Neonatal Pneumothorax Pressures Surpass Higher Threshold in Lung Recruitment Maneuvers: An In Vivo Interventional Study

Patricio González-Pizarro MD, Javier García-Fernández MD PhD, Susana Canfrán DVM PhD, and Fernando Gilsanz MD PhD

BACKGROUND: Causing pneumothorax is one of the main concerns of lung recruitment maneuvers in pediatric patients, especially newborns. Therefore, these maneuvers are not performed routinely during anesthesia. Our objective was to determine the pressures that cause pneumothorax in healthy newborns by a prospective experimental study of 10 newborn piglets (<48 h old) with healthy lungs under general anesthesia. METHODS: The primary outcome was peak inspiratory pressure (PIP) causing pneumothorax. Animals under anesthesia and bilateral chest tube catheterization were randomly allocated to 2 groups: one with PEEP and fixed inspiratory driving pressure of 15 cm H2O (PEEP group) and the second one with PEEP = 0 cm H2O and non-fixed inspiratory driving pressure (zero PEEP group). In both groups, the ventilation mode was pressure-controlled, and PIP was raised at 2-min intervals, with steps of 5 cm H2O until air leak was observed through the chest tubes. The PEEP group raised PIP through 5-cm H2O PEEP increments, and the zero PEEP group raised PIP through 5-cm H2O inspiratory driving pressure increments. RESULTS: Pneumothorax was observed with a PIP of 90.5 ± 15.7 cm H2O with no statistically significant differences between the PEEP group (92 ± 14.8 cm H2O) and the zero PEEP group (89 ± 18.2 cm H2O). The zero PEEP group had hypotension, with a PIP of 35 cm H2O; the PEEP group had hypotension, with a PIP of 60 cm H2O (P = .01). The zero PEEP group presented bradycardia, with PIP of 40 cm H2O; the PEEP group presented bradycardia, with PIP of 70 cm H2O (P = .002). CONCLUSIONS: Performing recruitment maneuvers in newborns without lung disease is a safe procedure in terms of pneumothorax. Pneumothorax does not seem to occur in the clinically relevant PIPs of <50 cm H2O. Hemodynamic impairment may occur with high driving pressures. More studies are needed to determine the exact hemodynamic impact of these procedures and pneumothorax PIP in poorly compliant lungs. Key words: barotrauma, mechanical ventilation; pediatrics; ventilator-induced lung injury; positive-pressure respiration; anesthesia [Respir Care 0;0(0):1–•. © 0 Daedalus Enterprises]

Introduction

Lung collapse invariably occurs during mechanical ventilation and commonly after induction of general anesthesia. The use of recruitment maneuvers has been proposed as a useful technique to reverse atelectasis during general anesthesia. Nevertheless, there is no standard,.
 universally accepted method of performing recruitment maneuvers.

There are many clinical trials described in the literature where different types of recruitment maneuvers have been used in trying to reopen collapsed lung regions, and discussion has focused on the minimum level of PEEP required to keep them open. Our goal was to determine the range of peak inspiratory pressures (PIPs) producing pneumothorax and compare it with the PIP range commonly used in recruitment maneuvers of healthy newborns in the operating theater setting.

One way of performing a recruitment maneuver was described by Tusman7 and is based on the slow increase of the inspiratory pressure with PEEP using step increments and a fixed inspiratory driving pressure (PIP – PEEP) to fully reopen collapsed lung regions, followed by a decremental PEEP titration in order to set the ideal open-lung PEEP that maintains the recruited lungs open. The aim of such a strategy is to prevent ventilator-induced lung injury by reversing lung collapse and hence avoiding cyclic tidal recruitment and to minimize lung overdistention by limiting the inspiratory driving pressure above the set open-lung PEEP.5–11 These slow stepwise increments in PIP, keeping inspiratory driving pressure <15 cm H2O, have less hemodynamic impact, particularly in children, and help to set the optimal PEEP. Other types of recruitment maneuvers frequently used in the operating theater are CPAP of 40 cm H2O for 8–40 s or a few breaths at a high rate and high pressure (PIP = 50 cm H2O/PEEP = 5 cm H2O).

Nevertheless, the recruitment maneuver has not yet gained widespread acceptance in routine pediatric mechanical ventilation. One of the main reasons is that there are concerns regarding the risks associated with recruitment maneuvers, including minor hemodynamic impairment,12,13 barotrauma,14,15 and tissue damage of the lung and distal organs.16,17 Barotrauma is one of the major clinical concerns, especially in neonates and infants, due to their infinite thorax compliance, which makes them particularly sensitive to increases in airway pressure and prone to pneumothorax.18,19 Most studies regarding recruitment maneuvers have been conducted in adult lungs with ARDS,1,10,11,20 and information regarding the response to recruitment maneuvers in either healthy or sick pediatric patients is scarce.

The lungs of healthy neonates and infants easily collapse after induction of anesthesia because their functional residual capacity is always below the airway closing volume.21 Therefore, the development of atelectasis during general anesthesia is a constant finding.3 There are reasons to believe that the pressures needed to recruit the lungs and the safety of recruitment maneuvers may differ in young healthy lungs compared with adult diseased lungs. If routine recruitment maneuvers are to be implemented in pediatric patients, their safety and efficacy must be explored in more detail. Therefore, it is relevant to determine the pressure range causing pneumothorax.

The aim of this study is to determine the PIPs causing pneumothorax in an experimental model using healthy newborn piglets. The hypothesis of the experiment is that recruitment maneuvers involving increasing PIP without increasing PEEP induce a greater degree of barotrauma and risk of pneumothorax as compared with maneuvers that maintain a constant PIP (PIP – PEEP). Therefore, we want to determine as well whether there is any difference in the pneumothorax PIP using a ventilation strategy with constant (PEEP group) or increasing inspiratory driving pressure (zero PEEP group).

We compared 2 different ventilation strategies producing pneumothorax: one with a fixed inspiratory driving pressure of 15 cm H2O and PIP raised upon PEEP increments (PEEP group) and one with zero PEEP (PEEP = 0 cm H2O) and PIP raised directly, thus having a non-fixed inspiratory driving pressure on every breath cycle and risking the production of cyclic overdistention and cyclic tidal recruitment (zero PEEP group). It is not the purpose of this study to determine the optimum PEEP after a recruitment maneuver but rather to help the clinician set a range of PIPs at which pneumothorax is likely to happen.

Methods

Ethics

The study was approved by the ethical committee for experimental research of La Paz University Hospital (Eth-
Table 1. Peak Inspiratory Pressure Resulting in Pneumothorax According to Group After Randomization

<table>
<thead>
<tr>
<th>Animal</th>
<th>Group</th>
<th>Pneumothorax Peak Inspiratory Pressure, cm H2O</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PEEP</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>Zero PEEP</td>
<td>65</td>
</tr>
<tr>
<td>3</td>
<td>PEEP</td>
<td>105</td>
</tr>
<tr>
<td>4</td>
<td>PEEP</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>Zero PEEP</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>Zero PEEP</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>Zero PEEP</td>
<td>115</td>
</tr>
<tr>
<td>8</td>
<td>Zero PEEP</td>
<td>95</td>
</tr>
<tr>
<td>9</td>
<td>PEEP</td>
<td>105</td>
</tr>
<tr>
<td>10</td>
<td>PEEP</td>
<td>85</td>
</tr>
</tbody>
</table>

Fig. 1. Ventilation protocol. The PEEP group raised peak inspiratory pressure (PIP) through 5-cm H2O PEEP increments every 2 min while keeping a fixed inspiratory driving pressure of 15 cm H2O. There is no current anesthesia workstation available supporting PEEP levels >50 cm H2O; therefore, breaking the fixed inspiratory driving pressure was necessary in those animals that already had reached PEEP of 50 cm H2O without signs of pneumothorax. In those cases, PIP was increased directly while keeping PEEP constant at 50 cm H2O was performed, and before the insertion of each chest tube, animals were disconnected from ventilation to ease lung collapse and avoid any possible risk of iatrogenic lung damage. Then each chest tube was carefully sutured to the skin to prevent leakages and connected to water traps. Tubes were covered by 1 cm H2O at their distal end in the water traps.

Ventilation Protocol

All animals were ventilated for 1 h before the experiment to allow atelectasis to occur with these same settings (pressure-controlled ventilation, PIP = 15 cm H2O, zero PEEP, 25 beats/min, I/E ratio 1:1, Fio2 60%, 1.0 L/min fresh gas flow, and end-tidal sevoflurane concentration of 1.5% in an air/oxygen mix). They were then randomly allocated to 2 groups. The first group (PEEP group) had a constant driving pressure of 15 cm H2O, and PIP was raised in 5-cm H2O increments every 2 min, starting from zero PEEP, until 50-cm H2O PEEP was reached. If no air leak was noticed, it was necessary to break the fixed pressure to keep raising the PIP, since no anesthesia workstations in the market support PEEP levels >50 cm H2O. From that point on, every step continued with 5-cm H2O PIP increments (Fig. 1).

The second group (zero PEEP group) kept zero PEEP during the whole experiment, and PIP was raised in 5-cm H2O increments every 2 min (Fig. 2), until bubbling was noticed in the water traps. Each single experiment lasted for a different time, until pneumothorax was witnessed in the form of a continuous air leak in the PEEP group or inspiratory air leak in the zero PEEP group.
The PEEP group had a higher PIP (mean PIP = 62.5 cm H2O) at which a 20% decrease in mean arterial pressure from baseline was noted in comparison with the zero PEEP group (mean PIP = 37.5 cm H2O) (P = .01). Similar results were found for systolic blood pressure and diastolic blood pressure (Table 3).

Regarding heart rate, the zero PEEP group presented a 20% decrease from baseline with a mean PIP of 42.5 cm H2O, whereas the PEEP group showed a pulse decreased by 20% from baseline with mean PIP of 72.5 cm H2O. These differences were highly significant (P = .002). Results are summarized in Table 3.

We found no significant (P = .058) difference in highest pulse values during the experiment between the zero PEEP group (highest heart rate value corresponds to a PIP of 22.5 ± 2.9 cm H2O) and the PEEP group (PIP of 43.8 ± 18.0 cm H2O), whereas there was a statistically significant difference (P = .03) for highest mean arterial pressure values (PEEP group, PIP 40.0 ± 14.7 cm H2O; zero PEEP group, PIP 18.8 ± 4.8 cm H2O) achieved in the experiment.

Mortality Analysis

PIP producing asystole in the PEEP group was 73.8 ± 4.8 cm H2O, whereas the zero PEEP group pressures for the same result reached 77.5 ± 18.5 cm H2O. No significant difference was found between the 2 groups. Figure 3 shows a box plot comparison regarding PIPs causing bradycardia, hypotension, asystole, and pneumothorax.

Discussion

Data describing precise pneumothorax pressures either in adults or in children are very scarce. In the current study, the only relevant factor that determines pneumothorax is the PIP. No difference was observed between the 2 groups.
VENTILATION STRATEGIES. The pneumothorax pressures that we describe greatly surpass the recommended recruitment PIPs in the literature, even in severely sick lungs. According to our results, a PIP of 90.5 ± 15.7 cm H₂O causes pneumothorax in healthy newborn piglets. Similar data were described in adult cadavers (100–110 cm H₂O pressure range) by Malhotra and Wright in 1961. These data are also compatible with the results from a newborn ex vivo open thorax model (50–70 cm H₂O PIP range) done by García-Fernández et al in healthy rabbits. In the latter study, pneumothorax PIPs are slightly lower, probably due to the fact that it used an open thorax model without any chest wall protection; these authors have already suggested that pneumothorax pressures in patients with an intact chest wall should be higher, since a closed system reduces transpulmonary pressure by raising pleural pressure, although a child’s chest wall is elastic, and the protection it supports is limited compared with adults, a hypothesis that our study supports. In the Malhotra and Wright study done with cadavers, barotrauma pressures rose up to the wide range of 180–260 cm H₂O if external chest wall compression was applied, thus reducing the transpulmonary pressure. Therefore, as described in the literature, transpulmonary pressure plays a key role in barotrauma development.

In our study, pneumothorax was observed mainly within the first 4–6 breaths rather than at the end of the 2-min pressure level. Just 1 of the 10 animals developed pneumothorax at the end of the pressure step. Therefore, PIP could be more relevant than the duration of pressure. Pneumothorax was found to be mainly an early dynamic event at excessive pressures; however, it remains possible that certain lungs may rupture when high pressures are maintained over a prolonged time. These results are consistent with the data obtained in the open thorax model discussed previously.

Although our study was not originally designed to assess the hemodynamic implications of these high pressures producing pneumothorax, we found interesting data that need to be discussed because barotrauma and hemodynamic impairment are among the main concerns of clinicians during recruitment maneuvers. The zero PEEP group did have greater hemodynamic impact than the PEEP ventilatory strategy. Hypotension is significantly greater in the zero PEEP group, with a 20% decrease from baseline in mean arterial pressure, systolic arterial pressure, and diastolic arterial pressure at the PIP range of 35–40 cm H₂O, whereas in the PEEP group, pressures associated with hypotension start at PIP = 60 cm H₂O/PEEP = 45 cm H₂O. Therefore, it was safe for the PEEP group to reach pressures up to 50 cm H₂O, both in terms of risk for pneumothorax development and hemodynamic repercussions, stressing the relevance of limiting driving-pressures when performing recruitment maneuvers, probably at inspiratory driving pressures <15 cm H₂O as recently described for adults. Pulse showed the highest endurance to high pressures: the zero PEEP group presented bradycardia significantly earlier, at PIPs of 40 cm H₂O, whereas the PEEP group showed bradycardia at PIP = 70 cm H₂O/PEEP = 50 cm H₂O. Bradicardia in the pediatric population is a well-known side effect of the sustained 40-cm H₂O CPAP recruitment maneuver, whose use is now strongly discouraged.

One of the more significant findings of the study is that hemodynamic compromise occurred in the zero PEEP group at considerably lower PIPs than those that caused pneumothorax. This important but unexpected finding, that a larger δ-pressure seems to induce more hemodynamic compromise with the same PIP, suggests that perhaps venous return is more compromised in this condition. Therefore, we find that hypotension and bradycardia, when an inspiratory driving pressure <15 cm H₂O is not preserved, are important side effects of PIP that actually occurred sooner than barotrauma in our experiment and, what is more important, at a common range of pressures in the...
clinical setting. Moreover, all animals suffered asystole before pneumothorax during our experiments. This fact stresses the relevance of the hemodynamic impact of high PIPs in the neonatal population and should raise concern about the hemodynamic impact and risk of death at pressures somewhat lower than those causing pneumothorax.

Regarding the mean arterial pressure highest values, in the PEEP group, these were achieved >35 cm H2O, the usual PIP goal during recruitment maneuvers, whereas the zero PEEP strategy reached maximum values at the level of 20 cm H2O and thereafter started hypotension. These findings add to the relevance that a fixed inspiratory driving pressure <15 cm H2O may have in the hemodynamics of recruitment maneuvers.27 Animals in the PEEP group slowly turned more tachycardic during the experiment, reaching the highest pulse values with PIPs of 45 cm H2O/PEEP of 30 cm H2O. This phenomenon could be due to a positive sympathetic stimulation with the increasing high pressures.28

The main limitation of our study may be the fact that it was done in healthy lungs, with no lung injury group with which to compare the results. Our idea was primarily to determine the pressures producing pneumothorax in healthy lungs, since this side effect may deter clinicians from performing recruitment maneuvers in the usual clinical setting of the operating theater. We found interesting data regarding hypotension and bradycardia that should be compared as well with lung-injured patients. Healthy lungs could, however, present earlier hemodynamic impairment than sick lungs due to their greater elasticity and the more efficient pressure transmission to the lung capillaries, thus being more likely to collapse.

There are, however, other limitations to our study: We did not perform computed tomography scanning to determine whether subtle lung damage was produced before pleural leaks were witnessed; nor did we check for other signs of barotrauma, such as pneumomediastinum. We did not make histological assessment of the lung afterward; nevertheless, there are studies available that have focused on high-pressure histologic lung lesions.29 Hemodynamic impact was a secondary goal, and the study was not designed for that purpose. Therefore, we did not measure cardiac output; nor was the preload status of our animals thoroughly assessed. A larger sample size could have shown significance in some values as mentioned previously.

Conclusions

This study is the first one to our knowledge measuring pneumothorax pressures in an in vivo model, either adult or pediatric, and shows similar data as those done ex vivo. According to our results, the recruitment maneuver pressures used in the clinical setting of the operating theater are considerably lower than those PIPs producing pneumothorax in our in vivo healthy newborn model.

We found unexpected results regarding hemodynamics: Animals in both groups had hemodynamic impact, but there are data pointing toward better hemodynamic performance to high ventilatory pressures when limiting inspiratory driving pressure, probably <15 cm H2O; a large δ-pressure seems to induce more hemodynamic compromise with the same PIP, and all animals suffered asystole and subsequently died before presenting pneumothorax. More studies should be performed specifically to assess the hemodynamic impact and barotrauma pressures in severely injured lungs.

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REFERENCES


