

Changes in intraocular pressures associated with inhalational and mixed anesthetic agents currently used in ophthalmic surgery

Sirisha Senthil, Mamata Nakka, Umashankar Rout¹, Hasnat Ali², Nikhil Choudhari, Swathi Badakere, Chandrasekhar Garudadri

Purpose: The aim of this study was to measure changes in intraocular pressures (IOPs) associated with inhalational and mixed anesthetic agents currently used for general anesthesia (GA) in ophthalmic surgery. **Methods:** In a cross-sectional study, 48 eyes from 48 consecutive subjects that underwent ophthalmic surgery under GA were included. Mixed anesthetics were used in 26 eyes and sevoflurane in 22 eyes. IOPs of the nonsurgery eyes were recorded at T1 (5 min before induction of anesthesia), T2 (5 min after intubation), and T3 (at the conclusion of surgery before extubation) using ICare PRO and Perkins tonometers. Linear mixed-effects models were used to compare differences in IOPs at various time points. Outcome measures were changes in IOP after induction of GA, intubation, and just before extubation and comparisons of decreases in IOPs induced by sevoflurane and mixed anesthetics. **Results:** Mean preanesthesia IOP for patients in this study (mean age \pm standard deviation = 26.9 \pm 18.3 years; range: 5–70 years) was 17.9 \pm 4.9 (range: 10–30) mm Hg. There was a significant decrease in the mean IOP (standard error (SE) (in mm Hg) at T2 (Perkins: -4.65 (0.57); ICare PRO: -5.16 (0.56) and T3 (Perkins: -5.63; ICare PRO: -5.36) as compared to the IOP at T1 ($P < 0.001$). The decreases in IOPs at T2 and T3 were similar in both anesthetic groups (T2: $P = 0.60$; T3: $P = 0.33$). **Conclusion:** Significant decreases in IOPs after GA were observed and the differences were not significantly different between sevoflurane and mixed anesthetic agents. For management decisions in pediatric glaucoma, the IOP measurements under GA are crucial, the underestimation of IOP as noted with currently used anesthetic agents has to be accounted for and decisions are taken appropriately.

Key words: General anesthesia, ICare PRO tonometer, inhalational anesthetics, intraocular pressure, Perkins tonometer

Intraocular pressure (IOP) is the most important parameter that is evaluated and treated in glaucoma.^[1] Accurate IOP measurement is essential for the appropriate management of glaucoma in both adults and children. IOP measurements may be affected by several ocular and nonocular factors,^[2,3] which need to be considered before management decisions concerning abnormal IOPs are taken. Obtaining reliable IOP measurements in young and uncooperative children is challenging and often requires sedation or anesthesia. Several agents used during the various stages of general anesthesia (GA) such as pre-anesthetic medications, inducing agents, and drugs used for maintenance and reversal have been shown to affect IOP measurements.^[4-9] Apart from the anesthetic agents themselves, other factors like the type of airway,^[10-12] tonometer, and method of IOP assessment,^[13-16] can also influence IOP measurements.

Sevoflurane (sevoflurane, USP) is the most commonly used halogenated inhalational anesthetic agent in ophthalmic

practice, as it causes faster induction, fewer systemic complications, minimal airway irritation, and is associated with faster recovery times^[17-21]; it is especially popular as a GA for short procedures in children.

Since several classes of drugs are used during induction and maintenance of GA, many of which can affect IOP, it is difficult to quantify the influences of each of these drugs on IOP. However, attempts to do so have been carried out in a few studies which used fixed anesthetic drug regimes in small cohorts of patients and compared the effects of individual anesthetic agents on IOPs.^[17-19] While fixed anesthetic drug regimens are ideal for research purposes, they cannot be practically applied in current day-to-day practices. This is because anesthesiologists usually use various drug cocktails for premedication and inducing anesthesia based on the patients' systemic status and safety, duration of surgery, and one's own experience.

VST Glaucoma Center, L V Prasad Eye Institute, Banjara Hills, Hyderabad, Telangana, ¹Department of Anesthesia, LV Prasad Eye Institute, Hyderabad, Telangana, ²Center for Biostatistics and Epidemiology, L V Prasad Eye Institute, Hyderabad, Telangana, India

Correspondence to: Dr. Sirisha Senthil, L.V Prasad Eye Institute, Kallam Anji Reddy Campus, Road No. 2, Banjara Hills, Hyderabad, Telangana - 500 034, India. E-mail: sirishasenthil@lvpei.org, sirishasenthil@gmail.com

Received: 12-Sep-2020

Revision: 15-Oct-2020

Accepted: 25-Feb-2021

Published: 18-Jun-2021

Access this article online

Website:

www.ijo.in

DOI:

10.4103/ijo.IJO_2923_20

Quick Response Code:



This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

Cite this article as: Senthil S, Nakka M, Rout U, Ali H, Choudhari N, Badakere S, et al. Changes in intraocular pressures associated with inhalational and mixed anesthetic agents currently used in ophthalmic surgery. Indian J Ophthalmol 2021;69:1808-14.

As of now, no studies have quantified the effects of mixed anesthetic agents on IOP measurements and compared them with Sevoflurane, which is the commonest inhalational anesthetic agent used. In this study, we have evaluated the changes in IOPs associated with different types of anesthetics used for GA during ophthalmic surgery.

Methods

In this cross-sectional study, conducted at our institute between January 2017 and August 2017, we evaluated the effects of different anesthetic agents on IOP at various time points and measured using two types of tonometers commonly used in children, the Perkins and rebound (ICare PRO) tonometers. Institutional review board approval was obtained (LEC-11-16-111) and the study adhered to all the tenets of the Declaration of Helsinki. Informed consent was taken from all patients; in the case of children, parental consent was obtained.

Inclusion criteria

Normal healthy individual without any systemic illness (known as ASA 1 as per American Society of anesthesiologists), individual with mild systemic illness under control with treatment (known as ASA 2) were included.^[20] Patients undergoing ophthalmic surgery under general anesthesia (ASA grade i, ii), and who were cooperative for IOP recording under topical anesthesia preoperatively, were included in the study.

Exclusion criteria

Patients allergic to anesthetic agents (as noted from prior history during preanesthetic check-up), and those with liver or kidney diseases, past history of vitreoretinal surgeries, refractive surgeries or any other intraocular surgeries known to affect IOP or its measurement, history of trauma, and eyes with corneal pathology that can influence IOP were excluded.

Procedures

In all cases, GA was induced via inhaled anesthetics. In children (sevoflurane group), anesthesia was induced with sevoflurane (8% for 30–60 s) along with nitrous oxide and oxygen (in a 1:1 mixture), and maintained with 2%–4% sevoflurane and nitrous oxide and oxygen (in a 1:1 mixture). In older children and adults (mixed anesthetics group), anesthesia was induced with a mix of propofol (2.0 mg/kg) or thiopentone sodium (4 mg/kg), fentanyl (2 µg/kg), and 2% sevoflurane (with nitrous oxide and oxygen in a 1:1 mixture); anesthesia was maintained with 2% sevoflurane and nitrous oxide and oxygen (in a 1:1 mixture). The muscle relaxant used was atracurium (0.5 mg/kg for induction and 0.1 mg/kg/30 min for maintenance). Oxygen saturation (SpO₂) levels of >98%, and end-tidal carbon dioxide partial pressures of 35–45 mm Hg were maintained throughout all surgeries. Use of endotracheal intubation or laryngeal mask airway was decided on by the anesthetist based on the duration of the procedure and age of the patient. Surgical procedures with expected surgical times of <2 h were included in this study.

The IOP of the eye not undergoing surgery (nonsurgical eye) was recorded at three time points with the patient in supine position by the same ophthalmologist. These time points were: 1) baseline IOP measured 5–10 min before induction of anesthesia (T1) in the preoperative room; 2) after induction of anesthesia and within 5 min after intubation (T2); and 3) at

the conclusion of surgery just before extubation (T3). The IOP was recorded first using an ICare PRO (handheld rebound tonometer that can be used in prone and supine position, ICare PRO; ICare Finland Oy, Helsinki, Finland), followed by a hand-held Perkins tonometer (Perkins; Clement-Clarke, Haag-Streit, UK). The Perkins IOP was recorded after instilling topical anesthetic drops and fluorescein staining. For measures of the Perkins IOP, an average of two readings were taken. The ICare PRO gives a digital display which is an average of five measurements, reliable ICare PRO readings as indicated by a green display were taken. The heart rates and blood pressures of patients were also recorded at all three time points. Central corneal thickness (CCT, Model Tomey SP 3000) measurements were also recorded in all eyes one day after the surgeries.

Statistical analysis

The calculated sample size was 48 subjects to detect a difference in IOP of >2 mm Hg with a power of 100% with an alpha error of 5%. Based on the normalities of the recorded continuous variables, descriptive statistics of either mean ± standard deviation (SD) or median and interquartile range (IQR) are reported for this study. A multiple comparison of means by Tukey contrast was used to compare the changes in IOP values at various time points pre- and post-anesthesia. A linear mixed-effects model was used to estimate between- and within-subject variability. Mixed-effects models do not assume independence among observations, and hence can be used in the presence of correlated observations within a unit or cluster, unlike traditional ANOVA models. An unpaired *t* test was used to compare mean IOPs between several pairs of groups: Perkins vs. ICare PRO, pediatric vs. adult patients, endotracheal intubation vs. laryngeal mask airway. In the results, a value of *P* < 0.05 was considered statistically significant. Statistical analyses were performed using R (version 3.3.2).

Results

Demographic and clinical characters

Between Jan 2017 and Aug 2017, 48 eyes of 48 patients aged between 5 and 70 years, all undergoing ophthalmic surgery under GA were enrolled in this study. There were 22 male and 26 female patients, 20 right eyes and 28 left eyes. Patients aged ≤16 years (*n* = 21) made up 44% of the sample. Only 18 patients (37.5%) in our study exhibited glaucoma and were on antiglaucoma medications. The mean pre-anesthesia IOP was 17.95 ± 4.9 mm Hg (range: 10–30 mm Hg). The type of airway management during anesthesia was either endotracheal intubation (in 41 subjects [85%]) or laryngeal mask airway (seven subjects [15%]). The general, ocular, systemic, and anesthesia parameters for all patients are shown in Table 1. Mean IOP values obtained at different time points using Perkins and ICare PRO tonometers are shown in Table 1. The mean heart rates, systolic, and diastolic blood pressures at various time points, and the end-tidal sevoflurane concentrations during anesthesia are given in Table 1. Surgical procedures consisted of 26 intraocular and 22 extraocular procedures, the mean durations of the surgeries were 42.5 ± 22.64 min (range: 5–95 min).

Reductions in IOP after induction of anesthesia

Table 2 and Figs. 1a and 2a show the mean differences and reductions in IOP values, respectively, at the three time points as measured with Perkins and ICare PRO tonometers.

Table 1: General, ocular, systemic, and anesthesia parameters in the study cohort (n=48)

Parameter	Number of observations	Mean	Standard Deviation	Minimum	Maximum
Age	48	26.94	18.33	5	70
CCT	48	550.31	47.65	470	687
Number of AGM	48	1.06	1.63	0	4
Duration of surgery (minutes)	48	42.5	22.64	5	95
Perkin_T1	48	17.95	4.9	10	30
Perkin_T2	48	13.29	4	8	28
Perkin_T3	48	12.31	4.33	5	32
ICare PRO_T1	48	19.45	4.9	7.7	31.9
ICare PRO_T2	48	14.3	3.91	6.8	26.3
ICare PRO_T3	48	14.09	3.66	6.6	23.5
HR at_T1	48	87.93	16.37	57	126
HR at_T2	48	82.25	15.97	53	126
HR at_T3	44	80.09	17.06	52	116
BP_Systolic_T1	48	113.48	17.82	87	157
BP_Diastolic_T1	48	69.1	11.47	50	98
BP_Systolic_T2	48	107.98	11.87	88	139
BP_Diastolic_T2	48	65.56	9.22	44	90
BP_Systolic_T3	36	104.72	16.05	80	160
BP_Diastolic_T3	36	66.17	13.4	46	94
End tidal sevoflurane concentration in %	41	1.55	1.31	0.2	8
End tidal CO ₂ concentration in mm Hg	22	35.68	4.36	26	46

CCT: central corneal thickness, CO₂: carbon dioxide, HR: heart rate, BP: blood pressure, AGM: antiglaucoma medications, T1: IOP measurement before anesthesia, T2: IOP measurement after anesthesia and intubation, T3: IOP measurement at the conclusion of surgery, before extubating

Table 2: Differences in IOP measurements at various time points in the study cohort. Multiple comparisons of means using linear mixed-effects models with Tukey's contrast; P values reported with Bonferroni's correction

	Mean difference	Std. error	95% CI		P
			LCL	UCL	
Perkins tonometer					
T2 - T1	-4.66	0.58	-6.13	-3.18	0.00
T3 - T1	-5.64	0.58	-7.11	-4.16	<0.001**
T3 - T2	-0.98	0.58	-2.46	0.50	0.55
ICare PRO tonometer					
T2 - T1	-5.16	0.56	-6.58	-3.74	<0.001**
T3 - T1	-5.36	0.56	-6.79	-3.94	<0.001**
T3 - T2	-0.20	0.56	-1.63	1.22	1.00

*Indicates $P < 0.05$; **Indicates $P < 0.01$. LCL: Lower confidence limits; UCL: Upper confidence limits

There were significant reductions in IOP values from T1 to T2 ($P < 0.01$) and T1 to T3 ($P < 0.01$) when measured with either Perkins or ICare PRO tonometers. The reductions in mean IOP values measured with Perkins and ICare PRO at T2 were -4.65 mm Hg and -5.16 mm Hg, respectively, and at T3 were -5.63 mm Hg and -5.36 mm Hg, respectively.

Effect of anesthetic regime on IOP

There were 22 eyes in the sevoflurane group (sevoflurane was used both for induction and maintenance) and 26 eyes in the mixed anesthetics group (where propofol or thiopentone sodium, fentanyl, and sevoflurane were used for induction

and maintenance of GA). The mean baseline IOP at T1 in both groups were similar ($P = 0.78$ for Perkins tonometer measurements and $P = 0.51$ for ICare PRO tonometer measurements). As shown in Table 3, and Figs. 1b and 2b, the decreases in IOP values after induction of anesthesia, at T2 ($P = 0.85$ for Perkins tonometer measurements and $P = 0.35$ for ICare PRO tonometer measurements) and T3 ($P = 0.42$ for Perkins tonometer measurements and $P = 0.20$ for ICare PRO tonometer measurements), were also not statistically significant.

Effect of endotracheal intubation and laryngeal mask airway on IOP

Although mean differences in IOP values measured using the Perkins tonometer were greater in cases where laryngeal mask airways were used (T2 = -6 mm Hg and T3 = -6.4 mm Hg), as compared to those which used endotracheal intubation (T2 = -4.4 mm Hg and T3 = -5.5 mm Hg), these differences were not statistically significant ($P = 0.35$ for T2 and $P = 0.66$ for T3). Similarly, mean differences in IOP values measured using the ICare PRO tonometer were greater for cases using laryngeal mask airways (T2 = -7.3 mm Hg and T3 = -9.3 mm Hg) than those using endotracheal intubation (T2 = -4.8 mm Hg and T3 = -6.8 mm Hg) though these differences were also not statistically significant ($P = 0.13$ for T2 and $P = 0.24$ for T3).

Effect of age on IOP

Our study had 27 adults and 21 children. The effect of age on IOP was compared at T1, T2, and T3, as shown in Figs. 1c and 2c. The baseline IOP at T1 as measured using a Perkins tonometer was not significantly different between the adult and pediatric patients ($P = 0.42$); similarly, decreases in IOPs after anesthesia

at T2 were not statistically different ($P = 0.15$) between the two groups. However, the decreases in IOP levels at T3 were significantly more in adults than those in children ($P < 0.02$), when IOPs were measured using the Perkins tonometer [Fig. 1c]. A similar result was obtained when the ICare PRO tonometer was used to measure IOPs [Fig. 2c]. Baseline IOPs at T1 were similar between adults and children ($P = 0.26$), as were the decreases in IOPs at T2 ($P = 0.45$). However, decreases in IOPs at T3 were significantly more in adults as compared to those in children ($P < 0.01$).

Decreases in IOP values in glaucomatous and nonglaucomatous eyes

The differences in IOP values for baseline (T1), T2, and T3 time points in glaucomatous ($n = 18$) and nonglaucomatous eyes ($n = 30$) were also compared. Differences between the two groups in the baseline IOPs at T1, when measured using the Perkins tonometer, were nonsignificant ($P = 0.26$), as were those for T2 ($P = 0.12$); IOP values at T3, however, were significantly different between the two groups with greater decrease in IOP

noted in nonglaucomatous eyes ($P < 0.03$). For measurements made with the ICare PRO tonometer, differences in T1 and T2 between the two groups were not statistically significant ($P = 0.1$ and $P = 1.0$, respectively). However, unlike the measurements made with the Perkins tonometer, differences in T3 were also found to be statistically nonsignificant ($P = 1.0$).

Changes in heart rate and blood pressure

Heart rates of patients were found to be significantly lower than baseline measures (T1) by averages of 5.6 beats/min and 8.0 beats/min at T2 ($P < 0.03$) and T3 ($P < 0.003$), respectively. However, although this difference was statistically significant, it was not clinically significant. The decreases in systolic blood pressures at T3 (when compared to those of T1) were statistically significant ($P < 0.01$), although these decreases were not significant at T2 ($P = 0$). Decreases in diastolic blood pressures were not clinically or statistically significant at T3 or T2 ($P = 0.78$ and $P = 0$, respectively). However, we did not find any significant association (p-value ranged from 0.27-0.92) between systolic blood pressure and

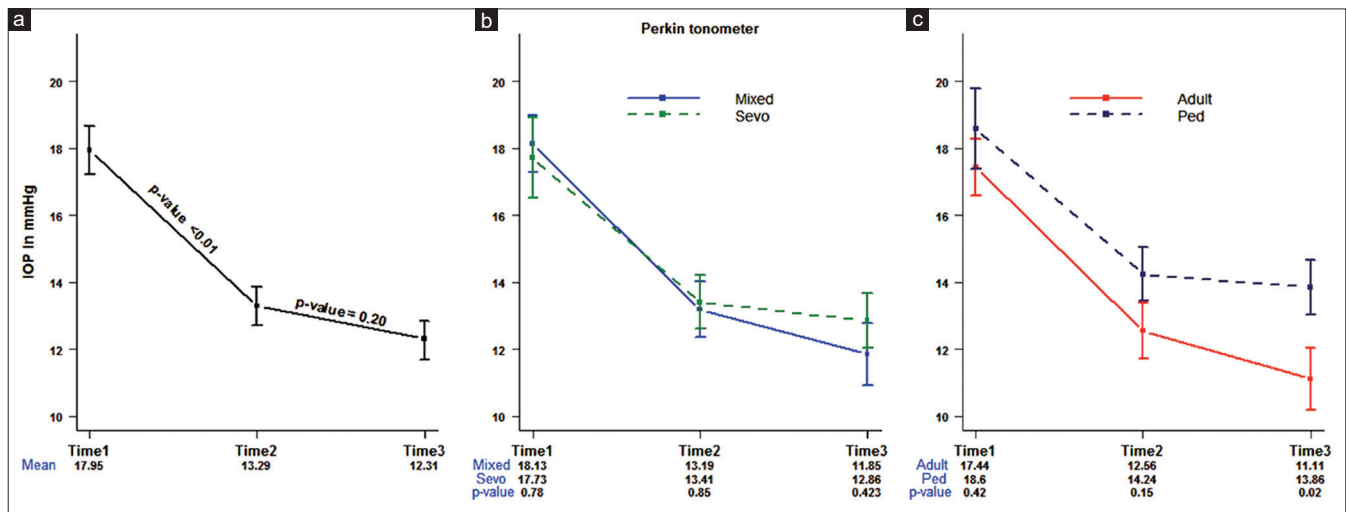


Figure 1: IOP measurements obtained using a Perkins tonometer. (a) Mean IOPs at different time points (T1, T2, and T3); (b) differences in IOPs at the 3 time points in the sevoflurane and mixed anesthetics groups; (c) variations in IOPs noted at the 3 time points in adults and children

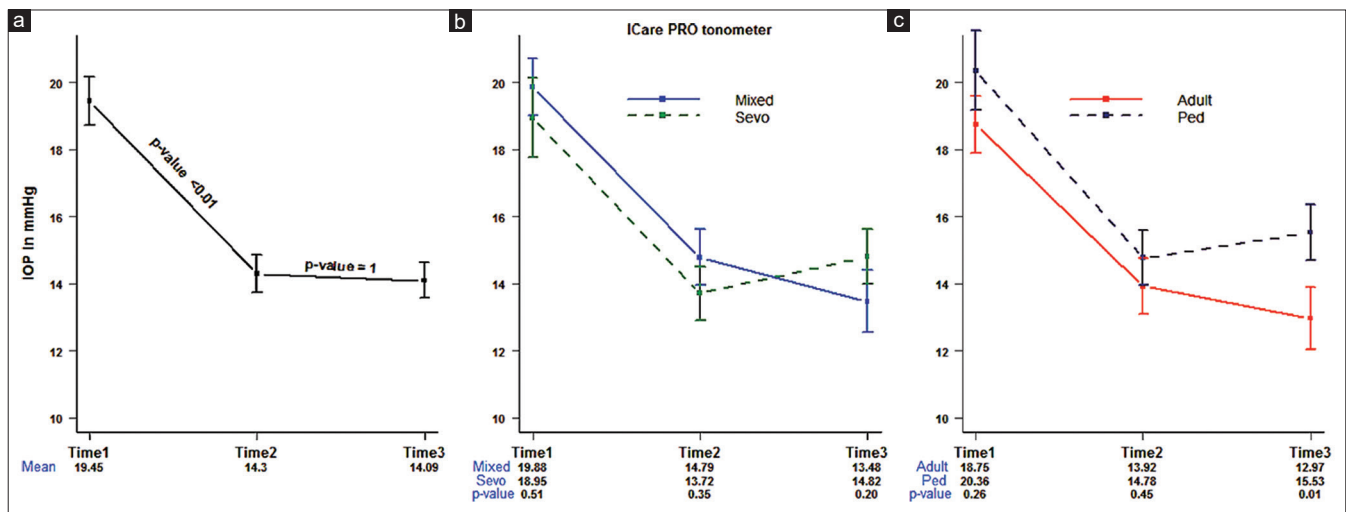


Figure 2: IOP measurements obtained using the ICare PRO tonometer. (a) Mean IOPs at different time points (T1, T2, and T3); (b) Differences in IOPs at the 3 time points in the sevoflurane and mixed anesthetics groups; (c) variations in IOPs noted at the 3 time points in adults and children

Table 3: Differences in intraocular pressures (IOPs) in patients under general anesthesia using sevoflurane or mixed anesthetic drugs between the baseline time point T1 (pre-anesthesia) and time points T2 (after induction) and T3 (at the conclusion of surgery) as measured with Perkins and ICare PRO tonometers. Test used: multiple comparison of means using linear mixed-effects models with Tukey's contrast; P values reported with Bonferroni's correction

Anesthetic	Difference in time points	Perkin tonometer					ICare PRO tonometer				
		Mean Difference	Std. Error	95% CI		P	Mean Difference	Std. Error	95% CI		P
				LCL	UCL				LCL	UCL	
Sevoflurane	T2 - T1	-4.32	0.97	-6.60	-2.04	<0.01	-5.23	0.89	-7.31	-3.16	<0.01**
	T3 - T1	-4.86	0.97	-7.14	-2.58	<0.01	-4.13	0.89	-6.21	-2.06	<0.01**
	T3 - T2	-0.55	0.97	-2.82	1.73	1.00	1.10	0.89	-0.98	3.18	0.64
Mixed anesthetics	T2 - T1	-4.94	0.74	-6.67	-3.21	<0.01	-5.10	0.72	-6.79	-3.40	<0.01**
	T3 - T1	-6.29	0.74	-8.02	-4.56	<0.01	-6.40	0.72	-8.10	-4.71	<0.01**
	T3 - T2	-1.35	0.74	-3.07	0.38	0.20	-1.31	0.72	-3.00	0.38	0.21

*Indicates $P < 0.05$; **Indicates $P < 0.01$

IOP or diastolic blood pressure on IOP measurements at the three time points.

A linear mixed-effects model with interactions was used to evaluate the effects of various parameters on IOP values. With both, Perkins and ICare PRO tonometers, CCT was found to have a significant positive effect ($P < 0.01$) on IOP values; i.e., patients with higher CCT values had slightly higher IOP values. However, the effect size was constant (ranged between 0.03 and 0.04) at every time point. Hence, the IOPs were not adjusted for the CCT.

The mean end-tidal sevoflurane concentration in this study cohort was $1.55 \pm 1.31\%$, and the mean end-tidal CO_2 concentration was 35.68 ± 4.36 mm Hg as shown in Table 1.

Discussion

In this nonrandomized, cross-sectional study, we evaluated the effects of commonly used inhalational anesthetics in decreasing IOP. During GA, several agents are used for induction and maintenance of anesthesia, muscle relaxation, analgesia, and sedation depending on the patient's systemic parameters and the type and duration of surgery. It is well known that many inhalational anesthetics reduce IOP.^[6,21,22] We conducted this study with drugs used for GA in regular clinical practice, rather than with a fixed anesthetic drug regimen as is mostly done for research purposes. We categorized patients into two cohorts based on anesthetic regimens commonly used in clinical practice; these were: 1) the sevoflurane group (where only sevoflurane along with nitrous oxide and oxygen are used to induce and maintain anesthesia) and 2) the mixed anesthetics group (where propofol or thiopentone sodium, fentanyl, and sevoflurane (with nitrous oxide and oxygen) are used to induce anesthesia, and sevoflurane with nitrous oxide and oxygen is used to maintain it). Although it would have been ideal to have had a cohort of uniform age in this study (specifically children, as they would have been the representative population to which this study's results would have applied), our study included both adults and children. This is because it is not practical to conduct such a study on very young children due to the very real challenges of acquiring reliable measures of IOP values using a Perkins tonometer (which is the gold standard in measuring IOPs) when the patient is awake.

In this study, IOP values recorded via both Perkins and ICare PRO tonometers showed a significant decrease (by 4–6 mm Hg)

after induction of anesthesia, intubation, and at the end of the surgery. While making diagnostic and therapeutic decisions, especially for children, it is important to be cognizant of this underestimation in IOP values during GA. We noted progressive reductions in IOPs (at T2 and T3) in both groups; though the differences in these reductions were not statistically significant between the two groups, these differences may be clinically significant. What we can infer from our data, is that IOP needs to be checked as soon as possible after induction of anesthesia to obtain IOP measurements closest to the true IOP. In children, while IOP is an important parameter that influences medical decisions, the effect of other parameters, such as corneal diameter, myopic shift in refraction, and structural progression, must also be considered.

Similar to our results, Park *et al.* (2013)^[18] showed IOP reductions of 5–6 mm Hg as measured by Tonopen, in patients anesthetized with either sevoflurane or desflurane. Schäfer *et al.* (2002)^[17] compared IOP measurements in patients anesthetized with a combination of anesthetics such as propofol with remifentanyl or sevoflurane with remifentanyl; IOPs were measured using Draeger's tonometer and the study reported greater IOP reductions in the group treated with propofol and remifentanyl than the one treated with sevoflurane and remifentanyl. However, the study lacked details on the degree of IOP reduction in the two groups. Gofman *et al.* (2017)^[21] compared IOP values in patients anesthetized with propofol administered by targeted control infusion, with those anesthetized with sevoflurane in the increasing vs. decreasing concentration (0.5%, 2%, and 5%). The authors showed that there were no significant changes in IOPs before and after induction of anesthesia, and that there were no differences in IOP values between the two groups of patients treated with the different anesthetics. The results of this study, however, are contradictory to those of other studies that have shown that both propofol and sevoflurane decrease IOP.^[17,18]

Endotracheal intubation has been shown to increase IOP via hemodynamic changes,^[10,11] and by stimulating the sympathetic nervous system, which leads to higher resistance in aqueous outflow at the level of the trabecular meshwork.^[10,11,23-26] Laryngeal airway mask induces lesser hemodynamic changes compared to endotracheal intubation.^[27] Although our primary aim was not to compare variations in IOP between the two types of airway maintenance (endotracheal tube or laryngeal

mask airway) used during GA, we had enough data to do so; this comparison is important for determining if IOPs recorded under GA with these two methods can be used interchangeably. In this study, although the mean reduction in IOP was slightly more for patients on whom laryngeal mask airways were used as compared to those on whom endotracheal intubation was used, the difference was not statistically significant, owing to small sample size. Similar to our study, Eltzschig *et al.* (2017)^[19] reported mean IOPs decreased by 3–4 mm Hg in endotracheal intubation and laryngeal mask airway groups with no differences noted between the two groups.

Our data, which includes almost equal numbers of adults and children, indicates that the IOPs at T1 and T2 in these two cohorts were similar; however, at T3, the decrease in IOP was much higher in the adult group. One-third of the patients included in this study suffered from glaucoma; however, since these patients were on antiglaucoma medication, the baseline IOPs between glaucoma patients were not very different from those of patients without glaucoma. A greater decrease in IOP at T3 was noted in adults compared to children, majority of adults were nonglaucomatous; and significantly larger number of children had glaucoma (15/21 vs. 3/27, $P < 0.0001$) in our study. Airway manipulation during GA causes rise in IOP due to increase in BP and increase in blood flow to the eye, increased sympathetic tone with higher resistance to aqueous outflow at the level of the trabecular meshwork. This increase in IOP is greater in eyes with glaucoma compared to nonglaucomatous eyes due to greater outflow resistance in glaucomatous eyes,^[28] which can explain the difference noted in our study between glaucomatous and nonglaucomatous eyes.

There is conflicting evidence in the literature on the effect of posture on IOP measurements.^[29–31] It is known that the IOP measurements are affected by position, elevated episcleral venous pressure is implicated to higher IOP measured in supine position compared to the sitting position.^[29,30] All the IOP measurements in our study were measured in supine position hence it is unlikely that the IOP differences noted at various time points in our study would be affected by postural variations. In the current study with no postural variations in IOP measurement, this factor is unlikely to affect the readings.

Several systemic parameters like heart rate and blood pressure, which may affect IOP, may be altered during GA. The end-tidal CO₂ level is another important parameter that can influence IOP in patients under GA.^[32,33] Levels of end-tidal CO₂ > 45 mm Hg can directly affect blood pressure, which can indirectly influence IOP. In our study, the end-tidal CO₂ levels were found to be maintained at a mean of 35.68 mm Hg. Since sevoflurane concentration in exhaled air is directly proportional to the decrease in IOP, maintaining sevoflurane at this concentration is desirable to prevent an excessive decrease in IOP decrease.^[21] In our study, the mean end-tidal sevoflurane concentration was 1.55%; it is possible that since these parameters (end-tidal CO₂ levels and end-tidal sevoflurane concentrations) were strictly maintained during surgery, their effects on IOP values were not evident.

The Perkins tonometer is a handheld variant of the Goldmann applanation tonometer and is the current gold standard for IOP estimation in the supine position for both adults and children.^[34] However, Rebound tonometers are increasingly used for IOP estimation in children and have

shown good agreement with Perkins tonometer estimations of IOP, although slightly overestimates when IOP values are higher than 19 mm Hg.^[15] Hence, we used both tonometers to measure all IOP readings at various time points. Significant reductions in IOP were measured by both tonometers at all time points after anesthesia; however, the IOP measurements obtained via the ICare PRO tonometer were higher than those obtained via the Perkins tonometer by an average of 1.4 mm Hg for all time points (these differences were statistically significant for time points T1 and T3); this result validates the results of several other studies.^[22,35,36]

Our study is different from other studies on this topic, as the comparisons of IOPs recorded at various time points with pre-anesthesia IOP values were carried out using linear mixed effect models. In addition, we believe that our study, which documents the effects of commonly used anesthetics (that are preferred in day-to-day practice) on IOP measurements and uses two tonometers to record IOPs, is more useful in understanding how different factors can affect IOP measures in patients under GA, than any other previous work on this subject. This work not only evaluates the effect of GA on IOP measurement, but also quantifies the reductions in IOP values at various time points after anesthesia. By not restricting this study to a single anesthetic agent, we were also able to gain some insights on how IOP is affected by the protocols followed in day-to-day practice; this makes our results applicable to a larger pool of patients.

The main limitation of this study is the involvement of multiple anesthetists and ophthalmologists (two ophthalmologists were involved in acquiring IOP measurements for this study), although all the IOP readings for a patient were taken by a single observer. The other limitations in this study are the very small sample sizes for the laryngeal mask airways cohort.

Conclusion

In conclusion, this work is a cross-sectional study comparing pre-anesthesia IOP measurements with IOP measurements obtained after induction of GA with inhalational anesthetics. We found that IOPs were significantly underestimated when patients are under GA. Since IOP is underestimated under GA, the 'actual IOP' should be ~4–6 mm Hg higher than the IOP measured in patients under GA; this difference has to be accounted for while making medical management decisions based on IOP values in children with glaucoma. While reporting IOPs in surgical studies, the "cut-offs" for IOP controls under GA and awake conditions should be different.

Financial support and sponsorship

Hyderabad Eye Research Institute.

Conflicts of interest

There are no conflicts of interest.

References

1. Musch DC, Gillespie BW, Niziol LM, Lichter PR, Varma R; CIGTS Study Group. Intraocular pressure control and long-term visual field loss in the Collaborative Initial Glaucoma Treatment Study. *Ophthalmology* 2011;118:1766-73.
2. Whitacre MM, Stein R. Sources of error with use of Goldmann-type tonometers. *Surv Ophthalmol* 1993;38:1-30.
3. Kawase K, Tomidokoro A, Araie M, Iwase A, Yamamoto T; Tajimi

- Study Group; Japan Glaucoma Society. Ocular and systemic factors related to intraocular pressure in Japanese adults: The Tajimi study. *Br J Ophthalmol* 2008;92:1175-9.
4. Self WG, Ellis PP. The effect of general anesthetic agents on intraocular pressure. *Surv Ophthalmol* 1977;21:494-500.
 5. Cunningham AJ, Barry P. Intraocular pressure-physiology and implications for anaesthetic management. *Can Anaesth Soc J* 1986;33:195-208.
 6. Murphy DF. Anesthesia and intraocular pressure. *Anesth Analg* 1985;64:520-30.
 7. Holloway KB. Control of the eye during general anaesthesia for intraocular surgery. *Br J Anaesth* 1980;52:671-9.
 8. Peuler M, Glass DD, Arens JF. Ketamine and intraocular pressure. *Anesthesiology* 1975;43:575-8.
 9. Jaafar MS, Kazi GA. Effect of oral chloral hydrate sedation on the intraocular pressure measurement. *J Pediatr Ophthalmol Strabismus* 1993;30:372-6.
 10. Watcha MF, Chu FC, Stevens JL, White PF. Intraocular pressure and hemodynamic changes following tracheal intubation in children. *J Clin Anesth* 1991;3:310-3.
 11. Duman A, Ögün CÖ, Ökesli S. The effect on intraocular pressure of tracheal intubation or laryngeal mask™ insertion during sevoflurane anaesthesia in children without the use of muscle relaxants. *Paediatr Anaesth* 2001;11:421-4.
 12. Bhardwaj N, Yaddanapudi S, Singh S, Pandav SS. Insertion of laryngeal mask airway does not increase the intraocular pressure in children with glaucoma. *Pediatr Anesth* 2011;21:1036-40.
 13. Hartley J, Song J. Evaluation of accuracy in Goldmann and perkins applanation tonometry. *Invest Ophthalmol Vis Sci* 2006;47:4431.
 14. Lasseck J, Jehle T, Feltgen N, Lagrèze WA. Comparison of intraocular tonometry using three different noninvasive tonometers in children. *Graefes Arch Clin Exp Ophthalmol* 2008;246:1463-6.
 15. Badakere SV, Rao HL, Ali MH, Mandal AK, Choudhari NS, Chandrasekhar G, *et al.* Comparison of rebound tonometry and handheld applanation tonometry in pediatric glaucoma with clear and scarred corneas. *Ophthalmology* 2019;126:1330-2.
 16. Bordon AF, Katsumi O, Hirose T. Tonometry in pediatric patients: A comparative study among Tono-pen, Perkins, and Schiötz tonometers. *J Pediatr Ophthalmol Strabismus* 1995;32:373-7.
 17. Schäfer R, Klett J, Auffarth G, Polarz H, Völcker HE, Martin E, *et al.* Intraocular pressure more reduced during anesthesia with propofol than with sevoflurane: Both combined with remifentanyl. *Acta Anaesthesiol Scand* 2002;46:703-6.
 18. Park JT, Lim HK, Jang K-Y, Um DJ. The effects of desflurane and sevoflurane on the intraocular pressure associated with endotracheal intubation in pediatric ophthalmic surgery. *Korean J Anesthesiol* 2013;64:117-21.
 19. Eltzschig HK, Darsow R, Schroeder TH, Hettesheimer H, Guggenberger H. Effect of tracheal intubation or laryngeal mask airway™ insertion on intraocular pressure using balanced anesthesia with sevoflurane and remifentanyl. *J Clin Anesth* 2001;13:264-7.
 20. Abouleish AE, Leib ML, Cohen NH. ASA provides examples to each ASA Physical Status Class. *ASA Newsletter* 2015;79:38-49.
 21. Gofman N, Cohen B, Matot I, Cattani A, Dotan G, Stolovitch C, *et al.* Do intraocular pressure measurements under anesthesia reflect the awake condition? *J Glaucoma* 2017;26:299-302.
 22. Mikhail M, Sabri K, Levin AV. Effect of anesthesia on intraocular pressure measurement in children. *Surv Ophthalmol* 2017;62:648-58.
 23. Şahin A, Tüfek A, Cingü AK, Çaça I, Tokgöz O, Balsak S. The effect of I-gel™ airway on intraocular pressure in pediatric patients who received sevoflurane or desflurane during strabismus surgery. *Pediatr Anesth* 2012;22:772-5.
 24. Prys-Roberts C, Greene LT, Meloche R, Foëx P. Studies of anaesthesia in relation to hypertension. II: Hemodynamic consequences of induction and endotracheal intubation. 1971. *Br J Anaesth* 1998;80:106-22.
 25. Casati A, Aldegheri G, Fanelli G, Gioia L, Colnaghi E, Magistris L, *et al.* Lightwand intubation does not reduce the increase in intraocular pressure associated with tracheal intubation. *J Clin Anesth* 1999;11:216-9.
 26. Brimacombe J. The advantages of the LMA over the tracheal tube or facemask: A meta-analysis. *Can J Anaesth* 1995;42:1017-23.
 27. Obsa MS, Kanche ZZ, Olana Fite R, Tura TS, Adema BG, Kinfe AA, *et al.* Effect of laryngeal mask airway insertion on intraocular pressure response: Systematic review and meta-analysis. *Anesthesiol Res Pract* 2020;2020:7858434. doi: 10.1155/2020/7858434.
 28. Madan R, Tamilselvan P, Sadhasivam S, Shende D, Gupta V, Kaul HL. Intra-ocular pressure and haemodynamic changes after tracheal intubation and extubation: A comparative study in glaucomatous and nonglaucomatous children. *Anaesthesia* 2000;55:380-4.
 29. Gautam N, Kaur S, Kaushik S, Raj S, Pandav SS. Postural and diurnal fluctuations in intraocular pressure across the spectrum of glaucoma. *Br J Ophthalmol* 2016;100:537-41.
 30. Sit AJ, Nau CB, McLaren JW, Johnson DH, Hodge D. Circadian variation of aqueous dynamics in young healthy adults. *Invest Ophthalmol Vis Sci* 2008;49:1473-9.
 31. Uzlu D, Akyol N, Türk A, Gürsoy N, Somuncu AM, Oruç Y. Effect of body position on intraocular pressure measured by rebound tonometer in healthy children. *Turk J Ophthalmol* 2020;50:271-4.
 32. Huber KK, Adams H, Remky A, Arend KO. Retrobulbar haemodynamics and contrast sensitivity improvements after CO2 breathing. *Acta Ophthalmol Scand* 2006;84:481-7.
 33. Klein B, Klein R, Knudtson M. Intraocular pressure and systemic blood pressure: Longitudinal perspective: The Beaver Dam Eye Study. *Br J Ophthalmol* 2005;89:284-7.
 34. Perkins ES. Hand-held applanation tonometer. *Br J Ophthalmol* 1965;49:591-3.
 35. Dosunmu EO, Marcus I, Tung I, Thiamthat W, Freedman SF. Intraocular pressure in children: The effect of body position as assessed by Icare and Tono-Pen tonometers. *Am J Ophthalmol* 2014;158:1348-52.e1.
 36. Jablonski KS, Rosentreter A, Gaki S, Lappas A, Dietlein TS. Clinical use of a new position-independent rebound tonometer. *J Glaucoma* 2013;22:763-7.