Kocatepe Veteriner Dergisi

Kocatepe Veterinary Journal ISSN: 1308-1594

ARAŞTIRMA MAKALESİ/RESEARCH ARTICLE

Comparison of the Effects of Sevoflurane and Isoflurane Anaesthesia on Intraocular Pressure in Dogs

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SUMMARY

This study aimed to compare the effects of sevoflurane and isoflurane on intraocular pressure (IOP) in dogs. The study animals were 12 healthy dogs of diverse age (1-4 years), sex and breed. The dogs were divided into two groups. The first (SEVO group, n = 6) was received anesthesia with atropine sulfate, xylazine hydrochloride (HCl), thiopental sodium and sevoflurane. Anesthesia in the second group (ISO group, n = 6) was carried out with isoflurane instead of sevoflurane, administered with the same doses of the same other drugs. IOP was measured by Schiøtz tonometer with 5.5 g, 7.5 g or 10 g weights. The obtained values were interpreted through to the calibration table of Peiffer and Friedenwald. The decrease in IOP was smaller in the SEVO group as compared to ISO. A decline in IOP during the maintenance phase was seen in both groups up to 60 minutes. The decrease in the ISO group was statistically significant (P<0.0001), however, while this was not the case in the SEVO group. An IOP increase was recorded 60 min after the anesthesia, while the finding on the first day was similar to that at the start of anesthesia maintenance. In this study, sevoflurane anesthesia was found to be safer than the one with isoflurane with regard to IOP and the examined hemodynamic parameters.

KEY WORDS: Cardiac Index, Central Venous Pressure, Dog, Heart Rate, Intra-Ocular Pressure, Isoflurane, Mean Arterial Pressure, Schiøtz Tonometry, Sevoflurane

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Köpeklerde Sevofloran ve İzofloran Anestezisinin İntraoküler Basınca Etkisinin Karşılaştırılması

ÖZET

Bu araştırmada köpeklerde sevofloran ve izofloran anestezisinin intraoküler basınca (İOB) etkisini karşılaştırılması amaç edinilmiştir. Araştırmanın materyalini 12 adet farklı yaş (1-4 yaş), cinsiyet ve ırkta köpek oluşturdu. Köpekler iki gruba ayrıldı. Birinci gruba (Grup SEVO, n=6); atropin sülfat, ksilazin hidroklorid, tiyopental sodyum ve sevofloran anestezisi uygulandı. İkinci gruba (Grup İZO, n=6); sevofluran yerine izofloran anestezisi ve diğer ilaçlar aynı dozda uygulandı. Köpeklerin İOB'ları 5,5, 7,5 ve 10.0 g. ağırlıkları bulunan Schiøtz tonometresi ile ölçüldü. Schiøtz tonometresi ile elde edilen değerler Peiffer ve Freindenwald adlı araştırıcıların kalibrasyon tablolarına göre değerlendirildi. İki grubun ölçüm sonuçları incelendiğinde; sevofloran anestezisinde İOB değerleri, izofloran anestezisi İOB değerlerine göre daha az düşmüştür. Her iki grupta da anestezi idamesi 60. dakikaya kadarki ölçüm sonuçları düşüş yönünde kaydedilmiştir. Bununla birlikte Grup İzo'daki düşüş istatistiksel olarak anlamlı bulunmuştur (P<0,0001), ancak sevo grubunda durum böyle değildir.Anestezi sonu 60. dakikada her iki grupta İOB yükselme yönünde kaydedilmiş ve 1. günde elde edilen bulgu, anestezi idamesi 0. dakika ölçüm sonuçlarına yaklaşmıştır. Araştırmada elde edilen bulgular ışığında, Sevofloran anestezisi gerek İOB'a gerekse hemodinamik parametrelere olan etkisi yönünden izofloran anestezisine göre daha güvenli bulunmuştur.

ANAHTAR KELİMELER: CI, CVP, Köpek, HR, İOB, İzofloran, MAP, Schiøtz Tonometresi, Sevofloran

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Introduction

Intraocular pressure (IOP) is determined by the dynamic equilibrium between its production by the ciliary body in the posterior ocular chamber and its elimination from the irido-corneal angle through Schlemm's canal (Gum 1991).

The measurement of intraocular pressure, or "tonometry", is essentially determined by three methods in veterinary ophthalmology: palpation, indentation tonometry and applanation tonometry (Slatter 1990). The cornea diameter is essential in measuring with indentation tonometry, which measures the IOB based on the indentation of the eye in response to pressure. The Schiøtz tonometer is the instrument used for such measurements (Peiffer and Petersen 1997). The fact that the curvature and rigidity of the human cornea is different than that of small animals necessitates the use of a translation table for optimal evaluation (Gum 1991).

The normal values in the Schiøtz tonometer pressure scale are approximately 3-7 for dogs and 2-6 for cats; it has been proposed that using a 5.5 g weight, a value of less than 3 on the scale would indicate an increased IOP, while more than 7 would mean ocular hypotension. The normal IOP values in dogs measured with the Schiøtz tonometer are 15-25 mm Hg (Gum 1991).

There is a weak correlation between arterial blood pressure and IOP. IOP was found to be low in diseases that are accompanied by low blood pressure (as for example hypoadrenocorticism, dehydration, hypovolemic or cardiogenic shock (Slatter 1990).

Immediate reduction of IOP is seen with sleep or at the start of anesthesia procedures, both situations where there is a loss of tonus of the extra-ocular tissues (Moses and Hart 1987).

Short-acting anesthetic agents are proposed for ocular surgery (Klett et al. 2002). Raw et al. observed a decrease in IOP within less than 10 minutes from intravenous diazepam administration (Raw and Mostafa 2001). They did not observe an effect on IOP when midazolam i.v. was given before induction. Sedatives and tranquilizers are used frequently, especially before intraocular surgery. All sedatives and tranquilizers reduce IOP, an effect probably mediated by the increase of aqueous humor drainage. Studies in different animals have shown that many narcotics slowly reduce IOP (Gelatt and Gelatt 2001). It has been reported that volatile anesthetic agents like halothane, enflurane, isoflurane, sevoflurane and desflurane reduce IOP on a dose-response curve (Raw and Mostafa 2001).

It is reported in a study that the heart rate (HR) in dogs increases during all stages of anesthesia, while systemic vascular resistance (SVR) diminishes by successive stages and blood pressure, both systolic and diastolic, sinks in a dose-dependent fashion with sevoflurane (Mutoh et al. 1997). As a conclusion, the cardiovascular effects of sevoflurane was more marked than that of halothane, similar to isoflurane but smaller than that of enflurane.

The objective of the present study was to compare the effects of sevoflurane anesthesia, used in veterinary practice during the last years, to isoflurane, with particular attention to IOP results.

Material and Methods

The study subjects were 12 stray dogs. Following a routine health check, the animals were observed for 10 days, during which they underwent a routine ophthalmic examination, vaccinations and anti-parasitic treatment. Approval was obtained from the Local Ethical Committee of Afyon Kocatepe University.

The animals were divided in two groups of six animals each, without consideration of age or sex. The IOP values were measured using a Schiøtz tonometer (Reister).

Anesthesia Protocol

All animals in the study were fasted for 24 hours before treatment. Premedication in both groups consisted of atropine sulfate (Belladon®), 0.04 mg/kg subcutaneous (s/c) and xylazine HCl (Rompun® Bayer), 2 mg/kg intramuscularly (i.m.) and, for induction, thiopental sodium (Pentotal® Abbot A.Ş), 15 mg/kg intravenously (i.v.). The

animals were intubated by the orotracheal route and connected to an anesthesia device (Vent 2000 SMS Ltd Şt., Turkey). A venous catheter was placed in the forearm cephalic vein and Ringer's Lactate solution was infused at a rate of 10 ml/kg/h. Animals in both groups were ventilated with a tidal volume of 15 ml/kg at a rate of 16 excursions/min. SpO2 was continuously monitored through a lingual probe.

General anesthesia was obtained with the use of sevoflurane 1.5% (Sevorane® Likid, Abbott Ltd Şt.) or isoflurane 1.5% (Forane® Likid , Abbott Ltd Şt.) according to the study group. Two drops of oxybuprocaine 0.4%, 4.5 mg/mL, were applied to each eye for local anesthesia. The results obtained by Schiøtz tonometry were evaluated using a calibration table for dogs.

Hemodynamic Monitoring

The left femoral arteries of all dogs were dissected using a soft tissue instrument kit after connecting the animal to the anesthesia device and aseptically preparing the medial femoral region. An arterial catheter (20 cm Deltacath, Becton-Dickinson, USA) was placed in artery under direct vision and connected to a transducer (Bıçakçılar Tıbbi Malzemeler A.Ş), allowing the monitoring of mean arterial blood pressure (MAP). A Swan-Ganz thermo-dilution catheter (7 F, 115 cm, Abbott Critical Care Systems, USA) was advanced into the pulmonary artery through the femoral vein and connected to a cardiac output (CO) monitor (Deseret 1000 Cardiac Output Computer, Deseret Med Inc., USA) ensuring continuous cardiac index (CI) recording. Electrocardiography (ECG) electrodes were placed on extremities and also connected to the multichannel monitor (PETAŞ Monitör Sistemleri Ltd.Şt., Turkey), allowing the follow-up of heart rate (HR) and ECG. The values of MAP, CI, CVP and HR were recorded at 0, 30 and 60 min of the anesthesia maintenance phase, from the start of post-induction stabilization.

IOP Measurements

After placing the animal's head in the upright position, benoxinate was dropped onto both eyes for local anesthesia. A Schiøtz tonometer was positioned on the cornea and the IOP values read using 5.5, 7.5 and 10 g weights at 0, 15, 30 and 60 minutes counting from post-induction stabilization. Ventilation with the anesthetic agent was interrupted after the 60 min measurement and the animals extubated after the return of spontaneous respiration. IOP measurement was repeated 60 minutes after the end of anesthesia, then again one day later, after which the study was terminated.

Statistical Analysis

The values at all the times of measurement were compared between the two study groups by the Two-sample t-Test and the values at different times were compared among themselves by ANOVA and Tukey's test, using a Windows-based SPSS software package. Descriptive statistics of measurement results were expressed as mean ± standard error (SE).

Results

The IOP values are summarized separately according to their interpretation by either Peiffer's or Friedenwald's calibration tables; the within-group comparisons of the different measurement time points are shown in Table 1 and the comparison between groups for each time point in Table 2. The drop in IOP from 0 to 60 min post-stabilization was statistically significant in the SEVO group according to pressure evaluation by the Peiffer calibration table ($P<0.0001$). IOP increase 60 min after the end of anesthesia for both SEVO and ISO groups (21.51±1.10 and 31.93±0.69 mm Hg, respectively) and its increase 24 hours later in the ISO group (40.1±1.30 mm Hg) were statistically significant ($P<0.0001$).

The values for CVP, MAP, HR and CI are summarized and their within-group and between-group comparisons shown in Tables 3 and 4, respectively. The CI values at 60 minutes from post-induction stabilization were 0.87±0.06 L/min/m2 for the SEVO group and 0.67±0.06 for the ISO group ($P=0.473$).

Table 1: Within-Group IOP Values as Interpreted with the Peiffer or Friedenwald Calibration Tables and their Comparison.

	0 min	15 min	30 min	60 min	60 min post	1 day
Peiffer						
SEVO (mm Hg)	24.18±1.51^{b}	19.81±1.50^{c}	19.31±0.50^{c}	19.71±0.62^{c}	21.51±1.10^{b,c}	27.01±1.06^{a}
ISO (mm Hg)	38.74±1.86^{a}	27.73±0.45^{d}	26.24±0.57^{d}	26.21±0.13^{d}	31.93±0.6^{b}	40.13±1.30^{a}
Friedenwald						
SEVO (mm Hg)	12.23±1.29^{a,b}	8.48±1.10^{b,c}	6.76±0.68^{c}	8.21±1.32^{b,c}	10.76±1.78^{a,b,c}	14.36±1.72^{a}
ISO (mm Hg)	23.50±1.64^{a}	14.19±0.67^{c}	13.61±0.50^{c}	13.86±0.22^{c}	17.54±0.61^{a}	24.73±1.14^{a}

SEVO: Sevoflurane group. **ISO:** Isoflurane group.,
The values marked with different letters from each other were found to be significantly different (P<0.05)

Table 2: Comparison Between Groups of IOP Values

	By Peiffer's Calibration Tables			By Friedenwald's Calibration Tables		
	SEVO	**ISO**	**P**	**SEVO**	**ISO**	**P**
0 min	24.18±1.51	38.74±1.86	**0.0001**	12.23±1.29	23.50±1.64	**0.0001**
15 min	19.81±1.50	27.73±0.45	**0.0001**	8.48±1.10	14.19±0.67	**0.001**
30 min	19.31±0.50	26.24±0.57	**0.0001**	6.76±0.68	13.61±0.50	**0.0001**
60 min	19.71±0.62	26.21±0.13	**0.0001**	8.21±1.32	13.86±0.22	**0.001**
60 min post	21.51±1.10	31.93±0.69	**0.0001**	10.76±1.78	17.54±0.61	**0.011**
1 day	27.01±1.06	40.13±1.30	**0.0001**	14.36±1.72	24.73±1.14	**0.001**

Table 3: CVP, MAP, HR and CI Values and Within-Group Comparisons

		0 min	15 min	30 min	60 min	P
CVP (mm Hg)	SEVO	8±0.73	6.83±0.31	7±0.58	7.67±0.42	P: 0.386
	ISO	7.50±0.34	7.33±1.28	8.17±0.79	7.67±1.05	P: 0.930
MAP (mm Hg)	SEVO	128.83±9.41	118.50±10.43	109±7.47	107.17±7.12	P: 0.299
	ISO	97.67±11.06	74.67±9.09	74±12.59	71.33±9.21	P: 0.290
HR (bpm)	SEVO	104.67±8.87	94±8.15	90.17±7.23	93.67±8.60	P: 0.635
	ISO	92.83±5.94	92.17±8.05	105.17±6.62	91.17±3.72	P: 0.371
CI (L/min/m^2)	SEVO	1.16±0.21	0.97±0.08	0.95±0.12	0.87±0.06	P: 0.473
	ISO	0.72±0.04	0.72±0.08	0.72±0.06	0.67±0.06	P: 0.925

SEVO: Sevoflurane. **ISO:** Isoflurane. **CVP:** Central venous pressure. **MAP:** Mean arterial pressure. **HR:** Heart rate. **CI:** Cardiac Index

Discussion

IOP varies according to multiple factors in the dog (Evans 1993, Gelatt and Gelatt 2001, Gum 1991, Klett et al. 2002, Moses and Hart 1987, Raw and Mostafa 2001). Age, sex and other possible factors were ignored in the two groups of dogs in this study, which were given the same premedication and induction, followed by anesthesia by either sevoflurane or isoflurane.

Even though a study using sevoflurane and desflurane anesthesia could not find a statistically significant difference in the IOP values of the sevoflurane group, Katzenschlager et al. in their study of propofol and sevoflurane showed that the reduction post-induction was significant for both groups without being different between the treatments (Almeida et al. 2004, Katzenschlager et al. 2002). Johnson et al. evaluated the effects of sevoflurane and isoflurane anesthesia in random dogs and pointed to the relatively more favorable character of the former (Johnson et al. 1998).

A statistically significant decrease was observed in IOP values of the ISO group in our study during the entire anesthesia period, as interpreted through Peiffer's calibration table, and a significant increase registered in this same ISO group at 60 minutes and at one day post-anesthesia.

The results reported above by different authors show some parallelism with ours when interpreted by the Peiffer calibration table. During the sixty minutes post-induction, sevoflurane reduced IOP less than isoflurane. The IOP values following the end of anesthesia, at 60 minutes and 1 day, however, showed an increase. Our data did not allow to examine a correlation between the increase in IOP after one day and the hemodynamic parameters.

It has been reported that IOP in healthy dogs mixed for race and sex vary between 15 and 25 mmHg (Gum 1991). According to the Peiffer calibration table, the values during the maintenance phase in our study were within the reference range. Akın, on the other hand, reported an IOP higher than the norm in dogs mixed for race and sex (Akın 1999). The values found 60-minute and 1-day post-anesthesia in the present study are superior to the norm, thus confirming Akın.

Even though IOP values during anesthesia were within the reference range for both groups, they fell less under isoflurane than in the other group. As for the IOP measurements interpreted through the Friedenwald calibration table, they were significantly falling from 0 to 60 minutes post-induction in the ISO group; the increases at 60 minutes and 1 day post-anesthesia were also statistically significant.

The measurements in either of the study groups were recorded as falling from the start for the maintenance phase to its 60th minute, with a statistical significance that could be detected only for the ISO group. One hour after the termination of anesthesia IOP increased in both groups and the value 24 hours later was approaching that at 0 minutes of the anesthesia maintenance phase. While the fall from 0 to 60 minutes of this phase was statistically important in the SEVO group, it remained more limited in absolute terms than in the ISO group. These results, obtained after interpretation with the Friedenwald calibration table, remain within the normal limits.

IOP is, on the average, at its lowest in the early morning and high in the evening in the sleep-wake cycle (Moses and Hart 1987). The present study was performed in the afternoon. The results we obtained according to either the Peiffer or the Friedenwald calibration tables were within the norm. As for the report by Akın on a study involving 104 eyes, it finds Schiøtz tonometry results above the normal range (Akın 1999). Having started our measurements at 0 minutes of the anesthesia maintenance stage, we observed a fall during this entire period and our values being within the normal range, we were unable to share the conclusions by Akın.

No statistically significant changes were registered in CVP during any stage in a study by Almeida et al. in 16 dogs evaluating cardiovascular parameters under treatment by propofol and sevoflurane or desflurane anesthesia (Almeida et al. 2004). Similarly, Apaydın failed to find a statistically significant variation in CVP values at all times under either sevoflurane or isoflurane anesthesia in 20 dogs premedicated by xylazine

Table 4: CVP, MAP, HR and CI Values and Comparisons Between Groups

	CVP			MAP		
	SEVO	**ISO**	**P**	**SEVO**	**ISO**	**P**
0 min	8±0.73	7.50±0.34	**0.549**	128.83±9.41	97.67±11.06	**0.057***
15 min	6.83±0.31	7.33±1.28	**0.713**	118.50±10.43	74.67±9.09	**0.010****
30 min	7±0.58	8.17±0.79	**0.262**	109±7.47	74±12.59	**0.038***
60 min	7.67±0.42	7.67±1.05	**0.990**	107.17±7.12	71.33±9.21	**0.012****

	HR			CI		
	SEVO	**ISO**	**P**	**SEVO**	**ISO**	**P**
0 min	104.67±8.87	92.83±5.94	**0.294**	1.16±0.21	0.72±0.04	**0.065**
15 min	94±8.15	92.17±8.05	**0.876**	0.97±0.08	0.72±0.08	**0.060**
30 min	90.17±7.23	105.17±6.62	**0.157**	0.95±0.12	0.72±0.06	**0.120**
60 min	93.67±8.60	91.17±3.72	**0.795**	0.87±0.06	0.67±0.06	**0.05***

***:P< 0.05 ****:P<0.01**

HCl and induced by thiopental sodium and fentanyl citrate (Apaydın and Koc 2005).

The present study failed to show a significant difference in CVP as in the published data. No variations were seen at the different measurement times in the dogs in the sevoflurane group and this parameter remained stable. Considering the fact that IOP fell during the anesthesia maintenance phase, we concluded that there were no correlations between IOP and CVP.

It has been reported that the reduction of MAP by isoflurane is stronger when compared to sevoflurane (Mutoh et al. 1997). Other authors report that there were no statistically significant changes in MAP (Klett et al. 2002, Almeida et al. 2004, Katzenschlager et al. 2002, Apaydın and Koc 2005).

Cantalapiedra et al., on the other hand, report a significant increase in MAP in dogs given sevoflurane (Cantalapiedra et al. 2000).

Several investigators report a correlation between systemic blood pressure and IOP, the changes in the former accompanying the relatively smaller variation in IOP. Bulpitt et al. calculated that a change by 2 mm Hg in IOP should correspond to a 100 mm Hg variation in blood pressure (Hoskins and Kassam 1989). As for Katzenschlager et al., they found no significant difference among groups for MAP and HR and no correlation between MAP, HR and IOP values (Katzenschlager et al. 2002).

Our results supported the reports of a fall of MAP parallel to IOP. The reduction in the ISO group MAP value parallels the IOP reduction. The available literature also reports no correlation between IOP and MAP values. In the present study, no correlation tests were performed among different parameters, while both IOP and MAP registered a statistically significant fall in the group given isoflurane anesthesia during its maintenance phase.

Mutoh et al. determined a relatively important increase in HR after the start of sevoflurane anesthesia in dogs receiving either sevoflurane or isoflurane, without being able to show a statistically significant difference in HR variation between the two groups (Mutoh et al. 1997).

A statistical increase in HR is reported by some authors (Mutoh et al. 1997, Cantalapiedra et al. 2000). Apaydın found a statistically significant difference in HR between his two groups at 0 and 60 minutes (Apaydın and Koc 2005).

Almeida et al. did not detect a significant change in HR at any moment in their study with sevoflurane or desflurane, while Katzenschlager et al., working with propofol and sevoflurane, reported a significant fall of HR in both groups (Almeida et al. 2004, Katzenschlager et al. 2002).

A weakly positive correlation between IOP and HR has been reported. There are some explanations for the correlation between IOP and blood pressure but not between IOP and HR (Moses and Hart 1987).

The present study could not determine any significant variations either within-group for the different measurement times, or between the two groups. The HR measurements seemed to be more stable from 0 to 15 minutes into the anesthesia maintenance phase in the isoflurane group. An increase at 30 minutes remained within normal limits.

Almeida et al. reported that no significant variations of CI were observed at any period in 16 dogs treated with sevoflurane or desflurane (Almeida et al. 2004). Apaydın and Koc similarly reported that the CO values remained stable throughout the study period in 20 dogs under sevoflurane or isoflurane anesthesia (Apaydın and Koc 2005). Johnson et al. evaluated the effects of sevoflurane and isoflurane anesthesia in random dogs, reporting that an increase in CO or decrease in ventilation could lengthen the awakening by increasing the solubility of the drug in the blood and the tissues, also stating that the time to awakening was short and regular (Johnson et al. 1998).

In this study, the CI values at the end of 60 minutes of anesthesia maintenance appeared to be different in comparing the treatment groups. The reports mentioned above do not seem to converge with our results. It was also established that the effects of sevoflurane on hemodynamic parameters were more limited than that of isoflurane.

The IOP values interpreted by either the Peiffer or the Friedenwald calibration tables moved in the direction of a decrease. Sevoflurane anesthesia was found to be safer both for its effect on IOP and that on hemodynamic parameters.

The data from the present study support the conclusion that sevoflurane anesthesia represents a safer choice than isoflurane for intraocular surgery.

Acknowledgement

This study is summarized from the same named master thesis.

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