Changes in Optic Nerve Sheath Diameter in Response to Various Levels of End-Tidal Carbon Dioxide in Healthy Patients under General Anesthesia

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Abstract

Background Intracranial pressure (ICP) monitoring is an essential component in management of traumatic brain-injured (TBI) patients. While invasive techniques are associated with many complications, noninvasive nature of ultrasonographic measurement of optic nerve sheath diameter (ONSD) is now becoming popular. Carbon dioxide (CO₂) alters the ICP by changing the size of cerebral vasculature. We aimed to assess the effect of (hypercarbia and hypocarbia) different levels of end-tidal carbon dioxide (EtCO₂) on ONSD.

Methods Thirty adult patients aged between 18 and 65 years, undergoing brachial plexus injury surgery under general anesthesia, were enrolled. Following standard anesthetic protocol, ONSD was measured at different time points of EtCO₂. ONSD was measured at EtCO₂ of 40 and then 30 mm Hg to assess change in ONSD due to hypocarbia (T_{hypocarbia}). Similarly, ONSD was measured at EtCO₂ of 50 mm Hg to assess change in ONSD due to hypercarbia (T_{hypercarbia}). The mean of three ONSD values at each time point was taken as the final value. The generalized estimating equation (GEE) was used to analyze correlation between different levels of EtCO₂ and ONSD.

Results The calculated 95% confidence interval (CI) for the difference of two measures (T_{hypocarbia}, EtCO₂ 40 and 30 mm Hg) on ONSD was −0.056 to −0.036, and the calculated CI for the difference of other two measures (T_{hypercarbia}, EtCO₂ 40 and 50 mm Hg) on ONSD was 0.044 to 0.077, and thus were observed to be significant.

Conclusions ONSD changes significantly in response to different EtCO₂ levels in healthy non-neurosurgical patients under general anesthesia.

Keywords

- ▶ optic nerve sheath diameter
- ▶ end-tidal carbon dioxide
- ▶ intracranial pressure
- ▶ hypocapnia
- ▶ hypercapnia

Introduction

Intracranial pressure (ICP) monitoring is an essential component in the management of traumatic brain injury (TBI). The clinical signs of raised ICP may be unreliable and may reflect relatively late cerebral decompensation. Similarly, papilledema and pupillary signs are late to develop and may not appear for hours after TBI. Moreover, in a sedated patient, clinical assessment may not be possible. Many studies have shown that early detection of elevated ICP with

timely intervention is associated with improved outcome of a TBI patient.¹ ICP may be monitored by invasive or noninvasive techniques. Though invasive techniques show the real-time values of ICP, they are associated with many complications, such as intracranial bleeding and infection, occlusion of the catheter tip by blood, debris, and difficult to locate ventricle in presence of cerebral edema. Moreover, invasive monitoring is contraindicated in presence of coagulopathies (which often accompanies the TBI patients). All these drawbacks of invasive methods can be averted by using noninvasive techniques

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of ICP monitoring. Although they do not show a real-time value, they are excellent tools to detect presence or absence of raised ICP. Elevated ICP can be detected by computed tomographic (CT) scan or magnetic resonance imaging (MRI); however, these techniques are time consuming and require transportation of patients who may be unstable. The quick and noninvasive nature of ultrasonography is fast becoming popular for rapid detection of elevated ICP at bedside in emergency and intensive care unit (ICU) by monitoring the optic nerve sheath diameter (ONSD). Its limitations notwithstanding, ultrasonographic ONSD monitoring is likely to be more reliable than clinical assessment in the diagnosis of intracranial hypertension, especially when the patient is under sedation that precludes proper clinical examination.² Therefore, in recent years, among noninvasive methods, bedside ocular ultrasonography to monitor ICP has gained popularity.^{3,4} Owing to direct communication with brain, intraorbital subarachnoid space around the optic nerve is subjected to the same pressure changes as intracranial compartment. Distension of optic nerve sheath increases its diameter in response to elevated ICP.

Carbon dioxide (CO₂) is a potent modulator of cerebral vascular tone, alters the ICP by changing the size of cerebral vasculature, and thereby cerebral blood flow (CBF), and this action occurs very rapidly over a period of few minutes. In a range of partial pressure of carbon dioxide (PaCO₂) 20 to 80 mm Hg, the CBF changes in a linear manner. End-tidal carbon dioxide (EtCO₂) concentration is a surrogate measure of PaCO₂ (especially in a hemodynamically stable patient with healthy lungs) and is routinely monitored continuously in patients subjected to general anesthesia. To date there is very little literature on the effects of changing EtCO₂ on ONSD. This prompted us to conduct this study to find out the effects of different levels of EtCO₂ on ONSD.

Materials and Methods

This observational study was performed after obtaining approval from the institutional ethics committee (Ref no.—IEC 128/05.02.2016, RP-23/2016). The study included American Society of Anesthesiologists (ASA) class I patients in age group of 18 to 65 years undergoing surgery for brachial plexus injury under general anesthesia. Patients with history of cardiopulmonary disease, smoking, eye disease/injury, and nonconsenting patients were excluded from the study. This was a crossover study, and the sequence of normocapnia, hypocapnia, and hypercapnia was randomized using a computer-generating program. Allocation concealment was done with the help of a sealed opaque envelop technique.

Preanesthesia checkup was performed a day prior to surgical procedure. Premedication consisted of oral ranitidine 50 mg and metoclopramide 10 mg orally 1 hour prior to induction of anesthesia. In the operating room, electrocardiogram (ECG), pulse oximeter (SpO₂), and noninvasive blood pressure (NIBP) cuff were attached. Anesthesia was induced with 2 µg/kg of intravenous (IV) fentanyl and 2 mg/kg of propofol. An appropriately sized laryngeal mask airway (LMA) was inserted without administering muscle relaxant. Anesthesia was

maintained with continuous infusion of 100 to 300 µg/kg/min of propofol with oxygen and air (1:1) along with intermittent fentanyl (1 µg/kg) administered hourly.

Mechanical ventilation was initiated with a fixed tidal volume of 8 mL/kg and adjusting respiratory rate (RR) to obtain the desired EtCO₂. Patients were given approximately 30-degree head-up tilt. After approximately 10 minutes, ONSD was measured by using 6 to 13 MHz linear probe of ultrasound machine (Sonosite S-Nerve; Bothell, Washington, United States) at EtCO₂ 30, 40, and 50 mm Hg. Sequence of measurement was determined by randomization. Ultrasonography was performed by the author (IK) who had sufficient experience of performing this procedure. The patients' eyes were covered with a transparent film, and a water-soluble jelly was applied over the probe. The probe was gently placed on the eyelid paying careful attention to exert minimal pressure on the eyeball. The probe was slid from temporal to nasal end to find a suitable angle for displaying the entrance of the optic nerve into the globe. The probe was adjusted to bring optic nerve in the center of ultrasound screen for measurement of size. The diameter was measured 3 mm behind the globe in fixed transverse plane. The diameter was measured 5 minutes after achieving the desired EtCO₂ level. Three measurements were taken at each EtCO₂ level in an eye, and average of the three readings was taken as final ONSD value. The person conducting the ultrasound was blinded to the EtCO₂ values. Other parameters such as SpO₂, heart rate (HR), and BP were also recorded simultaneously.

Data analysis was performed using software Stata 11.0 (College Station, Texas, United States). Data were summarized as mean ± standard deviation (SD). The effect of various levels of EtCO₂ on ONSD was compared using generalized estimating equation (GEE)—population averaged model with exchangeable correlation. The stability of hemodynamic parameters over various levels of EtCO₂ was also analyzed using GEE method. A *p*-value < 0.05 was considered significant.

Results

Total 30 patients participated in the study conducted over a period of 4 months, and data from all were analyzed. All patients were male with a mean age of 29.8 (8.84) years and mean weight of 65.6 (8.81) kg. Different hemodynamic parameters at all three values of EtCO₂ such as HR₃₀ (73), HR₄₀ (74), HR₅₀ (72), SBP₃₀ (105), SBP₄₀ (109), SBP₅₀ (105) and DBP₃₀ (62), DBP₄₀ (65), DBP₅₀ (63) were comparable (►Table 1).

The calculated 95% confidence interval (CI) for the difference of two measures (T_{hypocarb}, EtCO₂ 40 and 30 mm Hg) on ONSD was -0.056 to -0.036, and the calculated CI for the difference of other two measures (T_{hypercarb}, EtCO₂ 40 and 50 mm Hg) on ONSD was 0.044 to 0.077, and thus were observed to be significant (*p* < 0.0001) (►Table 2).

Discussion

In this study, we monitored the effect of hypocarb and hypercarb on ONSD. We observed a rapid response in ONSD with changes in EtCO₂. This again highlights the fact that

Table 1 Demographic and clinical profile (baseline)

Patient characteristics	Mean (SD)
Age (y)	29.8 (8.84)
Weight (kg)	65.6 (8.81)
HR (beats/min)	75.7 (9.67)
SBP (mm Hg)	121.8 (10.44)
DBP (mm Hg)	74.7 (10.22)

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure; SD, standard deviation.

Table 2 Change in ONSD in response to different EtCO₂ levels

	Mean (cm) (SD±)	Coefficient (95% CI)	p-Value
ONSD (40 mm Hg)	0.34 (0.04)		
ONSD (30 mm Hg)	0.29 (0.05)	-0.05 (-0.06, -0.04)	< 0.0001
ONSD (50 mm Hg)	0.40 (0.05)	0.06 (0.04, 0.08)	< 0.0001

Abbreviations: CI, confidence interval; EtCO₂, end-tidal carbon dioxide; ONSD, optic nerve sheath diameter; SD, standard deviation.

optic nerve being in direct communication with the brain, the pressure changes in the latter are reflected in the ONSD. The alteration in ONSD was immediate in response to EtCO₂ changes; moreover, changes in ONSD were parallel to the EtCO₂ changes. Since CBF and cerebral blood volume change in response to changes in PaCO₂, the ONSD also changes accordingly.

Over the years, advancements in monitoring of ICP have enabled the diagnosis of elevated ICP reliably by noninvasive techniques.⁵ ONSD measurement using bedside ultrasound has been shown to correlate with clinical and radiologic signs and symptoms of raised ICP.⁶⁻⁹ Despite the association between ONSD and PaCO₂,¹⁰ there is scanty literature on ONSD responsiveness to a more dynamic surrogate of PaCO₂, that is, EtCO₂. The pertinent advantages of EtCO₂ over PaCO₂ measurement is that the former is continuously monitored under anesthesia and avoids time-consuming process of arterial blood gas sampling.^{11,12} Moreover, the sensitivity of ICP to even small fluctuations in EtCO₂ has been reported in the literature.¹³ Animal studies have estimated that the rate of this increase in ONSD by 0.0034 mm/mm Hg increase in ICP.¹⁴

The ONSD was minimum (0.29 cm) at EtCO₂ 30 mm Hg and maximum (0.40 cm) at EtCO₂ 50 mm Hg, whereas it was 0.34 cm at EtCO₂ 40 mm Hg. These changes in ONSD are direct representation of changes in ICP brought about by changes in CBF due to PaCO₂ changes. Our results correlate well with the study by Kim et al.¹⁵ They studied ONSD responsiveness at two levels of EtCO₂, 40 and 50 mm Hg, each measured at 1 and 5 minutes, and observed significant changes in the diameter of ONSD. According to the available literature, the upper limit of ONSD used to define ICP greater than 20 mm Hg (raised ICP) ranges from 0.48 to 0.57 cm.^{6,9,16} In our study, the upper limit of ONSD at EtCO₂ level 50 mm Hg was average of 0.40 cm, which implies that even at EtCO₂ 50 mm Hg, intracranial hypertension is a remote possibility in healthy non-neurosurgical patients with normal brain compliance, and thus it may not be clinically significant. Factors such as position of patients, time of measurement after achieving target EtCO₂,

measuring ONSD in a single plane (transverse), and involving same experienced operator were kept constant, thereby avoiding any confounding factors.

The limitation of this study is that it was conducted in non-neurosurgical patients with normal brain compliance. Thus these results cannot be applied to patients with disturbed brain compliance in whom ONSD may behave in different manners in response to EtCO₂ alterations.

We conclude that ONSD changes significantly in response to different EtCO₂ levels in healthy non-neurosurgical patients under general anesthesia.

Conflict of Interest

None.

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