Medical Journal of South Punjab
www.mjsp.com

ORIGINAL ARTICLE-MJSP-0202

Comparing the Benefits of Titrated PEEP vs Low PEEP in terms of Mortality in Patients Suffering from Acute Respiratory Distress Syndrome

Asif Mahmood [1], Muhammad Adnan[2]

1. FCPS, Consultant Anesthetist Children hospital and Institute of Child Health, Multan

2. FCPS, Consultant Anesthetist Children hospital and Institute of Child Health, Multan

Objectives: To compare the benefits of titrated PEEP vs low PEEP in terms of mortality in patients suffering from acute respiratory distress syndrome. **Methods:** This randomized controlled trial was conducted at intensive care unit (ICU) of Nishtar hospital, Multan. Patients were randomly divided into two groups LP group and TP group. TP group received fluids and neuromuscular blockers. Lung recruitment maneuver was done with incremental PEEP level and in the second time by a decremental PEEP maneuver. **Result:** Of the outcome variables, numbers of death within 28 days were significantly higher in the low PEEP group (p-value 0.045 and 0.022, respectively). Development of pneumothorax requiring drainage and incidence of barotrauma within the first 7 days was significantly less in the titrated PEEP group. During the first 28 days, more number of patients in the titrated PEEP group had ventilator free days. **Conclusion:** In our study we find that the deaths within 28 days, development of pneumothorax requiring drainage and incidence of barotrauma within the first 7 days were significantly higher in the low PEEP group.

Keywords: Titrated PEEP. Low PEEP, ARDS

Article Citation: Asif M, Adnan M. Comparing the benefits of titrated PEEP vs Low PEEP interms of mortality in patients suffering from acute respiratory distress syndrome Med J South Punjab. 2021;2(2):17-21.

Correspondence Address:
Asif Mahmood
nishtarianasif@gmail.com
Mob #+923336365201

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is collection of fluid in tiny alveoli of lungs.[1] Quantity of fluid in alveoli is inversely proportional to amount of oxygen reaching the blood, so more fluid in the alveoli may deprive organ's functional need of oxygen. ARDS occurs in people who are severely ill, usually develops within a few hours to a few days after the precipitating injury or infection. [2] The signs and symptoms of ARDS can be severe shortness of breath, tachypnea, low blood pressure, restlessness. [3] The most common risk factor of ARDS include Sepsis, Inhalation of harmful substances, Severe pneumonia, Head, chest or other major injury, Pancreatitis (inflammation of the pancreas), massive blood transfusions and burns. [4, 5] People having history of chronic alcoholism are at more risk of developing ARDS. ARDS itself increases risk of clots formation in deep veins particularly in legs; in some cases it significantly raises the risk of pneumothorax among patients on ventilator machine along with high chances of infections and scarring or lung fibrosis.

Lab tests are done using blood from an artery in wrist to determine oxygen level. Other tests are used to evaluate infection or anemia. If lung infection is suspected then airway secretion are tested to know the reason of the infection. As some symptoms of ARDS are same as that of heart problems, so some test such as electrocardiogram has to be done to determine structural and functional problems of heart

As treatment is concerned the foremost goal is to increase the levels of oxygen in blood as oxygen is essential for the body organs to work effectively. [6] Some ways to increase oxygen level are supplemental oxygen in it oxygen is given through a mask and it is used in case of mild attack.

Second best option is Mechanical ventilation in which machine a mechanical ventilator is used to push air into lungs and forces some of the fluid out of the air sacs. As controlling the quantity of intravenous fluid is very important. [7] Balance is the key in case of intravenous fluid as too much fluid may increase fluid build-up in lungs and on the other hand too little fluid is dangerous for heart and other organs. Although this modality is a necessary part of the treatment but it can cause harm, as it can result a ventilator-associated lung injury (VILI) mainly due to baro-, volo-bio- and atelectrauma. [8, 9] it was estimated that patients with moderate/severe ARDS have high mortality (41-58%) and reduced long-term quality of life. Based on the risk of developing VILI, two different lung-protective ventilation methods can be used. [10] These are low tidal volume/ low plateau pressure and alveolar recruitment/ Positive End-Expiratory Pressure (PEEP) titration .Both of them are working well for decreasing the alveolar stress but the low tidal volume is lowering it by avoiding overexpansion at end-inspiration and the Positive PEEP do so by developing an 'open lung' at end-expiration.

Methodology

This study is a randomized clinical trial. Study was conducted in the intensive care unit (ICU) of Nishtar Hospital Multan over a period of January 2017 to January 2018. Ethical approval was obtained from hospital ethics committee. Informed consent was taken from the patients prior to the inclusion into this study. . Sample size was calculated from the reference study performed by Cavalcanti A et al. Non probability consecutive sampling technique was used to collect the sample size. Patients receiving invasive ventilation due to acute respiratory distress of less than 2 days duration and fall under the criteria of American European Consensus Conference were included in the study. In the screening phase patients who used high dose of vasopressor during last 120 minutes, mean arterial pressure of less than 65mm Hg and less than eighteen years old were excluded from the study. Patients with acute coronary syndrome, intracranial hypertension, subcutaneous emphysema and pneumothorax were also not involved in this study. For the conformation of inclusion into the study each patient receives low positive end expiratory pressure and low tidal volume for 180 minutes. After this the ratio of inspired oxygen (FIO_2) was fixed at 100%for half an hour as well as PEEP at 10 cm Hg or higher and ABGs were noted. Conformation is considered done if the ratio of partial pressure of oxygen (PaO_2) to FIO_2 was equal or less than 200 in less than 3 days.

Eighty patients were selected for our study. All the patients were randomly divided into two groups i.e. low peep group (LP group) and titrated peep group (TP group) by a person who didn't know about our study by a computer program. Patients in the TP group received fluids and neuromuscular blockers to maintain of hemodynamic status of the patient. Lung recruitment maneuver was done with incremental PEEP level and in the second time by a decremental PEEP maneuver for the best respiratory system static compliance. After PEEP titration and recruitment volume assisted control ventilation at the tittered value of PEEP was done and the ratio was noted and if levels of PaO_2 and FIO_2 were same or increasing during one day we stared to decrease the PEEP of 2cm Hg for every 8 hours. Excluding the lung recruitment and titration there is no difference in the care of two groups. Variables in our study are death in 4 weeks, length of hospital stay, pneumothorax requiring drainage, hospital mortality, 6 month mortality and ventilator free days in 4 weeks. Chi-square test was applied for percentages, independent T-test for mean SD, Mann Whitney U test for median. Computer software SPSS version 23 was used to statistically analyze the data. P value of less than or equal to 0.05 was taken as significant.

Results

We divided eighty patients into two equal groups. There were no significant differences between titrated PEEP and low PEEP groups in terms of age (p=0.390), gender distribution (p=0.390), number of extra pulmonary organ failure (p=0.555), hours since the development of acute respiratory distress syndrome (p=0.816), days intubated prior to randomization (p=0.095), SAPS-3 score (p=0.249), respiratory rate (p=0.341), tidal volume (p=0.114), PEEP (p=0.278), minute ventilation (p=0.495), PaO_2:FlO_2 (p=0.383) and the driving pressure (p=0.071). Table-I

The etiologies of the development of acute respiratory distress syndrome were also not significantly different between the two groups. (Table-II) Of the outcome variables, numbers of death within 28 days and within 60 days were significantly higher in the low PEEP group (p-value 0.045 and 0.022, respectively). Development of pneumothorax requiring drainage and incidence of barotrauma within the first 7 days was significantly less in the titrated PEEP group (p-value 0.048 and 0.043, respectively). During the first 28 days, more number of patients in the titrated PEEP group had ventilator free days (p=0.001). Number of days of hospital stay and ICU stay, and incidence of cardiopulmonary arrest on first day and severe acidosis were not significantly different between the two groups (p-value 0.497, 0.521, 0.396 and 0.499, respectively). Table-III

Table-I: Baseline Characteristics

Variable	Titrated PEEP (n=40)	Low PEEP (n=40)	p-value
Age, years	51.53±5.34	52.65±6.26	0.390
Gender, Male/Female	34/6	31/9	0.390
Extra pulmonary organs Failure, median(IQR)	2 (2-3)	2 (2-3)	0.555
Days intubated before randomization, median(IQR)	2 (1-4)	3 (2-4)	0.095
Hours since development of ARDS, median(IQR)	13 (6-29)	15 (6.75-29)	0.816
SAPS 3 score	56.35±14.96	60.05±13.51	0.249
Respiratory rate per minute	30.55±5.51	29.40±5.22	0.341
Tidal volume, ml/kg	5.95±0.94	5.63±0.82	0.114
PEEP, cm H_2O	11.65±2.34	12.13±1.44	0.278
Minute ventilation, L/min	7.03±1.64	7.30±1.94	0.495
PaO_2:FIO_2	115.13±13.07	112.63±12.42	0.383
Driving Pressure, cm H_2O	12.10±2.86	13.20±2.50	0.071

Data is mentioned as mean ± S.D unless mentioned otherwise.

Table-II: Etiology of Acute Respiratory Distress Syndrome

Cause	Titrated PEEP (n=40)	Low PEEP (n=40)	p-value
Pneumonia	20 (50)	18 (45)	0.654
Gastric Aspiration	9 (22.5)	11 (27.5)	0.606
Septic Shock	16 (40)	15 (37.5)	0.818
Aseptic Shock	6 (15)	9 (22.5)	0.390
Major Surgery	4 (10)	7 (17.5)	0.330
Smoking	12 (30)	9 (22.5)	0.446
Others	9 (22.5)	13 (32.5)	0.317

Data is mentioned as number (percentage)

Table-III: Outcome Data

Outcome	Titrated PEEP (n=40)	Low PEEP (n=40)	p-value
Death within 28 days	15 (37.5)	7 (17.5)	0.045
Death in ICU	7 (17.5)	6 (15)	0.762
Death in Hospital	12 (30)	8 (20)	0.302
Death within 6 months	21 (52.5)	11 (27.5)	0.022
Pneumothorax requiring drainage ≤7 days	6 (15)	1 (2.5)	0.048
Cardiorespiratory Arrest on 1st Day	4 (10)	2 (5)	0.396
Severe Acidosis	6 (15)	4 (10)	0.499
Barotrauma ≤7 days	8 (20)	2 (5)	0.043
Stay in ICU, days	16.01±8.82	17.23±8.59	0.531
Stay in Hospital, days	22.43±13.41	24.41±12.46	0.497
Ventilator free days within 28 days	10.58±5.13	16.38±8.97	0.001

Data is mentioned as number (percentage) or mean ± S.D; ICU=intensive care unit
(Note: tests applied are, chi-square for percentages, independent t-test for mean SD, Mann Whitney U test for median (IQR))

Discussion

In our study we find that the death within 28 days, development of pneumothorax requiring drainage and incidence of barotrauma within the first 7 days were significantly higher in the low PEEP group while the people in titrated group need less support of the ventilator for the first 4 weeks as compared to the low PEEP group. Number of days of hospital stay and ICU stay, and incidence of cardiopulmonary arrest on first day

and severe acidosis were not significantly different between the two groups. So we came to the conclusion that the titrated PEEP is better for the patients of ARDS.

Cavalcanti A et al. [11] in their study they concluded that the titrated peep leads to a higher rate of mortality during the first 4 weeks and risk of barotrauma is also high as compared to the low PEEP group although need of ventilator support is less in the titrated group during the first 4 weeks. Ewan C et al. [12] did a study to find out the response to higher PEEP and its effect on mortality in patients of ARDS and they saw that the rate of mortality is decreased in the patients receiving high PEEP oxygenation. Matthias B et al. [13] they done the review of many studies and they find out that the patients treated with low PEEP have higher mortality rate as compared to the patients with higher PEEP. Carol l et al. [14] in their study came to the conclusion that the titrated PEEP is associated with improved lung function and compliance as compared to the low PEEP.

Raul P et al. [15] did a study on one hundred and fifty nine patients and they saw that the death rate is decreased and lungs are functioning optimally when we used titrated PEEP. Allen J t al [16] did a study on 2728 patients of ARDS and they concluded that there is no significant benefit of using high titrated PEEP as compared to the low PEEP because the outcome like death rate, barotrauma, ventilator free days did not improved. Bime C et al. [17] wants to know the effect of high vs low PEEP in obese people suffering from ARDS and they came to know that the high PEEP strategy is beneficial for the obese patients as compared to the low PEEP strategy. Chikhani M et al. [18] found out in their study that the use of higher PEEP improves oxygenation and have a protective effect on alveoli in ARDS patients. More studies should be done on this topic to clear out the ambiguities and to know about the best approach.

Conclusion

In our study we find that the death within 28 days, development of pneumothorax requiring drainage and incidence of barotrauma within the first 7 days were significantly higher in the low PEEP group while the people in titrated group need less support of the ventilator for the first 4 weeks as compared to the low PEEP group. Number of days of hospital stay and ICU stay, and incidence of cardiopulmonary arrest on first day and severe acidosis were not significantly different between the two groups. So we came to the conclusion that the titrated PEEP is better for the patients of ARDS.

Conflict of interest: Nil

References

1. Force AD. Acute respiratory distress syndrome. Jama. 2012;307(23):2526-33.
2. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R, Osborn TM. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Inten Care Med. 2013 Feb 1;39(2):165-228.
3. Ferguson ND, Cook DJ, Guyatt GH, Mehta S, Hand L, Austin P, Zhou Q, Matte A, Walter SD, Lamontagne F, Granton JT. High-frequency oscillation in early acute respiratory distress syndrome. New Engl J Med. 2013 ;368(9):795-805.
4. Ong DS, Klouwenberg PM, Lunel FM, Spitoni C, Frencken JF, Dekker HA, Schultz MJ, Bonten MJ, Cremer OL. Cytomegalovirus seroprevalence as a risk factor for poor outcome in acute respiratory distress syndrome. Crit Care Med. 2015 ;43(2):394-400.
5. Thille AW, Esteban A, Fernández-Segoviano P, Rodriguez JM, Aramburu JA, Peñuelas O, Cortés-Puch I, Cardinal-Fernández P, Lorente JA, Frutos-Vivar F. Comparison of the Berlin definition for acute respiratory distress syndrome with autopsy. Am J Resp Crit Care Med. 2013 Apr 1;187(7):761-7.
6. Wilson JG, Liu KD, Zhuo H, Caballero L, McMillan M, Fang X, Cosgrove K, Vojnik R, Calfee CS, Lee JW, Rogers AJ. Mesenchymal stem (stromal) cells for treatment of ARDS: a phase 1 clinical trial. Lancet Resp Med. 2015;3(1):24-32.

7. Fuller BM, Mohr NM, Miller CN, Deitchman AR, Levine BJ, Castagno N, Hassebroek EC, Dhedhi A, Scott-Wittenborn N, Grace E, Lehew C. Mechanical ventilation and ARDS in the ED: a multicenter, observational, prospective, cross-sectional study. Chest. 2015 ;148(2):365-74.
8. Kuchnicka K, Maciejewski D. Ventilator-associated lung injury. Anaesthesiol Inten thera. 2013;45(3):164-70.
9. Saddy F, Sutherasan Y, Rocco PR, Pelosi P. Ventilator-associated lung injury during assisted mechanical ventilation. Sem Resp Crit care Med 2014 Aug (Vol. 35, No. 04, pp. 409-417). Thieme Medical Publishers.
10. Bein T, Weber-Carstens S, Goldmann A, Müller T, Staudinger T, Brederlau J, Muellenbach R, Dembinski R, Graf BM, Wewalka M, Philipp A. Lower tidal volume strategy (≈ 3 ml/kg) combined with extracorporeal CO2 removal versus 'conventional'protective ventilation (6 ml/kg) in severe ARDS. Intens Care Med. 2013 ;39(5):847-56.
11. Cavalcanti AB, Suzumura ÉA, Laranjeira LN, de Moraes Paisani D, Damiani LP, Guimarães HP, Romano ER, de Moraes Regenga M, Taniguchi LN, Teixeira C, de Oliveira RP. Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. Jama. 2017 318(14):1335-45.
12. Goligher EC, Kavanagh BP, Rubenfeld GD, Adhikari NK, Pinto R, Fan E, Brochard LJ, Granton JT, Mercat A, Marie Richard JC, Chretien JM. Oxygenation response to positive end-expiratory pressure predicts mortality in acute respiratory distress syndrome. A secondary analysis of the LOVS and ExPress trials. Am J Resp Crit care Med. 2014 ;190(1):70-6.
13. Briel M, Meade M, Mercat A, Brower RG, Talmor D, Walter SD, Slutsky AS, Pullenayegum E, Zhou Q, Cook D, Brochard L. Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. Jama. 2010;303(9):865-73.
14. Hodgson CL, Tuxen DV, Davies AR, Bailey MJ, Higgins AM, Holland AE, Keating JL, Pilcher DV, Westbrook AJ, Cooper DJ, Nichol AD. A randomised controlled trial of an open lung strategy with staircase recruitment, titrated PEEP and targeted low airway pressures in patients with acute respiratory distress syndrome. Crit care. 2011 ;15(3):R133.
15. Pintado MC, de Pablo R, Trascasa M, Milicua JM, Rogero S, Daguerre M, Cambronero JA, Arribas I, Sánchez-García M. Individualized PEEP setting in subjects with ARDS: a randomized controlled pilot study. Resp care. 2013 58(9):1416-23.
16. Walkey AJ, Del Sorbo L, Hodgson CL, Adhikari NK, Wunsch H, Meade MO, Uleryk E, Hess D, Talmor DS, Thompson BT, Brower RG. Higher PEEP versus Lower PEEP Strategies for Patients with Acute Respiratory Distress Syndrome. A Systematic Review and Meta-Analysis. Ann Am Thora Soc. 2017(Supplement 4):S297-303.
17. Bime C, Oren E, Fiero M, Parthasarathy S, Garcia JG. B96 VILI AND REGIONAL LUNG EFFECTS OF MECHANICAL VENTILATION: High Versus Low Peep And Ards Survival: Is There Effect Modification By BMI?. Am J Resp Crit Care. ;191:1.
18. Chikhani M, Das A, Haque M, Wang W, Bates DG, Hardman JG. High PEEP in ARDS: quantitative evaluation between improved oxygenation and decreased oxygen delivery. Brit J Anaesth. 2016 ;117(5):650-8.