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Effect of bronchoscopy on intracranial hypertension during different regimen of sedation by optic nerve sheath diameter

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Abstract

Objectives: Fiberoptic bronchoscopy (FOB) is a useful method for ventilator-associated pneumonia (VAP), aspiration, and atelectasis, especially in intensive care units. (ICU) We aimed to investigate the effect of FOB on intracranial pressure by ultrasonographic optic nerve sheath diameter (uONSD) during different sedation protocols in a tertiary ICU. *Methods:* Prospective randomized study included the patients with two groups as superficial (Group M; midazolam) and deep sedation (Group P; propofol). FOB was performed for VAP or aspiration and intracranial hypertension (ICH) was measured with uONSD, noninvasively. The values of uONSD were noted pre-procedure, on sedation, 1st – 5th, and 15th minute of the procedure. In addition, mean arterial pressures (MAP), oxygen saturation, and heart rate values were recorded from the monitor. *Results:* The mean age and indications of FOB for 33 patients as Group M (n=17) and Group P (n=16) were similar to each other. ONSD was increased with the procedure in both groups but in group P it was stabilized from the 5th minutes of FOB whereas became higher progressively in group M (p<0,001). Postoperative MAP values that may have an important role for ICH were also increased in Group M (MAP was 70.65 ± 16.18 at time of sedation in Group P and 75.63 ± 13.76 in Group M)**.**
Conclusion: This study showed that bronchoscopy results as a significant increase for OSND in both groups but that was less high in patients who had deep sedation with propofol and it returned to baseline after the procedure.

Keywords: Bronchoscopy, intensive care unit, optic nerve, propofol

INTRODUCTION

Fiberoptic bronchoscopy (FOB) is a tool to research for respiratory symptoms such as hemoptysis, wheezing, or coughing.[1-4] It is also used for both diagnoses of ventilator-associated pneumonia (VAP) and treatment of atelectasis – aspiration, especially in intensive care units (ICU).[2,3] Although major complications such as hypoxia, arrhythmia, pneumothorax have been reported in the literature, there are few studies showing the effects of FOB on cerebral hemodynamics.[5-7]

Intracranial pressure above 20 mmHg is defined as intracranial hypertension (ICH). Intraventricular and intraparenchymal measurements are the gold standard methods for ICH.[8] However, these techniques has limitation in clinical practice because of the risks, such as infection and bleeding.[9] Ultrasonographic measurement of optic nerve sheath diameter (uONSD) is a new non-invasive method that have been reported to be reliable when compared with invasive techniques.[8-10] It has been noted that the normal value of ONSD is 4.5mm, and it indicates intracranial pressure above 20 mmHg when it is measured above 5 mm.[8-10] Recent studies examining the effects of FOB was measured invasively using ventriculostomy drain.[5-9]

Volume changes of cerebrospinal fluid (CSF), skull, vascular, parenchymal structures are important for the intracranial pressure (ICP) and some maneuvers like coughing and straining may cause ICH.[9-11] Especially, cough increases intrathoracic pressure and central venous pressure (CVP), which affects CSF pressure so using deep sedation can prevent ICH.[12] High CVP has also been shown to increase ICP through several

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mechanisms, such as, decreased venous return to the heart, hypercapnia and respiratory acidosis.[11] Also, it is known that high airway pressures in mechanical ventilation may cause hemodynamic changes by increasing pleural pressures and causing a functional obstruction in the cerebral venous outlet through the jugular venous system.[13] In this study, we aimed to identify a regimen of anesthesia and sedation that could confer protection against increases in ICP during FOB by uOSND in ICU, noninvasively.

METHODS

Between March 2018 and July 2019, 33 patients needed FOB for diagnosis of VAP or aspiration in an ICU, a tertiary hospital. Patients with a history of head trauma, intracranial surgery, intracranial mass, using corticosteroid treatment, having bleeding diathesis, hemoglobin levels less than 10 mg/dl, pregnant women, and patients under 18 years of age were excluded from the study. And if patients in continuous sedation need extra doses, they were excluded too. This randomized prospective study was conducted in accordance with the Helsinki Declaration and with the permission of the Abant Izzet Baysal University Hospital ethics committee (Local Ethics Number: 2018/69). Written informed consent was obtained from first-degree relatives of all patients.

Anesthesia

All patients were intubated in ICU. Volume-controlled ventilation modes were preferred during FOB. The inspired FiO2 was raised to 100% before the procedure. Mean blood pressure, heart rate, oxygen saturation, and blood gas values were closely monitored during the procedure. Enteral feeding was stopped at least 6 hours before the procedure. The endotracheal tube position was checked at the end of the procedure. FOB was performed using a mobile bronchoscopy (Storz FB; 5.0 mm outer diameter). Patients were randomized into two groups by an anesthetist specialist who was blinded to the study. Patients in Group M received i.v. 0:02 to 0:04 mg / kg midazolam (zolamid 15 mg / 3 mL, and medications, Turkey), whereas patients in Group P received propofol i.v. 1.5 to 2.5 mg / kg(1% propofol, Fresenius, Turkey) were given. Neither any of the opioids such as fentanyl, remifentanil nor the muscle relaxants were used before the procedure.

Optic nerve sheath diameter

ONSD was performed with the B-Mode setting with the 6-10 MHz linear probe of the ultrasound device (L38/10-5 Mhz Transducer, SonoSite, Inc. Bothell, WA98021USA.). During measurements, the patients were placed in the supine position and the eyelid was closed with stretch film to protect the eyeball while the eyelids were closed. All ONSD measurements were performed by a single researcher experienced in the use of ultrasound who was blinded to the study. The transverse image of the eyeball was obtained in the axial plane without pressure on the eyeball using the high-frequency linear transducer. The best image was obtained for the optic nerves of both eyes and the image was frozen and the cursor was placed 3 mm posterior from the papilla to the external contours of the optic nerve and the measurement was completed. All values greater than 5.0 mm were evaluated as an ICH. The ONSD was measured by ultrasonography pre-procedure (T1), on sedation (T2), 1st minute (T3) - 5th minute (T4), and 15th minute (T5) of the procedure.

Statistical analysis

Univariate comparisons were made using various statistical tests. The normality of continuous variables was evaluated by Shapiro-Wilk tests. Variables showing normal distribution were analyzed by independent samples t-tests. Mann-Whitney U tests were used for continuous variables without normal distribution. Bonferonni corrected paired sample t-tests were used to compare the variables between the two groups. Categorical variables were analyzed by Chi-square test, and Fisher's exact correction was performed when necessary. After adjusting age, sex and BMI, multivariate repeated measures ANOVA was performed to see the effect of time and drug. Significance was set at $p < 0.05$ and analyzes were performed using the Social Sciences 25.0 Statistical Package for Windows (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Thirty-three patients, 17 female, and 16 male were included in two groups as Group M (n = 17) and Group P (n = 16) for this study. Bronchoscopy was performed on patients for diagnosis of VAP or aspiration. In both groups, mean age (Group M: 76.94±11.51; Group P: 68.75±19.30) and duration of the procedure (15 minutes) were similar. Also, physiological changes between the groups for arterial blood gas (pH, PCO2, PO2, SpO2, and lactate values) before and after the procedure were similar too. However, in Group M, heart rate and MAP values were elevated at all times of periods during the procedure. (Table 1) Repeated measurements according to the Greenhouse-Geisser corrected ANOVA assessment, there was a statistically significant difference between the time points of the ONSD. ($F(2.957, 82.805) = 0.880$, $p = 0.030$). As a result of post hoc tests using Bonferroni correction, significant differences were observed between T2-T3, T2-T4, and T2-T5 time frames in Group P. The ONSD of the midazolam group has significant increases between all the time periods. ($p < 0.005$) (Table 2) Also the level of ICP in Group P stayed on the

Table 1: Clinical and numerical values of physiological parameters observed during the procedure

	Group M	Group P
Number of patients	17	16
Mean age	76.94±11.51	68.75±19.30
Indication of FOB		
VAP	7	9
Aspiration	10	7
Mean arterial pressure (MAP)		
Pre-p	87.06±11.95	84.71±16.37
Sed	75.63±13.76	70.65±16.18
1st min	91.06±18.38	81.53±25.94
5th min	86.38±12.48	83.35±18.75
15th min	76.75±14.19	72.65±13.1
Heart rate (HR)		
Pre-p	106.71±25.57	95.69±15.86
Sed	106.29±26.49	94.38±22.91
1st min	113.59±30.42	101.63±27.77
5th min	114.53±31.54	100.44±29.53
15th min	115.82±30.53	96.25±24.23
Blood gases		
Ph Pre – p	7.41 ± 0.06	7.44 ± 0.09
15th min	7.39 ± 0.07	7.45 ± 0.08
pC02 pre - p	47.47 ± 10.92	39.94 ± 7.78
15th min	49.35 ± 11.41	39.81 ± 7.88
P02 pre - p	66.12 ± 19.76	70.31 ± 20.76
15th min	74.12 ± 22.15	79.63 ± 20.81
Sp02 pre – p	91.82 ± 9.17	95.25 ± 6.56
15th min	94.41 ± 6.71	95.44 ± 7.8
Lact pre -p	1.35 ± 0.37	1.25 ± 0.54
15th min	1.25 ± 0.37	1.43 ± 0.44
ONSD values		
Pre-p	4.5 ± 0.09	4.8 ± 0.12
Sed	4.4 ± 0.08	4.4 ± 0.08
1st min	4.9 ± 0.10	4.8 ± 0.07
5th min	5.3 ± 0.07	5.1 ± 0.06
15th min	5.4 ± 0.08	5.1 ± 0.07

Data expressed as mean ± SE. Paired samples t-tests were used. (lact: lactate, Sp 02: oxygen saturation, p02: oxygen pressure, pCo2: carbon dioxide pressure ONSD : optic nerve sheath diameter) (PreP : T1, sed : T2 , 1st min : T3, 5th min : T4, 15th min : T5)

Table 2: Comparison of ONSD measurements between groups with time points

	Group M (n=17)	Group P (n=16)
T1-T2	0.123	0.213
T1-T3	0.098	0.755
T1-T4	**<0.001**	0.419
T1-T5	**<0.001**	0.454
T2-T3	0.028	**0.004**
T2-T4	**<0.001**	**<0.001**
T2-T5	**<0.001**	**0.003**
T3-T4	0.042	0.093
T3-T5	0.021	0.181
T4-T5	0.540	0.937

p-values obtained with paired samples t-tests. The bold p-values indicate statistical significance with Bonferroni correction at $\alpha/10=0.005$.
(PreP : T1, sed : T2 , 1st min : T3, 5th min : T4, 15th min : T5)

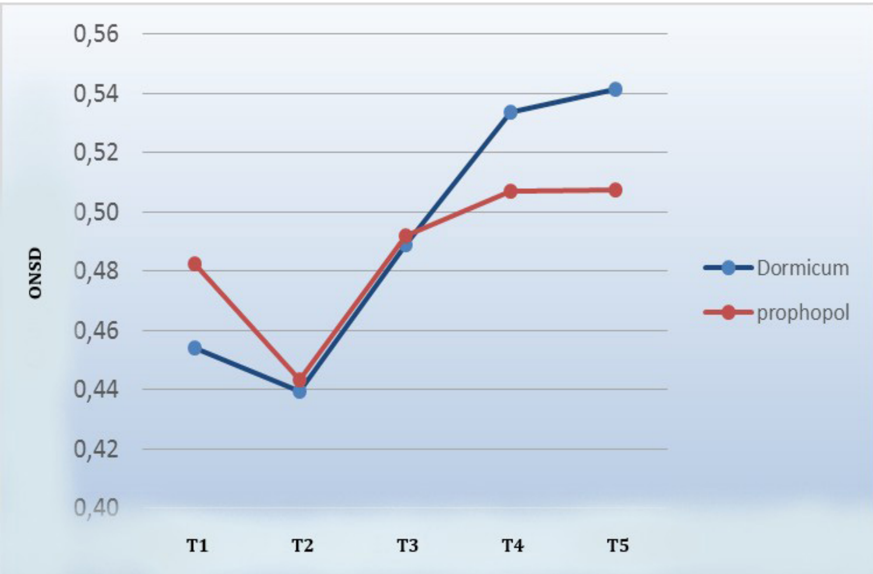

Figure 1. Measurements of ONSD between time intervals of two groups

same line during T3, T4, and T5 while ICP had been increasing all of the periods in Group M. (Figure 1). No neurological complications were observed in the postoperative period.

DISCUSSION

In our study, we evaluated the effects of bronchoscopy on ICP during different regimens of sedation with ultrasound-guided OSND before and after procedure non-invasively. All patients were divided into two groups as superficial (Group M) and deep (Group P) sedation. When a significant increase of OSND was observed between all time periods in Group M, there was a less increase and a parallel course after the 5th minute in Group P. Also we found that this increase was nearly the same as pre-procedure in group P.

Bronchoscopy is considered to be technically safe, but it is not completely uncomplicated. It has some risks of hypoxemia, hypercarbia, and respiratory failure, especially secondary to airway obstruction. Also, it may cause various complications such as arrhythmia, bleeding, hypotension/hypertension, pneumothorax, and ICH.[3-7]

Several factors that may lead to an increase in ICP during FOB should be considered. First of all, the position of the patient's head is important because ICP may be affected by resistance to venous outflow.[11] Second, the neck is extended to maximize the patient's airway patency especially critical for cerebral perfusion pressure in severe trauma.[12,14] Also while small changes in circulating volume within physiological limits may not cause pressure changes, ICP may change even with a minor increase especially in patients with trauma in ICU.[12] So it is recommended to avoid FOB, especially in the first 24 hours in such patients. Baiwa *et al*.[15] examined patients with cranial trauma who had both FOB and cranial computed tomography and found increased intracranial pressure findings on CT in 29 patients after FOB, retrospectively. They reported when patients were sedated with meperidine and atropine, there was no evidence of neurological complications was observed after 6 weeks post-procedure. In our study, ONSD was 4.9 ± 0.100 mm in Group M, while it was 4.8 ± 0.070 mm in Group P on 1st minute of the procedure(T3). And ONSD was stabilized on the 5th and 15th minutes of FOB in Group P whereas it became higher progressively in Group M ($p<0.001$).

In severe head trauma, it was concluded that high ICH may be balanced with the increase in MAP and sufficient CPP was maintained. Peerles *et al*.[16] anesthetized fifteen patients that had a brain injury, in need of FOB with thiopental and lidocaine and examined the values of ICP, MAP, and cerebral perfusion pressure(CCP) before and after the procedure with intracranial monitoring. They found an average increase in ICP after FOB 13.5 mm Hg above basal values. However, ICP has been shown to return to basal levels after treatment. In their study, the mean increase in MAP was 92.3: ±: 16.1 mm Hg to 111.5 ± 13.9 mmHg when ICP was highest. Similarly, in our study, MAP had increased from the beginning of the procedure in both groups. However, in Group P, the rises of the MAP values were less high than in group M. MAP was 70.65 ± 16.18 on sedation(T2) in Group P and 75.63 ± 13.76 in Group M. This was thought to be related to the depth of anesthesia. Kerwin *et al*.[7] used vecuronium, morphine sulfate, and midazolam as standard anesthetic regimens to prevent ICP increase during FOB, but they could not provide sufficient sedation or analgesia. These studies have shown that optimal sedation is required to reduce intracranial response during FOB and better comfort is achieved by the addition of muscle relaxants to the standard regimen.

There are much data in the literature about the effects of tracheostomy and endotracheal maneuvers on ICP. Some reasons for the ICH by endotracheal suctioning may be the stimulation of the airways, which may be due to the cough reflex, as well as to the endotracheal tube and PEEP.[18-22] These procedures have been suggested that should be performed with anti-edema treatment in patients in ICU. It has emphasized that the need to determine appropriate analgesia and sedation regimens in order to reduce this effect.[6,17] In a recent study, tracheostomy was performed in a group of patients at risk for ICP in neurology ICU. In that study, atropine, propofol, fentanyl, and atracurium were used and anti-edema treatment was started when the ICP exceeded 30 mmHg.[17] A recent study with endotracheal aspiration, lidocaine (1.5 mg/kg) before in 10 patients receiving head trauma anti-edema treatment and compared the results with placebo group given saline.[23] They found that although ICP increased above 20 mm Hg in all patients, the increase in ICP in lidocaine-treated group was lower than the increase in the placebo-treated group. To prevent ICP increase during intubation, White *et al*.[24] used i.v. fentanyl, lidocaine, thiopental. They suggested that neuromuscular blockers used in combination with topical anesthetics may be the most effective combination to prevent increases in ICP associated with endotracheal aspiration.

In our study, we performed routine sedation for FOB. We determined our sedation application deeply and superficially and researched the changes in ONSD. In patients who were given propofol and increased depth of anesthesia, fewer reflexes such as retching and straining during the procedure and a more stable HR value of the patients led to a less increase in the ONSD, thus reducing the increase in intracranial pressure.

There are some limitations of our study. Although evidence of persistent intracranial hypertension after FOB has not been demonstrated, we did not record the Glasgow coma score. Second of all, other factors influencing ICP like airway pressures, ETCO2 during bronchoscopy can be considered. Further studies are necessary with a large number of patients to identify ICP changes, especially in the population.

In conclusion, we suggest that patients who performed bronchoscopy with propofol had a lesser increase and a stable line in ONSD when compared to those receiving midazolam in the ICU population. As emphasized in our study, a regimen of anesthesia and sedation can be preferred for protection against increases in ICP during FOB measuring the diameter of optic nerve sheath by ultrasonographic method non-invasively.

DISCLOSURE

Availability of data and material: The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

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Conflicts of interest: There were no conflicts of interest in this study.

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