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Effect of positive end-expiratory pressure on optic nerve sheath diameter in mechanically ventilated traumatic brain injury patients

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Abstract:

Background: In patients with traumatic brain injury (TBI), positive end-expiratory pressure (PEEP) can change intrathoracic pressure and cerebral hemodynamics, which in turn affects intracranial pressure (ICP). This research aimed to determine varying PEEP levels on optic nerve sheath diameter (ONSD), an indirect predictor of ICP, in mechanically ventilated (MV) TBI and non-TBI patients. **Methods:** This prospective observational study enrolled 60 MV patients (30 TBI, 30 non-TBI controls). ONSD was measured bilaterally at 5, 10, and 15 mmHg PEEP levels. **Results:** At 15 mmHg PEEP, ONSD was considerably more remarkable in the TBI group (5.68±0.27 mm) compared to controls (5.4±0.18 mm, $p<0.001$). The median delta change in average ONSD between 15 mmHg and 5 mmHg was 0.55 mm (IQR: 0.31-0.65) in the TBI group and 0.27 mm (IQR: 0.20-0.35) in controls ($p<0.001$). TBI was an independent predictor of delta ONSD change. **Conclusions:** TBI patients exhibit a significantly greater increase in ONSD with higher PEEP levels than non-TBI controls, suggesting enhanced ONSD sensitivity to PEEP in individuals with brain injury. This highlights the need for careful PEEP titration to balance lung recruitment and ICP management in MV TBI patients.

Keywords:

Positive end-expiratory pressure, Optic nerve sheath diameter, Traumatic brain injury, Mechanical ventilation, Intracranial pressure

1. Introduction:

Positive end-expiratory pressure (PEEP) serves as a crucial ventilatory strategy for optimizing oxygenation and preventing alveolar collapse in mechanically ventilated (MV) patients [1]. However, in traumatic brain injury (TBI) patients, PEEP application presents a complex clinical challenge due to its effects on intracranial pressure (ICP) through alterations in intrathoracic pressure, which subsequently impacts cerebral venous drainage and cerebrospinal fluid outflow [2, 3].

Elevated ICP remains a significant concern in TBI management and is associated with substantial morbidity and mortality risks [4]. The most reliable method is invasive ICP observing, but the risks involved, incorporating infection and hemorrhage risks, have prompted the exploration of non-invasive alternatives [5].

As a non-invasive method for assessing ICP, ultrasound measurement of optic nerve sheath diameter (ONSD) has lately acquired interest [6, 7]. This method makes use of the fact that the optic nerve sheath is an extension of the dura mater and that it connects to the cerebral subarachnoid space anatomically [8]. The anterior portion's distensible nature allows for the transmission of ICP changes to the retrobulbar space, making ONSD dilation an early indicator of elevated ICP [9].

The relationship between PEEP and ICP is particularly nuanced in individuals with acute brain injury, where the ICP response varies based on factors such as chest wall elastance and respiratory system mechanics [10, 11]. This variability necessitates careful monitoring and individualized PEEP adjustments to maintain optimal cerebral hemodynamics while ensuring adequate pulmonary function [3]. The effects of PEEP on ONSD have been documented across various clinical scenarios, particularly during surgical procedures involving pneumoperitoneum and position changes [12].

Contemporary protocols emphasize the importance of personalizing PEEP levels to balance lung recruitment and cerebral perfusion [13, 14]. This consideration becomes especially critical in patients with concurrent brain injuries or conditions predisposing them to elevated ICP [15]. A comprehensive understanding of PEEP's impact on pulmonary function and cerebral dynamics is essential for clinicians managing MV patients with neurological conditions requiring careful ICP monitoring [16].

This study aims to evaluate the effect of varying levels of PEEP on ONSD as an indirect predictor of ICP in MV patients with or without TBI.

2. Patients and Methods:

This prospective observational study was conducted on 60 patients ≥18 years old, both sexes, Glasgow Coma Scale ≤8 and requiring MV with initial PEEP ≤5 mmHg at the intensive care unit of the Emergency Medicine and Traumatology Department at Tanta University Emergency Hospital, Egypt from September 2020 to October 2024. The Research Ethics Committee of Tanta University's Faculty of Medicine approved the study protocol (33934/7/20). Informed written consent was obtained from patients' relatives before enrollment.

There were two equal groups of participants: one group had severe head trauma and was called the TBI group, and the other group was called the control group.

Exclusion criteria encompassed severe cardiopulmonary disease, brain herniation, and hemodynamic instability.

All enrolled patients underwent initial resuscitation and comprehensive clinical assessment, including detailed neurological and ophthalmological examinations. Medical histories were obtained from patients' relatives when possible. Patients were MV under appropriate sedation and analgesia protocols.

The measurements were recorded by a well-trained emergency physician on ONSD evaluation by point-of-care ultrasonography using (Phillips Affinity 50) device. Both eyes and Averaged ONSD measurements were recorded. Measurements were taken at three PEEP levels (5, 10, and 15 mmHg) with 5-minute stabilization periods between adjustments.

The technique of optic nerve sheath diameter measurement [17]:

The patient was supine with their head lifted at 30° and aligned centrally during the ONSD measurements. After applying lubricant and protective film dressing to both contracted pupils, a 10 MHz linear array ultrasonographic probe was carefully positioned on the temporal region of the upper eyelid to avoid globe compression. The probe was oriented horizontally and vertically , and examinations were conducted bilaterally in both horizontal and vertical planes. Three millimeters behind the lamina cribrosa is where the measurements were taken, with the probe positioned perpendicular to the optic nerve. The primary outcome was the delta change in average ONSD between 15 mmHg and 5 mmHg PEEP. Secondary outcomes were ONSD of the right and left eye at 5 mmHg, 10 mmHg, and 15 mmHg PEEP.

Sample size calculation:

The sample size calculation was done by G*Power 3.1.9.2 (Universitat Kiel, Germany). We performed a pilot study (five cases in each group), and we found that the mean (± SD) of the delta change

between 15mmHg and 5mmHg was 0.43±0.12 mm in the TBI group and was 0.31±0.11 mm in the control group. We selected 30 patients in each group to account for the following factors: 1.04 effect size, 95% confidence level, 95% power of the trial, group ratio 1:1, and five cases added to each group to account for dropout.

Statistical analysis

Statistical analysis was done by SPSS v27 (IBM©, Armonk, NY, USA). The Shapiro-Wilks test and histograms were used to evaluate the normality of the data distribution. Quantitative parametric data were presented as mean and standard deviation (SD) and were analyzed by unpaired student t-test. The repeated measures of ONSD were compared using a repeated measure ANOVA test. The Mann-Whitney test was used to evaluate quantitative non-parametric data, which was reported as the median and interquartile range (IQR). The Chi-square test assessed qualitative variables, which were presented as frequency (%). We regarded a two-tailed P value < 0.05 to be statistically significant.

3. Results:

There were no statistically significant differences between the groups regarding age, sex, or GCS. Table 1

Table 1: Demographic data of the studied groups

		TBI group (n=30)	Control group (n=30)	P value
Age (years)		50.4 ± 15.88	54.73 ± 12.91	0.251
Sex	**Male**	20 (66.67%)	17 (56.67%)	0.426
	Female	10 (33.33%)	13 (43.33%)	
GCS		6(4 - 7)	6(5 - 7.75)	0.138

Data are presented as mean ± SD, frequency (%), or median (IQR). GCS: Glasgow Coma Scale.

There was no significant difference in ONSD at 5 and 10 mmHg between the two groups, but at 15 mmHg, the TBI group had a significantly higher ONSD than the control group (P <0.05). Table 2

At 5 and 10 mmHg, there was no significant difference in the average ONSD of both eyes between the two groups. However, at 15 mmHg, the TBI group had a considerably greater average ONSD than the control group (P <0.05). The average ONSD of both eyes was significantly higher at 15 mmHg than 5nnHg in both groups (P<0.05). Table 2

Table 2: ONSD of the right and left eye of the studied groups

	TBI group (n=30)	Control group (n=30)	P value
Right eye			
5 mmHg	5.14±0.19	5.11±0.15	0.501
10 mmHg	5.15±0.17	5.12±0.15	0.383
15 mmHg	5.65±0.25	5.39±0.16	<0.001
Left eye			
5 mmHg	5.21±0.17	5.15±0.18	0.223
10 mmHg	5.25±0.23	5.18±0.21	0.224
15 mmHg	5.71±0.3	5.41±0.22	<0.001
Average both eyes			
5 mmHg	5.17±0.17	5.13±0.16	0.314
10 mmHg	5.2±0.19	5.15±0.17	0.263
P#	0.134	0.228	
15 mmHg	5.68±0.27	5.4±0.18	<0.001
P#	<0.001	<0.001	

Data are presented as mean ± SD. ONSD: Optic nerve sheath diameter, P#: P value compared to 5 mmHg.

The median (IQR) of delta change between 15mmHg and 5mmHg was 0.55(0.31 – 0.65) in the TBI group and 0.27(0.2 - 0.35) in the control group. Delta change of average ONSD of both eyes between 15mmHg and 5mmHg was significantly higher in the TBI group than in the control group (P<0.001). Table 3

Table 3: Delta change of average ONSD of both eyes between 15mmHg and 5 mmHg of the studied groups

	TBI group (n=30)	Control group (n=30)	P value
Delta change between 15mmHg and 5mmHg	0.55(0.31 – 0.65)	0.27(0.2 - 0.35)	<0.001

Data are presented as median (IQR).

TBI was an independent predictor of delta change of ONSD (P =0.035), while age and sex were not. Table 4

Table 4: Linear regression of age, sex, and TBI versus delta change of ONSD

	Coefficient Interval (CI)	SE	P value
Age	-0.008	0.005	0.127
Sex	-0.100	0.160	0.534
TBI	-0.340	0.157	**0.035**

CI: Confidence interval. SE: Standard error. TBI: traumatic brain injury.

4. Discussion:

Our study demonstrated distinct patterns in ONSD responses to PEEP between TBI and non-TBI patients. At 5 mmHg and 10 mmHg PEEP, ONSD measurements were comparable between groups. However, the introduction of 15 mmHg PEEP revealed significant differences, with TBI patients exhibiting markedly higher ONSD values (5.65±0.25 mm right eye, 5.71±0.3 mm left eye) compared to controls (5.39±0.16 mm right eye, 5.41±0.22 mm left eye).

These findings align with but extend beyond those reported by Gupta et al. [18], who observed significant ONSD increases only when PEEP exceeded 10 cm H_2O in TBI patients. Our results particularly complement Balakrishnan et al. [19] observations, where ONSD values peaked at 5.24±0.49 mm on the pathologic side with 10 cm H_2O PEEP. The higher ONSD values in our study at 15 mmHg PEEP suggest a potential dose-dependent relationship between PEEP and ONSD expansion, especially in TBI patients.

The delta change analysis revealed a substantially larger ONSD increase in TBI patients [0.55 mm (IQR: 0.31-0.65)] compared to controls [0.27 mm (IQR: 0.2-0.35)] when PEEP was elevated to 15 mmHg. This finding is particularly noteworthy compared to Bala et al. [2], which reported smaller incremental changes (from 0.44±0.06 cm to 0.49±0.07 cm) with PEEP elevation to 15 cm H_2O in their general patient population. Our observed differential response between TBI and non-TBI patients suggests that brain injury may amplify ONSD sensitivity to PEEP changes.

This enhanced response in TBI patients aligns with Fenerci et al. [20], where patients with midline shifts showed increased vulnerability to PEEP effects, reaching critical ONSD values of 5.73 mm at 10 cm H_2O PEEP. The magnitude of change in our TBI group exceeds the normal PEEP-induced ONSD increases reported by Ertl et al. [21] in healthy volunteers ($\Delta = 0.21$ mm), highlighting the pathophysiological significance of TBI in ONSD response to PEEP.

Our regression analysis revealed that while age and sex showed no significant association with ONSD changes, TBI emerged as an independent predictor (coefficient: 0.340, SE: 0.157, p=0.035). This contrasts with Ertl et al. [21] in healthy subjects, where gender differences were significant and ONSD increased with age ($\Delta = 0.34$ mm). The disparity suggests that pathological conditions like TBI may override normal demographic influences on ONSD responses to PEEP.

However, our results align with Klinzing et al. [22], where TBI patients showed distinct

ONSD responses independent of demographic factors.

The bilateral ONSD measurements in our study showed consistent responses, similar to Suresh et al. [23] findings of strong correlation between right and left eye measurements ($r = 0.879$, $P < 0.001$).

This bilateral symmetry in ONSD response suggests that unilateral measurements might be sufficient for monitoring purposes, though bilateral measurements may provide more comprehensive information. The heightened ONSD response to PEEP in TBI patients suggests the need for careful PEEP titration in this population. This is especially relevant given Chin et al. [12] demonstrate ONSD stability with moderate PEEP (8 cm H_2O) in non-TBI patients.

The single-center design, relatively small sample size, and lack of direct ICP measurements limit generalizability. Long-term outcomes and clinical significance of ONSD changes at different PEEP levels were not assessed.

5. Conclusions:

The TBI patients showed a significant increase in ONSD when PEEP was increased to 15 mmHg, compared to non-TBI controls. The delta change in ONSD between 15 mmHg and 5 mmHg PEEP was substantially larger in the TBI group, suggesting TBI amplifies ONSD sensitivity to PEEP changes. This highlights the need for careful PEEP titration in TBI patients to balance lung recruitment and intracranial pressure management.

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Conflict of Interest: Nil

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