Original Article

Effect of Positive End-Expiratory Pressure on Optic Nerve Sheath Diameter in Pediatric Patients with Traumatic Brain Injury

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Background: The peak incidence of traumatic brain injury (TBI) has been reported in children and young adults. Intracranial pressure (ICP) as an important component can be measured with invasive technique, whereas noninvasive measurement of optic nerve sheath diameter (ONSD) is increasingly becoming popular. Positive end-expiratory pressure (PEEP) has been found to affect ICP. We aimed to compare the effect of different values of PEEP on ONSD and to obtain the correlation with ICP measurement. Setting and Design: Neurointensive Care Unit, Trauma Center, AIIMS, New Delhi. Materials and Methods: Pediatric patients with TBI, of either gender, between 1 and 18 years of age in whom ICP was measured using intraparenchymal Codman catheter admitted in neurointensive care unit were enrolled. For this crossover study, the sequence of PEEP (0 or 3 or 5 cm H2O) was randomized and ONSD was measured. The mean of three ONSD values was taken as final value. Statistical Method: The ONSD, ICP, peak airway pressure, and hemodynamic parameters at various stages were compared using two-way repeated measures analysis of variance with Bonferroni correction. A P value of <0.05 was considered to be significant. Results: Ten patients (seven males, three females) participated in the study. There was no significant increase in ONSD values when PEEP was increased from 0 to 3 cm H2O. However, increase in PEEP values from 3 to 5 cm H2O showed significantly increased ONSD values. Conclusion: PEEP up to 3 cm H2O can be safely applied in pediatric patients following TBI. Further increment of PEEP might accentuate the ICP values.

Keywords: Intracranial pressure, optic nerve sheath diameter, positive end-expiratory pressure

INTRODUCTION

Traumatic brain injury (TBI) is a major cause of disability, death, and economic cost to our society. The peak incidence has consistently been reported in children and young adults.[1] However, over the last 30 years, there has been a declining trend in mortality from 50% to 25% due to the systematic use of evidence-based protocols that emphasize monitoring and maintain adequate cerebral perfusion.[2,3] Protocols that emphasize intracranial pressure (ICP) monitoring have demonstrated improved outcomes particularly in trauma centers.[4,5] More recently, advancement in the field of research has enabled the diagnosis of raised ICP much reliably by noninvasive modalities. One such noninvasive modality includes estimation of optic nerve sheath diameter (ONSD) using bedside ultrasound.

The optic nerve sheath is an anatomical extension of the dura mater and the subarachnoid space around the optic nerve is continuous with the intracranial subarachnoid

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space. The anterior part of the optic nerve is loosely attached to the dural sheath and is surrounded only by orbital fat, thus making it distensible. Because of this direct communication, pressure changes in the intracranial compartment are transmitted to the intraorbital (particularly retrobulbar) subarachnoid space around the optic nerve. Dilatation of optic nerve sheath has been shown to be a much earlier manifestation of ICP rise. Ultrasound technology using high-frequency linear probes (>7.5 MHz) with improved spatial resolution has enabled excellent views of the optic nerve sheath.

Severe TBI is accompanied by both neurological and non-neurological complications. Involvement of respiratory system in the form of acute lung injury (ALI, 20%) and acute respiratory distress syndrome (ARDS, 15%) leading to hypoxemia is not uncommon after severe TBI and warrants early intervention. One of the established ventilation strategies to improve oxygenation index in lung injury is by recruiting collapsed alveoli through application of high positive end-expiratory pressure (PEEP). However, high PEEP therapy in adult patients with severe TBI has been shown to increase ICP and compromise cerebral perfusion pressure (CPP). Because of the lack of availability of literatures pertaining to the effect of PEEP on ICP in pediatric patients, optimal PEEP is yet to be ascertained.

The primary aim of our study was to compare the effect of different values of PEEP on ONSD and to obtain the correlation with ICP measurement. The secondary aim was to simultaneously evaluate the effect of similar values of PEEP on peak airway pressure (PAP), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP).

**Materials and Methods**

After approval from the Institutional Ethics Committee and written informed consent obtained from parents, we enrolled 10 pediatric patients with TBI, of either gender, between 1 and 18 years of age admitted in neurointensive care unit. For this crossover study, the sequence of PEEP (0 or 3 or 5 cm H₂O) was randomized using computer-generated program. This observational study was conducted over a period of 3 months. We included only those patients in whom ICP was measured using intraparenchymal Codman catheter. We excluded patients with associated respiratory or cardiovascular system disease or hemodynamically unstable patients. Patients with less than 1 year of age or more than 18 years of age were also excluded from the study. ONSD was measured using a 6- to 13-MHz linear probe of the ultrasound machine. The patients were placed in supine position with head-up tilt of 30°. Eyes were covered with transparent plaster. A water-soluble ultrasound-transmission jelly was applied over the probe. The probe was gently placed over the eyelid paying careful attention not to exert excessive pressure. The probe was adjusted from temporal to nasal end to find a suitable angle for displaying the entrance of optic nerve into the globe. The optic nerve was focused in the center of the image for measurement. The ONSD was measured 3 mm behind the globe. The ONSD was measured at PEEP values of 0, 3, and 5 cm H₂O. Simultaneously, invasive ICP values were also recorded at all these three PEEP values. The ONSD was measured 3 min after achieving desired PEEP value. We took three readings of ONSD and ICP at each PEEP setting, and mean of three values was taken as the final value. The average ONSD and ICP values were measured by an independent observer, who was blinded to ventilation setting. Other variables such as PAP, HR, SBP, DBP, and MBP were also recorded.

All the patients were mechanically ventilated with the following settings: mode, synchronized intermittent mandatory ventilation (SIMV); fraction of inspired oxygen (FiO₂), 0.4; square wave, inspiratory-expiratory ratio (I/E), 1:2; tidal volume (TV), 8 mL/kg; and respiratory rate set to keep the partial pressure of carbon dioxide (PaCO₂) at 34–36 mmHg. Factors such as position of the patient, time of estimation of ONSD after achieving desired PEEP, and measuring ONSD in a single plane (transverse) and involving two experienced observers in ONSD measurement were kept constant to minimize confounding factors.

**Statistical analysis**

Data were analyzed using software STATA 9.0 (StataCorp, College Station, TX). Data are expressed as median (range) or mean (SD) or number (%) as appropriate. The ONSD, ICP, PAP, and hemodynamic parameters at various stages were compared using two-way repeated measures analysis of variance with Bonferroni correction. A P value of <0.05 was considered to be significant.

**Results**

On the basis of statistical analysis, the median age, weight, Glasgow Coma Scale (GCS), and number of intensive care unit (ICU) days of all 10 patients were calculated and have been tabulated [Table 1]. Of
10 patients, 7 were males and 3 were females. Only noticeable variable was the median GCS (6) implying the severity of TBI. Table 2 shows the mean (SD) of all the hemodynamic variables at all the three levels of PEEP. Hemodynamic parameters such as HR, SBP, DBP, and MBP remained comparable to baseline values during sequential increase of PEEP from 0 to 3 and 3 to 5 cm H2O.

Although the median ONSD increased with sequential increase in PEEP, there was no significant increase in ONSD values when PEEP was increased from 0 to 3 cm H2O (P = 0.183). However, increase in PEEP values from 3 to 5 cm H2O showed significantly increased ONSD values (P = 0.000). Similarly, the ICP values showed no significant increase when PEEP increased from 0 to 3 cm H2O (P = 0.417) but showed significant increase when PEEP increased from 3 to 5 cm H2O (P = 0.001). PAP increased significantly during increment of PEEP both from 0 to 3 cm H2O (P = 0.001) and from 3 to 5 cm H2O (P = 0.000) [Table 3].

**DISCUSSION**

TBI is classified as, either closed or penetrating (open). It is defined as any traumatically induced structural injury or physiological disruption of brain function as a result of an external force. Non-neurological organ dysfunction in severe TBI most commonly involves respiratory system, of which ALI and ARDS are the most severe and are associated with worse neurological outcomes and longer hospitalization. PEEP plays an important role in the ventilation management of ALI/ARDS because it improves oxygenation by recruiting small airways and collapsed alveoli, increases functional residual capacity, and decreases the incidence of ventilator-induced lung injury. Studies addressing the effect of PEEP on the intracranial system have focused mainly on ICP, showing conflicting results. It is still a matter of debate worldwide as to what should be the maximum level of PEEP that can correct hypoxemia without escalating ICP in patients with severe TBI. Although, there are few studies available in the literature defining the optimal PEEP in adult patients, there are none pertaining to pediatric patients with TBI.

According to Cooper et al., a PEEP value of 10 cm H2O slightly increased ICP and was clinically safe for adult patients with severe TBI. In a pilot study conducted by Nemer et al. in 20 patients with severe TBI, PEEP application even up to 15 cm H2O did not significantly increase ICP or decrease CPP. Similarly, Frost found no change in ICP even with PEEP as high as 40 cm H2O. On the contrary, Shapiro and Marshall observed an ICP increase of 10 mm Hg or more after the administration of 4–8 cm H2O of PEEP along with a CPP decrease in 50% of the cases. In a study conducted by Videtta et al., PEEP was raised from 5 (basal) to 15 cm H2O in steps of 5 cm H2O. They observed that PEEP at 10 and 15 cm H2O produced a significant increase in ICP without change in CPP. McGuire et al. postulated that ICP increase following PEEP administration of 10 cm H2O or more occurs in patients with normal ICP but is well tolerated in patients with intracranial hypertension. This suggests that intracranial hypertension, by compressing the cerebral venous system, may avoid the transmission of intrathoracic pressure to the intracranial compartment.

Ours is the first study to determine the effect of three sequentially increasing PEEP values (0, 3, and 5 cm H2O) primarily on ONSD in children with severe TBI. In this study, we also measured ICP invasively.

### Table 2: Hemodynamic variables at all three levels of PEEP

| PEEP levels (cm H2O) | HR (beats/min) Mean (SD) | SBP (mm Hg) Mean (SD) | DBP (mm Hg) Mean (SD) | MBP (mm Hg) Mean (SD) |
|----------------------|--------------------------|-----------------------|-----------------------|-----------------------|
| 0                    | 127.3 (15.82)            | 106.6 (7.84)          | 64.6 (5.89)           | 63.7 (9.69)           |
| 3                    | 127.5 (21.88)            | 108.7 (7.74)          | 65.7 (6.52)           | 63.4 (11.55)          |
| 5                    | 127.2 (20.02)            | 107.7 (7.08)          | 66.6 (7.90)           | 63.3 (11.89)          |

| PEEP levels (cm H2O) | ONSD (mm) Median (range) | ICP (mm Hg) Median (range) | PAP (cm H2O) Median (range) |
|----------------------|-------------------------|----------------------------|-----------------------------|
| 0                    | 3.1 (2.3–3.9)           | 11.5 (3–14)                | 11.5 (7–16)                 |
| 3                    | 3.3 (2.4–4.3)           | 12 (3–15)                  | 12.5 (10–18)                |
| 5                    | 3.5 (3.0–5.5)           | 13 (3–18)                  | 15 (11–19)                  |
| PEEP increments      |                         |                           |                            |
| 0–3                  | P = 0.183               |                           | P = 0.417                   |
| 3–5                  | P = 0.000               |                           | P = 0.001                   |
Our results showed that both ONSD and ICP did not increase significantly when PEEP increased from 0 to 3 cm H\textsubscript{2}O though the increase was significant when PEEP increased from 3 to 5 cm H\textsubscript{2}O. However, this significant increase in ICP did not apparently change the clinical status. It would be unjustifiable to compare the results of our study with those conducted previously in adults because of significant differences in intracranial dynamics and autoregulation among the two populations. In a study conducted by Pulitanò et al.\cite{22} in 21 pediatric patients undergoing surgery for intracranial neoplasm, they did not find any significant difference in ICP values after increasing PEEP from 0 to 8 cm H\textsubscript{2}O. This can probably be attributed to the chronic nature of the disease itself where the intracranial compensatory mechanisms reinforce over the time in contrast to acute and severe brain injury following trauma where the autoregulatory mechanisms are completely at stake.

Simultaneously, the effect of these three sequentially increasing PEEP values did not show any significant difference in the values of HR, SBP, DBP, and MBP. However, PAP values showed significant increase during increase of PEEP values both from 0 to 3 cm H\textsubscript{2}O and then from 3 to 5 cm H\textsubscript{2}O. Although the median PAP increased from 11.5 (PEEP, 0) to 15 cm H\textsubscript{2}O (PEEP, 5), no complications pertaining to this increase could be noticed. This is because large changes in the intrathoracic pressure in children are accompanied by only small changes in chest wall pressure due to steep volume-pressure relationship. As such, large changes in ventilator pressure have only a limited effect on pleural pressure. This explains the generally higher cardiovascular tolerance of children to the application of high airway pressures.\cite{22}

Our study has few limitations. First, the study is limited by its small size and results need to be validated in larger population. Second, we did not measure CPP that indeed is a more robust determinant of cerebral autoregulation. Third, we did not measure compliance of the respiratory system, which according to literature is one of the main factors affecting the transmission of PEEP to the intracranial compartment. Fourth, we did not investigate the effect of PEEP in children with high ICP because the median ICP in these patients is not elevated. Fifth, because our patients had severe TBI (median GCS, 6), we feel that the results might have varied in patients with mild-to-moderate TBI, and thus further studies should categorize the patients into the three types of TBI. Finally, we also did not look for any specific adverse effects such as increased cerebral edema or intracranial bleeding pertaining to increased ICP, even though apparently there was no change in clinical status.

**Conclusion**

Thus, we conclude that, if required, PEEP up to 3 cm H\textsubscript{2}O can be safely applied in pediatric patients following TBI. Further increment of PEEP might further improve oxygenation but at the cost of accentuation of ICP. At present, it is difficult to comment whether such increment of ICP resulting from PEEP application has any bearing on clinical outcome. Large trials are required to further validate the effect of PEEP on ICP in pediatric patients with TBI.

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**Conflicts of interest**

There are no conflicts of interest.

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