Original Article

Is the Lung Recruitment and Titrated Positive End Expiratory Pressure a Better Strategy as Compare to Low PEEP on Mortality in Patients with Acute Respiratory Distress Syndrome

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ABSTRACT

Objective: To establish whether lung recruitment maneuver with PEEP titration reduces 28-day mortality in patients with moderate to severe ARDS in comparison to low PEEP strategy.
Study Design: A Randomized Control Trial.
Place and Duration: This study was conducted at the Intensive Care Unit Nishtar Hospital, Ibn e Sina Hospital, City Hospital, Multan from February 2016 to January 2018.
Materials and Methods: A total of 490 patients were divided in two equal groups on the base of technique use as Lung recruitment maneuver with PEEP titration RP Group and in patents low PEEP (LP Group) was used to treat ARDS. Primary outcome was all-causes mortality up till 28 days. Secondary outcome included length of ICU and hospital stay, ventilator-free days, pneumothorax or barotrauma within seven days. Chi square test and student T tests were used to analyze data. P value ≤ 0.05 was considered significant.
Results: Death ≤28 days was observed as (58%) and (51%) for lung recruitment maneuver with PEEP titration group and low-PEEP group respectively. The difference was statistically insignificant (p=0.058). Deaths in intensive care unit, in hospital and within 6 months was observed as (62%) and (51.8%), (59.6%) and (50.6%), (70.6%) and (58%) for lung recruitment maneuver with PEEP titration group and low-PEEP group respectively
Conclusion: There is no significant difference of 28-day survival and decrease hospital stay, ICU Stay, and on ventilator duration, so lung recruitment maneuver and PEEP titration is not a better and effective strategy as compare to low PEEP.

Key Words: Positive end expiratory pressure, Mechanical ventilation, Acute respiratory distress syndrome, PEEP titration, recruitment maneuver

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INTRODUCTION

One of the common and grave clinical conditions encountered by severely ill patients is acute respiratory distress syndrome (ARDS)[1]. It is correlated with increased levels of mortality and decreased levels of health-related quality of life[2.] There is reduction in functional lung size as a result of non-aeration or poor aeration of multiple lung units due to consolidation, flooding or collapse[3]. There is an increased risk of ventilator induced injury among such patients as a result of over expansion of lungs and rhythmic opening and closure of small alveoli [4].

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The target of recruitment strategies and positive end expiratory pressure (PEEP) is the opening of collapsed lungs and keep them opened, thereby reducing the atelectasis[5,6]. There were two randomized trials that compared analogous recruitment strategy following a decrease in PEEP versus well-adjusted reduced PEEP maneuver proves to be propitious with regards to oxygenation, inflammation, respiratory tree compliance in the absence of increasing risk of barotrauma or other adverse effects [7, 8]. Further systemic reviews showed a decrease in mortality rate in the absence of barotrauma[9,10]. Thence, we conducted Alveolar Recruitment for ARDS Trial (ART) in order to determine if lung recruitment maneuver along with PEEP in accordance with best respiratory tree compliance versus well-adjusted low PEEP strategy ameliorates clinical outcomes in patients having moderate to severe ARDS.

MATERIALS AND METHODS

It was a randomized control trial conducted in Intensive Care Unit Nishtar Hospital, Ibn e Sina Hospital, City Hospital, Multan from February 2016 to January 2018.

A total of 490 patients were divided into two equal groups. Group RP in which lung recruitment maneuver and titration PEEP and group LP in which Low PEEP used.

Patients having invasive mechanical ventilation suffering from moderate to severe ARDS no more than 72 hours were included in the study. Exclusion criteria included less than 18 years of age, having mean arterial pressure lower than 65mmHg, vasoconstrictor drug usage in previous two hours, contraindicated to hypercapnia. Mechanical ventilation was given for three hours with low PEEP and low tidal volume.

The patients belonging to LP group received the low PEEP strategy. While the RP group received neuromuscular blocker in the form of a bolus and maintenance of hemodynamic status was done through IV fluids administration when the signs of fluid responsiveness were seen. Then the maneuver of lung recruitment was performed with increasing levels of PEEP, following decreasing levels of PEEP titrated in accordance with respiratory system compliance and secondary recruitment maneuver. The levels of PEEP were weaned once the PaO2:FIO2 became stable or kept on increasing within 24 hours. It was reduced by 2cmH2O in every eight hours. Other than PEEP titration and lung recruitment maneuvers, rest of the clinical care was similar for both the groups.

Primary upshot was 28-day mortality. Secondary outcome included duration of hospital and ICU stay, pneumothorax needing drainage within seven days, ventilator-free days, and mortality in hospital, ICU or 6-month mortality. The other exploratory outcomes included hypoxemia within seven days, death with barotrauma or refractory acidosis within seven days.

The effects of intervention on categorical variables were determined and presented as frequency and percentages. X2 test was used for the comparison among differences between two groups. P value equal or less than 0.05 was taken significant.

RESULTS

Base line findings for both groups were described in (Table **I**).

Table No. I: Baseline characteristics of the patients

Variables	RP Group n=245	LP Group - n=245	P Value
Age	45.88±4.89	48.34±3.99	0.000
Gender: Male	(60%) n=147	(61.6%) n=151	0.711
Female	(40%) n=98	(38.4%) n=94	
SAPS 3 score	62.76±9.64	62.19±8.64	0.493
No. of non-pulmonary organ failures	2.08±0.82	2.04±0.64	0.583
Septic shock	(63.3%) n=155	(63.7%) n=156	0.925
Cause of ARDS			
Pulmonary ARDS	(63.3%) n=155	(55.5%) n=136	0.081
Pneumonia	(52.7%) n=129	(49%) n=120	0.000
Gastric aspiration	(6.5%) n=16	(2%) n=5	0.014
Lung contusion	(4.1%) n=10	(1.6%) n=4	0.104
Near drowning	(5.7%) n=14	(2.0%) n=5	0.000
Extra pulmonary ARDS	(39.2%) n=96	(41.0%) n=100	0.000
Non-septic shock	(20%) n=49	(2.9%) n=7	0.000
Sepsis or septic shock	(19.6%) n=48	(19.6%) n=48	0.000
Trauma without lung contusion	(0.8%) n=2	(0%) n=0	0.156
Cardiac surgery	(9.0%) n=22	(7.3%) n=18	0.509
Other major surgery	(4.1%) n=10	(1.2%) n=3	0.049
Head trauma	(8.6%) n=21	(0.4%) n=1	0.000
Smoke inhalation	(9.4%) n=23	(6.1%) n=15	0.177
Multiple transfusions	(1.2%) n=3	(3.7%) n=9	0.079
Drug or alcohol abuse	(1.6%) n=4	(1.6%) n=4	0.000
Other	(5.7%) n=14	(4.1%) n=10	0.402
Prone position	(6.5%) n=16	(11.4%) n=28	0.058
time since onset of ARDS,	0.11±0.32	0.12±0.33	0.783
Days intubated prior to randomization	15.03±3.61	16.03±2.67	t0.000
Respiratory measures,			
PaO_2:FIO_2	1.97±0.94	1.97±0.67	1.0
Tidal volume, mL/kg predicted body weight	119.14±3.36	114.75±6.60	0.000
Plateau airway pressure, cm H_2O	5.78±1.18	5.65±2.03	0.398
Minute ventilation, L/min	25.78±3.23	27.13±2.98	0.000
Respiratory rate, breaths/min	8.87±2.42	8.87±2.98	0.991
Driving pressure, cm H_2O	25.22±3.12	25.97±2.93	0.006
Positive end-expiratory pressure, cm H_2O	13.41±2.25	14.13±3.96	0.014
Respiratory system static compliance, mL/cm H_2O	12.28±2.13	13.0±1.73	0.000

Table No.2: Outcomes among Patients Treated With Lung Recruitment Maneuver With Positive End-Expiratory Pressure (PEEP) vs Low-PEEP Strategy

Variables	Lung Recruitment Maneuver With PEEP Titration Group n=245	Low-PEEP Group n=245	P value
Primary Outcome			
Death ≤28 day	(58%) n=142	(51%) n=125	**0.058**
Secondary Outcome			
In intensive care unit	(62%) n=152	(51.8%) n=127	**0.023**
In hospital	(59.6%) n=146	(50.6%) n=124	**0.046**
Within 6 months	(70.6%) n=173	(58%) n=142	**0.003**
Length of stay			
Intensive care unit	20.42±14.58	22.35±10.81	**0.000**
Hospital stay	28.45±15.65	31.25±9.61	**0.000**
No. of ventilator-free d from d 1 to d 28	6.87±4.56	8.47±5.10	**0.000**
Pneumothorax requiring drainage ≤7 d	(6.9%) n=17	(1.0%) n=3	**0.235**
Barotrauma ≤7 d	(5%) n=12	(4%) n=10	**0.051**
Exploratory Outcomes			
Death			
Within 7 d	(7.3%) n=18	(2.4%) n=6	**0.012**
With refractory hypoxemia ≤7 d	(37.6%) n=92	(4.5%) n=11	**0.000**
With refractory acidosis ≤7 d	(10.6%) n=26	(11%) n=27	**0.884**
With barotrauma ≤7 d	(12.2%) n=30	(12.7%) n=31	**0.891**
Cardiorespiratory arrest on day 1	(2.0%) n=5	(2.4%) n=6	**0.760**
Need of commencement or increase of vasopressors or hypotension (MAP <65 mm Hg) within 1 h	(3.3%) n=8	(5.7%) n=14	**0.191**
Refractory hypoxemia (PaO2<55 mm Hg) ≤1 h	(36.3%) n=89	(29%) n=71	**0.083**
Severe acidosis (pH<7.10) ≤1 h	(0.4%) n=1	(2.0%) n=5	**0.100**

Table No.3: Effects of the Lung Recruitment Maneuver With Titrated PEEP vs the Low-PEEP Group on Mortality According to Subgroups

Variables	Lung Recruitment Maneuver With PEEP Titration Group n=245	Low-PEEP Group n=245	Test of Sig.
PaO_2:FIO_2			
≤100 mm Hg	(42%) n=103	(58%) n=142	**0.000**
>100 mm Hg	(58%) n=142	(42%) n=103	
Simplified Acute Physiology Score 3			
<50	(43.3%) n=106	(48.6%) n=119	**0.239**
≥50	(56.7%) n=139	(51.4%) n=126	
Type of ARDS			
Extrapulmonary	(43.3%) n=106	(55.9%) n=137	**0.005**
Pulmonary	(56.7%) n=139	(44.1%) n=108	
Duration of ARDS at randomization, hours			
≤36	(45.3%) n=111	(46.9%) n=115	**0.717**
>36 to <72	(54.7%) n=134	(53.1%) n=130	
Position 1 h after randomization			
Supine (dorsal decubitus) or lateral decubitus	(38%) n=93	(30.2%) n=74	**0.070**
Prone	(62%) n=152	(69.8%) n=171	
Duration of mechanical ventilation before randomization, day			
0-4	(49%)n=120	(47.3%) n=116	**0.718**
≥5	(51%) n=125	(52.7%) n=129	
Protocol modification			
Before	(38%) n=93	(53.5%) n=131	**0.001**
After	(62%) n=152	(46.5%) n=114	

The difference was statistically significant for age (p=0.000), pneumonia (p=0.000), near drowning (p=0.000), extra pulmonary ARDS (p=0.000), non-septic shock (p=0.000), sepsis or septic shock

(p=0.000), head trauma (p=0.000), drug or alcohol abuse (p=0.000), days intubated prior to randomization (p=0.000), tidal volume (p=0.000), minute ventilation (p=0.000), driving pressure (p=0.006), positive end-expiratory pressure (p=0.014) and respiratory system static compliance (p=0.000). (Table **1**).

The difference was statistically significant of secondary outcome in intensive care unit (p=0.023), in hospital (p=0.046), within 6 months (p=0.003), length of stay in intensive care unit (p=0.000), hospital (p=0.000) and no. of ventilator-free d from d 1 to d 28 (p=0.000). The difference was statistically significant death with refractory hypoxemia ≤7 d (p=0.000). (Table **2**). Effects of the lung recruitment maneuver with titrated PEEP versus the low-PEEP Group on mortality according to subgroups were shown in (Table **3)**. The difference was statistically insignificant simplified acute physiology score 3 (p=0.239), duration of ARDS at randomization, hours (p=0.717), position 1 h after randomization (p=0.070) and duration of mechanical ventilation before randomization, day (p=0.718) (Table. 3).

DISCUSSION

A recruitment maneuver by Povoa P et al [11] was performed in which effect of constant positive inspiratory pressure along with high PEEP was determined upon the static compliance and oxygenation in patients having severe ARDS. It was concluded that this recruitment maneuver was "safe and useful" in attempt to ameliorate the oxygenation and compliance static in patients having severe ARDS having lung ventilation added with lung protective strategy.

Neto AS et al [12] compared ventilation at various levels of PEEP in ICU patients without suffering from ARDS, it was observed that there was no difference between two levels of PEEP in seven RCTs as well as the duration of mechanical ventilation.

PEEP serves as protective role in preventing from atelectasis in patients undergone general anesthesia even when coupled with high inspired oxygen concentration, says Neumann P et al [13]. The results showed significant decrease in levels of atelectasis in patients where moderate levels of PEEP were maintained. There was a noteworthy relationship between PaO2 and atelectasis and similar study done by Martin JB et al [14] established the effect of PEEP and decreased levels of inspired oxygen and VC in preventing atelectasis in patients having general anesthesia.

With regards to arresting the postoperative pulmonary complications and reducing mortality in patients undergoing anesthesia, Barbosa FT et al [15] studied the effects of intraoperative PEEP. There were no complications reported. However, due to insufficient evidence, it cannot be said clearly if intraoperative PEEP ameliorates the postop complications and mortality.

The application of alveolar recruitment maneuver in patients with ARDS or acute lung injury is still controversial as said by Badet M et al [16]. There is no standard strategy in this regard. According to the results, the optimal levels of PEEP were found to be was 12 +/- 4 cm H(2)O., the other findings were as such "The measurements from the standardization periods were comparable between the 3 PEEP groups. In the optimal-PEEP-plus-sighs group the changes in P(aO(2)) (85 +/- 96%) and static compliance (14 +/- 20%) were significantly greater than in the 2 other groups".

Toth L et al [17] determined the hemodynamic and respiratory changes during lung recruitment maneuver and decreasing PEEP titration among patients suffering from ARDS. Whereas a negative correlation was found between CI and CVP and no correlation was present between mean arterial pressure and CI. After performing lung recruitment maneuver and decreasing PEEP titration, the levels of PaO2 ameliorates remarkably in the absence of variation in EVLW up till one hour. It shows that reduction in formation of atelectasis is due to the recruitment rather than due to reduction in EVLW. Although a change in CI is seen during the maneuver, however, CVP, MAP, or heart rate fail to show these changes.

Cruz S et al [18] compared high and low levels of PEEP in patients having ARDS or ALI on mechanical ventilation. The mortality as a result of ALI or ARDS can be reduced by mechanical ventilation. However, there is high risk of ventilator induced injury in these patients. It is assumed that higher levels of PEEP are helpful in reducing the injury and improving the survival of patient. PEEP is thought to improve the gaseous exchange as well as respiratory compliance but on the other hand, it may as well reduce the tissue injury and inflammation [19,20].

CONCLUSION

There is no significant difference of 28-day survival and decrease hospital stay, ICU Stay, and on ventilator duration, so lung recruitment maneuver and PEEP titration is not a better and effective strategy as compare to low PEEP.

Author's Contribution:

Concept & Design of Study:	Nadeem Ahmed Khan
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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