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Randomized Trial

The Effect of Different Posture on Normal Saline Injection in Optic Nerve Sheath Diameter in Thoracic Epidural Anesthesia

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Background: Thoracolumbar or caudal epidural anesthesia affects intracranial pressure (ICP) in both animals and humans. Epidural injection increases ICP at least transiently. Measurement of the optic nerve sheath diameter (ONSD) using ultrasonography is one of the noninvasive methods for ICP assessment.

Objectives: The purpose of this study was to investigate the effect of the different posture during epidural saline injection to the ONSD under awake conditions.

Study Design: Prospective, randomized trial.

Setting: An interventional pain management practice in South Korea.

Methods: This study included 44 patients receiving thoracic epidural catheterization for pain management after upper abdominal or thoracic surgery. Following successful epidural space confirmation, patients were randomized to receive epidural saline while supine (A group) or in sitting position (B group), respectively. Transorbital sonography was performed for the measurement of the ONSD, and the ONSD was measured at 3 mm posterior to the optic nerve head.

Results: Both A and B groups showed significant increases of ONSD according to time. Mean ONSD values measured at T10, T20, and T40 significantly increased from the baseline value (T0) ($^{*}P < 0.05$ vs. T0, $^{\dagger}P < 0.001$ vs. T0, $^{\ddagger}P < 0.005$ vs. T0). The mean ONSD values measured at any of the time points and degrees of changes (T10-T0, T20-T0, and T40-T0) between groups A and B did not show any significant changes.

Limitations: Epidural pressure and ONSD measurement can make this study more reliable. Further study showing changes of epidural pressure with ONSD measurement is required.

Conclusions: Thoracic epidural injection of 10 mL of normal saline resulted in a significant increase of ONSD compared with the baseline. However, the different posture did not affect the increase of ONSD.

Key words: Epidural, optic nerve sheath diameter, posture, saline

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Analgesia using a thoracic epidural catheter is one of the popular methods for postoperative pain control of hepatobiliary, thoracic, or gastric surgery due to its favorable safety and efficacy. (1-3).

Previous studies showed that thoracolumbar or caudal epidural anesthesia affected intracranial pressure (ICP) in both animals and humans. Epidural injection increases ICP at least transiently (4-6). Increased ICP has long been considered as a contraindication to epidural anesthesia. Early diagnosis and management of increased ICP plays an essential role for preventing brain damage. Despite the importance of increased ICP during surgery, ICP is rarely monitored intraopera-

tively due to invasiveness of ICP measurement. Direct measurement of ICP includes measuring pressure in the ventricle or the brain parenchyma directly (7). However, such an invasive method makes the popular use of ICP monitoring difficult. One of the noninvasive methods for ICP assessment is using the optic nerve sheath diameter (ONSD) measurement by ultrasonography (8-10). Numerous studies suggested that ONSD correlates well with the degree of ICP and is able to detect intracranial hypertension (7-10). Optimal cutoff point for identifying increased ICP was 5.5 mm (11).

Epidural pressure changes have been demonstrated to reflect real-time changes in ICP. Both ICP and epidural pressures have been shown to reach peak pressure just after epidural injection and begin decline thereafter. After decline, epidural pressure starts to maintain residual pressure approximately 30 seconds after completion of injection (4,5,12-14). Our previous study demonstrated that different speeds of the injection of normal saline did not affect the increase of ONSD. The residual epidural pressure, not the peak epidural pressure, is thought of as a main factor to determine the increase of ONSD (6,15).

Cervical and thoracic epidural pressure demonstrated lower epidural pressure in the sitting group compared with the lateral or prone group (16,17). In addition, the lumbar epidural pressure measured in patients with spinal stenosis demonstrated dynamic changing patterns depending on body position with higher epidural pressure compared with the normal individual patient (18,19). Variable patient position also influenced the extent of spread of contrast medium during the thoracic epidural injection (20).

We hypothesized that lower epidural pressure while sitting (16,17) can affect the increase of ONSD because epidural pressure is closely related to the changes of ICP (4,12,13).

The primary endpoint of this study was to compare the values of ONSD using ultrasonography measured in 2 groups (supine vs. sitting) with thoracic epidural saline injection.

Methods

Patients

This prospective and randomized study was approved by the institutional review board (IRB #11-039-004) of our institution. Written and verbal information about the potential benefits and risks of the study were provided. All patients provided informed consent. This study was registered before patient enrollment at clinical trials.gov (NCT03785314, date of registration: December 20, 2018).

Inclusion criteria were patients undergoing hepatobiliary, pancreas, lung, and gastric surgery due to cancer scheduled to receive thoracic epidural catheterization for postoperative pain control. Eight patients refused to participate in this study; therefore final enrollment included 44 patients aged between 19 and 79 years (January–December 2019). Patients with the following conditions were excluded: coagulopathy, infection, previous history of thoracic spine surgery, ophthalmic disease, and history of increased ICP.

Procedure of Thoracic Epidural Catheter Insertion

A pain physician with more than 14 years of experience in C-arm-guided intervention performed all thoracic epidural catheterization 1 day before the elective surgery at the pain management clinic. In the prone position on a fluoroscopy table, the patient's upper back was draped in a sterile fashion. An 18-gauge Tuohy needle was inserted slowly via the paramedian approach targeting the interlaminar space of the eighth to ninth thoracic vertebra. Epidural space was confirmed using loss of resistance with air when the Touhy needle approached the expected spinolaminar line using a lateral view. Final thoracic epidural space was confirmed in the anteroposterior (AP) and lateral views using 2 mL of contrast medium. All AP and lateral fluoroscopic views were saved on the hard disc of the C-arm after confirming the successful epidural injection. After final confirmation of epidural space, an epidural catheter was inserted through the Touhy needle and advanced until the seventh thoracic vertebrae. The catheter was firmly fixed with an adhesive plaster.

Group Allocation

This study focused on measuring the ONSD using ultrasonography with different patient posture. Therefore patients in groups A and B were randomly assigned to receive 0.9% normal saline while supine (A group) or sitting (B group) using a computer-generated randomization table. Normal saline was injected through an epidural catheter just after finishing each procedure. Patients of groups A and B were asked to switch to supine or sitting to be injected with normal saline. The assigned position of groups A and B was maintained until serial measurement of ONSD was completely finished.

Measurement of ONSD

One investigator with experience of more than 100 cases of ONSD measurement and fully experienced with previous studies (6,20,21) measured ONSD using saved ultrasonography images. This investigator was blinded to the group assignment.

Transorbital sonography using a hockey stick probe (Logiq S8; GE Healthcare, Milwaukee, WI) was performed to measure ONSD. The power output was reduced (mechanical index, 0.2; thermal index, 0) to minimize the risk of ultrasound-induced eye injury. Patients were asked to close their eyes, and a sterile gel was applied on each closed upper eyelid. The hockey stick probe was gently placed to minimize the exerted pressure on the eyeball. The probe was moved using the heel-toe method to capture the best axial image of the orbit in the plane of the optic nerve. The depth parameter was controlled within 3.0 to 4.0 cm. ONSD was measured 3 mm posterior to the optic nerve head (Fig. 1) (5,6,22). ONSD images were obtained when the postural effects were stabilized with no further external stimuli.

Each ONSD was measured serially in each eye at the following time points: before (baseline, T0), 10 minutes (T10), 20 minutes (T20), and 40 minutes (T40) after injection of normal saline.

At each time point, to obtain more accurate value of ONSD, this measurement was performed twice on the right and left side, respectively. Therefore the mean value of the 4 measurements was considered to be the ONSD at each time point. If the measured ONSD was more than 5.5 mm, which was the cutoff point of the previous study, such patients were considered to have increased ICP (11).

After finishing the ONSD measurement, presence of possible complications of increased ICP such as headache, nausea, vomiting, dizziness, or blurred vision were checked. Patients were sent to their admission room if no complications related to increased ICP or the procedure of thoracic epidural catheterization were found.

Statistical Analysis

This study was designed to identify whether there would be any differences in ONSD according to the position of normal saline injection. Previous study demonstrated that a difference in ONSD greater than 0.5 mm (10% of mean ONSD in asymptomatic normal adults [mean ONSD 4.9 mm]) would be clinically relevant (11). Twenty patients were required in each group considering a significance level of 5%, a power of 80%, and a dropout rate of 15%.

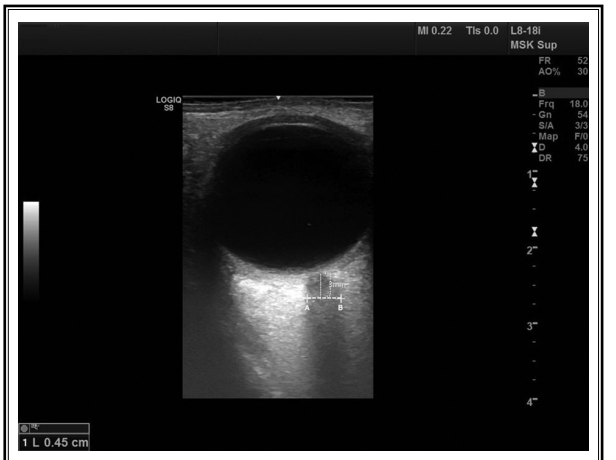

Fig. 1. *ONSD measurement by ultrasonography. ONSD was measured 3 mm posterior to the optic nerve head (A-B) in the axial image of the orbit in the plane of optic nerve.*

Continuous variables are presented as mean (standard deviation [SD]) or median (interquartile range). Categorical variables are presented as number (percentile). Demographic data were compared by unpaired t-test, the χ^2 test, or the Fisher exact test. The repeated measurement of ONSD was performed to evaluate the differences between the 2 groups by repeated-measures analysis of variance. Intergroup comparison of the changes in ONSD over time was performed through group-by-time interaction. Post hoc analyses for ONSD with Bonferroni correction were performed. All statistical values were 2-tailed, and P values < 0.05 were considered to be statistically significant. Statistical evaluations were performed using SPSS Version 22.0 (IBM Corporation, Armonk, NY).

Results

Eligibility was assessed in 52 patients, and 44 of these patients completed the study (January–December 2019) without dropout (Fig. 2). Demographic data and type of disease requiring thoracic epidural catheterization were compared between groups A and B. The number of male patients was nearly twice that of female patients. Various surgeries of lobectomy of lung or liver, Whipple's operation, donor surgery for liver transplantation, and laparoscopic gastrectomy were included (Table 1).

Both groups A and B showed significant increases of ONSD according to time. Mean ONSD values mea-

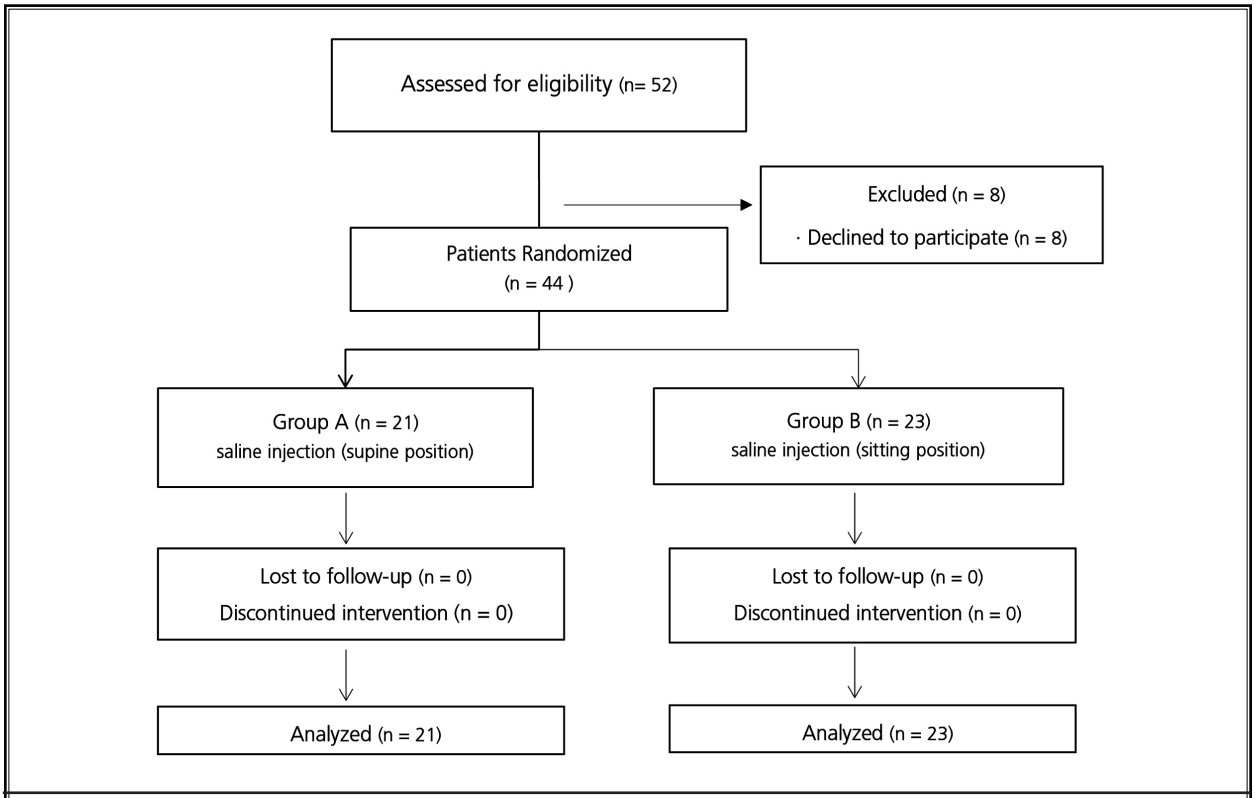

Fig. 2. *Flow chart showing patients who participated in this study.*

Table 1. *Demographic data and type of disease required for thoracic epidural catheterization.*

	Group A (n = 21)	Group B (n = 23)	*P* Value
Gender (male/female)	14/7 (66.7/33.3)	17/6 (73.9/29.5)	0.599
Age (years)	54.6 ± 15.0	62.2 ± 11.0	0.177
BMI (kg/m^2)	25.0 (24.0–26.5)	23.2 (21.0–26.0)	0.071
Type of disease			
Gastric cancer	4 (19.0)	12 (52.1)	
Lung cancer	8 (38.0)	4 (17.4)	
Hepatobiliary cancer	6 (28.5)	5 (21.7)	0.175
Pancreas cancer	1 (4.7)	1 (4.3)	
Donor for liver transplantation	2 (9.5)	1 (4.3)	

Values are presented as mean ± SD or median (interquartile range) for quantitative variables and n (%) for qualitative variables. There were no significant differences between Groups A and B. Group A: injection of normal saline with supine position. Group B: injection of normal saline with sitting position.

sured at T10, T20, and T40 significantly increased from the baseline value (T0) ($^{*}P < 0.05$ vs. T0, $^{\dagger}P < 0.001$ vs. T0, $^{\ddagger}P < 0.005$ vs. T0; Table 2, Fig. 3). Both groups A and B showed peak values of ONSD at T40. The mean ONSD values measured at any of the time points and degrees of changes (T10-T0, T20-T0, and T40-T0) between groups A and B did not show any significant changes (Tables 2 and 3). Although there was no significance, the degree of changes at T40 was more pronounced in group A compared with group B. From T10, nearly half of patients in both groups started to demonstrate ONSD of more than 5.5 mm (Table 4).

Possible complications of increased ICP such as headache, nausea, vomiting, dizziness or blurred vision were not found.

Discussion

Significant increases of ONSD after epidural saline or local anesthetic injection were reported through previous studies. If injected epidural volume was higher, the level of increase of ONSD was more pronounced, although the speed of injection did not show such a

Table 2. *Mean values of ONSD at each time point.*

	Group A (n = 21)	Group B (n = 23)	Adjusted *P* Value
ONSD (mm)			
T0	5.06 (0.43)	5.07 (0.41)	> 0.999
T10	5.36 (0.56)*	5.39 (0.55)*	> 0.999
T20	5.65 (0.44)†	5.65 (0.72)‡	> 0.999
T40	5.94 (0.64)†	5.73 (0.55)†	0.716

Values are presented as mean (SD). Adjusted *P* value indicates the Bonferroni-corrected *P* value. *$P < 0.05$ vs. T0; †$P < 0.001$ vs. T0; and ‡$P<0.005$ vs. T0 in each group. T0, baseline; T10, 10 minutes after epidural normal saline injection; T20, 20 minutes after epidural normal saline injection; T40, 40 minutes after epidural normal saline injection. Group A: injection of normal saline with supine position. Group B: injection of normal saline with sitting position.

Table 3. *Degree of changes in ONSD between time points.*

	Group A (n = 21)	Group B (n = 23)	Adjusted *P* Value
Changes in ONSD (mm)			
T10-T0	0.36 (0.53)	0.32 (0.52)	> 0.999
T20-T0	0.65 (0.50)	0.59 (0.66)	> 0.999
T40-T0	0.94 (0.36)	0.67 (0.54)	0.171

Values are presented as mean (SD). Adjusted *P* value indicates the Bonferroni-corrected *P* value. T0, baseline; T10, 10 minutes after epidural normal saline injection; T20, 20 minutes after epidural normal saline injection; T40, 40 minutes after epidural normal saline injection. Group A: injection of normal saline with supine position. Group B: injection of normal saline with sitting position.

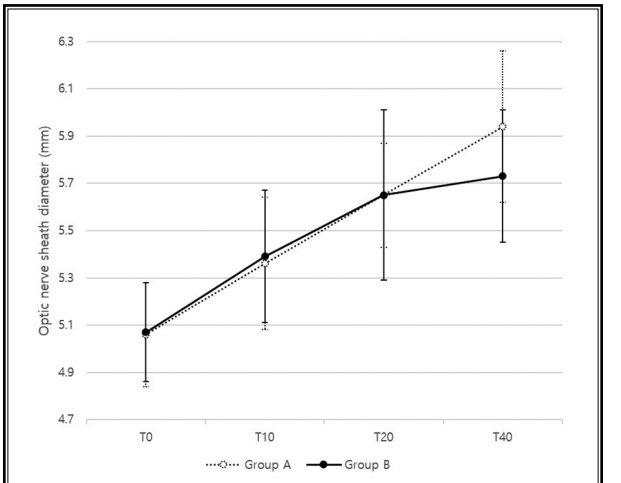

Fig. 3. *Changes in ONSD according to time. Values are mean ± SD. T0, baseline; T10, 10 minutes after epidural normal saline injection; T20, 20 minutes after epidural normal saline injection; T40, 40 minutes after epidural normal saline injection. Group A: injection of normal saline with supine position. Group B: injection of normal saline with sitting position.*

relationship (5,6,23). This study investigated whether different posture (supine vs. sitting) has any attenuating effect on such increase of ONSD after injection of epidural saline. Our hypothesis was that lower epidural pressure while sitting (16,17) can result in the attenuation of increase of ONSD because epidural pressure is closely related to the changes of ICP (4,12,13). However, mean ONSD values in group B (sitting) did not show any attenuation compared with group A. Although there was a tendency of supine position (group A) showing higher increase of ONSD at T40, this trend was not statistically significant between the 2 groups.

In this study, 10 mL of normal saline was injected in the low-thoracic level via epidural catheter. The epidural pressure and incidence of true subatmospheric (negative) pressure demonstrated different values according to the measured level of thoracic spine. Mid-thoracic level (T3-5) showed lower epidural pressure compared with low-thoracic level (T7-10). Accordingly, the incidence of true subatmospheric pressure was higher in the mid-thoracic level than the low-thoracic level (24).

Sitting showed lower epidural pressure compared with lateral decubitus position. However, such difference of epidural pressure was compared using pressure transducer just after needle entry into the epidural space without injecting any material (16,17). It is thought that this difference of epidural pressure between sitting and supine is not maintained if any injection is performed, although preinjected epidural pressure is different between the 2 groups. The equilibration of epidural pressure between the 2 groups after injection of normal saline may explain the failure of attenuation of ONSD increases in group B. Further study is required showing pressure changes after normal saline injection in epidural spaces of higher and lower pressure.

Real-time changes of ICP were demonstrated through epidural pressure monitoring. Both ICP and epidural pressures have been shown to reach peak pressure just after epidural injection and begin to decline thereafter. The peak, descent, and residual part are the components of the epidural pressure curve. Among the 3 parts mentioned earlier, the final extent of the block and ICP were determined mainly by the residual epidural pressure (4,12,13,15). A previous animal study using a porcine model showed that peak

Table 4. *Number of patients (%) who showed ONSD more than 5.5 mm.*

	Group A (n = 21)	Group B (n = 23)
ONSD ≥5.5 mm		
T0	0 (0%)	0 (0%)
T10	9 (42.8%)	12 (52.1%)
T20	12 (57.1%)	15 (65.2%)
T40	15 (71.4%)	17 (73.9%)

T0, baseline; T10, 10 minutes after epidural normal saline injection; T20, 20 minutes after epidural normal saline injection; T40, 40 minutes after epidural normal saline injection. Group A: injection of normal saline with supine position. Group B: injection of normal saline with sitting position.

ICP was significantly greater in group R (increased ICP group) after epidural injection, but this difference was not significant by 30 minutes compared with group N (normal ICP group). This result means that although baseline ICP was different between the 2 groups, the residual epidural pressure, which is important for ICP, was equalized after epidural normal saline injection in both groups.

The epidural injected fluid volume led to an increase in epidural pressure. This increase in epidural pressure translated into the subarachnoid space to the optic nerve sheath. The optic nerve is encircled by the expansible subarachnoid space (25). If an ICP is increased by various reasons, cerebrospinal fluid is shifted from the intracranial cavity to the perineural space causing an ultimate increase of ONSD. Previous studies have shown that ONSD values measured by ultrasonography are closely related to ICP and is a noninvasive and valuable method for detecting increases in ICP (7-10).

In adults, increased ICP was associated with prone position and neck flexion when measured directly (26). ICP depends on the cerebral blood volume and cerebrospinal fluid for which the vascular component is influenced by systemic blood pressure, modified by cerebral autoregulation and venous outflow resistance. If cerebral autoregulation and systemic blood pressure regulation is intact, the main determinant of ICP during positional changes is venous pressure (27). Conversely, being prone with neck extension in infants was not associated with changes in ONSD. Pressure transmission between subarachnoid space and optic nerve sheath is not solid and may not directly increase ONSD (28).

This study includes several limitations. First, ONSD was measured with different posture under the assumption of different baseline epidural pressure in such positions demonstrated by previous studies (16,17). However, actual changes of epidural pressure of baseline and after normal saline injection were not measured in this study. Further study is required showing changes of epidural pressure before and after normal saline injection in groups showing different baseline epidural pressure.

Second, after epidural saline injections, the main determinant of ONSD increase is changes of epidural pressure. However, in normal adult without any epidural injection, but maintaining with intact cerebral autoregulation and systemic blood pressure, venous pressure is a crucial factor in regulating the ICP during positional change. Therefore further study showing measurement of venous pressure in addition to epidural pressure can make this result more reliable, although our study could not present such pressure measurement.

Conclusions

Both groups of different posture showed significant increases of ONSD according to time. However, there were no significant differences in ONSD values between groups and degrees of change in ONSD at any of the time points.

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