Positive End-Expiratory Pressure Alters Intracranial and Cerebral Perfusion Pressure in Severe Traumatic Brain Injury

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Background: Optimizing intracranial pressure (ICP) and cerebral perfusion pressure (CPP) is important in the management of severe traumatic brain injury (TBI). Intracranial pressure (ICP), directly measured via a catheter transducer system, represents pressure in the cranium exerted by brain tissue, cerebrospinal fluid, and blood. Targeted care aimed at optimizing ICP and cerebral perfusion pressure (CPP) has shown benefits in survival and neurologic outcomes. Further, cerebrospinal fluid, and blood. Targeted care aimed at optimizing ICP and cerebral perfusion pressure (CPP) has similarly, avoiding tracheal stimulation, altering mode of mechanical ventilation, paralysis, and reduction in positive end-expiratory pressure (PEEP) may decrease intrathoracic pressure.

Management of intracranial hypertension and avoidance of systemic hypotension constitute mainstay therapies in the care of critically ill patients with severe traumatic brain injury (TBI). Intracranial pressure (ICP), directly measured via a catheter transducer system, represents pressure in the cranium exerted by brain tissue, cerebrospinal fluid, and blood. Targeted care aimed at optimizing ICP and cerebral perfusion pressure (CPP) has shown benefits in survival and neurologic outcomes. Furthermore, facilitating venous drainage from the head may reduce intracranial blood volume. Clinically, maneuvers that help improve venous drainage include elevation of head of bed to 30 degrees, midline position, removal of internal jugular venous catheters, and minimizing intrathoracic pressure. Simultaneously, avoiding tracheal stimulation, altering mode of mechanical ventilation, paralysis, and reduction in positive end-expiratory pressure (PEEP) may decrease intrathoracic pressure.

Patients who develop acute lung injury, either by direct pulmonary contusion or as a consequence of the systemic inflammatory response syndrome, require the application of PEEP to maintain adequate oxygenation. In trauma patients with acute lung injury, PEEP offered therapeutic benefits and improved survival. The use of PEEP for treatment of concomitant pulmonary dysfunction in patients with TBI may potentially elevate ICP. Empiric administration of PEEP could increase intrathoracic pressure and diminish venous return, causing lowering of blood pressure. Thereby, PEEP may affect CPP, both by raising ICP and reducing mean arterial pressure (MAP) (CPP = MAP – ICP). However, the direct effect of PEEP on ICP, and hence CPP, has not been well demonstrated.

Indeed, the extent to which moderate use of PEEP impacts ICP has been questioned. In a study by Ropper et al., PEEP values up to 20 cm H₂O did not increase ICP even in patients with low intracranial compliance. More recently, McGuire et al. showed that in patients with intracranial hypertension, varying levels of PEEP produce no significant changes in CPP. The influence of mode of ventilation on ICP has also been examined. In a prospective crossover study involving nine patients with severe TBI, pressure control...
inverse ratio ventilation led to no changes in ICP or CPP compared with volume cycled ventilation. Nevertheless, these studies did not examine hemodynamic parameters and intracranial hypertension in relation to increasing PEEP.

In this study, we sought to determine the relationship between increasing levels of PEEP and ICP, CPP, and hemodynamic endpoints. Retrospectively, we examined 20 critically ill patients (Injury Severity Score of 28) with severe TBI (Glasgow Coma Scale [GCS] score < 8) requiring mechanical ventilation and invasive monitoring. Our hypothesis is as follows. Increases in PEEP levels, leading to augmented intrathoracic pressure and diminished venous return, alter hemodynamics and worsen intracranial hypertension. We found that the strategy of increasing PEEP to optimizing oxygenation is not associated with worsened intracranial hypertension or compromised oxygen transport. Overall mortality is comparable to that reported in the literature for similar patient populations.

**PATIENTS AND METHODS**

**Patient Selection Criteria**

A retrospective chart review was performed for an 18-month period from June 1997 to January 1999 for patients admitted to the trauma intensive care unit at Carolinas Medical Center, an American College of Surgeons–verified Level I trauma center. Two hundred critically injured patients (mean Injury Severity Score of 28) with severe traumatic brain injury (GCS score < 8) met criteria for initial analysis. Of these, 20 patients required simultaneous ICP and invasive hemodynamic monitoring for severe TBI and pulmonary dysfunc-

Data Points

All patients met criteria for ICP monitoring, according to *Guidelines for the Management of Severe Head Injury* (Brain Trauma Foundation, 1995). These indications included severe head injury (GCS score < 8) with an abnormal head computed tomographic scan (e.g., hematomas, contusions, edema, or compressed basal cisterns). In each case, the attending neurosurgeon decided on the type of ICP device (Camino 110-4B, Camino Medical Products, San Diego, CA; or Monitor 10-102, Clinical Neurosyst, Inc., Exton, PA). Brain-specific endpoints included ICP (mm Hg) and CPP (mm Hg). Patients had their heads elevated at 30 degrees when appropriate. In all instances, the trauma team provided pulmonary and critical care support, and neurosurgeons collaborated on brain-specific therapeutic maneuvers.

All patients required mechanical ventilation, initially via intermittent mandatory volume mode, and switched over to pressure control inverse ratio when peak airway pressures exceeded 45 mm Hg. Our institutional practice management guidelines for patients with severe head injury recommend invasive hemodynamic assessment when ICP monitoring is instigated. The Continuous Cardiac Output pulmonary artery catheter (CCO REF-746HF8, Baxter, Irvine, CA) was used. The application of increasing PEEP proved necessary to keep oxygen saturation > 92% or PaO₂ > 60 mm Hg. The following hemodynamic parameters were obtained. Central venous pressure (CVP), PAOP, cardiac index (CI), oxygen delivery index (Do₂i), and oxygen consumption index (Vo₂i).

**Statistical Analysis**

Brain-specific and hemodynamic data are categorized on the basis of levels of PEEP, and reported as mean ± SE. Three arbitrary groups, consisting of PEEP 0 to 5, 6 to 10, and 11 to 15 cm H₂O, were available for comparison. Differences among groups were assessed using Kruskal-Wallis analysis of variance, with p < 0.05 considered significant. When differences between two groups were examined, pairwise multiple comparison procedures were used (Dunn method).

**RESULTS**

There were 16 male subjects (80%) and 4 female subjects (20%). Overall mortality was 30%. Two patients died from isolated head injuries with intractable intracranial hypertension. Three patients died from traumatic brain injury with associated pulmonary failure. One death resulted from early multiple organ dysfunction syndrome. Mechanisms of injury included motor vehicle collision (65%), motorcycle crash (15%), fall (10%), and assault (10%). Ten patients had intracerebral hemorrhage, and two had intracerebral and subarachnoid blood. Five patients had subdural hematoma with midline shift, and three had epidural hematomas necessitating surgical decompression.

**PEEP versus ICP and CPP**

The average number of data points were 1,287 for each brain-specific dataset, and 335 for each hemodynamic dataset. Table 1 shows the association between increasing PEEP and changes to ICP and CPP. As PEEP increased, ICP showed a decreasing trend. The reduction in ICP gained statistical significance at higher PEEP levels (11–15 cm H₂O) when compared with ICP values at PEEP of 0 to 5 cm H₂O. When PEEP levels were increased to support oxygenation, CPP improved. The increases in CPP with rising levels of PEEP were significant. There was no temporal relationship between changes in PEEP levels and therapeutic maneuvers for controlling ICP levels.

**PEEP versus CVP and PAOP**

Figure 1 illustrates the correlation between increasing PEEP and hemodynamic parameters. As PEEP levels rose from 0 to 5, 6 to 10, to 11 to 15 mm Hg, CVP increased.
accordingly. These changes were significant. Similarly, PAOP increased with elevating levels of PEEP.

### DISCUSSION

Our results showed that in trauma patients with severe head injury, the strategy of increasing PEEP to optimize oxygenation was not associated with a reduction in oxygen transport or worsening of intracranial hypertension. We observed that as PEEP levels increased, CVP and PAOP measurements were accordingly elevated, whereas CI, Do\textsubscript{O\textsuperscript{2}i}, and Vo\textsubscript{O\textsuperscript{2}i} remained unaffected. In relation to brain-specific pressures, increases in PEEP correlated with reduction in ICP, and augmented CPP. These data support judicious use of PEEP to maximize oxygen transport in the management of head-injured patients with concomitant acute lung injury.

Application of PEEP in the care of critically ill patients after TBI remains controversial. Clinically, PEEP exerts beneficial effects on oxygenation by increasing functional residual capacity, reducing intrapulmonary shunt via alveolar recruitment, and lowering supplemental oxygen.\textsuperscript{7} Excessive PEEP can create volutrauma, hamper venous drainage, reduce MAP, and increase ICP.\textsuperscript{9,12,13} These deleterious effects can worsen CPP, and can negatively impact a head-injured patient. Presently, the influence of PEEP on brain-specific pressures, hemodynamics, and oxygen transport after TBI remains to be established.

### Table 1

PEEP vs. Cranial Pressures and Oxygen Kinetics (Mean ± SE)

<table>
<thead>
<tr>
<th>PEEP (cm H\textsubscript{2}O)</th>
<th>ICP (mm Hg)</th>
<th>CPP (mm Hg)</th>
<th>CI (L/min/m\textsuperscript{2})</th>
<th>Do\textsubscript{O\textsuperscript{2}i} (mL O\textsubscript{2}/min/m\textsuperscript{2})</th>
<th>Do\textsubscript{O\textsuperscript{2}i} (mL O\textsubscript{2}/min/m\textsuperscript{2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–5</td>
<td>14.7 ± 0.2</td>
<td>77.5 ± 0.3\textsuperscript{*}</td>
<td>3.8 ± 0.1</td>
<td>593 ± 9</td>
<td>167 ± 6</td>
</tr>
<tr>
<td>6–10</td>
<td>13.6 ± 0.2</td>
<td>80.1 ± 0.5</td>
<td>4.0 ± 0.1</td>
<td>629 ± 21</td>
<td>167 ± 6</td>
</tr>
<tr>
<td>11–15</td>
<td>13.1 ± 0.3\textsuperscript{†}</td>
<td>78.9 ± 0.7\textsuperscript{‡}</td>
<td>3.8 ± 0.1</td>
<td>560 ± 21</td>
<td>153 ± 6</td>
</tr>
</tbody>
</table>

\textsuperscript{*}p < 0.001 vs. PEEP 6–10 cm H\textsubscript{2}O; \textsuperscript{†}p < 0.001 vs. PEEP 0–5 cm H\textsubscript{2}O.

In patients with acute respiratory distress syndrome, the effect of PEEP on hemodynamic parameters has been well documented.\textsuperscript{14,15} Elevated airway and pleural pressure resulting from increases in PEEP may cause artificially inflated CVP and PAOP.\textsuperscript{16} This may lead to a false sense of assurance that the intravascular status is “adequate.” Our data support previous observations showing increases in CVP and PAOP corresponding to elevating levels of PEEP. Furthermore, we found that oxygen transport in our study remained unaffected, despite changes in PEEP levels.

Optimized oxygen transport parameters (e.g., CI, Do\textsubscript{O\textsuperscript{2}i}, and Vo\textsubscript{O\textsuperscript{2}i}) have resulted in survival benefits.\textsuperscript{17–20} However, other clinical trials of a heterogeneous group of patients with unclear timing of resuscitation have demonstrated no difference\textsuperscript{21} or higher mortality rates using high doses of inotropic support.\textsuperscript{22} In addition, these calculated values have been shown to be less affected by PEEP,\textsuperscript{23} compared with CVP or PAOP values. Incorporated in our goal-directed resuscitation regimen, we found that despite increases in PEEP levels, oxygen transport parameters (CI, Do\textsubscript{O\textsuperscript{2}i}, and Vo\textsubscript{O\textsuperscript{2}i}) remained unchanged in our head-injured patients. This is attributable to the endpoints selected on our trauma services being CI, Do\textsubscript{O\textsuperscript{2}i}, and Vo\textsubscript{O\textsuperscript{2}i}, as opposed to CVP or PAOP.

Thus far, our findings agree with previously published data regarding the effects of PEEP on hemodynamic indices (CVP and PAOP) and oxygen transport endpoints. Evidence
on the impact of PEEP on brain-specific pressures remains less substantiated.

Two earlier studies reported detrimental effects of PEEP on ICP and CPP in head-injured patients. In one study, baseline CPP was not measured, thus the changes in CPP could not be independently explained by the addition of PEEP. In the other, patient head position was not recorded. Because 30 degrees of head elevation is important in the care of head-injured patients, lack of monitoring head position in this study rendered the data difficult to interpret.

Earlier, Cooper et al. showed that application of PEEP at 10 cm H2O (range, 5–15 cm H2O) to baseline of 0 to 6 cm H2O in 33 patients with severe head injury significantly increased ICP by 1.3 mm Hg. The authors concluded, however, that the increase in ICP was not clinically relevant.

Two recent studies also failed to demonstrate any negative impact of PEEP on intracranial hypertension. McGuire et al. found that, although application of PEEP at 10 or 15 cm H2O increased ICP, this maneuver produced no effect on CPP. Moreover, in a study involving nine patients with TBI and concomitant pulmonary dysfunction, switching the mode of ventilation from volume control to pressure control inverse ratio significantly increased PEEP, yet had no impact on MAP, ICP, or CPP.

In this study, we observed a decreasing ICP trend with increased levels of PEEP. At PEEP of 11 to 15 cm H2O versus PEEP at 0 to 5 cm H2O, the reduction in ICP became significant. Moreover, CPP improved with escalation of PEEP. Inherent to the retrospective nature of our study, we could not exclude time as an independent variable contributing to changes in ICP levels. As such, we emphasize the associative relationship between PEEP and alterations in ICP. Our goal-directed therapy in the management of critically ill patients with TBI aims at the judicious use of PEEP. Targeted endpoints include oxygen saturation > 92% (or PaO2 > 60 mm Hg), normal CI and Do2i, and avoiding alveolar overdistention with high plateau airway pressures. Thus, PEEP is increased by increments of 2 cm H2O to optimize oxygen kinetics. This regimen of cautious use of PEEP may explain, in part, the maintenance of oxygen transport and avoidance of exacerbating intracranial hypertension during PEEP therapy in the severely head-injured patient.

CONCLUSION

After TBI, the avoidance of hypotension and management of intracranial hypertension constitute mainstay therapies. In severely head-injured patients with concomitant pulmonary dysfunction, use of PEEP to support oxygenation may interfere with optimizing brain-specific parameters (ICP and CPP). In this study, we examined the effects of PEEP on preload values (CVP and PAOP), oxygen transport kinetics (CI, Do2i, and Vo2i), and intracranial hypertension (ICP and CPP). We found that with increasing levels of PEEP, preload values were elevated. Concurrently, oxygen transport remained unchanged. Furthermore, escalating PEEP levels did not worsen intracranial hypertension, as reflected by the associated reduction in ICP and augmentation of CPP. We concluded that in patients with TBI and concomitant pulmonary dysfunction, the strategy of increasing PEEP to maintain oxygenation is not associated with compromised oxygen transport or exacerbated intracranial hypertension.

REFERENCES

I have four issues for the authors. First, Could you clarify your ventilator management? PEEP is one of several ways in which we can increase mean airway pressure. It is mean airway pressure that is the parameter that must closely correlate to the beneficial and adverse effects of PEEP. What we need to know is that when you turn the PEEP knob up, what did you do with the other ventilator knobs? Did mean airway pressure truly increase?

Second, did your patients have stiff lungs? This is an important issue, because as pulmonary compliance decreases, airway pressure transmission to the intrapleural space decreases. If your patients did have stiff lungs, it’s not surprising that modest elevations in PEEP had little effect.

Third, how were your patients managed from a hemodynamic perspective? As we’ve heard today, it appears that it’s variable among institutions. But again, if your patients were volume loaded as PEEP levels were increased, which I expect from the filling pressure data, then one would not anticipate that cardiovascular function would be compromised.

Fourth, your data indicate that increased PEEP decreases ICP. Can you provide a physiologic explanation, or does this represent an alpha error or simply a flaw in retrospective data?

I would like to congratulate the authors for refocusing attention on an important issue. Their conclusions clearly support my bias, but unfortunately their retrospective data are a bit difficult to interpret. Finally, I would like to thank the Association for the privilege of the floor.

Dr. Alex B. Valadka (Houston, Texas): I’d like to congratulate the authors and ask them whether or not they elevated the head of the bed of these patients. As you know, one school of thought says that elevating the head of the head-injured patient’s bed will promote venous drainage, and perhaps lower the ICP. A contrary school says that keeping the head of the bed flat will optimize their cerebral perfusion. I’m wondering whether the authors consistently have elevated the head of the bed or kept it flat, and if they have any other thoughts on that.

Dr. Lawrence H. Pitts (San Francisco, California): Sort of a follow-on to that same point; that is, whether elevation of the head improves or worsens cerebral perfusion pressure, and probably is very intimately tied to brain compliance at any given point in time, as I think the question about PEEP might change compliance. If one has poor compliance, then a relatively small change in cerebral venous outflow might have a substantial effect on ICP. In point of fact, your group should be congratulated for having quite normal ICP levels in the population that you’re reporting here. The mean ICP levels were 13 or 14 in each of your groups. I would not expect compliance to be compromised at that level.

My question is, in whatever subgroup of patients had elevated ICP, did you have a more profound effect of PEEP on changing ICP? I wouldn’t expect much change in this particular group with a mean ICP of less than 15.
Dr. Steven R. Shackford (Burlington, Vermont): In 18 months, did you only put in 20 monitors? If you put more monitors in, did you look at patients who didn’t have respiratory failure who also ventilated? I’m sure many of these patients, since the entry criterion was traumatic coma, were intubated.

Dr. Toan Huynh (closing): I’d like to thank you for the insightful comments, especially Dr. Moore’s review of the article. To address Dr. Moore’s question on ventilator management in these patients, there’s almost a uniform approach at our institution of keeping peak airway pressures at about 45 mm Hg, beyond which the patient would be switched to a pressure-targeted mode. Now, inherent to a retrospective study, compliance variables were not consistently recorded, hence the compliance issue remains inconclusive.

Your third question had to do with the hemodynamic management. Again, we had a goal-oriented approach, not targeting CVP or wedge pressure alone, but looking at other endpoints such as oxygen delivery and consumptions as well as other parameters. I think you are right that the patients were volume loaded adequately.

Your last question has to do with a possible explanation for why the increases in PEEP would lead to an ICP decrease. I have no physiologic explanation for that, and anything I say would be a speculation. I almost agree with you that maybe this is an alpha error. I think the point that we like to emphasize again is that in a hypoxic patient, PEEP therapy is probably safe if you have a goal-directed strategy.

Dr. Valadka asked about the elevation of the head of bed. We actually have a guideline for managing these head-injured patients, and all these patients had the head elevated to 30 degrees if there were no other contraindications to that.

Dr. Pitts mentioned subgroup analysis. Unfortunately, the number for this study was small enough that it was impossible to perform a subgroup analysis of the patients with severe elevations in their ICP levels.

Dr. Shackford asked about the number of catheters and the number of patients being monitored over an 18-month period. We aimed to examine patients who had simultaneous invasive monitoring. By that, I mean ICP monitor as well as pulmonary artery catheters, which limits the number of patients selected for the study.