CLINICAL STUDY

Can Arterial Minus End-Tidal Carbon Dioxide Gradient Be Used for Peep Titration?

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Abstract

Objectives: There is a debate about how to find optimal positive end-expiratory pressure (PEEP) in the current literature. Our aim was to determine whether arterial minus end-tidal carbon dioxide can be used to find optimal PEEP in acute respiratory distress syndrome (ARDS) patients.

Setting: Eight beds, postsurgical intensive care unit of a university hospital.

Patients: Eight patients with ARDS were included in the study. One patient was excluded due to desaturation in the initial phase of the study.

Interventions: The patients were sedated and paralyzed. PEEP levels were applied in random sequence as 5, 10, 15 and 20 cmH_2O.

Results: $PaCO_2$-$PetCO_2$ gradient was 11.0 (2.8-20.0) at 5 cmH_2O of PEEP and decreased to 9.0 (1.2-20) with 10 of PEEP, further decreased to 7.0 (2.0-16.1) with 15 of PEEP and increased to 17.0 (4.6-22.0) with 20 cmH_2O PEEP. Qsp/Qt was 0.4 (0.28-0.71) and 0.4 (0.19-0.45) with 5 and 10 cmH_2O of PEEP and decreased to 0.31 (0.11-0.71) with 15 cmH_2O of PEEP and to 0.30 (0.29-0.32) with 20 cmH_2O PEEP. V_D/V_T decreased to 0.21 (0.2-0.36) and 0.15 (0.6-0.36) with 10 and 15 cmH_2O of PEEP from 0.35 (0.05-0.41) at 5 cmH_2O of PEEP and increased to 0.31 (0.05-0.47) with 20 cmH_2O of PEEP. As we increase PEEP we observed that the intrapulmonary shunt was decreasing although $PaCO_2$-$PetCO_2$ decreased up to 15 cmH_2O PEEP and increased at 20 cmH_2O PEEP just as V_D/V_T. $PaCO_2$-$PetCO_2$ gradient was minimal when PaO_2 was maximal.

Conclusion: $PaCO_2$-$PetCO_2$ gradient is a useful and easily available parameter to find optimal PEEP in patients with ARDS.

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Key words: *end-tidal carbon dioxide, PEEP, ARDS, respiratory failure*

Introduction

It has been shown that positive end-expiratory pressure (PEEP) increases functional residual capacity, decreases intrapulmonary shunt (Qsp/Qt) and improves oxygenation in patients with adult respiratory distress syndrome (1). The optimal PEEP is the PEEP the beneficial effects of which are superior to its harmful effects. PEEP should be titrated to improve PaO_2 while minimizing a decrease in cardiac output (CO), in dead space volume and barotrauma (2,3,4). A decrease in CO may impair O_2 delivery (DO_2) and thus offset the benefit of a higher PaO_2 (5). Suter and colleagues pointed out that changes in O_2 delivery should be used as the reference standard for titrating PEEP (6). They found that increases in PEEP caused an increase in DO_2 up to a certain point and further increases in PEEP caused a decrease in DO_2. Use of DO_2 and CO for PEEP titration can be helpful for finding optimal

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Table. Baseline characteristics of the patients

Patients	Primary Diagnosis	PaO_2/FIO_2	$PaCo_2$ (mmHg)	$PetCO_2$ (mmHg)	PEEP (cmH_2O)	SBP (mmHg)	PAOP (mmHg)
1	Abdominal sepsis	90	43	34	8	124	18
2	Abdominal sepsis	183	33	23	13	129	17
3	Abdominal sepsis	143	33	31	7	142	16
4	Pneumonia (COPD)	197	49	27	6	105	11
5	Pneumonia	191	37	28	12	123	14
6	Pneumonia (COPD)	165	68	65	16	137	16
7	Pneumonia	114	47	39	15	132	15

PEEP but invasive interventions such as Swan-Ganz catheter placement are required. Such invasive techniques may be harmful, expensive and laborious. Excessive levels of PEEP would increase the dead space and dilute alveolar CO_2 by a larger volume, resulting in an increase in $PaCO_2$-$PetCO_2$ gradient (7). $PaCO_2$-$PetCO_2$ gradient has been proposed to be a useful non-invasive means of titrating PEEP (8). In another study, it is reported that CO_2 elimination is not helpful in titrating PEEP (9). These studies seem conflicting. The aim of our study was to determine whether the $PaCO_2$ - $PetCO_2$ gradient can be used for titration in patients with adult respiratory distress syndrome (ARDS), since it is a noninvasive and almost universally available parameter.

Patients and Methods

Eight patients with ARDS and on mechanical ventilatory support were included in the study. The median age of the patients was 57 years (36-74 years). The criteria for ARDS were as follows (a) PaO_2/FIO_2 <200, (b) bilateral diffuse infiltrates on chest X-ray, (c) pulmonary artery occlusion pressure (PAOP) <18 mmHg, (d) existence of a definite reason for ARDS. Patients were included in the study if they had a pulmonary artery catheter. FIO_2 was increased to 1.0 before the initiation of the study and kept on 1.0 during the study. The patients were sedated and paralyzed with 1-5 mg/h midazolam and intermittent dosing of vecuronium during the study period to prevent spontaneous movement throughout the study. The ventilator (Siemens Servo 300, Elama, Sweden) was set to deliver 8 ml/kg tidal volume with volume-controlled mode. Respiratory rate was maintained between 8 and 16 breaths/min to keep arterial CO_2 between 35and 45 mmHg. $PetCO_2$ was monitored with HP capnograph monitor (HP Virida 24C, Boeblingen, Germany). The capnograph sensor was placed between the Y-piece and the endotracheal tube. PEEP was applied as 5, 10, 15 and 20 cmH_2O in random sequence. CO was measured with thermodilution technique with 10 mL of normal saline at 0 to +8°C by using the mean of three determinations (10). Arterial blood was drawn from the radial artery and mixed venous blood was drawn from the pulmonary artery catheter for blood gas determinations (Chrion Diagnostics, Essex, England). Intrapulmonary shunt was calculated according to the following formula: $Qsp/Qt= (CcO_2-CaO_2)/(CcO_2-CvO_2)$. CcO_2: pulmonary end capillary O_2 content, CaO_2: arterial O_2 content and CvO_2: mixed venous O_2 content. O_2 content was calculated according to the following formula: $CO_2=1.34x$ Hemoglobin (g/dl)$xSO_2+0.003xPO_2$. For CcO_2, PO_2 was taken as alveolar PO_2 and SO_2 was taken as 1.0. Dead space to tidal volume ratio (V_D/V_T) was calculated from the following formula: $V_D/V_T= PaCO_2-PetCO_2 / PaCO_2$. All measurements and calculations were done 30 minutes after each PEEP change.

All data are presented as median (range) values. Kruskal-Wallis and Mann-Whitney U tests were used for the statistical analysis. $p<0.05$ was accepted as statistically significant.

Results

Eight patients were included in the study. One of the patients showed a significant decrease in SaO_2 just after decreasing PEEP to 5 cmH_2O and was excluded. Five patients were in the surgical intensive care unit (ICU) and two patients in the medical ICU. Three patients had ARDS due to abdominal sepsis and four had ARDS due to pneumonia (Table). $PaCO_2$-$PetCO_2$ gradient was 11.0 (2.8-20.0) at 5 cmH_2O of PEEP and decreased to 9.0 (1.2-20.0) with 10 of PEEP, further decreased to 7.0 (2.0-16.1) with 15 of PEEP and increased to 17.0 (4.6-22.0) with 20 cmH_2O PEEP without any statistical significance (Figure). V_D/V_T decreased to 0.21 (0.2-0.36) and 0.15 (0.6-0.36) with 10 and 15 cmH_2O of PEEP respectively from 0.35 (0.05-0.41) at 5 cmH_2O of PEEP and increased to 0.31 (0.05-0.47) with 20 cmH_2O of PEEP without any statistical significance (Figure). $PaCO_2$ and pH did not change significantly during the study. PaO_2 was 216 (54-315), 240 (61-391), 258 (76-284) and 214 (67-340) mmHg with 5, 10, 15 and 20 cmH_2O of PEEP respectively (Figure). All these PaO_2 values were with 1.0 of FIO_2. As we increase PEEP we observed that intrapulmonary shunt was decreasing (significant difference only between 5 and 20 cmH_2O of PEEP, $p<0.05$) although PaCO2-PetCO2 decreased up to 15 cmH_2O PEEP and increased at 20

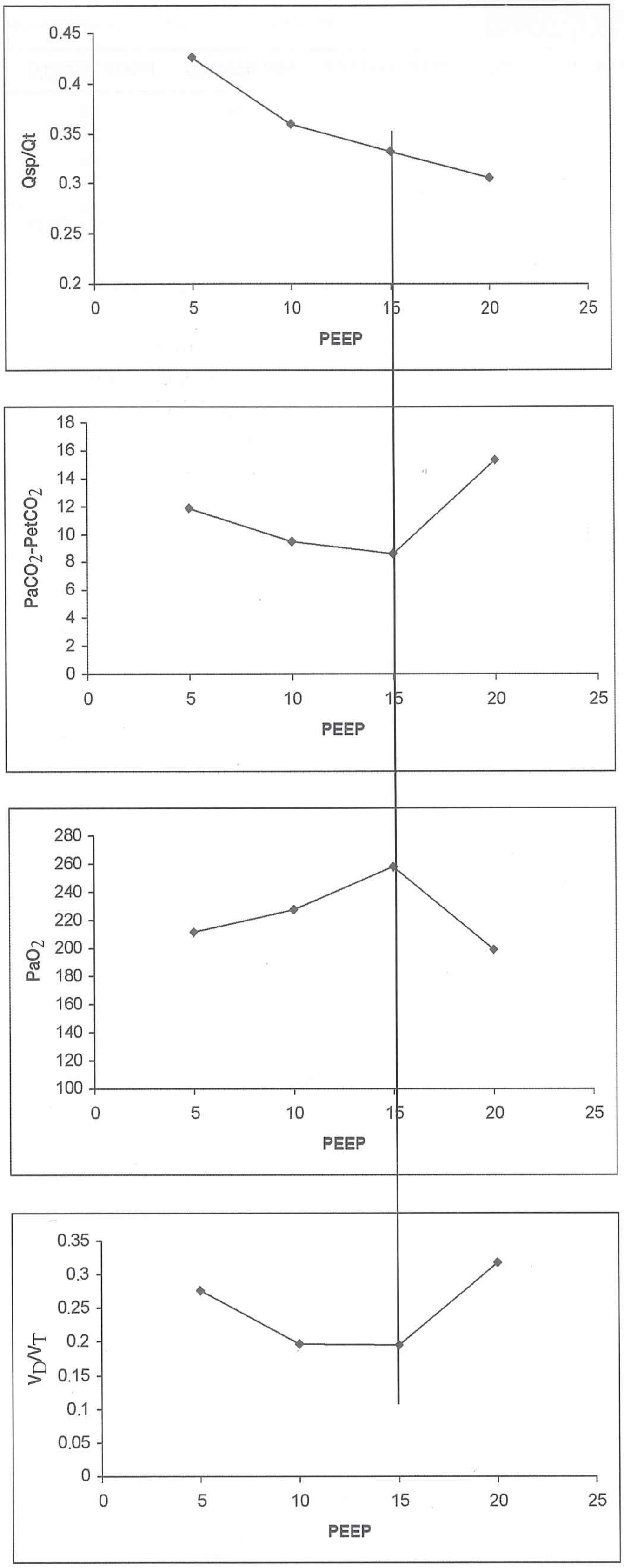

Figure. *Changes in shunt (Qsp/Qt), $PaCO_2$-$PetCO_2$, PaO_2 and dead space to tidal volume ratio(VD/VT) with increasing levels of PEEP. Notice that $PaCO_2$-$PetCO_2$ is minimal when PaO_2 is maximal and V_D/V_T is minimal (mean values).*

cmH_2O PEEP just as V_D/V_T. Change in intrapulmonary shunt was independent from the changes from CO because CO was 8.2 (5.6-14), 9 (6.1-13.6), 8.9 (6.0-13.0) and 8.9 (5.9-13.4) L/min with increasing levels of PEEP (5, 10, 15 and 20 cmH_2O respectively). These values were quite similar and were not statistically significant.

Discussion

What is the optimal PEEP? There is not a certain answer to this question yet. Optimal PEEP should provide all expected beneficial effects and should not cause harmful effects. PEEP should improve PaO_2 and should have a minimal effect on cardiac output, on alveolar overdistension and barotrauma (2,3,11). Barotrauma is a life threatening complication of positive pressure ventilation, observed especially in patients with ARDS (12). It is accepted that ventilation to perfusion ratio (V_A/Q) mismatching is one of the main reasons of hypoxemia in ARDS. PEEP causes improvement in V_A/Q relationships (13). The distribution of V_A/Q ratios is altered in ARDS, which was shown by multiple inert gas elimination technique. PEEP causes reduction in pulmonary blood flow including shunting regions, meaning obliteration of low V_A/Q regions (14). These changes account for improvement in PaO_2 with PEEP (15). It is claimed that changes in DO_2 should be used as guide to titrate PEEP (6). This may be an appropriate way of titrating PEEP but it is clear that to measure DO_2 pulmonary artery catheter is required and this is an invasive procedure. A group from the University of Florida claimed that PEEP should be increased until the intrapulmonary shunt decreases below 15% of CO (16). This approach was never studied in a controlled study and with this technique PEEP may be as high as 40 or 50 cmH_2O. The physiological dead space calculated from the arterial and mixed expired partial pressures of CO_2 is markedly elevated in oleic acid induced lung injury. Up to a certain point of PEEP physiological dead space decreases but with higher PEEP physiological dead space increases (8). In a model of oleic acid induced lung injury, analysis of expired gas was proposed as a useful method of PEEP titration (8). In this study, $PaCO_2$-$PetCO_2$ significantly deteriorated when oleic acid was injected into the pulmonary artery. The application of PEEP significantly decreased $PaCO_2$-$PetCO_2$ and additional PEEP beyond that which minimized the $PaCO_2$-$PetCO_2$ gradient produced a statistically significant increase in $PaCO_2$-$PetCO_2$ gradient but this was not reflected by concomitant changes in Qsp/Qt or PaO_2 in spite of further changes in CO. Our study was a human study performed in patients with ARDS. We observed that $PaCO_2$-$PetCO_2$ gradient decreased with application of PEEP and minimized with 15 cmH_2O of PEEP but increased again with 20 cmH_2O of PEEP. Calculated V_D/V_T followed the same course with $PaCO_2$-$PetCO_2$ gradient. V_D/V_T values that we found seem to be much smaller than that expected for patients with ARDS. Two reasons may be responsible for these low values; first, PaO_2/FIO_2 ratios of our patients did not show severe ARDS and secondly, the formula we used requires mixed expired PCO_2 values, but we used $PetCO_2$ values. However, these results still show a trend. When the $PaCO_2$-$PetCO_2$ gradient is minimal PaO_2 was also at the highest level. Intrapulmonary shunt also decreased with increasing levels of PEEP and was minimal with 20 cmH_2O of PEEP. In a study done in dogs by Coffey and co-workers, the effect of PEEP on V_D/V_T was studied with multiple inert gas elimination technique and it was shown that the decrease in V_D/V_T was due to reductions in shunt and midrange V_A/Q heterogeneity and the increase in V_D/V_T with higher PEEP levels was due to increased ventilation to high V_A/Q regions and a larger anatomical dead space (17). We showed that the shunt decreased in our patients also. The other mechanisms mentioned by Coffey and co-workers probably play a role also in human patients. Another method to identify the optimal PEEP is supersyringe measurement of the volume-pressure curve; optimal PEEP with this method was defined as the positive pressure level just above inflection point (18). This method requires disconnection of patients from the ventilator, which is not possible at all times. $PaCO_2$-$PetCO_2$ gradient is easy to monitor. A blood gas analysis and a simple capnogram are enough for monitorization. Measuring the dead space volume with single breath CO_2 elimination technique needs relatively expensive equipment and most of the other methods need pulmonary artery catheterization, which is an invasive technique. It was concluded that $PaCO_2$-$PetCO_2$ gradient is a useful and easily available parameter for PEEP titration in ARDS patients.

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