The effects of positive end-expiratory pressure in alveolar recruitment during mechanical ventilation in pigs[1]

Os efeitos da pressão positiva expiratória final no recrutamento alveolar durante a ventilação mecânica em porcos

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ABSTRACT

Purpose: To evaluate the effects of alveolar recruitment based on mean airway pressure (MAP) on pig lungs submitted to thoracotomy through blood gas exchange and hemodynamic parameters. **Methods:** Twelve pigs weighting approximately 25Kg were intubated and ventilated on volume controlled ventilation (tidal volume 10ml/Kg, respiratory rate 16min, FiO_2 1.0, inspiratory:expiratory ratio 1:2, PEEP 5cmH$_2$O). The animals were then randomized into two groups: control and left lateral thoracotomy. The PEEP was increased at each 15-minute intervals to reach a MAP of 15, 20 and 25cmH$_2$O, respectively. Hemodynamic, gas exchange and respiratory mechanic data were measured immediately before each PEEP change. **Results:** There were no significant differences between both groups in all parameters analyzed (P=1.0). The PaO_2, $PaCO_2$, MAP, PAP and plateau pressure were significantly worse at MAP of 25cmH$_2$O, when compared with the other values of MAP (P=0.001, P=0.039, P=0.001, P=0.016 e P=0.027, respectively). The best pulmonary performance according to the analyzed parameters was observed at MAP of 20cmH$_2$O. **Conclusion:** PEEP adjusted to MAP of 20cmH$_2$O resulted in best arterial oxygenation, without compromising the venous return, as opposed to MAP of 25cmH$_2$O, which caused deterioration of gas exchange, hemodynamics and respiratory mechanic.
Key words: Respiration, Artificial. Positive-Pressure Respiration. Pulmonary Alveoli. Swine.

RESUMO

Objetivo: Avaliar os efeitos do recrutamento alveolar baseado na pressão média das vias aéreas (Pmédia) sobre os pulmões de porcos submetidos a toracotomia, através de dados gasométricos e hemodinâmicos. **Métodos:** Doze porcos machos pesando em média 25Kg receberam indução anestésica, sendo intubados e ventilados a volume (FiO_2=1.0, volume corrente=10 ml/kg/min, FR=16 cpm, relação I:E=1:2 e PEEP 5 mmHg). Os animais foram randomizados em dois grupos: controle e toracotomia lateral esquerda. Os valores de PEEP em cada grupo foram aumentados a cada 15 minutos para atingir valores de Pmédia de 15, 20 e 25cmH$_2$O, sendo coletados dados hemodinâmicos, gasometria arterial e mecânica respiratória imediatamente antes de cada acréscimo do PEEP. **Resultados:** Não houve diferença estatisticamente significativa entre os 2 grupos em todos os parâmetros analisados (P=1,0). Ocorreu piora significativa da PaO_2, $PaCO_2$, pressão arterial média, pressão da artéria pulmonar e pressão de platô com Pmédia de 25cmH$_2$O comparado com os demais valores de Pmédia (P=0.001, P=0.039, P=0.001, P=0.016 e P=0.027, respectivamente). O melhor desempenho pulmonar pelos parâmetros analisados ocorreu com a Pmédia de 20cmH$_2$O. **Conclusão:** As manobras de recrutamento alveolar alteram o desempenho pulmonar e função hemodinâmica independente da cavidade torácica estar aberta ou fechada. O PEEP ideal para o recrutamento alveolar independente dos grupos estudados foi obtido a uma Pmédia de 20cmH$_2$O em relação a todos os parâmetros analisados.
Descritores: Respiração Artificial. Respiração com Pressão Positiva. Alvéolos Pulmonares. Suínos.

Introduction

Mechanical ventilation has been incorporated into the basic life support for several decades, but numerous potential drawbacks and complications have been identified early in the use of mechanical ventilation[1].

Artificial mechanical ventilation is used to improve patient's oxygenation with compromised lung function. Such support measures might ultimately cause ventilator-induced lung injury, which includes edema, pneumothorax and rupture of alveolar walls. Ventilator-induced lung injury occurs in 0.5–38% of all mechanically ventilated patients and in up to 83% of those with underlying chronic lung disease. The additional mortality rate of patients who develop ventilator-induced lung injury as a complication of mechanical ventilation is as high as 13–35%[1].

A large number of animals and clinical studies have shown that mechanical ventilation can worsen preexisting lung injury or produce acute lung injury *de novo* in previously normal lungs[2]. The postulated mechanisms responsible for ventilator-induced lung injury is the mechanical stress induced by shear forces that might initiate or worsen pulmonary inflammatory processes and alter the alveolar-endothelial barrier, as well as the surfactant function[3].

In response to concerns about the potential adverse effects of mechanical ventilation, lung protective strategies that limit tidal volumes, plateau pressures and positive airway pressure have been suggested in the literature as alveolar recruitment enhancement strategies. It has been shown in a number of experimental models of acute lung injury that ventilation with high positive end-expiratory pressure (PEEP) attenuates lung injury by reducing the number of atelectasis or edematous alveoli at end-expiration[5].

Patients with the acute respiratory distress syndrome are particularly prone to overdistention, particularly when conventional tidal volumes are used (10 to 15 ml per kilogram of body weight), since the number of lung units available for ventilation is markedly reduced as a result of fluid accumulation, consolidation, and atelectasis[6]. Ventilation strategies that limit airway pressure and volume often result in hypercapnia and respiratory acidosis, which could ultimately be harmful to extremely ill patients. Nonetheless, observational studies have reported reduced mortality when patients with the acute respiratory distress syndrome undergo ventilation at decreased pressures and tidal volumes[7].

Amato et al showed that the use of low tidal volume plus moderate/high PEEP and the use of periodic recruitment maneuvers (RM) in patients with acute lung injury and ARDS improved patients' outcomes. Since then, many studies have considered RM as a tool to improve oxygenation and perhaps survival in ARDS[8,9].

Following such initial enthusiasm, a number of issues have been raised regarding optimal lung recruitment. Many different RM were proposed, and the ideal frequency and duration have not yet been established. A number of experimental models of lung injury have shown that the best RM seems to be the use of mechanical ventilation with low tidal volumes and PEEP adjusted to the lower inflection point in the pressure-volume curve[4,10]. The amount of positive pressure and the length of time that the airway is submitted to such pressure are factors estimated by the mean airway pressure (MAP), that is the pressure required to open de airway during the entire respiratory cycle, corresponding to the pressure that causes alveoli to distend. It also has a relationship with the mean alveolar pressure, and thus with alveolar recruitment[11].

The objective of this study is to analyze the effects of MAP on gas exchange and hemodynamics in pigs submitted to mechanical ventilation, and compare the findings between animals with a closed chest (control) versus an open chest (thoracotomy), in order to exclude thoracotomy as a confusion factor for further studies on mechanical ventilation.

Methods

The animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" (National Institutes of Health Publication 85-23, revised, 1985). Twelve pigs weighing 25kg in average, received general anesthesia (induction with Ketamine 20mg/kg and Xylazine 2mg/kg IM, followed by thiopental 10 mg/kg IV and fentanyl 10μg/Kg IV). Muscle relaxation was done with pancuronium bromide (0,15mg/Kg IV bolus, followed by intermittent doses of 0,1mg/Kg/h). Following induction, the animals were intubated with a 7.0mm outer diameter endotracheal tube. Each animal had a pulmonary artery catheter placed percutaneously via the jugular vein. An indwelling arterial and venous line placed in the femoral artery and vein, respectively, for blood sampling and hemodynamic measurements. The animals were ventilated in a volume-cycled, pressure-limited ventilator (Servo 900C, Siemens Elema-Sweden) with a peak inspiratory pressure (PIP) of less than $35cmH_2O$, tidal volume of 10ml/Kg, respiratory rate of 16breaths/minute, FiO_2 1.0, inspiratory: expiratory ratio 1:2 and a $5cmH_2O$ PEEP. No vasoactive drugs were used in the experiments. Five minutes after stabilization, the animals were randomized into two groups: group 1 (control - no thoracotomy) and group 2 (thoracotomy), in which pigs were submitted to a left lateral thoracotomy and chest tube drainage with posterior close of the wound. In each animal, the PEEP was increased to reach a MAP of 15, 20 and $25cmH_2O$ every 15 minutes, respectively. Immediately before each incremental adjustment, the PEEP was returned to a baseline of 5mmHg for 5 minutes. At the end of the 15-minute observation period of each MAP, hemodynamic data was recorded (mean arterial blood pressure-MABP; pulmonary arterial pressure-PAP), arterial blood gas analysis (PaO_2 and $PaCO_2$) and dynamic respiratory parameters measurements (plateau pressure-Ppl) were obtained.

Statistical analysis was performed using the SPSS12.0 software. Differences between groups were evaluated using Chi-Square test. McNemar Test was used for within the groups analysis of the different values of MAP. Statistical significance was considered for *P* less than 0.05.

Results

All animals survived the observation period. There were no significant differences between the groups in all parameters (P=1.0). When the values of MABP between MAP 15 cmH_2O and 20 cmH_2O with MAP 25 cmH_2O were compared, there were significant differences in both groups (P=0.001) (Figure 1).
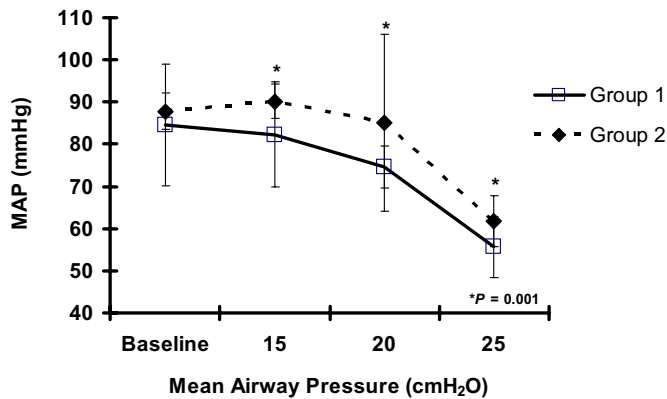
The values of PaO_2 when MAP was adjusted at 25cmH_2O were significant lower when compared to all other MAP adjustments in both groups (P=0.001, Figure 3).

FIGURE 1 - Mean Arterial Blood Pressure: MABP significant lower in MAP 25 cmH_2O when compared with MAP 15 cmH_2O and 20 cmH_2O (P=0.001)
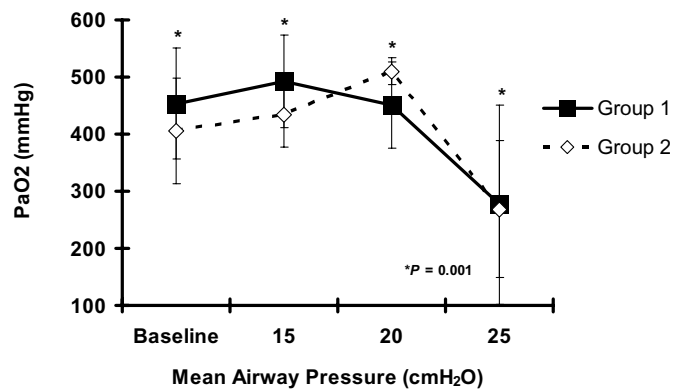
FIGURE 3 - Partial Oxygen Pressure: PaO_2 significant lower when MAP was adjusted at 25cmH_2O were when compared to all other MAP (P=0.001)

A significant difference was observed when values of PAP between MAP 15cmH_2O and 20cmH_2O were compared with the values of PAP in MAP 25cmH_2O in both groups (P=0.016 and P=0.031, respectively; Figure 2).

There was a significant difference between the $PaCO_2$ values when the MAP was 15cmH_2O when compared to the MAP at 25cmH_2O (P=0.039), however there was no significant difference between MAP 20cmH_2O and MAP 25cmH_2O (P=0.07). When comparing dynamic respiratory measurements, all values of PEEP until MAP 25cmH_2O did not increase plateau pressure above 30cmH_2O. On the other hand, a MAP 25cmH_2O caused a significant increase of Ppl (P=0.027, Figure 4).
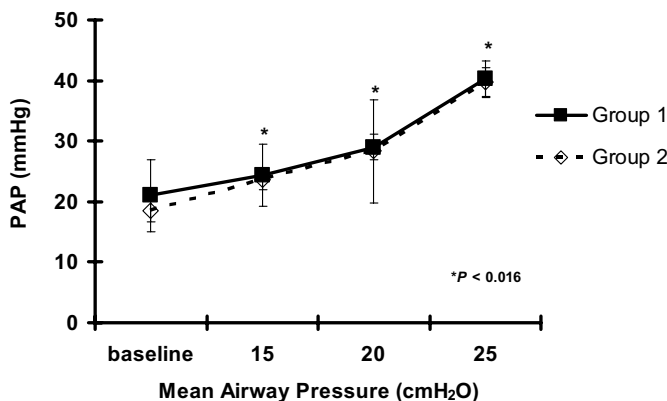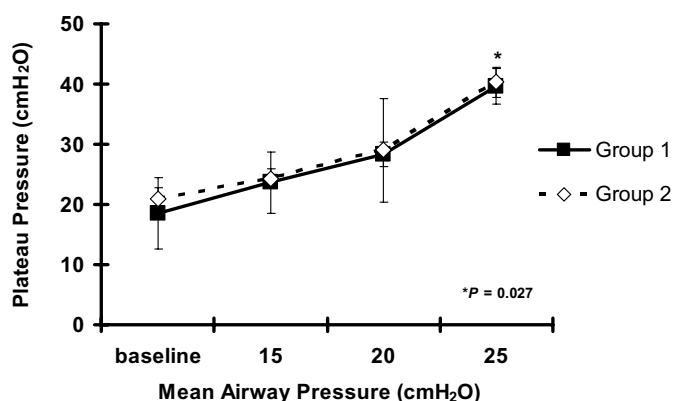

FIGURE 2 - Pulmonary Arterial Pressure: PAP significant higher when values of PAP between MAP 15cmH_2O and 20cmH_2O were compared with the values of PAP in MAP 25cmH_2O in both groups (P=0.016 and P=0.031)

FIGURE 4 - Plateau Pressure: MAP 25cmH_2O caused a significant increase of Ppl (P=0.027)

Discussion

The primary objective of this study was to develop a new strategy of recruitment maneuver in an animal model of open and closed chest, in to assess the influence of the thoracotomy under different PEEP levels. This technique is easier to use routinely in the clinical setting when compared to the PEEP adjusted to the lower inflection point of the pressure-volume curve. This new strategy is similar to that one based on lower tidal volume and higher PEEP[3,9]. Our results are similar from those of the literature, showing a good gas exchange and hemodynamic performance in this model of RM[9].

According to the literature, recruitment maneuvers yield different effects depending on the type and severity of lung insult, as well as on the use of different combinations of tidal volume and PEEP, either before or after the RM. The beneficial effects of RM were demonstrated mostly in animal models of alveolar collapse induced by surfactant depletion[13]. In animal models of lung injury other than produced by surfactant depletion, the effect of RM on lung function is less evident[14]. Insofar, there has been no consensus on the best level of PEEP for effective lung protection. The ideal PEEP should be high enough to be able to maintain or improve arterial oxygenation as well as low enough to avoid hemodynamic collapse.

We found a significant improvement on arterial oxygenation when PEEP was adjusted to MAP 20cmH$_2$O. Conversely, when higher MAP (25cmH$_2$O) was used, it resulted in lower PaO$_2$ and worsened the hemodynamic parameters, resulting in hemodynamic collapse.

RM based on the blood gas analysis alone as a ventilatory strategy has failed to improve outcome in some studies[15], and there are physiological mechanisms of practical relevance that might explain such findings. In the clinical scenario, ventilator settings are often adjusted to achieve predetermined arterial blood gas values. This approach seems adequate when only oxygenation and carbon dioxide removal are considered. Once the changes on ventilator settings are carried out, one is temped to conclude that an improvement on arterial oxygenation reflects alveolar recruitment, whereas recruitment may indeed be the cause for improved oxygenation. Furthermore the increase in PaO$_2$ may simply reflect the consequences of the changes in the ventilator settings upon hemodynamics[15].

The increase in intrathoracic pressure resulting from the increments in PEEP can also reduce venous return to the right atrium. The subsequent reduction on right ventricular end-diastolic volume leads to a substantial decrease in cardiac output[15]. In contrast, a decrease in cardiac output may improve the effectiveness of hypoxic pulmonary vasoconstriction, which is seldom taken into consideration. Improved arterial oxygenation may be the result of improved hypoxic pulmonary vasoconstriction after a decrease in venous return rather than a result of alveolar recruitment itself. Indeed, single or periodic sustained increase in intrathoracic pressure can induce adverse hemodynamic effects and compromise cardiac performance in a patient who is already critically ill. Unintentional lung overinflation can increase pulmonary vascular resistance with blood flow diversion from overinflated alveoli to consolidated but perfused alveoli, thus incrementing intrapulmonary shunt[16]. It is therefore advisable to consider gas exchange, hemodynamic parameters and dynamic respiratory mechanics measurements altogether, in order to obtain an ideal alveolar recruitment. We expected the animals in the thoracotomy group to have had an altered intra-thoracic pressure, however no significant differences were observed between the two groups in regards to hemodynamic parameters.

Conclusions

The PEEP adjusted to MAP of 20cmH$_2$O can be used as an "Ideal PEEP", based on improved arterial oxygenation, without any sizeable hemodynamic and respiratory impairment, regardless the presence of thoracotomy. Such findings may potentially represent a practical modality of alveolar recruitment, easily transposed into apply the clinical setting. Such strategy is currently being applied to a pig lung model of severe lung injury as part of an ongoing study of this research line, in which this "Ideal PEEP" will be used in a model of lung injury caused by oleic acid as well as in a lung transplant model of severe reperfusion injury.

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