas or hemodynamic instability were excluded. The main causes of acute lung injury (ALI) were sepsis (n = 6), chest trauma (n = 2) and aspiration pneumonia (n = 2) (Table 1).

All patients were intubated and ventilated with pressure controlled mode with a mechanical ventilator (Puritan Bennett 7200 AE, Puritan Bennett, California, USA). The investigation was performed with patients in a semi-recumbent position with continuous infusion of midazolam (0.5-2µg/kg/min), fentanyl (2-3µg/kg/min), ketamine (5-15µg/kg/min) and vecuronium (4 mg bolus) for comfortable ventilator management.

Patients were ventilated according to the ARDS net protective ventilatory strategy.[9] Patients were ventilated with pressure control mode. The pressure was set to the exhaled tidal volume (V_T) of 6-8 ml/kg predicted ideal body weight and PEEP and F_IO_2 were set to obtain an arterial oxygen saturation (SaO_2) value of 90−95% or an arterial oxygen pressure (PaO_2) of 60-80 mmHg (baseline) or both. The ventilator was initially set to pressure controlled ventilation mode with PEEP and all ventilator parameters were set by an intensivist. The ventilator was then adjusted to deliver a sustained inflation by switching to the CPAP mode and gradually increasing the CPAP to an inflation pressure of 40 cmH_2O over a period of 5-10 seconds. The inflation pressure was maintained for 40 seconds then the CPAP was reduced to a PEEP level that was determined by monitoring of P/F ratio, SaO_2 and compliance. We conducted RM three times with high-sustained airway pressure in ARDS patients considering physician in charge round time and nursing shifts. The level of CPAP was maintained unless systolic blood pressure decreased to 90 mmHg or less or increased by 30 mmHg or more, heart rate increased to 140 beats/min or more or by 20 beats/min or more, or a cardiac dysrhythmia developed. In case of hypotension during sustained inflation with CPAP, we used norepinephrine to prevent further decrease of systolic and diastolic pressure. And oxyhemoglobin saturation measured by pulse oximetry (SpO_2) was maintained $> 90\%$ or was not decreased by $> 5\%$.

After each RM, previous ventilator settings of pressure control mode were reestablished. F_IO_2 was determined by monitoring SaO_2 or PaO_2. The PEEP level was determined by the peak airway pressure. Before, during and after RMs, we monitored and recorded continuously oxygen saturation by pulse oximetry (SpO_2) and arterial blood pressure. Arterial blood gas analysis was done and respiratory compliance was calculated (tidal volume/[plateau pressure - PEEP]) from ventilator monitor at 30 min pre and post recruitment. All patients had radial artery and central venous catheters for continuous monitoring of the systemic blood pressure and central venous

Table 1. Patient Characteristics

	Sex (M/F)	Age (yrs)	F_IO_2	PaO_2 (mmHg)	P/F ratio	LIS	APACHE	Diagnosis
1	M	34	1.0	72	72	3.5	73	Sepsis
2	M	80	0.8	102	127	2.8	38	Sepsis
3	F	35	1.0	118	118	3.7	67	Sepsis
4	M	56	0.9	123	136	3.5	45	Chest trauma
5	M	48	0.8	80	100	2.8	54	Sepsis
6	M	60	1.0	46	46	3.3	57	Pneumonia
7	M	28	1.0	95	95	2.9	45	Chest trauma
8	M	59	0.8	70	88	3.8	55	Pneumonia
9	M	56	1.0	89	89	3.0	47	Sepsis
10	M	65	0.7	82	117	3.3	39	Sepsis

M: male, F: female, LIS: lung injury score, APACHE: acute physiologic and chronic health evaluation.

pressure respectively. For the patient's safety, we recorded their lowest blood pressure, highest pulse rate and lowest SpO_2 during the 30 minutes following RMs. Chest radiographs were obtained after RMs for barotraumas (pneumothorax, subcutaneous emphysema). We monitored patients for at least 24 hours and looked for the development of adverse events such as barotraumas, hypotension or desaturation.

Statistics

Data were expressed as mean ± standard deviation. The effect of individual RM was compared by analysis of variance for repeated measures with Bonferroni correction. Bonferroni adjusted P-value was obtained by multiplying the corresponding P-value by the number of tests. A P-value of less than 0.05 was considered significant. Analysis was carried out with a SAS 8.1 software.

RESULTS

The time intervals from first RM to second RM and from second RM to third RM were 8.42 ± 0.56 hours and 12.43 ± 1.45 hours, respectively. Mean duration of ventilator support and ICU stay were 13.6 ± 9.3 and 18.1 ± 12.7 days, respectively. Eight patients were survived, but two patients expired.

Ventilator parameters at pre and post RMs are summarized in Table 2. Compliance of the respiratory system of post third RM improved significantly compared with those of pre and post first RM. The changes in plateau pressure, peak inspiratory pressure, exhaled tidal volume and compliance from pre first RM to post third RM were statistically significant ($P < 0.05$) (Table 2).

F_IO_2 decreased from 0.9 at pre first RM to 0.5 at post third RM. F_IO_2 of post second RM, pre third RM and post third RM decreased significantly compared with that of pre first RM (Table 3). PaO_2/F_IO_2 (P/F ratio) improved from 98 at pre first RM to 288 at post third RM. P/F ratio of post second RM, pre third RM and post third RM improved significantly compared with that of pre first RM (Table 3).

F_IO_2 decreased significantly ($P < 0.05$) and PaO_2/F_IO_2

Table 2. Ventilator Parameters at Pre and Post Recruitment Maneuver

	Pre FRM	Post FRM	Pre SRM	Post SRM	Pre TRM	Post TRM
Plateau pressure (cmH_2O)	21.1 ± 0.9	17.8 ± 0.9	17.4 ± 4.1	14.7 ± 5.1	14.4 ± 0.4	13.1 ± 4.7*
PEEP (cmH_2O)	10.2 ± 4.3	13.2 ± 6.6	13.7 ± 4.0	13.4 ± 3.8	13.2 ± 4.6	13.1 ± 2.3
Peak pressure (cmH_2O)	33.5 ± 3.7	29.2 ± 6.5	30.6 ± 4.7	27.3 ± 5.4	27.4 ± 6	25.9 ± 4.3*
V_T (ml)	447 ± 23	447 ± 92	478 ± 47	451 ± 124	503 ± 121	520 ± 83*
Compliance (ml/cmH_2O)	26.7 ± 5.5	27.0 ± 5	28.9 ± 6.2	31.8 ± 8.1	34.5 ± 8.8	41.3 ± 14*
RR (breaths/min)	18 ± 4	16 ± 2	16 ± 3	17 ± 3	15 ± 3	16 ± 3

Values are mean ± SD. Pre FRM: pre first recruitment maneuver, Post FRM: post first recruitment maneuver, Pre SRM: pre second recruitment maneuver, Post SRM: post second recruitment maneuver, Pre TRM: pre third recruitment maneuver, Post TRM: post third recruitment maneuver, PEEP: positive end expiratory pressure, V_T: exhaled tidal volume, RR: respiratory rate. *: $P < 0.05$ compared with pre first recruitment maneuver.

Table 3. Arterial Blood Gas Analysis at Pre and Post Recruitment Maneuver

	Pre FRM	Post FRM	Pre SRM	Post SRM	Pre TRM	Post TRM
pH	7.41 ± 0.0	7.35 ± 0.1	7.33 ± 0.2	7.33 ± 0.1	7.33 ± 0.0	7.37 ± 0.0
$PaCO_2$ (mmHg)	44 ± 4	44 ± 13	47 ± 11	46 ± 5	44 ± 4	40 ± 3
F_IO_2	0.9 ± 0.1	0.8 ± $0.1^{\dagger}$	0.7 ± 0.1	0.6 ± $0.1^{*\dagger}$	0.6 ± 0.1*	0.5 ± $0.1^{*\dagger}$
PaO_2 (mmHg)	99 ± 20	122 ± 46	106 ± 19	116 ± 19	107 ± 19	135 ± 28
PaO_2/F_IO_2	98 ± 27	164 ± $53^{\dagger}$	166 ± 51	221 ± $47^{*\dagger}$	204 ± 51*	288 ± $63^{*\dagger}$
SaO_2 (%)	93 ± 1	98 ± 2	97 ± 2	97 ± 2	98 ± 2	99 ± 1

Values are mean ± SD. Pre FRM: pre first recruitment maneuver, Post FRM: post first recruitment maneuver, Pre SRM: Pre second recruitment maneuver, Post SRM: post second recruitment maneuver, Pre TRM: pre third recruitment maneuver, Post TRM: post third recruitment maneuver. *: $P < 0.05$ compared with pre first recruitment maneuver, †: $P < 0.05$ compared to the value before RM.

Table 4. Hemodynamic Data at Pre and Post Recruitment Maneuver

	Pre FRM	Post FRM	Pre SRM	Post SRM	Pre TRM	Post TRM
SBP (mmHg)	139 ± 31	144 ± 26	123 ± 23	130 ± 29	117 ± 5	136 ± 19
DBP (mmHg)	62 ± 8	73 ± 8	68 ± 7	65 ± 5	57 ± 5	64 ± 5
PR (bpm)	82 ± 14	81 ± 14	87 ± 19	88 ± 19	86 ± 19	85 ± 18
CVP (mmHg)	7 ± 1	6 ± 1	6 ± 1	6 ± 1	5 ± 1	5 ± 1

SBP: systolic blood pressure, DBP: diastolic blood pressure, PR: pulse rate, CVP: central venous pressure, Pre FRM: pre first recruitment maneuver, Post FRM: post first recruitment, Pre SRM: pre second recruitment, Post SRM: post second recruitment, Pre TRM: pre third recruitment, Post TRM: post third recruitment.

improved significantly at each RM ($P < 0.001$). Compliance of the respiratory system improved significantly only at the third RM ($P = 0.0071$). PaO_2 increased at each RMs without statistical significance and $PaCO_2$, pH, remained unchanged during the RMs.

Systolic blood pressure, diastolic blood pressure, pulse rate and central venous pressure were maintained during the RMs without inotropes or vasopressors as norepinephrine (Table 4). No patients showed barotrauma developed by RMs on chest radiograph.

DISCUSSION

We conducted RM three times with high sustained airway pressure (CPAP of 40 cmH_2O, for 40 seconds) and assessed the effects of each RM on oxygenation and compliance in ARDS patients. We conducted our study in a manner that was similar to the technique used in a previous trial of a lung protective ventilation approach.3) Between each RM the patients were supported with a protective lung strategy of lower tidal volume with higher PEEP. The issue of full lung opening has been mainly emphasized by Bohn and Lachman10) who suggested a recruitment maneuver with plateau pressure exceeding 35 cmH_2O for a short period of time to resolve the sticky atelectasis problem. Lower pressure was thought to be enough thereafter to keep the lung open if adequate PEEP was provided.

Pelosi et al.11) reported that RMs improved lung mechanics and oxygenation only in patients with extrapulmonary ARDS but Grasso et al.12) showed that underlying disease did not influence the amount of improvement in arterial oxygenation after application of RM. In the study by Pelosi,11) V_T was 0.56 L (approximately 10 ml/kg) and the static end-inspiratory pressure of respiratory system was 31.6 cmH_2O during baseline ventilation. In the study of Grasso et al,12) the same parameters were 0.38 L (6 ml/kg) and 23.3 cmH_2O respectively during baseline ventilation. The larger potential for alveolar recruitment by lower V_T and end-inspiratory pressure of respiratory system in the study of Grasso et al. could explain the improvement in arterial oxygenation with RMs. It was also noted in pulmonary ARDS from Grasso's study which suggested as non-responder patients in Pelosi's study.

Application of RM improved oxygenation only in early ARDS patients who did not have impairment of chest wall mechanics.12) Improvement of oxygenation at first RM was not consistent with the causes of ARDS in our patients. The baseline P/F ratio and P/F ratio after first RM in our patients was lower than that of non-responder patients of the Grasso et al. study.13) This suggests that our patients' lung injuries were severer than their patients. In our study the improvement of P/F ratio at first recruitment was not more than 50% in all patients defined as a responder with RM in Grasso study. The effect of first RM on oxygenation and compliance might be limited because the mean difference between peak pressures during tidal ventilation, 33.5 ± 3.7 cmH_2O and RM pressure was approximately 7 cmH_2O in our study (Table 1). In the study by Grasso et al.12) improvement of P/F ratio after RM was 175% in responders and our data showed 288% improvement after three RMs.

The composition of inspired gas can also play a role in maintaining the recruitment effect, because more rapid de-recruitment and reabsorption atelectasis occurs at a higher F_IO_2.8,14) F_IO_2 should be reduced to the lowest acceptable level to prevent lung injury as well as to reduce the rate of de-recuitment.7,15) In our study, the improvement effect of RM on compliance and increase of exhaled tidal volume were statistically significant only after the third RM ($P < 0.05$). Repetitive RMs might cause increase of exhaled tidal volume by way of compliance increase.

The RM pressure used in this study was not as high as in other studies of RMs in ALI/ARDS patients[8] and in animal models of ALI.[16,17] One may argue that application of a higher level of continuous positive airway pressure for a longer period of time may have a greater effect on gas exchange.[12] Foti et al.[8] suggested that RM could improve oxygenation at relatively low PEEP (9.4 ± 3 cmH_2O), but it was less effective than a higher PEEP level (16 ± 2 cmH_2O). More aggressive RMs might worsen the hemodynamic impairment[8] and therefore limit the clinical use of RMs at pressures greater than 40 cmH_2O.

The PEEP after RMs could be used to maintain recruitment. Favorable effects of RMs at time points after the first 10 minutes could have been reversed in some patients if PEEP was decreased after RM.[18] Loss of the beneficial effects of the RM during a 4 hour follow up was noted in 4 patients in Lapinsky's study.[5] This might be the result of the insufficient level of PEEP to maintain the recruitment in those 4 patients who all had PEEP levels less than or equal to 10 cmH_2O (mean 7.5 cmH_2O). We increased PEEP after the first RM and maintained that level between RMs through the study. This might maintain the effect of RM to 8.42 ± 0.56 hours until the second RM and 12.43 ± 1.45 hours until the third RM compared to the 4 hours of Lapinsky's study.[5] Each RM improved oxygenation in our patients and the improvement was maintained until the next RM. We could not determine if the improvement of oxygenation and compliance was due to the effect of repetitive RM, or higher PEEP between RMs or both. It might be speculated that repetitive RMs had the effect of changing non-responders to responders as evidenced by the improvement of oxygenation and compliance of their respiratory system.

A limitation of our study was that we did not measure pressure-volume curves. In the group ventilated with the protective strategy, the PEEP level had to be individualized in each patient at a value 2 cmH_2O greater than the lower inflection point of the PV curve. Concerns with this approach include the difficulty in measuring a static PV curve, the potential risks to the patient of paralysis and loss of PEEP during the maneuver.[19]

Our results show that three consecutive RMs improved P/F ratio and compliance significantly within one day. Although the number of patients was small in our study, results suggest that repetitive recruitment could be beneficial if used earlier for ARDS patients who are supported with a lung protective ventilator strategy of higher PEEP and lower tidal volume.

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