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The effects of propofol and a diazepam/alfentanil combination in dogs aged 10 years and above on heart rate, respiratory rate, pulse oximetry data, intraocular pressure, and body temperature*

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Abstract: In older patients, it is important to minimise anaesthesia-related deaths and complications. In this study, 2 separate anaesthesia inductions were evaluated with respect to their effects on heart rate, respiratory rate, pulse oximetry data, intraocular pressure, and body temperature. A total of 22 dogs were evaluated and 2 separate anaesthesia groups were formed. Propofol (6 mg/kg) was administered to group G1 via a slow intravenous (IV) injection. In group G2, diazepam (0.5 mg/kg) was first administered via an IV injection, followed immediately by alfentanil (40 µg/kg), administered via a slow IV route. Each parameter was recorded prior to anaesthesia (T_0), immediately after anaesthesia induction (min 0–T_1), 5 min after induction (T_2), immediately after intubation (min 0–T_3), and 5 min after intubation (T_4). Statistical analysis was performed by repeated measurements of ANOVA and independent samples t-test methods in SPSS 10.0. While no difference was observed between the times of measurements in group G1 regarding heart rate, respiratory rate, and pulse oximetry data, differences were determined between the measurement times in group G2. In group G1, a drop occurred in intraocular pressure immediately after anaesthesia induction. In group G2, a decrease in intraocular pressure was observed in the measurement taken 5 min after induction. Body temperature dropped significantly in both groups. It was concluded that, in the anaesthesia induction of patients aged 10 years and above, propofol, with more reliable findings, should be preferred over the diazepam/alfentanil combination.

Key words: Propofol, diazepam/alfentanil, heart rate, intraocular pressure, dog

1. Introduction

Anaesthetic drugs and endotracheal intubation have vitally significant effects on the cardiovascular and pulmonary systems. At the same time, they cause sudden increases in intraocular pressure. This leads to severe complications occurring in surgical interventions performed on patients, in particular, those with ocular trauma or glaucoma (1–5).

Propofol is a nonbarbiturate, nonsteroidal, short-acting anaesthetic drug belonging to the alkylphenol group, used commonly in veterinary medicine. It achieves rapid and uncomplicated induction and recovery and does not affect cardiac output or heart rate. Its most common complications are apnoea and hypotension (5–8).

It has been reported that slow intravenous injection of propofol in dogs does not affect heart rhythm; however, it does cause an increase in heart rate that begins to drop 5 min after administration and then continues within normal limits (9).

Respiration may become depressed following propofol administration. This situation, however, is related to the drug administration rate and dose (5,6,8,9).

Propofol also causes some changes in intraocular pressure. When used on its own, it decreases intraocular pressure. However, it cannot prevent the increase in intraocular pressure caused by endotracheal intubation (1,2,10,11). Studies are present in which propofol is reported to lead to an increase in intraocular pressure (4,12).

Hofmeister et al. (5) have stated that propofol administration increases intraocular pressure. They reported that this increase may not have originated from changes in the cardiovascular or blood gas parameters, but may have occurred in relation to the changes produced by propofol in the extraocular muscle tone, scleral rigidity, or humour aqueous production and drainage.

Diazepam is a benzodiazepine group drug and does not produce any significant changes in heart rate, myocardial contractility, cardiac output, or arterial blood pressure. It has no analgesic effect, and significantly suppresses the laryngeal reflex and enables endotracheal intubation. It produces reliable sedation, particularly in older dogs.

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Diazepam can be combined with opioids. Hence, the amount of anaesthetic drug to be used can be decreased, as well as producing excellent analgesia (6,13,14).

Following diazepam administration, no changes occur in intraocular pressure (4).

Alfentanil is a structural analogue of the opioid fentanyl. Its half-life is shorter than that of fentanyl and it takes effect more rapidly. It has a strong analgesic effect (3,11,15). Opioids provide cardiovascular stability during anaesthesia. However, high doses and administration rates lead to a decrease in heart rate and depressed respiration. It is stated that, in the suppression of haemodynamic changes, alfentanil is more effective than fentanyl. Opioids are combined with a sedative drug and produce an ideal anaesthesia protocol (7,8,16–18).

Opioids decrease intraocular pressure. Alfentanil is also effective in decreasing the intraocular pressure increase caused by intubation (1,11).

The state of advanced sedation produced by the combined use of an opioid and tranquiliser is termed "neuroleptanalgesia". When used together, opioids and benzodiazepines do not produce myocardial depression or vasodilation. Particularly in critical patients due to old age or hypovolaemia, cardiogenic shock, septic shock, or dehydration, it produces a safe anaesthesia induction until endotracheal intubation can be achieved (11,19,20).

In their study, Psatha et al. (8) performed anaesthesia induction with diazepam and alfentanil. They stated that this combination did not produce a significant change in heart rate and that the anaesthetic effect was satisfactory. However, they also reported the need for supplementary propofol for intubating patients.

Laryngoscopy and endotracheal intubation stimulates the larynx. The cough reflex caused by this stimulation leads to a sympathetic tone increase. This in turn produces tachycardia and hypertension (4,18).

Neuroleptanalgesia causes less haemodynamic changes produced by endotracheal intubation (14,21,22).

Endotracheal intubation also causes an increase in intraocular pressure. The highest intraocular pressure increase occurs immediately after laryngoscopy and starts to drop within the following 15 s (1,4).

The propofol and alfentanil combination prevents an intraocular pressure increase caused by both laryngoscopy and intubation, and provides sufficient depth of anaesthesia (1).

Hypothermia may occur during sedation or anaesthesia. This may be caused by factors such as cessation of body activity, temperature of the surgical area, thermoregulation suppression, or a decrease in the rate of metabolism (3,23).

Particularly in older patients, it is important to minimise anaesthesia-related deaths and complications. In this study, in order to achieve a safe and controlled anaesthesia, 2 separate anaesthesia inductions of the patients, aged 10 years and above, consisting of propofol and a diazepam/alfentanil combination were evaluated with respect to their effects on heart rate, respiratory rate, pulse oximetry data, intraocular pressure, and body temperature. In light of the findings, and in order to prevent anaesthesia-related complications, particularly in intraocular surgical procedures and older patients, the aim of this study was to determine the preferred drug for anaesthesia induction.

2. Materials and methods

The study material consisted of a total of 22 dogs of different breeds and sex, aged 10 years and above, brought to the İstanbul University Veterinary Faculty Surgery Department Clinics to be operated on for various reasons.

Permission was obtained from the İstanbul University Animal Experiments Local Ethics Committee (Protocol No. 36/2011).

In the preoperative period, haemograms [erythrocyte (red blood cells), haemoglobin (HGB), haematocrit, and leucocyte (white blood cells)] and some blood biochemical results (aspartate aminotransferase, alanine aminotransferase, glucose, urea, creatinine, and total protein) were evaluated. Blood analyses were carried out at the İstanbul University Veterinary Faculty Central Laboratory. According to the results obtained, intravenous fluids and other medical treatments were given to the relevant patients.

In the study, 2 separate anaesthesia groups were formed. Each group comprised 11 dogs. All of the dogs were given no food for 12 h and no water for 2 h prior to anaesthesia induction.

The 1st group (G1) was determined as the propofol group and the 2nd (G2) was the diazepam/alfentanil group.

In both groups, intravenous injections were performed via a 22-gauge catheter (Vasofix; B. Braun Melsungen AG, Germany) placed in the antebrachial cephalic vein.

Before anaesthesia, routine physical examinations of all of the dogs in both groups were carried out. The patients' heart rate, respiratory rate, pulse oximetry data, and body temperature were recorded. At the same time, all of the patients underwent a routine eye examination to determine the presence of any underlying problem that could affect intraocular pressure, after which, the intraocular pressure was measured in both eyes.

Heart rate and arrhythmia checks were carried out with an electrocardiography monitor (Advisor V9212 AR; Surgivet, Waukesha, WI, USA) using the second derivation.

The oxygen saturation of HGB (SpO_2) was obtained from the cheek mucosa in a medium where the animal was

breathing atmospheric air using a pulse oximeter (Advisor V9212 AR; Surgivet, Waukesha, WI, USA).

The respiratory rate was determined by observing the chest movements that occurred during breathing.

In order to investigate the effects of the administered drugs on intraocular pressure, applanation tonometry (Tono-Pen Vet; Reichert, Inc., USA) was used to determine the intraocular pressure in both eyes. Tono-pen calibration was carried out before the measurements.

The intraocular pressure was measured with the patients in a standing position prior to anaesthesia and in a sternal position following injection of the anaesthetic substances. Hence, factors that could change the intraocular pressure by obstructing the jugular vein or the eye were avoided.

Throughout the induction period, body temperature was measured rectally using a digital thermometer (Omron, the Netherlands).

Propofol (Propofol 1%, 200 mg/20 mL; Fresenius, Sweden) was administered at a dose of 6 mg/kg via a slow intravenous (IV) injection to group G1.

Diazepam (Diazem 10 mg/2 mL; Deva, Turkey) was first administered at a dose of 0.5 mg/kg via a slow IV injection to group G2. This was followed immediately by alfentanil (Rapifen 0.5 mg/mL; Janssen-Cilag, Belgium) at a dose of 40 µg/kg via a slow IV injection.

Following relaxation of the jaw muscles, the patients were intubated using intubation tubes (Rüsch, Germany) of suitable sizes.

All of the parameters to be evaluated were recorded immediately before anaesthesia (T_0), immediately after anaesthesia induction (min 0–T_1), 5 min after induction (T_2), immediately after intubation (min 0–T_3), and 5 min after intubation (T_4).

The statistical analysis was carried out by the İstanbul University Veterinary Faculty Department of Animal Breeding and Husbandry.

Repeated measurements of ANOVA in SPSS 10.0 (SPSS, 1999) were used to analyse the data for the heart rate, respiration rate, pulse oximetry findings, body temperature, and intraocular pressure. The model included the measurement time (T_0, T_1, T_2, T_3, and T_4) as a within-subject effect and the group (G1 and G2) as a between-subject effect, as well as the measurement time × group interaction. Significance control was assessed using the least significant difference procedure. In order to determine the effect of the group on the investigated parameters in the specific measurement time, independent samples t-tests were also performed. Values were considered significant when $P < 0.05$.

3. Results

The study material consisted of a total of 22 dogs of different breeds and sex, aged 10 years and above, brought to the İstanbul University Veterinary Faculty Surgery Department Clinics and operated on for various reasons.

The patients were split into 2 groups, with 11 dogs in each group. The age, sex, and body weight of all of the patients are shown in Table 1.

The age and body weight distribution between groups G1 and G2 was seen to be balanced and the difference between the 2 groups was found to be statistically insignificant ($P = 0.826$ and $P = 0.415$, respectively).

Following anaesthesia induction, rapid and uncomplicated anaesthesia was achieved in both groups. None of the patients developed apnoea. After loss of the swallowing reflex and jaw muscle tone, intubation was achieved without difficulty.

The means for heart rate, respiration rate, pulse oximeter, intraocular pressure, and body temperature for groups G1 and G2 at different measurement times are presented in Table 2. The group, as a main effect, had a significant influence on heart rate ($P < 0.001$). At all of the measurement times, the heart rate in group G1 dogs was higher than that in group G2 dogs. While a significant difference with respect to heart rate was not found in group G1 dogs ($P = 0.324$), the heart rate in group G2 dogs decreased at the T_1 measurement; this decrease continued

Table 1. Means and (standard deviations) for the age and body weight of dogs in the propofol (G1) and diazepam/alfentanil (G2) groups and the distribution of the groups according to sex.

Parameter	G1 (n = 11)	G2 (n = 11)
Age (years)[a]	12.73 (3.47)	13.00 (2.10)
Body weight (kg)[b]	18.73 (12.06)	14.91 (9.29)
Distribution of groups		
Female (number)	2	2
Male (number)	9	9

[a]: The difference between groups G1 and G2 in terms of age was not significant ($P = 0.826$).
[b]: The difference between groups G1 and G2 in terms of body weight was not significant ($P = 0.415$).

Table 2. Means and (standard deviations) for heart rate (HR), respiration rate (RR), pulse oximeter, body temperature, and intraocular pressure (IOP) for the propofol (G1) and diazepam/alfentanil (G2) groups at different measurement times.

Parameter	Measurement time (MT)					P-value[e]	Significance of main effects[f]		
	T0	T1	T2	T3	T4		G	MT	G × MT
HR (beats min^{-1})									
G1	166.4 (35.7)	168.3 (27.0)	150.6 (22.4)	157.9 (21.9)	159.4 (21.9)	0.324			
G2	135.6^{a} (23.2)	108.5^{bc} (28.1)	102.8^{c} (28.7)	112.9^{bc} (29.5)	123.8^{ab} (32.7)	0.002	<0.001	0.004	0.149
P-value[d]	0.026	<0.001	<0.001	<0.001	0.007				
RR (breaths min $^{-1}$)									
G1	36.4 (16.7)	29.9 (11.1)	27.6 (14.1)	26.2 (7.5)	34.8 (10.1)	0.175			
G2	42.6^{ab} (32.2)	27.7^{b} (18.9)	31.6^{b} (17.3)	66.2^{a} (54.4)	63.8^{a} (47.2)	0.002	0.101	0.002	0.003
P-value[d]	0.578	0.744	0.559	0.025	0.060				
Pulse oximeter (%)									
G1	89.5 (6.2)	83.1 (9.5)	84.9 (7.0)	88.3 (5.3)	89.1 (4.6)	0.087			
G2	93.9^{a} (4.2)	87.4^{b} (4.7)	87.3^{b} (2.8)	87.1^{b} (3.4)	88.2^{b} (5.2)	<0.001	0.220	<0.001	0.177
P-value[d]	0.062	0.195	0.310	0.542	0.669				
Body temperature (°C)									
G1	38.96^{ab} (0.42)	39.06^{a} (0.34)	38.87^{bc} (0.42)	38.86^{bc} (0.40)	38.67^{c} (0.38)	0.004			
G2	38.89^{a} (0.49)	38.85^{ab} (0.66)	38.72^{ab} (0.60)	38.64^{b} (0.49)	38.40^{c} (0.64)	<0.001	0.346	<0.001	0.678
P-value[d]	0.712	0.363	0.491	0.267	0.240				
IOP (mmHg)									
G1	23.59^{a} (4.96)	19.77^{bc} (7.13)	17.23^{bc} (4.66)	20.73^{ab} (9.15)	16.64^{c} (5.31)	<0.001			
G2	19.00^{a} (5.60)	18.09^{a} (7.70)	15.32^{b} (6.24)	23.14^{a} (9.42)	22.86^{a} (15.06)	0.016	0.952	0.002	0.005
P-value[d]	0.006	0.457	0.257	0.394	0.075				

[a, b, c]: Differences between the means of the measurement times carrying various letters in the same line are significant.

[d]: Significance level of the differences between the groups for the same measurement time according to independent samples t-test statistics.

[e]: Significance level of the differences between the measurement times for the same group according to repeated measurements of ANOVA statistics.

[f]: Significance of the main effects according to repeated measurements ANOVA statistics.

until T_4 and at 5 min after intubation, returned to its preanaesthesia level (P = 0.002).

As a main effect, the influence of the group (G) was not significant on the respiration rate (P = 0.101), while the measurement time (MT) and G × MT interaction significantly affected the respiration rate (P = 0.002 and P = 0.003, respectively). While the difference between various measurement times with respect to the respiration rate was not found to be significant in group G1 (P = 0.175), in group G2, the respiration rate immediately after induction (T_1) was seen to decrease and then return to its preanaesthesia level immediately after intubation (P = 0.002).

At various times, the difference between the pulse oximetry data of the dogs in both group G1 and group G2 was not significant (P > 0.05). On the other hand, while the effect of measurement time was not significant in group G1 (P = 0.087), it was significant in group G2 (P < 0.001). In group G2, the oxygen saturation ratio was seen to decrease immediately after anaesthesia induction and not return to preanaesthesia levels at any of the subsequent measurements.

The effect of the group, as a main effect, on intraocular pressure was not significant (P = 0.952). However, the measurement time and G × MT interaction significantly affected the level of intraocular pressure (P = 0.002 and P = 0.005, respectively). In group G1, a decrease occurred in intraocular pressure immediately after anaesthesia induction, followed by an increase immediately after

intubation. However, in the measurement 5 min after intubation in group G1, the lowest intraocular pressure was recorded. In group G2, a decrease in intraocular pressure was observed in the measurement taken 5 min after induction, after which it returned to its preanaesthesia level immediately after intubation and no further decrease was recorded.

As a main effect, the measurement time significant influenced body temperature ($P < 0.001$), but the effect of the group was not significant ($P = 0.346$). Statistically significant decreases were observed at the T_2 measurement in group G1 and at the T_3 measurement in group G2. Further decreases were observed in the T_4 measurements for both groups.

4. Discussion

In geriatric patients, and especially in intraocular surgical procedures, it is important to minimise anaesthesia-related complications and fatalities. In this study, in order to achieve safe and controlled anaesthesia in dogs aged 10 years and above, the effects of 2 different anaesthesia induction protocols, consisting of propofol and a diazepam/alfentanil combination, on heart rate, respiration rate, pulse oximetry values, intraocular pressure, and body temperature were evaluated.

In group G1, following a slow intravenous injection of propofol, rapid anaesthesia induction was achieved in all of the patients, without apnoea or any other complications developing. After loss of the swallowing reflex and jaw muscle tone, intubation was achieved without any problem (5,6,8).

In group G2, where the induction agent was diazepam/alfentanil, rapid anaesthesia was also achieved without any complication and intubation was performed smoothly (6,11,15,19). Psatha et al. (8) stated that a satisfactory level of anaesthesia was achieved with the diazepam/alfentanil combination; however, patients needed supplementary propofol administration for intubation. In our study, intubation was performed successfully using the diazepam/alfentanil combination without the need for any additional injectable anaesthetic drug.

In group G1, the heart rate remained unchanged between measurement times. This is consistent with the literature (5,6,8). However, in contrast to sources (4,18) reporting laryngoscopy and endotracheal intubation leading to tachycardia, a statistically significant increase was not observed in the measurements recorded either immediately after endotracheal intubation (T_3) or 5 min later (T_4).

In group G2, the heart rate decreased with drug administration (T_1) and this state remained unchanged with endotracheal intubation (7,18,21,22). The increase observed at the T_4 measurement time was thought to have occurred due to the waning of the effect of the anaesthesia.

The findings obtained for the heart rate at all of the measurement times monitored in the propofol group patients exhibited that with respect to cardiac stability, propofol was more reliable than diazepam/alfentanil, especially in patients aged 10 years and above.

The main complication of propofol administration is depressed respiration. The frequency of this occurring depends on the dose and administration rate of the drug (5,6). In our study, a significant difference was not observed between the measurement times of the respiration rates and no respiratory depression was seen. This state was linked to the slow intravenous injection of the drug.

In group G2, the respiration rate started to decrease together with the drug administration (T_1). This decrease was thought to have originated from the respiratory depression effects of the opioids (7,8,18). The respiratory rate increased again at the T_3 measurement time and then returned to its preanaesthesia level. It was concluded that this increase may have been the result of endotracheal intubation.

In group G1, with respect to pulse oximetry data, a significant difference between all measurement times was not observed. This was thought to have resulted from the fact that drug administration had not produced respiratory depression in patients and the results obtained were found to be compatible.

In the group G2 patients, the pulse oximetry data was seen to decrease in direct proportion to the respiration rate decreasing with the diazepam/alfentanil administration. In addition, while the respiratory rate increased following endotracheal intubation, there was no increase in the pulse oximetry data. This suggested that the depth of respiration was not sufficient to raise the oxygen saturation level of the HGB.

In light of the respiratory rates and pulse oximetry data, with respect to respiratory system stabilisation in patients aged 10 years and above, the fact that propofol was better than the diazepam/alfentanil combination was regarded as an advantage.

While there are publications stating that propofol administration decreases intraocular pressure (1,2,10,11), some researchers report that this administration increases intraocular pressure (4,12). In the present study, in group G1, propofol administration at the T_1 measurement time was determined to decrease intraocular pressure. With endotracheal intubation of the patients, the values increased at the T_3 measurement time and, at the subsequent measurement time (T_4), reached their lowest level. The findings obtained as a result of endotracheal intubation were compatible with other sources (1,4,5).

In group G2, intraocular pressure decreased approximately 5 min after (T_2) the drug combination

administration. This decrease was thought to be related to the drop in heart rate seen in diazepam/alfentanil administration. The decreased intraocular pressure returned to preanaesthesia levels with endotracheal intubation (T_3) and showed no further (T_4) decrease. This result was found to be incompatible with research into neuroleptanalgesia decreasing haemodynamic changes and preventing intraocular pressure increase with endotracheal intubation (1,14,21,22).

In light of the intraocular pressure change findings obtained at the end of this study, especially in intraocular surgery administrations, propofol was observed to be more reliable than the diazepam/alfentanil combination.

With respect to body temperature, a significant difference was not observed between the 2 groups. Values dropped in the later stages of anaesthesia induction and the results were compatible with sources reporting that hypothermia may develop during anaesthesia (3,23).

In conclusion, contrary to research stating that neuroleptanalgesia provides a reliable anaesthesia induction, especially in geriatric patients and those in poor general condition, with the present study it was concluded that for the anaesthesia induction of patients aged 10 years and above, due to more reliable findings than the diazepam/alfentanil combination regarding heart rate, respiration rate, and intraocular pressure, propofol should be the drug of choice.

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