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ORIGINAL RESEARCH PERIOPERATIVE MEDICINE

Comparison of the effects of general anesthesia and combined spinal-epidural anesthesia on intraocular pressure in lower extremity surgeries employing pneumatic tourniquets: a randomized clinical trial

Gokhan Yildiz, MD[1], Handan Gulec, MD[2], Esra Ozayar, MD[3], Eyup Horasanli, MD[4]

Author affiliation:

1. Gokhan Yildiz, Department of Algology, Ankara Bilkent City Hospital, Ankara, Turkey; E-mail: gkoyldz@gmail.com; ORCID {0000-0001-5905-938X}
2. Handan Gulec, Anesthesiology and Reanimation Department, Yildirim Beyazid University, Ankara, Turkey; E-mail: handandrhandan@yahoo.com.tr, ORCID {0000-0002-3547-9336}
3. Esra Ozayar, Anesthesiology and Reanimation Department, Kecioren Education and Research Hospital, Ankara, Turkey; E-mail: eozayar@yahoo.com.tr; ORCID {0000-0002-1309-9279}
4. Eyup Horasanli, Anesthesiology and Reanimation Department, Yildirim Beyazid University, Anesthesiology and Reanimation Department, Ankara, Turkey; E-mail: eyuphorasanli@gmail.com; ORCID {0000-0002-6077-8549}

Correspondence: Gokhan Yildiz, E-mail: gkoyldz@gmail.com; Mobile: +905059272589

Abstract

Background & Objective: Induction of general anesthesia has been known to raise the intraocular pressure (IOP). The effect is more pronounced at the time of intubation. Similarly, applying pneumatic tourniquets is associated with rise in IOP. We compared the effects of general anesthesia and combined spinal-epidural anesthesia (CSEA) on IOP in lower extremity surgeries employing pneumatic tourniquets.

Methodology: A total of 50 patients, aged over 18 y, completed the study. Patients were randomly divided into the general anesthesia group (Group GA) and CSEA group (Group CSE). IOP and hemodynamic parameters including systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP) and heart rate (HR),were measured at baseline (T0), and after general anesthesia induction (T1), after intubation or after initiation of CSEA (T2), after placement of tourniquet (T3), and on removal of tourniquet (T4).

Results: There was no difference in IOP between the groups at T0 ($P > 0.05$), but it was higher at T2, T3, and T4 in Group CSE than in Group GA ($P < 0.05$). SAP was only higher in Group CSE at T3 ($P < 0.05$). İn Group GA IOP at T1, T3, and T4 was lower than that at T0 ($P < 0.01$) but were similar at T2 and T0 ($P > 0.05$). SAPs at T1, T3, and T4 were lower than those at T0 ($P < 0.05$) but were similar to those at T2 and T0 ($P > 0.05$). İn Group CSE although SAP was lower at T2, T3, and T4 than that at T0 ($P < 0.05$), IOP at T2 was higher than that at T0 ($P < 0.01$). IOP was the same at T3, T4, and T0 ($P > 0.05$).

Conclusion: Increased systolic arterial pressure and intraocular pressure due to tourniquet use can be managed better with general anesthesia. Neuraxial interventions such as CSEA may elevate IOP by raising cerebrospinal fluid (CSF) pressure. General anesthesia would benefit critical patients with increased risk for IOP. More studies with larger sample size, and meta-analyses are required to further validate our results.

Abbreviations: IOP: intraocular pressure; CSEA: combined spinal-epidural anesthesia; SAP: systolic arterial pressure; DAP: diastolic arterial pressure; MAP: mean arterial pressure

Key words: Intraocular Pressure; Anesthesia, Spinal; Anesthesia, General; Anesthesia, combined spinal-epidural; Tourniquet

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1. Introduction

Elevated intraocular pressure (IOP) leads to degenerative changes in the retina and optic nerve.[1] These changes are initially asymptomatic and they get noticed when visual complaints begin. Therefore, management of IOP and early management of the degeneration in the optic nerve may prevent loss of vision. A delay may cause permanent blindness.[2]

To our knowledge, there are no clinical studies that compare the effects of general anesthesia and combined spinal-epidural anesthesia (CSEA) on IOP in lower extremity surgeries employing a tourniquet. Increased IOP may be of critical importance in patients who may be at risk for postoperative vision loss and selection of the anesthetic technique is vital in susceptible patients.

The pressure by the needles used in CSEA on the dura mater as well as the fluids and local anesthetics injected into the epidural and subarachnoid space increase the CSF pressure in the subarachnoid space. Therefore, increased IOP can be observed due to increased central retinal venous pressure when sections of the optic nerve and retinal veins located in the subarachnoid space are compressed.[3, 4] IOP is also affected by the central effect of general anesthetics, the effect of muscle relaxants on extraocular muscles and to adrenergic reflexes to laryngoscopy and intubation.[5]

In lower extremity surgeries, tourniquets are frequently used to reduce blood loss and create a bloodless surgical field. A tourniquet placed on the lower extremity increases blood volume in the systemic circulation almost by 500–1000 ml, leading to increased blood pressure. This is called tourniquet-induced hypertension. Moreover, hypertension caused by a tourniquet may also lead to increased intracranial pressure and IOP.[6]

We compared the IOP values in patients who were administered general anesthesia or CSEA during lower extremity surgeries, employing a tourniquet to demonstrate the sudden spikes in intraocular pressure. We aimed to disclose other factors affecting IOP as a secondary objective.

2. Methodology

Approval for the study was obtained from the institutional Clinical Research Ethics Committee. Written consent was obtained for each patient. The study was designed as a randomized, prospective study. When calculating the sample size with the G power 3.1.9.2. program, the standard effect size was determined as 0.96 with a 5% margin of error (alpha), 95% (1-beta) power. We could not find any study comparing the effects of GA and CSEA on IOP in the literature. When we analyzed the study within itself, the calculation for effect size was made according to T3, which is the most statistically significant measurement with $P < 0.001$. When analyzed with 85% power with the G power 3.1.9.2 program, at least 34 patients were required for the study. In our study, the effect size was determined as 96% with 50 patients. We enrolled 56 ASA physical status I–II patients, aged 18–65 y who were scheduled to undergo lower extremity surgery. Exclusion criteria were as follows: the presence of ocular disease, a systemic disease that could affect IOP, pregnancy, and coagulopathy.

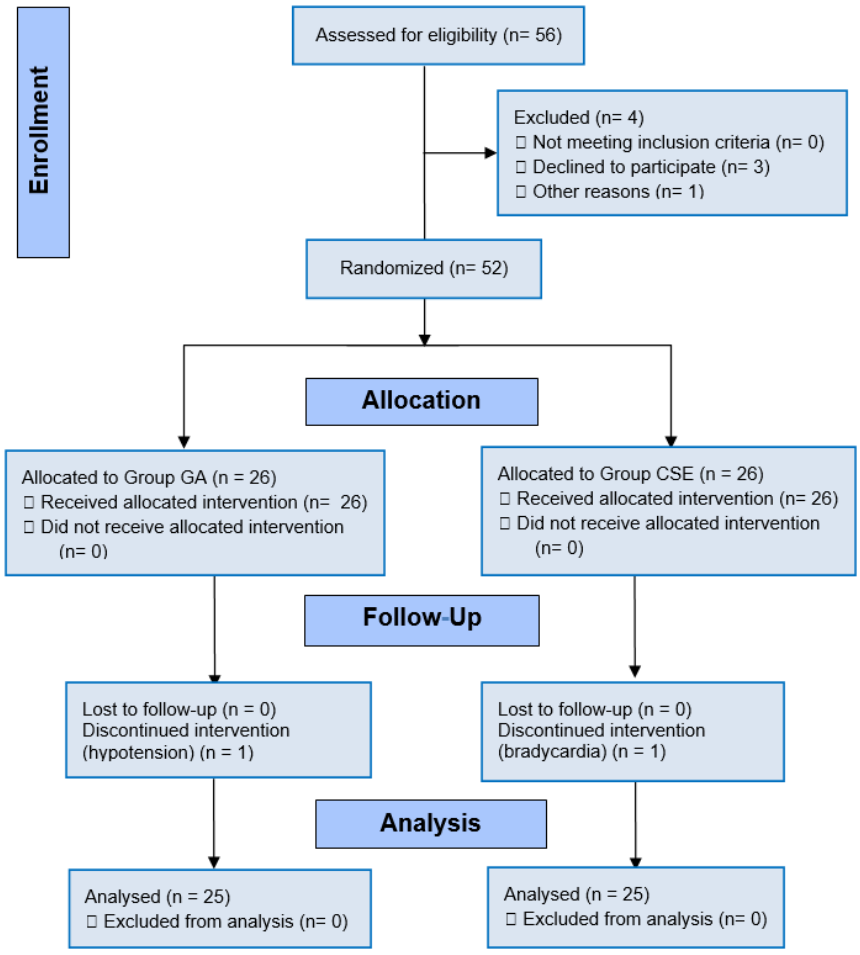

Figure 1. CONSORT flow diagram

Preoperative eye examination was performed by the same ophthalmologist in all patients included in the study. Intraocular disease was ruled out with the following findings:

- No autorefractometric refraction defects,
- Visual acuity complete in both eyes,
- No pathology detected on fundus examination.

Out of 56 patients (112 eyes) who satisfied the inclusion criteria were enrolled in the study, but 50 patients (100 eyes) completed the study. The patients excluded from the study are shown in the CONSORT flow diagram in Figure 1.

The patients were informed before the surgery and all patients signed the informed consent forms. The computer program and sealed envelope method were applied for randomization. After the computer program assisted randomization, the ranking was written on papers and put in envelopes by a blind researcher. The anesthesia method to be applied was determined according to the order in the envelope. The patients were assigned to two groups, i.e. patients who received CSEA (Group CSE) and general anesthesia (Group GA). All patients were selected in the morning to minimize the effects of circadian changes on IOP. Midazolam 0.05 mg/kg was administered intravenously (IV) as premedication. Fluid replacement was calculated as follows; 4 mL/kg/h for the first 10 kg of body weight, 2 mL/kg/h for 10–20 kg and 1 mL/kg/h for over 20 kg. Preoperative and other intraoperative losses were replaced. One drop of proparacaine HCl 0.5% was instilled in each eye. The pen-sized applanation tonometer Tono-Pen AVIA (TPA, Reichert Inc., NY), Reichert® that weighed 71 g, did not require calibration, and highly correlated with Goldmann Applanation Tonometry was used for IOP measurements in both groups. IOP measurements were conducted by the same ophthalmologist on all patients. The Tono-Pen provides the mean of four independent measurements after slight contact with the cornea within a 1.5 mm contact area. A disposable sterile sleeve was placed on the device before each measurement. All anesthesia procedures were performed by the same anesthesiologist. Besides, it was not possible for the person administering anesthesia and measuring IOP to be blind due to different anesthesia techniques (GA and CSEA).

The patients who were brought to the operating room were monitored and IOP, systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), and heart rate (HR) were noninvasively measured and recorded (T0).

The measurements were made in the supine position at the following timepoints:

T0: At baseline when the patient was placed on the operating table.

T1: After the induction of general anesthesia.

T2: After intubation-CSEA.

T3: After placement of the tourniquet.

T4: After removal of the tourniquet.

2.1. General anesthesia protocol

Group GA was administered lidocaine 1 mg/kg, propofol 2.5 mg/kg, rocuronium 0.6 mg/kg, and fentanyl 1 µg/kg intravenously for induction of GA. Anesthesia was maintained with sevoflurane 2–4% in 50% air and 50% O_2, and an infusion of remifentanil 0.05–0.25 µg/kg/min. Bispectral Index (BIS) was used to adjust the depth of GA. For remifentanil and sevoflurane dose adjustment, a BIS value of 40–65 was targeted. Nitrous oxide was not used since it could lead to increased IOP. To administer a maintenance dose for rocuronium, 2–3 responses to four consecutive stimuli were expected in the TOF (train-of-four) response, and 0.15 mg/kg rocuronium was added when necessary. TOF value was expected to be 0.9 before extubation.

Thirty seconds after induction (T1) and thirty seconds after intubation (T2), both IOP values, SAP, DAP, MAP and HR values were recorded. The surgical team used Esmarch bandages to exsanguinate the lower extremity that was going to be operated on and then inflated the tourniquet to a pressure of 100 mmHg above the SAP. IOP and other measurements were repeated 2 min after the tourniquet was inflated (T3). IOP and other measurements were repeated once more after 2 min after the tourniquet was deflated (T4) at the end of the surgery.

2.2. Combined spinal-epidural anesthesia protocol

Patients in the CSEA group (Group CSE) were placed in the sitting position and the skin was disinfected using povidone-iodine. Local anesthesia of 3–5 ml of 2% lidocaine was administered to the injection site at the L3–L4 intervertebral space; skin, subcutaneous tissue, and interspinous ligament were infiltrated. The epidural space was identified by using the “loss of resistance” method with an 18G Tuohy needle using normal saline (combined spinal-epidural set, B.Braun®, Germany). A 27G spinal needle was inserted through the epidural needle to access the subarachnoid space. After passing through the dura with the spinal needle and observing the CSF flow, the patients were injected with 15 mg (3 ml) of 0.5% hyperbaric bupivacaine (Marcain® Spinal heavy 0.5%) into the subarachnoid space. The spinal needle was then removed and a 20G epidural catheter was advanced 4.5 cm through the epidural needle and fixed for postop analgesia. The patients were again placed in the supine position, and IOP measurements were conducted for both eyes 2 min after the administration of the drug into the subarachnoid space (T2). SAP, DAP, MAP, and HR values were also recorded simultaneously with IOP.

After determining that the sensory block was at the T10–T11 dermatome level with the loss of pinprick sensation in all patients, it was allowed to exsanguinate the lower extremity using an Esmarch bandage and then the tourniquet was applied to perform the surgery. IOP measurements were repeated for both eyes 2 min after the placement of the tourniquet (T3). At the end of the surgery, the tourniquet was deflated, and IOP and other measurements were repeated 2 min after the tourniquet was removed (T4).

2.3. Statistical Analysis

SPSS (Statistical Package for the Social Sciences) for Windows
22.0 (SPSS Inc, Chicago, IL) was used for statistical analysis. Descriptive statistics were expressed with mean ± standard deviation, median (25%–75%), frequency distribution, and percentage values. Categorical variables were evaluated using Pearson's chi-square test and Fisher's exact test. The normal distribution of the variables was analyzed using visual (histograms and probability graphs) and analytical (Shapiro-Wilk Test) methods. For variables that were found to have a normal distribution, statistical significance was assessed using Student's T-Test for two independent groups and a paired samples T-Test for two dependent groups. For variables that did not have a normal distribution, statistical significance was assessed using the Mann-Whitney U test for two independent groups and the Wilcoxon signed-Rank test for two dependent groups. $P < 0.05$ was considered statistically significant.

3. Results

There was statistically no significant difference between the patients in terms of demographics, gender, height and weight ($P > 0.05$).

Evaluating each group separately, there was no significant difference between the IOP values of the left and right eyes at every measurement time (Table 2).

Each group was again evaluated separately to compare the IOP values measured at the baseline (T0) and the IOP values measured at various times. Accordingly, the patients who received GA (Group GA) had significantly lower IOP values at T1, T3, and T4 than

at T0 for both eyes ($P < 0.01$). On the other hand, there was no statistically significant difference between the IOP value at T2, i.e. after intubation, and the IOP value at T0 for both eyes ($P > 0.05$) (Table 1). In Group CSE, the IOP value at T2, i.e. the measurement after the administration of CSEA, was significantly higher than the IOP value at T0 ($P < 0.01$), whereas the IOP values were similar at T3, T4, and T0 for both eyes ($P > 0.05$) (Table 1).

Comparison of the groups showed no statistically significant difference in terms of the IOP values of both

Table 1: Intergroup and intragroup comparison of the distribution of the right and left intraocular pressure in time (Data presented as Mean ± SD)

IOP	Group GA		P[1]	Group CSE		P[2]	P[3]	P[4]
	Right Eye (n = 25)	Left Eye (n = 25)		Right Eye (n = 25)	Left Eye (n = 25)			
T0	21.08 ± 3.29	21.04 ± 3.16	0.655	21.88 ± 2.72	21.48 ± 2.90	0.070	0.271	0.456
T1	12.88 ± 3.53**	13.04 ± 3.56**	0.102	----	----	----	**----**	**----**
T2	21.00 ± 5.29	21.08 ± 5.22	0.157	25.80 ± 4.59**	25.36 ± 5.04**	0.465	**0.004**	**0.011**
T3	15.96 ± 4.58**	16.00 ± 4.50**	0.564	23.72 ± 3.52	23.20 ± 4.02	0.334	**<0.001**	**<0.001**
T4	18.76 ± 3.87**	18.72 ± 3.91**	0.564	22.84 ± 3.30	22.64 ± 3.45	0.131	**<0.001**	**0.001**

T0: Baseline; T1: After the induction of general anesthesia (Group G only); T2: After intubation-CSEA; T3: After placement of the tourniquet; T4: After removal of the tourniquet

**P < 0.05 according to the comparison with T0; **P < 0.01 according to the comparison with T0*

[1] A comparison of right and left intraocular pressure in the GA group

[2] A comparison of right and left intraocular pressure in the CSEA group

[3] A comparison of the RIGHT intraocular pressure between the GA and CSEA groups

[4] A comparison of the LEFT intraocular pressure between the GA and CSEA groups

Table 2: Intergroup and intragroup comparison of the distribution of systolic arterial pressure in time

SAP (mmHg)	Group GA (n = 25)	Group CSE (n = 25)	P
T0	139.32 ± 20.80	147.20 ± 27.54	0.259
T1	109.16 ± 20.64**	----	----
T2	139.20 ± 25.90	136.00 ± 16.61*	0.605
T3	112.12 ± 17.59**	131.40 ± 21.47**	**0.001**
T4	127.08 ± 23.31*	138.68 ± 26.19*	0.105

T0: Baseline; T1: After the induction of general anesthesia (Group GA only); T2: After intubation-Group CSEA; T3: After placement of the tourniquet; T4: After removal of the tourniquet

SAP: Systolic arterial pressure; Data presented as Mean ± standard deviation

**P < 0.05 according to the comparison with T0; **P < 0.01 according to the comparison with T0*

eyes at T0; i.e. the baseline measurement (P > 0.05). IOP values of Group CSE were significantly higher than the IOP values of Group GA at T2, T3, and T4 for both eyes (Table 1).

SAP values at T1, T3, and T4 were significantly lower than at T0 in patients included in Group GA (P < 0.05). On the other hand, SAP values were similar at T2 and T0 (P > 0.05) (Table 2).

SAP values at T2, T3, and T4 were significantly lower than at T0 in patients included in Group CSE (P < 0.05) (Table 2).

Comparison of the patients in Group GA and Group CSE showed that the SAP values at T3 were significantly higher in patients who received CSEA than those who received GA (P < 0.05). There was no significant difference in other measurement times (Table 2).

4. Discussion

In this study, there was no significant difference between the groups in terms of blood pressure at T2, whereas the IOP values for both eyes were significantly higher in Group CSE at T2, i.e. time of measurement after intubation for the Group GA and after subarachnoid block and epidural catheter placement for the Group CSE. Moreover, the IOP values of the patients in Group CSE were significantly higher at T2 than at baseline (T0). The increase in IOP in Group CSE starts as a result of increased CSF pressure due to the pressure on the dura matter from the Tuohy needle. Normal saline is given to the epidural space to enter the epidural space. Thereafter, the increase may continue due to the local anesthetic delivered into the CSF via the spinal needle and due to the inserted epidural catheter. The increased CSF pressure moves into the cranium along the neural axis and increases the IOP by putting pressure on the optic nerve and vascular structures.[7] Kang et al. found that the IOP started increasing after the insertion of the Tuohy needle during a neuraxial intervention and continued to increase for 2 min after the intervention.[8] It was commonly reported in various studies and reviews that sudden IOP spikes could be observed due to the increased CSF pressure observed in neuraxial interventions. It has been reported that increased trans-lamina cribrosa pressure could be of critical importance in patients who were at risk of loss of vision.[7,9–14]

Similar to the case in the general anesthesia group, the main determinant of IOP is the arterial blood pressure when a neuraxial intervention does not cause increased CSF pressure.[15,16] In Group GA, SAP values were significantly lower at T1, T3, and T4 than at T0. In correlation, the IOP values were lower at T1, T3, and T4 than at T0 for both eyes. On the other hand, the SAP and IOP values were similar at T2 and T0. In a study by Reitsamer et al. conducted on rabbits, it was reported that the ciliary process perfusion increased due to high blood pressure, which led to increased IOP. It was also stated that a decrease in the SAP reduced the perfusion of the ciliary process, which led to decreased IOP.[17]

In Group GA, SAP, and IOP at T3, i.e. the measurement after placement of the tourniquet, were even lower than at T0, which suggests that GA could lead to an ideal suppression of the hemodynamic and sympathetic responses associated with the tourniquet. Measurements at T3 showed that both SAP and IOP were higher in Group CSE, and the difference was statistically significant. Exsanguination of the lower extremity and application of a tourniquet increases the blood volume in the systemic circulation by 500–1000 mL. The tourniquet itself also applies pressure on underlying tissues, thereby increasing sympathetic response. IOP values were found to be lower under GA. This effect of CSEA on IOP should be considered in patient groups in which even a slight increase in IOP is clinically important. Previous studies asserted that the said IOP-decreasing effect was caused by general

anesthetics, opioids, and muscle relaxants that are administered to provide general anesthesia.[18,19]

Glaucoma is the second leading cause of blindness followed by cataracts and it affects nearly 60 million people worldwide.[20] Increased IOP is the most common cause of visual impairment in glaucoma; however, it is a treatable risk factor. Successful management of IOP reduces optic nerve damage and slows down the progress of the disease. Increased IOP puts pressure on vascular structures and disrupts the blood flow to the optic nerve, which in turn leads to a gradual deterioration of the optic nerve fibers that provide vision.[2]

The central retinal vein travels in the subarachnoid space with the optic nerve after exiting the lamina cribrosa and drains into the pterygoid plexus and cavernous sinus.[21] Therefore, drainage of the central retinal vein depends on a venous blood pressure that is higher than the cerebrospinal fluid (CSF) pressure. An increased CSF pressure will be directly deflected to the optic nerve and vascular structures. Increased pressure in the subarachnoid space due to any cause would be rapidly transferred to all neuraxial structures that contain CSF, thereby causing occlusion of the optic nerve and the accompanying vascular structures and preventing venous drainage, which would lead to increased IOP.[22] Similar to the observation in patients who are administered anesthetics during orthopedic surgery, practices that commonly employ neuraxial interventions may also lead to increased CSF pressure and prevent venous drainage, which in turn can increase IOP. Prevention of IOP fluctuations would reduce postoperative visual defects.

To our knowledge, no studies have compared the effects of general anesthesia and regional anesthesia on IOP. We believe that neuraxial regional anesthesia techniques may lead to higher IOP in comparison to general anesthesia. We also think that tourniquet-induced elevations in IOP could be managed better with general anesthesia.

5. Limitations

The limitations of this study are that the tourniquet times were not recorded and that there was a variety of knee and below-knee surgeries. Besides, all operations were performed by the same surgical team, and patients were not included in the study in any unexpected intraoperative condition such as bleeding or hypotension. Moreover, it is a single-center study. More studies with a large sample size are required to validate our findings.

6. Conclusion

The results of our research reveal that the patients who receive general anesthesia have significantly lower intraocular pressures at more time points than the CSEA group. This result may be beneficial to provide a better outcome in terms of safety in patients who are at high risk of increased intraocular pressure and subsequent loss of vision.

7. Data availability

The numerical data generated during the conduct of this study is available with the authors.

8. Conflict of interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

9. Acknowledgements

None

10. Authors' contribution

All authors took part in the concept and conduct of the study, data collection and statistical analysis and manuscript preparation. All authors have read the manuscript and approve it for publishing.

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