Effect of Repeated Recruitment Manoeuvres on Patients with Severe Acute Respiratory Distress Syndrome

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ABSTRACT

Objective: *The study aimed to evaluate the influence of repeated recruitment manoeuvres (RRMs) on lung injury in patients with acute respiratory distress syndrome (ARDS).*

Methods: *Forty-one ventilated patients with severe ARDS were selected for this study. Recruitment manoeuvres (RMs) were conducted with continuous positive airway pressure (CPAP; 30 cm H_2O for 40 seconds). Recruitment manoeuvres were repeated every two hours for all three groups. Changes in haemodynamics, pulmonary compliance, gas exchange and extravascular lung water index (EVLWI) were monitored before RM (pre-RM), 10 minutes after each RM, and four hours after RM3 (4 hours post-RRM). Pulmonary inflammatory factors (tumour necrosis factor-alpha [TNF-α] and interleukin [IL]-6 and -10) were also analysed.*

Results: *Compared with those in pre-RM, pulmonary compliance, oxygenation index (ratio of partial pressure of arterial oxygen to fraction of inspired oxygen [PaO_2/FiO_2]) and EVLWI remarkably improved in RM1, RM2, RM3 and 4 hours post-RRM (*$p < 0.05$*). The PaO_2/FiO_2 ratio increased significantly in RM1 and RM3 (*$p < 0.05$*). Extravascular lung water index decreased significantly in RM1 compared with that in RM3 and 4 hours post-RRM (*$p < 0.05$*). There was no significant difference in cytokines.*

Conclusion: *Repeated recruitment manoeuvres during lung-protected ventilation can improve pulmonary compliance and oxygenation and significantly decrease extravascular lung water in ARDS patients. Lung injury was not worsened by RRMs in patients with severe ARDS.*

Keywords: Acute respiratory distress syndrome, extravascular lung water, gas exchange, haemodynamics, inflammatory reaction, pulmonary compliance, repeated recruitment manoeuvres

Efecto de las Maniobras de Reclutamiento Repetidas en Pacientes con Síndrome de Dificultad Respiratoria Aguda Severa

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RESUMEN

Objetivo: *El estudio tuvo por objeto evaluar la influencia de las maniobras de reclutamiento repetidas (MRR) en la lesión pulmonar en pacientes con síndrome de dificultad respiratoria agudo (SDRA).*

Métodos: *Para este estudio se seleccionaron cuarenta y un pacientes ventilados, con SDRA severo. Se realizaron maniobras de reclutamiento (MR) con presión positiva continua de las vías respiratorias (CPAP; 30 cm H2O durante 40 segundos). Las maniobras de reclutamiento se repitieron cada dos horas para los tres grupos. Los cambios de hemodinámica, distensibilidad pulmonar, intercambio gaseoso e índice de agua pulmonar extravascular (EVLWI) fueron monitoreados antes de MR (pre-MR), diez minutos después de cada MR y cuatro horas después de MR3 (4 horas post-MRR). También se analizaron los factores de inflamación pulmonar: factor de necrosis tumoral alfa, e interleucina-6 y-10 (TNF-α, IL-6 e IL-10).*

Resultados: *En comparación con los de pre-MR, la distensibilidad pulmonar, el índice de oxigenación, la proporción de la presión parcial de oxígeno arterial con respecto a la fracción de oxígeno inspirado (PaO_2/FiO_2) y EVLWI mejoraron notablemente en MR1, MR2, MR3, y cuatro horas post-MRR (*$p <$

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0.05). La razón PaO_2/FiO_2 aumentó significativamente en MR1 y MR3 (p < 0.05). El índice de agua pulmonar extravascular disminuyó significativamente en MR1, en comparación con la de MR3 y cuatro horas de post-MRR (p < 0.05). No hubo diferencias significativas en las citocinas.

Conclusión: *Las maniobras de reclutamiento repetidas durante la ventilación de protección pulmonar puede mejorar la oxigenación y la distensibilidad pulmonar, y disminuir considerablemente el agua pulmonar extravascular en pacientes con SDRA. La lesión pulmonar no fue empeorada por MRR en pacientes con SDRA grave.*

Palabras claves: Síndrome de dificultad respiratoria agudo, agua pulmonar extravascular, intercambio gaseoso, hemodinámica, reacción inflamatoria, distensibilidad pulmonar, maniobras de reclutamiento repetidas

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INTRODUCTION

Mechanical ventilation is an indispensable means for acute respiratory distress syndrome (ARDS) treatment. The lung protective ventilation strategy, which focusses on low tidal volume and positive end-expiratory pressure (PEEP), reduces ventilator-induced lung injury and mortality (1). However, this ventilation mode accelerates part of the alveolar collapse and affects gas exchange (2). Lung recruitment manoeuvres (RMs) can open collapsed alveoli. Recruitment manoeuvre is favourable for gas exchange and lung protection. However, the limited time available for maintaining lung recruitment (3), repeated suctioning, and other operations cause the alveoli to collapse. Thus, repeated recruitment manoeuvres (RRMs) are requested in clinical applications, but few trials have indicated that RRMs aggravate alveoli damage. Thus, we conducted this study to evaluate the clinical efficacy and safety of RRM by observing the haemodynamics, respiratory mechanics, and inflammatory reaction in severe ARDS patients and provide more evidence for clinical implementation.

SUBJECTS AND METHODS

All patients were admitted to five intensive care units (ICUs) at tertiary teaching hospitals from January 2008 to December 2012. According to the American-European Consensus Conference Committee 1994 diagnostic criteria for ARDs (4), we chose 41 ARDS patients with severe hypoxaemia (ratio of partial pressure of arterial oxygen to fraction of inspired oxygen [PaO_2/FiO_2] < 100 mmHg at PEEP ≥ 10 cm H_2O, after 30 minutes) and pulmonary infiltrates based on a chest radiograph or computed tomography (CT). The patients were 27 males and 14 females aged 18 to 80 (mean 57.4 ± 16.3) years with a mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score of 21.5 ± 10.1 and a lung injury score of 3.1 ± 0.4. The causes of ARDS of these patients included pneumonia (12 cases), multiple trauma (n = 6), acute pancreatitis (n = 5), lung contusion (n = 6), intestinal perforation (n = 7) and severe systemic infection (n = 5). This study was conducted in accordance with the Declaration of Helsinki and with approval from the Ethics Committee of Xuzhou Hospital Affiliated to Southeast University. Written informed consent was obtained from all participants.

Treatment methods

The patients were asked to lie in a supine position and then sedated with midazolam (0.03 mg/kg·h to 0.20 mg/kg·h). A double-lumen intravenous tube was introduced to the right internal jugular vein and connected to a pressure sensor to continuously record central venous pressure (CVP), which was adjusted from 8 cm H_2O to 12 cm H_2O. A Pulsiocath PV2014L16A PiCCO catheter (Pulsion Medical Systems, Munich, Germany) was placed into the left/right femoral artery and then connected with the PiCCO instrument to monitor the mean arterial pressure (MAP), cardiac index (CI) and extravascular lung water (EVLW). An HP monitor was used to continuously record electrocardiograms and blood oxygen saturation (SpO_2). A Connect Drager Evita 4 (Drager Medical Systems, Lubeck, Germany) or PB840 ventilator (Puritan Bennett, America) with tracheal intubation or tracheotomy tube was used to set the ventilation mode for bi-level positive pressure ventilation and assist spontaneous breathing. Pressures were lower than the lower inflection point plus 4 according to the dynamic pressure-volume curve; tidal volume was set to 6 mL/kg to 8 mL/kg of the predicted body weight, the respiratory rate to 16, inspiratory to expiratory time ratio (I:E) to 1:1.5 and FiO_2 to ≤ 0.60.

Recruitment manoeuvre implementation: RM was performed by changing the ventilator mode to continuous positive airway pressure (CPAP) and gradually increasing it to 30 cm H_2O and maintaining it for 40 seconds. The CPAP was then decreased for over five seconds and reverted to the initial ventilator settings (mode, PEEP and FiO_2). Recruitment manoeuvres were conducted three times every two hours (RM1, RM2 and RM3). The airway was kept clear before each RM.

Data collection

The APACHE II score and injury severity score of the pre-RM were calculated by score software. The SpO_2, peak airway pressures, mean airway pressure, plateau pressure, tidal volume, dynamic compliance, airway resistance, continuous electrocardiographic monitoring, CVP, arterial blood pressure, CI and EVLW were determined during the whole period. Gas exchange: The arterial blood gases (pH, PaO_2, $PaCO_2$, and PaO_2/FiO_2) pre-RM, 10 minutes after RM (RM1, RM2 and RM3) and four hours post-RRM were examined. Determina-

tion of plasma cytokines: about 2 mL of non-anticoagulant blood was extracted before RM, four hours after RM3, and 24 hours after RRM. The sample was centrifuged for 10–15 minutes within 30 minutes after blood collection. The samples were stored in a refrigerator after the separation of serum. The cytokines were analysed by enzyme-linked immunosorbent assay. Chest radiographs were obtained before and after RM, and the number of ventilator-free days, ICU mortality and 28-day mortality were determined.

Statistical analysis

Results are expressed as mean ± standard deviation. Statistical analysis was performed with SPSS 12.0 software and by one-way analysis of variance (ANOVA). Any two of the multiple samples were compared by a Q-test. *P*-values < 0.05 were considered significant.

RESULTS

Forty-one patients were enrolled in this study. All patients tolerated the RRMs. No barotrauma was observed on the lung X-rays after the treatment.

Comparison of haemodynamic parameters

No statistical difference was observed in the haemodynamic parameters (heart rate [HR], MAP, CVP and CI) of RM1, RM2, RM3 and four hours post-RM3 [$p > 0.05$] (Table 1).

Comparison of pulmonary compliance, oxygenation index and EVLW

Compared with pre-RM, RM1, RM2, RM3 and four hours post-RRM increased pulmonary compliance and PaO_2/FiO_2 but decreased the EVLW index ($p < 0.05$). A comparison of RM3 and four hours post-RRM with RM1 indicated that pulmonary compliance and PaO_2/FiO_2 increased significantly and the changes were statistically different. Extravascular lung water index significantly decreased ($p < 0.05$); by contrast, $PaCO_2$ had no statistical difference [$p > 0.05$] (Table 2).

Comparison of cytokine levels between pre-RM and post-RM

Compared with those in pre-RM, tumour necrosis factor-alpha (TNF-α), interleukin (IL)-6 and -10 decreased four and 24 hours post-RRM, but without significant difference [$p > 0.05$] (Table 3).

Table 3: Comparison of cytokine levels in pre-RM, four hours and 24 hour post-RRM

	Pre-RM	4 hours post-RRM	24 hours post-RRM
TNF-α	434.21 ± 104.72	401.56 ± 95.83	391.77 ± 121.11
IL-6	502.56 ± 318.64	489.01 ± 295.75	480.95 ± 276.92
IL-10	127.33 ± 43.57	98.76 ± 37.82	111.37 ± 51.46

*$p < 0.05$: comparison with pre-RM
RM – recruitment manoeuvre; RRM – repeated recruitment manoeuvre; TNF-α – tumour necrosis factor-alpha; IL – interleukin

Comparison of lengths of ICU stay and mortality

The number of ventilator-free days was 8.7 ± 10.1, the length of ICU stay was 20.8 ± 22.4 days, the ICU mortality was 34.1% (14/41) and the 28-day mortality was 31.7% (13/41).

DISCUSSION

The reduction of aerated alveoli caused by alveolar collapse is an important pathophysiological feature of ARDS. This feature increases pulmonary shunt and ventilation/perfusion ratio

Table 1: Comparison of haemodynamic parameters between pre-RM and post-RM

	Pre-RM	RM1	RM2	RM3	4 hours post-RRM
HR	117 ± 17	120 ± 13	118 ± 17	109 ± 15	110 ± 19
MAP	83 ± 13	84 ± 14	86 ± 16	85 ± 15	86 ± 12
CVP	10.4 ± 2.9	11.9 ± 2.3	12.8 ± 1.8	12.6 ± 2.5	12.1 ± 1.8
CI	2.8 ± 0.7	2.9 ± 0.4	3.1 ± 0.5	3.0 ± 0.4	3.1 ± 0.6

*$p < 0.05$: compared with pre-RM. #$p < 0.05$: compared with RM1.
RM – recruitment manoeuvre; RRM – repeated recruitment manoeuvre; HR – heart rate; MAP – mean arterial pressure; CVP – central venous pressure; CI – cardiac index

Table 2: Comparison of pulmonary compliance, PaO_2/FiO_2 and EVLWI between pre-RM and post-RM

	Pre-RM	RM1	RM2	RM3	4 hours post-RRM
Cdyn	28.1 ± 2.3	33.8 ± 2.2*	38.1 ± 1.8*	40.9 ± 2.0*#	40.4 ± 1.2*#
$PaCO_2$	36.8 ± 8.5	37.7 ± 6.4	38.6 ± 5.3	42.8 ± 5.4	40.0 ± 4.5
PaO_2/FiO_2	98 ± 54.26	121 ± 78.75*	147 ± 85.20*	165 ± 89.61*#	182 ± 75.95*#
EVLWI	20.56 ± 7.23	16.95 ± 5.47*	15.90 ± 4.54*	14.25 ± 5.15*#	13.87 ± 3.92*#

*$p < 0.05$: comparison with pre-RM. #$p < 0.05$: comparison with RM1
RM – recruitment manoeuvre; RRM – repeated recruitment manoeuvre; Cdyn – dynamic compliance; $PaCO_2$ – partial pressure of arterial carbon dioxide; PaO_2/FiO_2 – ratio of partial pressure of arterial oxygen to fraction of inspired oxygen; EVLWI – extravascular lung water index

imbalance, producing hypoxaemia, which is difficult to correct (5). To improve patient oxygenation, the lungs should be kept open. Thus, lung recruitment is proposed as a part of lung protective ventilation. Many reports on the single RM technique have been published (6); however, few studies have shown the clinical efficacy and safety of RRMs in ARDS patients (7). Recruitment manoeuvre as a part of a protective ventilation strategy can reopen poorly aerated alveoli and maintain alveolar recruitment (8). Thus, we conducted this study to evaluate the effectiveness of RRMs during lung protective ventilation in severe ARDS patients. The results showed that, compared with pre-RM, RRM during lung protective ventilation can significantly increase pulmonary compliance and PaO_2/FiO_2 and decrease EVLW index but maintain the inflammatory index. The haemodynamic parameters also did not show statistical changes. The changes in oxygenation and haemodynamics were consistent with Cruces *et al* (9) who conducted an experiment on RMs in ARDS patients. Injured alveolar recruitment is generally maintained through the RRM period; thus, RRMs significantly increase gas exchange and improve oxygen delivery.

Repeated recruitment manoeuvres improved ICU and 28-day mortality in severe ARDS patients compared with the control group in the study by Xi *et al* (10). Methods using high CPAP in RRM studies (11) are efficient in severe ARDS cases.

The severity of pulmonary oedema can be directly reflected by EVLW through PiCCO monitoring. Extravascular lung water index is the most specific quantitative index for monitoring pulmonary oedema (12) and is closely related to the prognosis of critically ill patients (13). Chew *et al* (14) studied a prospective, observational cohort of 51 patients with shock and found that EVLW is associated with the degree of lung injury and mortality. Michard *et al* (15) examined 29 patients with severe infection and found that EVLW is significantly interrelated with the oxygenation index, duration of mechanical ventilation and hospital mortality. This study suggests that EVLW significantly affects the evaluation of changes in patient condition and prognosis. Repeated recruitment manoeuvres also significantly reduce EVLW but improve oxygenation, which may be attributed to the following: i) RRM can keep the alveoli open, prevent alveolar shear, reduce type II alveolar epithelial cell injury and increase alveolar water clearance. Recruitment manoeuvres reduce lung endothelial cell injury and the EVLW of acute lung injury in rats (16); ii) Keeping the alveoli open can increase the clearance area of lung water; iii) RRM develops high airway pressure and iv) increases ambient pressure, inhibiting the generation of lung water.

Abnormal mechanical force (including excessive stretch, pressure and shear) caused by mechanical ventilation can lead to biological injury (17) when it affects lung epithelial and endothelial cells. The mechanical force signals delivered into these cells stimulate inflammatory cells to release massive inflammatory factors, causing biological injury, thereby aggravating pulmonary inflammation (18, 19). Macrophages and polymorphonuclear cells in the alveoli are also involved in the release of ventilator-associated cytokines (20). Cell stretch caused by mechanical ventilation generates cytokines, including TNF-α, IL-1β, IL-6, IL-8, IL-10 and matrix metalloproteinase-2 (21). In this study, the degree of lung injury was evaluated by measuring TNF, IL-6 and IL-10 in serum. The RRM group was not statistically significant but had lower TNF-alpha, IL-6 and IL-10 than the pre-RRM group. This result indicates that RRM did not worsen pulmonary inflammation and lung injury.

CONCLUSION

Repeated recruitment manoeuvres during lung protective ventilation can improve oxygenation and significantly decrease EVLW without increasing lung injury in severe ARDS patients.

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