






Comparing the Effects of Sevoflurane and Desflurane on Intracranial Pressure in Patients Undergoing Laparoscopic Cholecystectomy Via Ultrasonographic Measurement of the Optic Nerve Sheath Diameter

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ABSTRACT

Objective: Anesthetics have various effects on intracranial pressure (ICP). We aimed to compare the effects of sevoflurane and desflurane on intracranial pressure during laparoscopic cholecystectomy.

Methods: After obtaining ethical approval and patients' informed consent, 69 patients scheduled for laparoscopic cholecystectomy were randomized into Group-S and Group-D. Demographic data, hemodynamics, and ultrasonographic optic nerve sheath diameter (ONSD) values were recorded. Patients were administered propofol, fentanyl, and rocuronium for induction of anesthesia. Anesthesia was maintained by administering sevoflurane in Group-S, desflurane in Group-D, and remifentanyl infusion. The respiratory rate was adjusted, with end-tidal carbon dioxide (ETCO₂) values of 35–40 mmHg. The ONSD measurements, hemodynamics, and ETCO₂ levels were recorded at 5 minutes after induction (T1), 3 minutes after creating pneumoperitoneum and reverse Trendelenburg position (T2), 20 minutes of pneumoperitoneum (T3), and 5 minutes after terminating pneumoperitoneum (T4). All parameters were recorded by an anesthesiologist blinded to the groups.

Results: Patients had similar demographic data, intraoperative hemodynamic parameters, SpO₂, and end-tidal CO₂ levels. There was no difference between the groups in ONSD measured at T0, T1, T2, T3, and T4. Intragroup comparisons revealed that the ONSD was higher at all measurement times than the baseline in both groups.

Conclusion: Sevoflurane and desflurane had similar effects on ICP during laparoscopic cholecystectomy, and the intraoperative ICP was higher than the baseline in both groups.

INTRODUCTION

Organ systems are affected differently during anesthesia applications. Anesthetic agents cause perfusion and pressure changes in the central nervous system, which is their site of action. Inhalation anesthetics are known to slightly

increase intracranial pressure (ICP) during anesthesia.^[1] However, there are no reported adverse effects of these minimal intracranial pressure changes on postoperative neurological outcomes in healthy patients. Laparoscopic surgery is widely performed as an alternative to open surgery due to its advantages such as reduced bleeding, post-

operative pain, and length of hospital stay. However, pneumoperitoneum and the resulting intra-abdominal pressure (IAP) may cause many systemic physiological outcomes such as decreased venous return, hypercapnia due to CO₂ absorption through the peritoneal surface, and respiratory acidosis. Studies with animal models have reported the use of CO₂ pneumoperitoneum to be associated with ICP. Increases in intracranial pressure can decrease cerebral perfusion pressure, leading to cerebral ischemia. Therefore, anesthetic agents that would minimize fluctuations in intracranial pressure should be chosen in procedures known to increase intracranial pressure, such as laparoscopic surgeries.^[2] There is a scarcity of research comparing the effects of inhalation anesthetics on intracranial pressure in humans.

Measurement of the optic nerve sheath diameter (ONSD) with ultrasound is a simple, reliable, and non-invasive technique for ICP assessment, which has been shown to detect compliance with the degree of ICP, and the increase in ICP in clinical settings.^[3]

We aimed to compare the effects of sevoflurane and desflurane—commonly used agents in general anesthesia practice—on intracranial pressure during laparoscopic cholecystectomy via measuring the optic nerve sheath diameter with ultrasound.

MATERIALS AND METHODS

This study was carried out between 15.03.2019 and 15.03.2020. After ethical committee approval (2019/28) and obtaining informed consent forms from the patients, this prospective, randomized, double-blind study was carried out in accordance with the Helsinki Declaration. We randomized 69 ASA I-3 risk group patients who were scheduled for laparoscopic cholecystectomy into Group S and Group D using the sealed envelope method. The patients were not provided any information about their group. Those with a history of increased intracranial pressure or with any condition that might cause an increase in intracranial pressure (ischemic cerebrovascular event, intracranial hemorrhage, brain tumor), those with eyeball diseases, glaucoma patients, those with a history of cataract surgery, and those <18 years of age were excluded from the study. Routine monitoring, which includes electrocardiography, non-invasive blood pressure, pulse oximetry, and the bispectral index, was performed, and the levels were recorded, followed by the optic nerve sheath diameter measurement on the right and left eyelids before induction (T0). Measurements were made 3 mm beneath the point where the optic nerve enters the globe by a USG (My Lab30 Gold, Esaote, Genova, Italy) 12 MHz linear probe placed transversely on the closed eyelid and at an angle of around 15 degrees. The measurements were repeated twice in both eyes, and the average was recorded. The patients were not premedicated, and 2 – 2.5 mg/kg propofol and 2 mcg/kg fentanyl were administered for anesthesia induction with a BIS value of <60, and 0.6 mg/

kg rocuronium for muscle relaxation. After intubation, the patients were ventilated with volumes of 6–8 ml/min according to their ideal body weight. The respiratory rate was adjusted to 10–14/min, with the patient's end-tidal carbon dioxide values between 35–40 mmHg. Using a mixture of 40% oxygen and 60% air, anesthesia was maintained by administering 1–2% sevoflurane in Group S, 4–6% desflurane in Group D, and 0.05–0.5 mcg/kg remifentanyl infusion, with a BIS value of 40–60. The vaporizers were adjusted according to randomization by a specialist who was not involved in the study follow-up, and the top of the vaporizers was covered with gauzes to block the view of the measurer. The pneumoperitoneum pressure was maintained at 12 mmHg during the surgery. The mean blood pressure, heart rate, peripheral oxygen saturation, end-tidal carbon dioxide level, and optic nerve sheath diameter were recorded at 5 minutes after induction (T1), 3 minutes after creating pneumoperitoneum and placing the patient in the reverse Trendelenburg position (T2), 20 minutes of pneumoperitoneum (T3), and 5 minutes after terminating pneumoperitoneum and placing the patient in the supine position. In addition, the average of the right and left optic nerve diameters was recorded. After the gallbladder was removed, 1 g paracetamol and 1 mg/kg tramadol were intravenously administered for postoperative analgesia, and 4 mg ondansetron for postoperative nausea prophylaxis. Following the completion of the skin sutures, the inhalation anesthetic was discontinued, and 0.02 mg/kg atropine and 0.05 mg/kg neostigmine were intravenously administered to reverse the neuromuscular blockade. Patients with a BIS value of >85 and adequate spontaneous ventilation were extubated. All perioperative parameters were recorded by an anesthesiologist who was not involved in patient follow-up and blinded to the inhalation anesthetic used.

The findings of the study were assessed using IBM SPSS Statistics 22 (IBM SPSS, Türkiye) for statistical analyses. The normality of the parameters was tested by the Shapiro-Wilk test. The assessment of the study data included descriptive statistical methods (mean, standard deviation, frequency) as well as the Student's t-test to compare normally distributed parameters between two groups, and the Mann-Whitney U test to compare non-normally distributed parameters between two groups for the comparison of quantitative data. A repeated-measures analysis of variance was used for within-group comparisons of normally distributed parameters, and the Bonferroni test was used to reveal the period causing the difference. The Friedman test was used for within-group comparisons of non-normally distributed parameters. The Fisher-Freeman-Halton's test and Yates's correction for Continuity were used to compare qualitative data. A p-value of <0.05 was considered statistically significant.

A study using sevoflurane found the ONSD measured at 3 minutes after the creation of pneumoperitoneum to be 4.9±0.4 mm.^[4] Assuming that the ONSD in anesthesia with sevoflurane was 10% different from that in anesthesia

with desflurane, the mean difference between sevoflurane and desflurane was 0.49 mm. Accordingly, the number of samples was calculated to be at least 25 patients for each group, at 90% power, and a p level of <0.05. Considering the losses during follow-up, a total of 69 patients were included in the study.

RESULTS

A total of 69 patients were included in the study. Three patients were excluded due to desaturation in one patient and deteriorated hemodynamic parameters in two patients. The data were assessed for 66 patients, with 33 per

Table 1. Demographic data

	Group S Mean ± SD	Group D Mean ± SD	
Age (years)	47.94±11.93	49.45±11.47	¹ 0.604
BMI (kg/m ²)	29.73±5.52	29.34±5.23	¹ 0.770
	n (%)	n (%)	
Sex			
Male	8 (22.9%)	6 (19.4%)	² 0.964
Female	27 (77.1%)	25 (80.6%)	
ASA			
1	29 (82.9%)	22 (71%)	³ 0.162
2	6 (17.1%)	6 (19.4%)	
3	0 (0%)	3 (9.7%)	

¹Student t test, ²Continuity (yates) correction, ³Fisher freeman halton test. BMI: Body Mass Index.

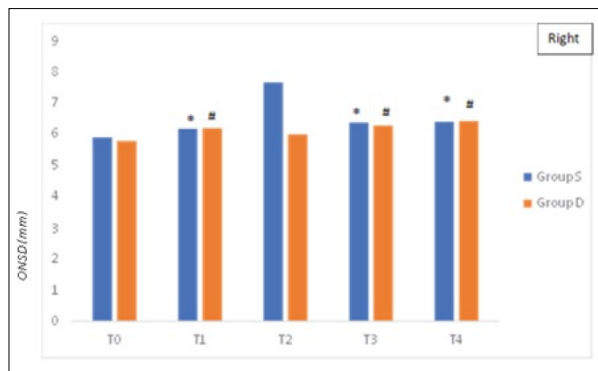


Figure 1. Right Optic Nerve Sheath Diameter Measurements. Student t test, Bonferroni test, * $p < 0.05$ indicates significant difference compared with the baseline measurements for Group S; # $p < 0.05$ indicates significant difference compared with the baseline measurements for Group D.

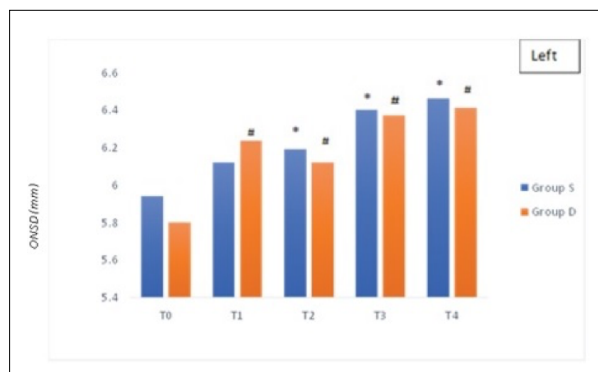


Figure 2. Left Optic Nerve Sheath Diameter Measurements. Student t test, Bonferroni test, * $p < 0.05$ indicates significant difference compared with the baseline measurements for Group S; # $p < 0.05$ indicates significant difference compared with the baseline measurements for Group D.

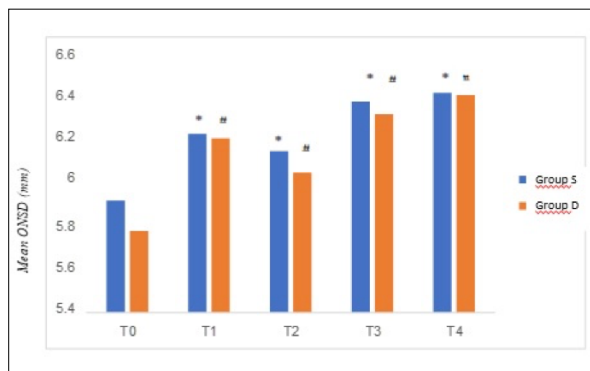


Figure 3. Mean Optic Nerve Sheath Diameter Measurements. Student t test, Bonferroni test, * $p < 0.05$ indicates significant difference compared with the baseline measurements for Group S; # $p < 0.05$ indicates significant difference compared with the baseline measurements for Group D.

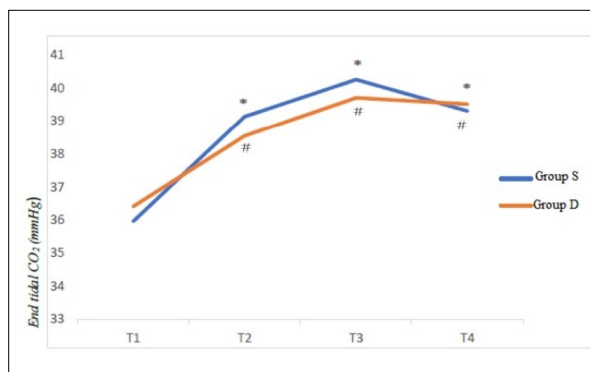


Figure 4. End-tidal Carbon Dioxide Levels. Student t test, Bonferroni test, * $p < 0.05$ indicates significant difference compared with the baseline measurements for Group S; # $p < 0.05$ indicates significant difference compared with the baseline measurements for Group D.

group. The demographic data of the study patients were similar (Table 1).

Right, left, and mean ONSD values were similar in both groups at all measurement times. The within-group comparison revealed that the mean ONSD was higher than the baseline value at all measurements (Figure 1-2-3).

The mean blood pressure (MBP) was similar. In Group S, the MBP was lower than the baseline value after intubation and at 5 minutes after terminating pneumoperitoneum (T4) ($p=0.000$; $p=0.006$). In Group D, the MBP was lower than the baseline value at all measurement times ($p=0.000$; $p=0.003$; $p=0.000$; $p=0.000$).

The mean heart rate was similar in both groups. There was no difference in the $ETCO_2$ levels between the two groups of patients, but the $ETCO_2$ levels in both groups were higher at all measurement times compared to the first measurements (Figure 4).

DISCUSSION

It is known that inhalation anesthetics, which are frequently used agents during anesthesia applications, have vasodilator effects. These effects become evident with increasing concentrations, and general anesthesia significantly increases cerebral blood flow, and thus may result in increased intracranial pressure.^[5] Sujata et al.^[2] compared the effects of propofol and sevoflurane on intracranial pressure during laparoscopic pelvic surgeries by measuring the ONSD and reported that the highest mean ONSD was significantly lower in the propofol group than in the sevoflurane group. Limited studies are exploring the effects of two inhalation agents on intracranial pressure. Fraga et al.^[6] reported no difference in the effects of desflurane and isoflurane on intracranial pressure in normocapnic patients. Sponheim et al.^[7] investigated the effects of isoflurane, desflurane, and sevoflurane on intracranial pressure in children with a suspected increase in intracranial pressure, showing that isoflurane and sevoflurane did not increase ICP from the baseline value, while desflurane caused an ICP higher than the baseline value. Holmström et al.^[1] also demonstrated a greater effect of desflurane on ICP than sevoflurane. Our study assessed the effects of sevoflurane and desflurane on intracranial pressure during laparoscopic cholecystectomy by measuring optic nerve sheath diameter in patients without intracranial disease and established that the two inhalation agents had similar effects on intracranial pressure at all measurement times.

Laparoscopic surgery, which is preferred to conventional open surgery, has advantages such as being minimally invasive, reduced bleeding, and early discharge.^[8] However, laparoscopic surgery requires the creation of pneumoperitoneum with CO_2 in the abdomen to achieve a better view of the surgical site. This may cause some hemodynamic, respiratory, and cerebrovascular side effects. The study by Kamine et al.^[9] measured intracranial pressure with a ventricular catheter and reported an increase in ICP during laparoscopy. The study by Min et al.^[8] with pediatric patients assessed intracranial pressure by ultrasonographic

measurement of ONSD in cases undergoing elective laparoscopic surgery and found an increased ONSD to be correlated with pneumoperitoneum. In our study, ONSD was higher than baseline values during pneumoperitoneum. The study by Sahay et al.^[10] showed that the mean optic nerve sheath diameter was higher at 5 minutes after desufflation than the baseline value. Our study also observed that the increase continued at the measurements after the pneumoperitoneum was created, and the values after desufflation were higher than the baseline value.

The study by Yashwashi et al.^[11] reported that intracranial pressure increased with increasing pneumoperitoneum pressures during laparoscopic cholecystectomy. In our study, the pressure of pneumoperitoneum was fixed at 12 mmHg, and an increased ONSD was detected during the surgery performed at this pressure. Our findings suggest that the use of high pneumoperitoneum pressures, especially in patients with high intracranial pressure, may result in adverse neurological conditions.

In addition to the pressure effect of the pneumoperitoneum during laparoscopic surgery, the gas used for insufflation may also change intracranial pressure. The study comparing pneumoperitoneum with CO_2 , helium, and nitrous oxide in pigs observed that the intracranial pressure increased significantly in pneumoperitoneum with CO_2 compared to other gases. This was attributed to an increase in $PaCO_2$, a decrease in pH values, and an increase in cerebral perfusion.^[12] When intracranial pressures were compared during hyperventilation and hypoventilation after pneumoperitoneum with CO_2 in pigs, hypoventilation was found to cause an increase in intracranial pressure.^[13] In our study, end-tidal CO_2 values were similar in both groups and were statistically higher than baseline values. In both groups, there was an increase in ONSD at the measurement times when carbon dioxide was higher than the baseline measurement. It was concluded that this finding supported the relationship between CO_2 and intracranial pressure reported in previous studies.

The extraventricular drainage system is considered the gold standard for the measurement of ICP. However, it has side effects such as brain damage, infection, and hemorrhage. With noninvasive CT and MRI, it is not possible to make simultaneous and repeated measurements during surgery. The ultrasonographic measurement of ONSD has been found correlated with increased intracranial pressure and produced reliable results in previous studies.^[14] Also, it has become important as it enables instant monitoring.^[15-17] Our study used the ultrasonographic measurement of the ONSD to evaluate ICP during the operation.

A study on the hemodynamic effects of inhalation anesthetics reported that when 1 MAC sevoflurane and desflurane were used, desflurane exhibited more potent vasodilator properties and reduced blood pressure more.^[18] A study with patients undergoing bariatric surgery showed that the effects of sevoflurane and desflurane on hemodynamic parameters were similar when the inhalation agent concentration was titrated by maintaining BIS

levels between 40 and 60.^[19] A study on intracranial surgeries found similar effects of sevoflurane and desflurane on blood pressure, while the heart rate was lower in the desflurane group.^[20] Our study performed volatile agent titration to maintain the bispectral index in the range of 40-60 and found the heart rate and mean blood pressure to be similar between groups throughout the operation.

The limitation of our study was that the patients included in the study had no intracranial diseases. If patients with intracranial diseases were included, the effect of sevoflurane and desflurane on ICP might be different.

Conclusion

Sevoflurane and desflurane have similar effects on intracranial pressure and hemodynamic parameters during laparoscopic cholecystectomy. Laparoscopic cholecystectomy causes an increase in intracranial pressure. We believe that this should not be ignored in risk-group patients, and negative outcomes should be prevented by taking necessary precautions.

Ethics Committee Approval

This study approved by the University of Health Sciences Fatih Sultan Mehmet Health Application and Research Center Ethics Committee (Date: 14.03.2019, Decision No: FSMEAH-KAEK 2019/28).

Informed Consent

Informed consents were obtained from all patients.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: M.Ö.İ., S.A., D.E.A.; Design: S.A., M.Ö.İ., C.K.; Supervision: D.E.A., Ö.D.; Materials: M.Ö.İ., S.A., D.E.A.; Data: M.Ö.İ., S.A., Ö.D.; Analysis: S.A., C.K.; Literature search: M.Ö.İ., S.A.; Writing: M.Ö.İ., S.A.; Critical revision: D.E.A., Ö.D., C.K.

Conflict of Interest

None declared.

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Laparoskopik Kolesistektomi Geçiren Hastalarda Sevofluran ve Desfluranın İntrakraniyal Basınca Etkisinin Ultrasonografik Optik Sinir Kılıf Çapı Ölçümü İle Karşılaştırılması

Amaç: Anestezik ajanların intrakraniyal basınca (İKB) farklı etkileri mevcuttur. Çalışmamızda laparoskopik kolesistektomi operasyonlarında sevofluran ve desfluranın intrakraniyal basınca etkilerini karşılaştırmayı hedefledik.

Gereç ve Yöntem: Etik kurul onayı ve hastalardan bilgilendirilmiş onam alındıktan sonra laparoskopik kolesistektomi planlanan 69 hasta, Grup-S ve Grup-D olarak randomize edildi. Demografik ve hemodinamik veriler ile ultrasonografik optik sinir kılıfı çapı (OSKÇ) değerleri kaydedildi. İndüksiyon için propofol, fentanil ve rokuronyum kullanıldı. Grup-S'ye sevofluran, Grup-D'ye desfluran uygulandı; remifentanil infüzyonu yapıldı. OSKÇ ölçümleri ve hemodinamik veriler indüksiyondan 5 dk sonra (T1), pnömoperitonyum oluşturulduktan ve ters Trendelenburg pozisyonundan 3 dk sonra (T2), pnömoperitonyumdan 20 dk sonra (T3) ve pnömoperitonyum sonlandırıldıktan 5 dk sonra (T4) kaydedildi. Tüm parametreler gruplara kör bir anestezi uzmanı tarafından takip edildi.

Bulgular: Hastaların demografik verileri, intraoperatif hemodinamik parametreleri, SpO2 ve ETCO2 düzeyleri benzerdi. T0, T1, T2, T3 ve T4'te ölçülen OSKÇ'de gruplar arasında fark yoktu. Grup içi karşılaştırmalarda, OSKÇ'nin tüm ölçüm zamanlarında her iki grupta da başlangıca göre daha yüksek olduğu görüldü.

Sonuç: Sevofluran ve desfluranın laparoskopik kolesistektomi sırasında İKB üzerine etkileri benzerdir; laparoskopik cerrahi esnasında her iki ajan ile intraoperatif İKB bazale göre yüksek seyretmektedir.

Anahtar Sözcükler: Desfluran; laparoskopik kolesistektomi; optik sinir kılıfı çapı; sevofluran.