Original Article

Effect of sevoflurane, propofol and propofol with dexmedetomidine as maintenance agent on intracranial pressure in the Trendelenburg position during laparoscopic surgeries

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Abstract

Background and Aim: Pneumoperitoneum (PP) and the Trendelenburg position (TP) in laparoscopic surgeries are associated with rise in intracranial pressure (ICP). The optic nerve sheath diameter (ONSD) is a surrogate marker of ICP. The study aimed to evaluate the effect of sevoflurane, propofol and propofol with dexmedetomidine as maintenance agent on ICP in TP during laparoscopic surgeries.

Material and Methods: A total of 120 American Society of Anesthesiologists (ASA) physical status I/II patients, aged 18–65 years were randomly allocated into three groups: sevoflurane as group S, propofol as group P, and propofol with dexmedetomidine as group PD. The intra-abdominal pressure (IAP) was kept in the range of 12–14 mmHg and TP varied between 15°– 45° angle. The primary objective was comparison of ICP and secondary objectives were IOP, intraoperative hemodynamic and postoperative recovery characteristics among groups. The ONSD and IOP were measured in both eyes 10 min after endotracheal intubation (T0), 5 min after CO_2 insufflation (T1), 5 min after TP (T2) and 5 min after deflation of gas (T3). The data were analyzed by using the Statistical Package for Social Sciences version 23.

Results: ONSD and IOP at T1 and T2 were significantly higher than T0 in all groups, but no significant difference was found among the intergroup groups. Significantly lower heart rate and mean blood pressure were observed in PD group at T1 and T2 compared to group S and group P.

Conclusion: The rise in ICP was comparable among sevoflurane, propofol, and propofol–dexmedetomidine combination as a maintenance agent during laparoscopic surgeries in TP.

Keywords: Intraocular pressure, laparoscopic surgeries, optic nerve sheath diameter, pneumoperitoneum, trendelenburg position

Introduction

Laparoscopic surgical procedures are being preferred over conventional open surgery because of its various advantages like minimal invasiveness, less risk of hemorrhage, minimal postoperative pain and earlier discharge.[1] Pneumoperitoneum (PP) and the Trendelenburg

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position (TP) are an integral part of lower abdominal and pelvic laparoscopy surgeries. Laparoscopy surgery causes a rise in intra-abdominal and intracranial pressure (ICP), due to its multicompartment transmission of pressure.[2] The optic nerve sheath diameter (ONSD) is a surrogate marker of ICP because the optic nerve sheath is a direct anatomical extension of the brain dura mater and subarachnoid space. An increase in ONSD is one of the earliest manifestations of rise in ICP.[3-5] Several other neurological complications like cerebral ischemia, cerebral edema and postoperative visual loss (POVL) have been attributed to raised ICP.[6]

Laparoscopic surgeries are usually performed under general anesthesia (GA). The GA was maintained through either inhalational agents or total intravenous anesthesia (TIVA). The inhalation anesthetic agents have direct dose-dependent vasodilation effect on cerebral circulation, which in turn leads to the rise in ICP.[7] This rise in ICP may be further increased with the TP.[8]

On the other hand, theoretically, TIVA decreases both cerebral blood flow (CBF) and cerebral metabolic rate via cerebral vasoconstriction, and thus causes a reduction in ICP. Propofol is the most commonly used anesthetic agent for TIVA.[9,10] Besides hemodynamic stability in laparoscopic surgeries, dexmedetomidine has a cerebral vasoconstrictive effect, which is mediated by post synaptic $\alpha 2$ receptors.[11,12] PP and the TP during laparoscopic or robotic surgeries also lead to a significant rise in IOP,[13,14] but effects of inhalational agents and TIVA have not been evaluated much.

Our hypothesis was that TIVA in the form of propofol and propofol–dexmedetomidine combination would be better than sevoflurane inhalational anesthesia as a maintenance agent to prevent rise in ICP during laparoscopic surgeries. This study aimed to compare the effect of inhalational TIVA as maintenance agent on ONSD as surrogate marker of ICP and on IOP in patients undergoing laparoscopic surgeries performed in TP and to find the optimal anesthetic technique.

Material and Methods

After institutional ethical clearance (AIIMS/IEC/2018/1082) and Clinical Trial Registry- India (CTRI/2018/07/015078) registration, this single center, prospective, randomized study was conducted between January 2018 and December 2019 in a tertiary care hospital. Written informed consent was taken from all the patients.

A total of 120 American Society of Anesthesiologists (ASA) I/II patients aged 18–65 years who underwent laparoscopic surgeries were enrolled for the study. These patients were randomly divided into three groups: sevoflurane as group S, propofol as group P, and propofol with dexmedetomidine as group PD. Forty patients were randomly allocated in each group according to the anesthetic techniques, using computer-generated random number table and group allocation was done by sealed opaque envelope method, which was opened just before induction. The intra-abdominal pressure (IAP) was kept in the range of 12–14 mmHg and TP varied between 15°– 45° angle during surgery. Patients with a history of neurological illness or surgeries, glaucoma or ophthalmic diseases other than myopia or hypermetropia, acute or chronic ocular infections, allergy to study drugs, history of bradycardia or cardiac conduction defects, body mass index (BMI) greater than 35 kgm^{-2}, and surgeries requiring TP >45° were excluded from the study.

All patients were in a fasting state as per ASA fasting guidelines. On arrival of patients in the operation theatre, electrocardiogram (ECG), non-invasive blood pressure (NIBP), pulse oximetry, neuromuscular transmission (NMT) monitoring and bispectral index (BIS) were attached. Baseline heart rate (HR), NIBP and peripheral oxygen saturation (SpO_2) were recorded. After securing 18-gauge (G) intravenous (iv) access, ringer lactate 10 ml/kg was initiated. All patients were pre-medicated with iv midazolam 20–50 μg/kg and iv dexamethasone 0.1–0.2 mg/kg. In group PD, 1 μg/kg of dexmedetomidine was loaded over 10 min before induction and continued at 0.4 μg/kg throughout the surgical procedure until skin closure. Muscle relaxation was achieved with iv rocuronium 1 mg/kg and the airway was secured with appropriately sized endotracheal tube. Patients were ventilated with the air-oxygen mixture (50:50) with a tidal volume of 6–8 mg/kg keeping $EtCO_2$ target of 35–40 mmHg. The BIS was maintained between 40 and 60 during the surgical procedure.

The anesthesia was maintained according to the group assigned. The intermittent doses of iv rocuronium were given according to train of four (TOF) count. Analgesic supplementation was done with iv fentanyl 1 μg/kg when the HR and/or mean blood pressure (MBP) increased by more than 20% of baseline value, after excluding the of light plane of anesthesia.

The ONSD was measured with linear probe (5–10 MHz) of ultrasound machine (Sonosite Micromax, Sonosite Inc., Bothell, WA) after application of conductive ultrasonography gel over the closed eyelid. We adjusted the angle and depth of ultrasound probe to clearly visualize ONSD images. Then ONSD width measurements were done at 3 mm posterior to the orbit [Figure 1]. These measurements were performed by an anesthesiologist who was unaware of the study groups.

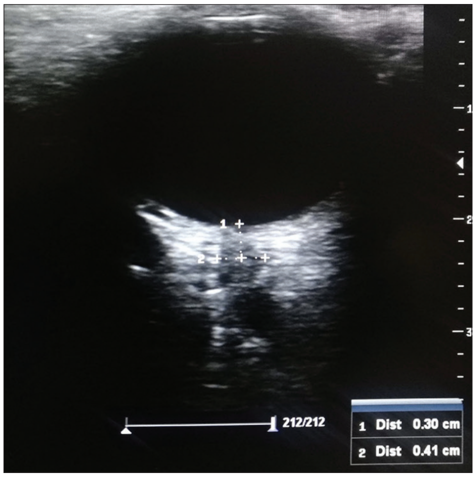

Figure 1: Optic nerve sheath diameter measurement by ultrasound

The measurements were averaged in both eyes to yield a mean ONSD, to minimize intraoperator variability.

IOP was measured in both eyes at central cornea with a Schiotz tonometer after topical instillation of 0.5% proparacaine. The mean IOP was obtained after averaging the IOP of both eyes. Tonometer consists of a spherical mold and a 5.5 g weight in the box. The noted scale readings were converted into the IO*P* value using the scale card.

ONSD and IOP were measured in both eyes at the following time intervals: 10 min after endotracheal intubation (T0), 5 min after $C_{O}2$ insufflation in neutral position (T1), 5 min after TP (T2), and 5 min after gas deflation in neutral position (T3). The time of recovery from the anesthesia (to achieve full consciousness and respond to verbal command state) and postoperative sedation score by using Richmond agitation sedation scale (RASS) were noted.

The primary objective of this study was comparison of ICP which was measured with ONSD and secondary objectives were IOP, intraoperative hemodynamics, relation of ICP with TP, and mean time of recovery from anesthesia.

Statistical analysis

The sample size was calculated on the basis of a pilot study of 10 cases in each group. The mean difference of ONSD in three groups was 0.2 and the standard deviation 0.3; the effect size was calculated to be 0.2/0.3, i.e., 0.666. Taking the level of significance (α) as 5% and power of the test (1-β) as 80%, the sample size was calculated in each group to be 35. Considering about 10% loss of data, the sample size was increased to 40 in each group.

Data was entered into Microsoft Excel sheet and analyzed using the Statistical Package for Social Sciences (SPSS, IBM Corp. Armonk, NY) version 23. The categorical variables were expressed as number (%) and continuous variables as mean ± standard deviation (SD) or median (interquartile range [IQR]) for non-normally distributed data. Normality of data was checked using the Shapiro–Wilk test. The normally distributed data were analyzed with one-way analysis of variance (ANOVA) test. For non-normally distributed data, a non-parametric test (Kruskal–Wallis test) was used for data analysis. A P value of <0.05 was considered statistically significant.

Results

A total of 135 patients were recruited in the study, out of which 8 were refused to participate and 7 patients converted to open surgery. The remaining 120 patients were randomized in three groups of 40 patients each [Figure 2]. The demographic and intraoperative variables were comparable and not clinically significant between three groups [Table 1].

We observed a rise in median ONSD values measured at T1 and T2 compared to T0 in all the three groups [Table 2]. However, there was no significant difference found in the intergroup comparison between the three groups. At T3 (5 min after gas deflation), median ONSD returned to nearby baseline values (T0) in all groups [Figure 3]. Similar to ONSD, the median IO*P* value increased at T1 and T2 compared to T0 in all three groups, but was found to be insignificant on the intergroup comparison [Figure 4].

The hemodynamic parameters (HR, MBP and $EtCO_2$) were also recorded at different intervals and compared in the three groups. The intergroup comparison in baseline mean HR, MBP, and $EtCO_2$ values were statistically insignificant ($P > 0.05$). But significant difference was found in mean HR and MB*P* values measured at different intervals between three groups ($P < 0.05$), while mean $EtCO_2$ value was not found to be statistically significant [Figure 4]. The median anesthesia recovery time was 12.5 (5) in group S, 15.0 (9) in group P, and 20.0 (5) in group PD [Table 1]. It was found to be significantly shorter in group S as compared to group P and group PD ($P < 0.001$).

Discussion

The main findings of our study were the significant rise in ONSD and IOP in comparison to baseline values in all groups at PP and TP. On deflation of PP in neutral position, the values of ONSD and IOP reached near to baseline values in all groups. This study emphasized that the rise in ICP associated with TP was not clinically significant in normal

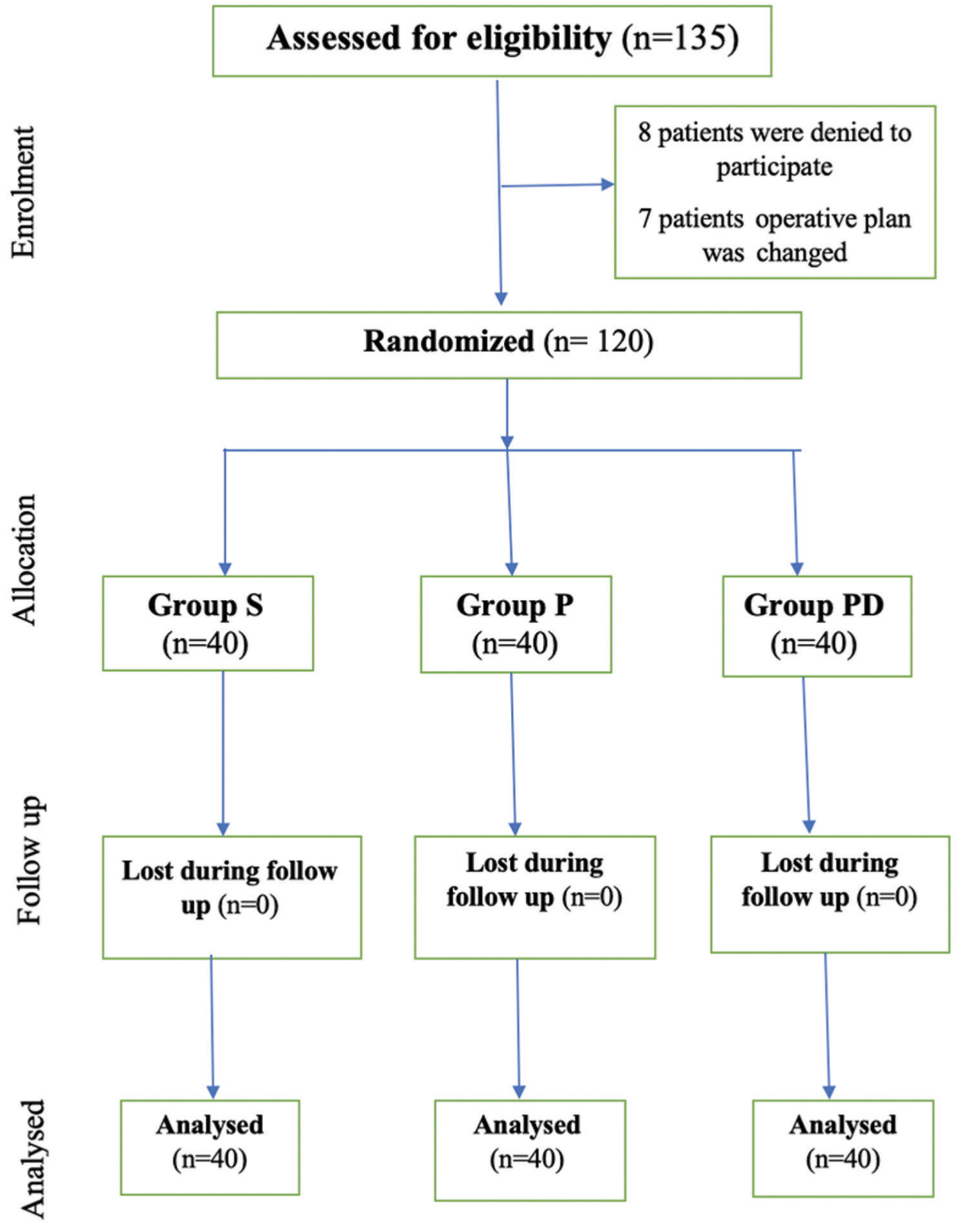

Figure 2: CONSORT flow diagram

patients, but it may be important in patients with pre-existing intracranial and intraocular hypertension. On intergroup comparison, the rise in ONSD and IOP were similar in all three maintenance techniques of general anesthesia. The TIVA is a better technique compared to volatile anesthesia in patients undergoing laparoscopy surgical procedures with Trendelenburg angle >35°.

In our study, we used ONSD by ultrasonography as a surrogate measure for ICP because it is non-invasive, reproducible, easy to learn and can be readily performed in patients undergoing laparoscopic surgery. Major R *et al*.[15] demonstrated a good correlation between ultrasonographic ONSD measurement and raised ICP in 26 patients in the emergency department. Monitoring of ONSD can provide useful information on changes in ICP intraoperatively.[16]

The adequate cerebral perfusion pressure (CPP) and minimizing fluctuations in ICP, CBF and cerebral oxygen requirement are the goals of anesthesia for laparoscopic procedures. Propofol-based total TIVA has been reported to be more effective than inhalation anesthesia in attenuating in rise of ICP.[17-19] Propofol is neuroprotective, as it is known to prevent the rise of ICP with stable hemodynamics.[20,21] Yu J *et al*.[22] observed a significant decrease in ONSD during propofol anesthesia than during sevoflurane anesthesia 60 min after PP and TP, suggesting that propofol anesthesia may help minimize ICP changes in robotic prostatectomy patients.

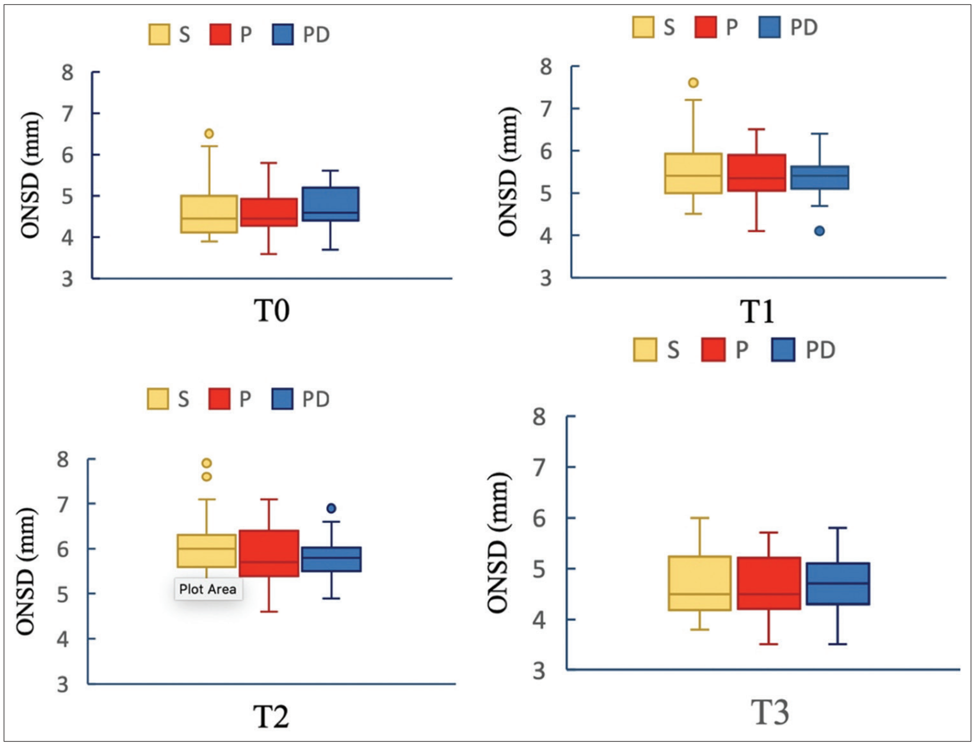

Figure 3: Boxplot and whiskers chart of ONSD at different intervals in the three groups

Table 1: Demographic and intraoperative variables in the three groups

Variables	Group S (*n*=40)	Group P (*n*=40)	Group PD (*n*=40)	*P*
Age (years)	42.65±14.22	41.90±13.19	43.03±10.36	0.922
Gender				
Female *n* (%)	22 (55.0)	27 (67.5)	25 (62.5)	0.512
Male *n* (%)	18 (45.0)	13 (32.5)	15 (37.5)	
BMI (kgm^{-2})	23.21±2.64	22.69±3.47	23.65±2.80	0.362
ASA class				
I *n* (%)	33 (82.5)	32 (80.0)	33 (82.5)	0.946
II *n* (%)	7 (17.5)	8 (20.0)	7 (17.5)	
IAP (mmHg)	13.05±1.01	13.35±0.95	13.40±0.93	0.216
Trendelenburg angle (mean)	29.50±12.49	31.63±13.02	32.25±12.95	0.554
PP Time (min)	102.50 (85)	125.00 (88)	112.50 (89)	0.061
Duration of Anesthesia (min)	130.00 (79)	145.00 (90)	135.00 (89)	0.093
Anesthesia recovery time (min)	12.50 (5)	15.00 (9)	20.00 (5)	<0.001

Values are mean±SD, numbers (%), or median IQR. BMI, Body mass index; ASA, American Society of Anesthesiologists; IAP, Intra-abdominal pressure; PP, Pneumoperitoneum

In our study, ONSD measured at 10 min after intubation was considered as baseline, which was comparable in all three groups. There was an increase in ONSD after creation PP and TP in all the three groups compared to baseline values. But on intergroup comparison, we found that none of the anesthetic agents (sevoflurane, propofol, and propofol with dexmedetomidine) resulted in a significant reduction in ONSD as contrary to findings of Yu J *et al*.[22]

The combination of PP and the need for head-down position during surgery results in a gravitational shift of the fluid which can have severe perturbing effects on the body's physiology. PP is an independent factor for ICP increase through the impaired venous drainage of the lumbar venous plexus. PP with a steep TP may have synergic detrimental consequences on the central nervous system homeostasis.

Volatile anesthetics have a direct relaxation effect on vascular smooth muscles. The vasodilatory effects are more pronounced beyond 1.0 minimum alveolar concentration (MAC); consequently, CBF and ICP increase.[23] In our study, depth of anesthesia was guided by BIS. To achieve BIS of 40–60 in sevoflurane group, the average MAC values were 0.9 which was <1 MAC; hence the vasodilatory effect of a volatile

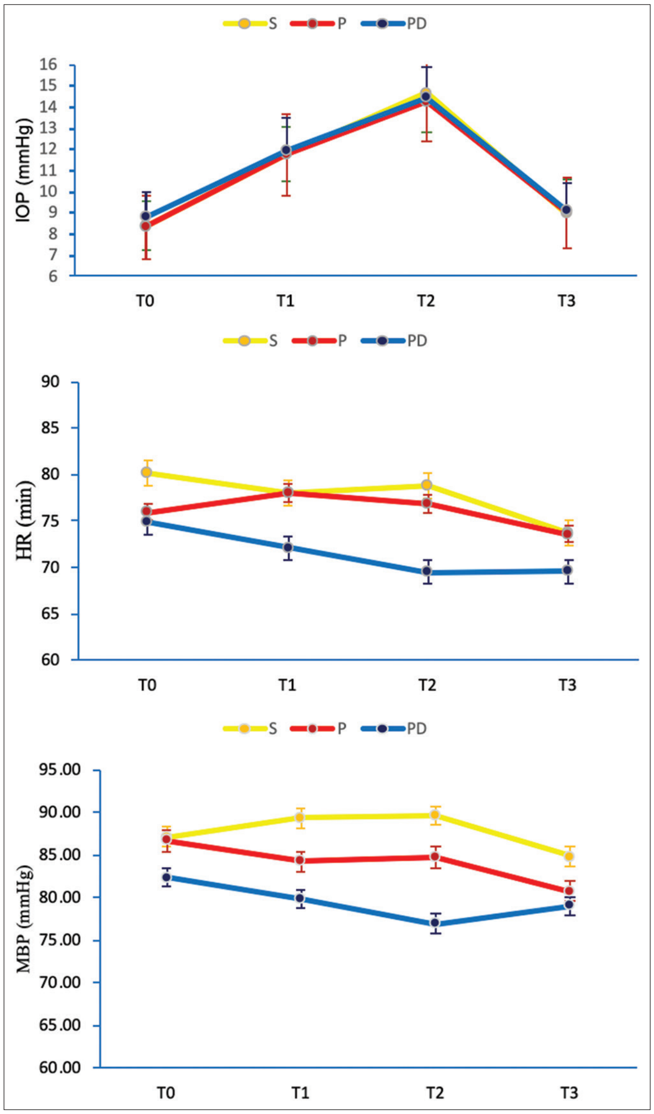

Figure 4: IOP, HR and MBP comparison at different intervals in the three groups

agent was probably not appreciable. In our study, we found that ONSD returned near to the baseline values within a few minutes after patients were brought back to neutral position after deflation of PP. Colombo R *et al.*[24] found similar results.

Dexmedetomidine is a selective α2agonist drug that is used to decrease the requirement of anesthetics and opioids. It attenuates the sympathoadrenal response to stress and provides a good recovery profile during laparoscopic surgeries. Dexmedetomidine has also been found to possess neuroprotective properties and it reduces CBF through direct cerebral vasoconstriction mediated by α2 receptor activation. Reduced CBF may be detrimental in conditions where ICP is already higher (e.g., acute stroke). However, it has an advantage when ICP rises due to vasogenic conditions as in laparoscopy. Catecholamine pathways play an important role in the neuroprotective property of dexmedetomidine, possibly by modulating neurotransmitter release in the central and peripheral sympathetic nervous systems. The dexmedetomidine infusion during the intraoperative period may prevent the rise in ICP due to PP in TP.[25] In our study, we noted that the addition of dexmedetomidine with propofol over propofol-based TIVA did not provide any additional benefit in decreasing ONSD after PP and TP during laparoscopic surgery. The probable reason was that the dose of dexmedetomidine used may not provide effective arterial vasoconstriction.

Table 2: ONSD and IOP measured at different intervals and their median values

ONSD (mm)	Group S Median (IQR)	Group P Median (IQR)	Group PD Median (IQR)	*P*
T0	4.45 (0.90)	4.45 (0.75)	4.60 (0.80)	0.260
T1	5.40 (0.97)	5.35 (0.95)	5.40 (0.58)	0.584
T2	6.00 (0.70)	5.70 (1.00)	5.80 (0.57)	0.108
T3	4.50 (1.15)	4.50 (1.00)	4.70 (0.80)	0.845
IOP (mmHg)				
T0	8.40 (2.14)	8.30 (2.35)	8.90 (1.85)	0.178
T1	11.50 (1.66)	11.75 (2.50)	11.85 (2.57)	0.862
T2	14.55 (2.70)	14.60 (2.72)	14.65 (2.10)	0.811
T3	9.50 (2.88)	9.30 (2.70)	9.25 (2.40)	0.935

ONSD, Optic nerve sheath diameter; IOP, Intraocular pressure

The physiological changes in the form of IOP due to PP and TP is well tolerated in normal patients. But it may be detrimental in patients with pre-existing raised IOP. Similar to the study by Mondzelewski *et al.*[13] and Blecha *et al.*[14] with the establishment of PP and TP, there was an increase in IOP in all the groups, but it was not statistically significant at any time. Kaur G *et al.*[26] evaluated the effect of propofol-based TIVA with sevoflurane anesthesia on IOP in patients scheduled for lower abdominal laparoscopic surgery performed at TP. They concluded propofol that was more effective than sevoflurane in reducing the raised IOP during laparoscopic surgery performed with CO_2 PP with TP.

Lee YY *et al.*[27] found no significant difference in IOP between sevoflurane anesthesia and propofol-based TIVA in relatively short operations. In our study, we also did not find any difference among inhalation agents or TIVA in attenuating the increased IOP associated with PP and TP.

Dexmedetomidine has a marked influence on HR and MBP, and provides better hemodynamics during laparoscopic surgery.[28] In our study, we observed that group PD had a significantly lower HR and MBP compared to other groups.

During laparoscopic surgery with CO_2 PP, there is peritoneal stretching and irritation, which increases the risk of postoperative nausea and vomiting (PONV). The increase in PONV might be caused due to raised ICP.[29] The anti-emetic property of propofol is well known.[30] In our study, nine patients in group S and one in group PD had PONV. Based on the results of our study, TIVA proved to be a better anesthetic technique compared to volatile agents in terms of PONV in laparoscopic surgery. Further large-scale studies will be required to elucidate the effects of increased ICP on PONV in patients undergoing laparoscopic surgeries or whether the increased incidence of PONV was directly due to anesthetic agents.

There were a few limitations to our study, which included limiting surgical procedures performed to <45° and IAP of 12–14 mmHg so the results of our study cannot be extrapolated to IAP >14 mmHg and angle >45°. IOP was not measured before induction of anesthesia as we considered it unethical to subject the patients to tonometry when they were awake only for the sake of the study, relationship between the duration of surgery and ONSD and IO*P* values was not studied.

Conclusion

Sevoflurane, propofol, and propofol with dexmedetomidine as maintenance agents have no effect on intracranial pressure in the Trendelenburg position during laparoscopic surgeries. The addition of dexmedetomidine with propofol over propofol would not provide any additional benefit in decreasing ONSD after PP and TP during laparoscopic surgery.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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