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RESPIRATORY AND HAEMODYNAMIC CHANGES DURING DECREMENTAL RECRUITMENT IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME

SUMMARY

The aim of the paper was to investigate the haemodynamic and respiratory changes during lung recruitment and decremental positive endexpiratory pressure (PEEP) titration for open lung ventilation in patients with acute respiratory distress syndrome (ARDS). A prospective, clinical trial was performed involving 10 adult patients with ARDS treated in the surgical intensive care unit in our hospital.

Recruitment (pressure-controlled ventilation with fixed PEEP at 20 cmH_2O and increased driving pressures at 20, 25 and 30 cmH_2O for two minutes each) and PEEP titration (PEEP lowered by 2 cmH_2O every two minutes, with tidal volume set at 6 ml/kg) were applied. The open lung PEEP (OL-PEEP) was defined as the PEEP level achieving maximum dynamic respiratory compliance plus 2cmH_2O. Gas exchange, respiratory mechanics and central haemodynamics were measured at the following steps: at baseline (T0), during the final recruitment step with PEEP at 20cmH_2O and driving pressure at 30 cmH_2O (T20/30), at OL - PEEP, following another recruitment manoeuvre (TOLP).

The ratio of partial pressure of arterial oxygen (PaO_2) to fraction of inspired oxygen (FiO_2) increased from T0 to TOLP (130 ± 49 versus 156 ± 64 mmHg, $P < 0.005$); dynamic respiratory compliance also increased (23 ± 5 versus 27 ± 6 ml/cmH_2O, $P < 0.005$). At constant PEEP (14 ± 3 cmH_2O) and tidal volumes, peak inspiratory pressure decreased (32 ± 3 versus 29 ± 3 cmH_2O, $P <$ 0.005), although partial pressure of arterial carbon dioxide ($PaCO_2$) was unchanged (58 ± 22 versus 53 ± 18mmHg). No significant decrease in mean arterial pressure was noted.

A standardised open lung strategy increased oxygenation and improved respiratory system compliance. No major haemodynamic compromise was observed.

Key words: **ventilatory management, ARDS**

INTRODUCTION

Cyclical opening and closing of atelectatic alveoli and distal small airways with tidal ventilation is a basic mechanism leading to ventilator-induced lung injury (VILI) (1).To prevent alveolar cycling and derecruitment in acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), high levels of positive end-expiratory pressure (PEEP) have been proposed. In a partially collapsed lung, high levels of PEEP alone result in limited lung protection. "Open lung concept' has been proposed

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to open up all recruitable alveoli by applying high inflation pressures (lung recruitment manoeuvre (RM) to 'open up the lung') (2). Once the lung is thought to be recruited, the open lung PEEP (OL-PEEP) is defined as the level of PEEP that prevents end-expiratory collapse ('to keep the lung open'). A decremental PEEP has been proposed, after full lung recruitment. We observed the changes in both oxygenation and respiratory mechanics during that decremental PEEP. However, high intrathoracic pressures applied during lung recruitment and PEEP may cause barotrauma or haemodynamic instability. That could be the limitation of the open lung concept. On the other hand, re-establishing a 'normal' functional residual capacity (FRC) by optimum PEEP should result in hemodynamic changes. The aims of the present study were to investigate the effects of a standardised, open lung strategy on the respiratory function and haemodynamics in patients with ARDS already being ventilated in a lung protective mode (3,4).

MATERIAL AND METHODS

Every mechanically ventilated patient with ARDS (5) (lung injury score ≥ 2.5) was considered. Exclusion criteria were: age younger than 18 years, severe head injury, aortic or femoral aneurysms, inherited cardiac malformations, presence of arrhythmias, immunosuppression, end-stage chronic organ failure. Before interventions, patients had to be haemodynamically stable. Adequate sedation (Richmond agitation sedation scale score -5) (6) was ensured with intravenous midazolam (5 to 15 mg/hour) and fentanyl (0.5 to 2.5 mg/hour) throughout the study. Paralysing agents were not used.

The ventilator was set in the pressure-control mode with tidal volumes ranging between 5 to 8 ml/kg, an inspiration:expiration ratio of 1:1 and respiratory rate (RR) set to keep arterial pH greater than 7.20. PEEP was set during an incremental PEEP trial using the oxygenation response as the primary endpoint. Improvement in oxygenation was defined as an increase in PaO_2 exceeding 10 mmHg, as described previously. All patients had a triple lumen central venous catheter (via the subclavian or internal jugular vein). Haemodynamic stability was defined as a MAP higher than 65 mmHg, HR less than 130 beats/min.

Respiratory mechanics

Lung recruitment and PEEP titration was guided and standardised during the clinical application of a recruitment strategy. End-inspiratory pressure (EIP), PEEP, inspired and expired tidal volumes and dynamic compliance of the respiratory system (Cdyn) were observed. Cdyn was calculated as Vtinsp/EIP – PEEP.

The open lung procedure was divided into two distinct parts: the lung recruitment phase and the open lung PEEP titration.

First, baseline measurements (time = T0) were taken at the settings determined in the pressure control mode. PEEP was set at 20cmH_2O and the lungs were recruited by increases of the driving pressure up to 30 cmH_2O (time = T20/30). PEEP was kept constant at 20 cmH_2O, but EIP was reduced in order to achieve about the same Vt as at baseline. Every two minutes, PEEP was reduced in steps of 2 cm H_2O keeping driving pressure constant and recording Cdyn. OL-PEEP was defined as the PEEP achieving highest Cdyn +2 cmH_2O. The RM was repeated and OL-PEEP was set along with the EIP that resulted in the same Vt as at T0 (time = TOLP). All measurements were taken in the pressure-controlled mode, without changing fraction of inspired oxygen (FiO_2) or RR.

Lung recruitment and PEEP titration

The open lung procedure was divided into two distinct parts: the lung recruitment phase and the open lung PEEP titration. PEEP was set at 20 cmH_2O and the lungs were recruited by increases of the driving pressure up to 30 cmH_2O (time = T20/30). Following RM, OL-PEEP was titrated PEEP and kept constant at 20 cmH_2O, but EIP was reduced in order to achieve about the same Vt as at baseline. Every two minutes, PEEP was reduced in steps of 2 cmH_2O keeping driving pressure constant and recording Cdyn. OL-PEEP was defined as the PEEP achieving highest Cdyn +2 cmH_2O. The RM was repeated and OL-PEEP was set along with the EIP that resulted in the same Vt as at T0 (time = TOLP). All measurements were carried out in the pressure-controlled mode, without changing the fraction of inspired oxygen (FiO_2) or RR.

Statistics

All data are presented as mean ± standard deviation. To test normal distribution, the Kologomorow-Smirnov test was used. To analyse statistical differences, paired sample *t*-test was applied if two times points were compared; otherwise, the analysis of variance for repeated measurements was used. To investigate the relationship between the observed variables, Scheffe's test was performed.

RESULTS

After fulfilling the inclusion criteria, 10 patients were enrolled over a period of one year in a prospective autocontrol clinical trial *(Table1)*.

Table 1.Patients' characteristics

Patient No.	Diagnosis	PaO2/FiO2	PEEP
1	Sepsis	108	16
2	Sepsis	98	16
3	Pneumonia	54	18
4	Pneumonia	61	12
5	Pneumonia	103	12
6	Sepsis	170	17
7	Pneumonia	156	10
8	Sepsis	83	14
9	Pneumonia	144	15
10	Pneumonia	151	14

FiO2 = fraction of inspired oxygen
PaO2 = partial pressure of arterial oxygen
PEEP = positive end-expiratory pressure

At baseline conditions, patients were on a lung protective strategy with low tidal volume (5.4 ± 0.8 ml/kg IBW) and high PEEP (14 ± 3 cmH_2O). Compared with baseline, RM followed by OL-PEEP ventilation increased oxygenation (PaO_2/FiO_2 at T0 120 ± 59 vs 146 ± 64 mmHg at TOLP, $P < 0.005$) *(Table 2)*.

Table 2.Respiratory variables presented as mean ± standard deviation

	TO	TOLP
PH	7.22 ± 0.2	7.22 ± 0.3
PaO_2/FiO_2 (mmHg)	120 ± 59	146 ± 64
$PaCO_2$ (mmHg)	58 ± 22	53 ± 18
Peak inspiratory pressure (cmH_2O)	32 ± 3	29 ± 3
PEEP (cmH2O)	14 ± 3	14 ± 3
Dynamic compliance (ml/cmH_2O)	23 ± 5	27 ± 6
Tidal volume (ml/kg)	5.4 ± 0.8	5.6 ± 0.7
Respiratory rate (breaths/min)	19 ± 3	19 ± 3

FiO_2 = fraction of inspired oxygen;
$PaCO_2$ = partial pressure of arterial carbon dioxide;
PaO_2 = partial pressure of arterial oxygen;
PEEP = positive end-expiratory pressure;
T0 = time at baseline;
TOLP = time at open lung-positive end-expiratory pressure.

From T0 to TOLP, PEEP was increased in four patients and decreased in six patients, leaving mean PEEP unchanged (14 ± 3 cmH_2O). From T0 to TOLP, Cdyn significantly improved (23 ± 5 vs 27 ± 6 ml/cmH_2O, $P < 0.05$), peak inspiratory pressures (29 ± 3 at TOLP vs 32 ± 3 cmH_2O at T0, $P < 0.05$) was lower. There was a significant correlation between the percentage changes from T0 to TOLP in oxygenation and Cdyn (r = 0.62, $P < 0.005$). There was a significant correlation between the changes in Cdyn and the changes in partial pressure of arterial carbon dioxide ($PaCO_2$) from T0 to TOLP (r = -0.52, $P < 0.05$). Tidal volume, $PaCO_2$ and pH remained constant.

There were no significant changes in mean arterial pressure (MAP), heart rate (HR) and central venous pressure (CVP) *(Table 3)*.

Table 3. Haemodynamic characteristics

	TO	T20/30	TOLP
Heart rate (beats/min)	86 ± 20	89 ± 20	85 ± 18
Mean arterial pressure (mmHg)	79 ± 13	71 ± 17	79 ± 13
Central venous pressure (mmHg)	22 ± 6	26 ± 4	21 ± 5

T0 = time at baseline;
T20/30 = time when positive end-expiratory pressure at 20 cmH2O and
driving pressure at 30 cmH2O;
TOLP = time at open lung-positive end-expiratory pressure.

DISCUSSION

This study shows that a standardised open lung strategy consisting of a RM followed by a decremental PEEP trial was effective in patients with ARDS (5,6) (while already being ventilated with low tidal volume and high PEEP). No clinically significant haemodynamic compromise occurred during the stepwise RM. Two different methods were proposed for recruiting the lung: high-level continuous positive airway pressure (CPAP) and pressure control ventilation with high peak and end-expiratory pressure. In this study we used the pressure control strategy, applying a stepwise increasing peak inspiratory pressure up to 50 cmH_2O at a high level of PEEP. We found an increase in PaO_2/FiO_2 of 22% following the RM and decremental PEEP trial. Furthermore, the improvement in oxygenation was associated with an increase in the dynamic respiratory compliance, suggesting the presence of alveolar recruitment. The oxygenation response in our study was in line with that reported by Villagra et al. (7).

The primary complications possibly occurring during RMs are barotrauma and haemodynamic compromise. RMs may impair haemodynamics, most commonly MAP, HR and CVP (4,8,9).

RMs may impair hemodynamics, most commonly assessed by MAP or cardiac output (10). A recent systematic review (9) revealed hypotension (12%) and desaturation (9%) as the most frequent complications, although serious adverse events such as barotrauma were rare (1%).

In our study, we did not have major complications. In particular, we did not observe any significant decrease in MAP, HR, CVP. In some studies, there was a decrease in cardiac pumping capability, assessed by the cardiac power index, which combines both pressure and flow domains of the cardiovascular system (11). Our findings of relative hemodynamic stability during the RMs are in line with those reported in the ARDS Network study (12,4) showing a 10.6 ± 1.2 mmHg decrease in systolic blood pressure during lung recruitment manoeuvre using CPAP over 5 to 10 seconds at 35 to 40 cmH_2O and the study by Borges et al. (13) using peak airway pressures up to 60 cmH_2O, where none of the patients investigated experienced hemodynamic compromise during the RMs.

According to our results this manoeuvre in patients with ARDS is a safe way to recruit the collapsed alveoli and to keep them opened.

CONCLUSION

Our study demonstrates that a standard recruitment manoeuvres during protective ventilation can be associated with haemodynamic changes that could not be observed by conventional haemodynamic monitoring. A decremental titration of PEEP aimed to achieve maximum dynamic compliance was associated with an improvement in oxygenation and dynamic respiratory system compliance.

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RESPIRATORNE I HEMODINAMSKE PROMENE ZA VREME OPADAJUĆEG ALVEOLARNOG PRODUVAVANJA KOD BOLESNIKA SA AKUTNIM RESPIRATORNIM DISTRES SINDROMOM

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SAŽETAK

U prospektivnoj kliničkoj studiji koja obuhvata 10 bolesnika sa akutnim respiratornim distres sindromom (ARDS) ispitivali smo hemodinamske i respiratorne promene za vreme alveolarnog produvavanja (recruitment) i održavanja otvorenim prethodno aeriranih alveola pomoću opadajućeg pozitivnog endekspiratornog pritiska (PEEP).

Produvavanje je izvođeno primenom pritiskom kontrolisane ventilacije sa fiksnim pozitivnim endekspiratornim pritiskom (PEEP) od 20 cm H_2O i radnim pritiskom postepeno povećanim na 20, 25 i 30 cm H_2O (pojedinačno trajanje u periodu od dva minuta). Nakon ovih postupaka, kako bi pluća ostala otvorena, tj. alveole ostale otvorene, na kraju ekspirijuma, smanjivali smo PEEP za 2 cm H_2O na svaka dva minuta, sa udisajnim volumenom od 6ml/kg tt. PEEP koji drži pluća otvorenim (OL PEEP) je definisan kao PEEP, koji je za 2 cm H_2O veći od maksimalne dinamičke respiratorne komplijanse. Gasna razmena, respiratorni mehanizmi i hemodinamske karakteristike mereni su na sledeći način: T0- nulto vreme, T20/30 - vreme kada je pozitivni endekspiratorni pritisak 20, a radni pritisak 30 cm H_2O, što predstavlja trenutak na kraju alvelarnog produvavanja, tj. recruitment manevra i TOLP vreme, kada se zadaje pozitivni endekspiratorni pritisak (PEEP) koji drži otvorene alveole na kraju ekspiriuma (OL PEEP).

Odnos parcijalnog pritiska kiseonika (PaO_2) i frakcije inspiratornog kiseonika (FiO_2) uvećao se od početnog (T0) do TOLP trenutka merenja (130±49 vs 156± 64 mmHg,P<0.005), uz istovremeno uvećanje dinamičke respiratorne komplijanse (23±5 vs 27±6 ml/cm H2O,p<0.005).

Za vreme konstantnog pozitivnog endekspiratornog pritiska (14±3 cmH_2O) i konstantnog disajnog volumena, umanjio se maksimalni inspiratorni pritisak (32±3 prema 29 ±3 cm H_2O p<0.005), a parcijalni pritisak ugljen dioksida ($PaCO_2$) ostao je nepromenjen (58±22 prema 53 ±18 mmHg). Nije postojalo značajno sniženje srednjeg arterijskog pritiska.

Standardizovana strategija otvorenih pluća uvećava oksigenaciju i poboljšava respiratornu komplijansu. U ispitivanoj grupi bolesnika nisu zapaženi veći hemodinamski poremećaji.

Ključne reči: **ventilatorni menadžment, ARDS**