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Evaluation of the cardiorespiratory effects of the alpha-2 adrenoceptor agonists xylazine, medetomidine and dexmedetomidine in combination with ketamine in dogs

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ABSTRACT: In this study, we compared the effects of xylazine, medetomidine and dexmedetomidine in combination with ketamine on heart rate, respiratory rate, blood gas values, temperature and sedation scores. A total of 30 dogs were evaluated. The dogs were randomly allocated into three anaesthesia groups, each of which included ten dogs. The first group, denoted the xylazine/ketamine group, intravenously received xylazine (0.5 mg/kg) for premedication and ketamine (5 mg/kg) for induction. The second group, the medetomidine/ketamine group, intravenously received medetomidine (10 μg/kg) followed by ketamine (5 mg/kg). The third group received the dexmedetomidine/ketamine combination. This group intravenously received dexmedetomidine (3 μg/kg) for premedication and ketamine (5 mg/kg). Heart rate, respiratory rate, oxygen saturation, blood gas parameters and temperature were recorded for all patients immediately before sedation onset (T_0), five minutes after sedation onset (T_1) and five minutes after endotracheal intubation following ketamine injection (T_2). The end tidal carbon dioxide level was recorded at T_2. A significant decrease in heart rate occurred following premedication in all groups. However, the decrease was most marked in the medetomidine/ketamine group. An increase was observed in venous partial pressure of carbon dioxide values at T_2 in the xylazine/ketamine group compared to the medetomidine/ketamine and dexmedetomidine/ketamine groups. The end tidal carbon dioxide levels were higher in the medetomidine/ketamine group than in the other two groups, and oxygen saturation of haemoglobin levels in the same group were found to be lower than in the others. It was determined that none of α_2-agonists, namely xylazine, medetomidine or dexmedetomidine, had superior properties over the others. If medetomidine is used, special care should be taken because of the rapid decrease in heart rate.

Keywords: α2-agonist; cardiorespiratory effect; dog

The safety of anaesthesia is crucial for the survival of the patient. Since no anaesthetic agent that has been developed to date can be considered completely safe, multiple agents are used in combination in order to reduce the risk factors. Alpha-2 adrenoceptor agonists (α_2-agonists) are considered to be components of balanced anaesthesia. Owing to their sedative, myorelaxant and analgesic properties, the administration of these agents for premedication enables the use of lower amounts of general anaesthetics. Xylazine, medetomidine and dexmedetomidine are extensively used α_2-agonists. Medetomidine and dexmedetomidine have higher selectivity towards adrenergic receptors than xylazine (Sinclair 2003; Lamont et al. 2012; Quiros-Carmona et al. 2017).

Physiological consequences of the administration of α_2-agonists in dogs include normo- or hypotension and bradycardia followed by an initial state of hypertension (Murrell and Hellebrekers 2005; Lemke 2007; Cardoso et al. 2014; Webb et al. 2014; Kellihan et al. 2015). All α_2-agonists cause an approximately 50% reduction in cardiac output (Sinclair 2003; Carter et al. 2010; Pascoe 2015). Potential adverse effects of α_2-agonists on cardiovascular parameters restrict the use of these agents

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in healthy dogs (Murrell and Hellebrekers 2005; Restitutti et al. 2017).

All α_2-agonists decrease the rate of respiration, which does not cause an increase in the partial pressure of carbon dioxide ($PaCO_2$) in arterial blood (Lee 2011; Lamont et al. 2012; Lee et al. 2015; Restitutti et al. 2017) but may reduce the respiratory response to hypercapnia (Cardoso et al. 2014). Furthermore, α_2-agonists contribute to an insignificant decrease in body temperature (Sinclair 2003; Carter et al. 2010; Silva et al. 2010).

Rapid sedation and analgesia develop following the parenteral administration of xylazine. Blood pH, arterial partial pressure of oxygen (PaO_2) and $PaCO_2$ levels remain constant. The decrease in respiratory rate is compensated for by an increase in tidal volume (Lemke 2007).

Medetomidine is an equivalent mixture of two optical enantiomers: the pharmacologically inert levomedetomidine and the active form of dexmedetomidine (Murrell-Hallebrekers 2005; Lamont et al. 2012; Kellihan et al. 2015). Intravenous (*i.v.*) administration of medetomidine results in more pronounced cardiovascular effects than those that manifest following administration through the intramuscular (*i.m.*) route (Silva et al. 2010).

Dexmedetomidine, which is the pharmacologically active isoform of medetomidine (Silva et al. 2010), has minimal cardiopulmonary effects in dogs at low doses (0.5 µg/kg, *i.v.*), whereas at higher doses (3 µg/kg, *i.v.*) well-recognized cardiopulmonary effects of α_2-agonists are observed (Murrell and Hellebrekers 2005; Lemke 2007; Cardoso et al. 2014; Lee et al. 2015; Pascoe 2015; Quiros-Carmona et al. 2017). Respiratory depression produced by the agent decreases blood pH by causing respiratory acidosis, but lactate levels remain unchanged (Quiros-Carmona et al. 2014).

In healthy dogs, α_2 agonists are administered along with opioids or dissociative anaesthetics and general anaesthetics such as ketamine, propofol and isoflurane in order to produce sedation and analgesia (Murrell and Hellebrekers 2005; Silva et al. 2010; Lamont et al. 2012). Anaesthesia induced by xylazine, medetomidine or dexmedetomidine in combination with ketamine produces a safe state of anaesthesia in terms of haemodynamic parameters (Lemke 2007; Silva et al. 2010).

In the present study, we administered xylazine, medetomidine and dexmedetomidine, which are extensively used for premedication, in combination with ketamine to dogs and compared heart rate, respiratory rate, blood gas values, body temperature and sedation scores. Our aim was to determine which of these combinations carries the least risk for the vital functions of the patient.

MATERIAL AND METHODS

The study was conducted in accordance with ethical principles approved by the local Animal Experiments Ethics Committee (Protocol No. 35980450-050. 01.04/2017). All patient owners were informed regarding the use of their dogs in the clinical trial.

Animals. A total of 30 dogs aged between one and six years of age of different breeds and genders which underwent surgical procedures due to miscellaneous conditions were evaluated. The dogs weighed 10–30 kg. In the preoperative period, all dogs were subjected to routine physical inspection. Haemograms (erythrocyte, RBC; haemoglobin, HGB; haematocrit, HCT; leukocyte, WBC), as well as certain biochemical indicators (alanine aminotransferase, ALT; aspartate aminotransferase, AST; glucose; urea; creatinine; total protein) were assessed. The selected patients were classified as having ASA 1 and ASA 2 physical status.

Experimental design. The dogs were allocated into three anaesthesia groups, each of which included ten dogs. The food and water intake of the patients were restricted 12 hours and one hour before the induction of anaesthesia, respectively. Intravenous (*i.v.*) injections were performed via a 22G-angiocath (Vasofix; B. Braun Melsungen AG, Germany) inserted into the v. cephalica antebrachii.

The first group was the xylazine/ketamine (XK) group, and this group intravenously received 0.5 mg/kg of xylazine HCl (Rompun, Bayer, Turkey) for premedication. This was followed by ketamine HCl (Alfamine 10%, Ege-Vet, Turkey) at a dose of 5 mg/kg by slow *i.v.* injection for the induction of anaesthesia, five minutes after xylazine.

The second group was the medetomidine/ketamine (MK) group which intravenously received 10 µg/kg of medetomidine (Domitor, Pfizer, Turkey) followed by 5 mg/kg of ketamine by slow *i.v.* injection, five minutes after medetomidine.

Dogs receiving dexmedetomidine/ketamine (DK) constituted the third group. This group intravenously received 3 µg/kg of dexmedetomidine (Precedex 200 µg/2 ml, Meditera, USA) for premed-

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ication by slow *i.v.* injection, and anaesthesia was likewise induced with 5 mg/kg of ketamine by slow *i.v.* injection, five minutes after dexmedetomidine.

Heart rate (HR; beats/minute), respiratory rate (*f*R; breaths/minute), oxygen saturation of haemoglobin (SpO_2; %), blood gas parameters and body temperature were recorded for all patients at three different time points: immediately before sedation onset (T_0), five minutes after sedation onset (T_1) and five minutes after endotracheal intubation following ketamine injection (T_2). The end-tidal CO_2 concentration ($EtCO_2$; mm Hg) level of all dogs was recorded at T_2.

Heart rate and arrhythmia were assessed using second derivatives by a multifunctional ECG monitoring system (Advisor V9212 AR; Surgivet, Waukesha, USA).

Respiratory rate was determined by monitoring chest movements while breathing. $EtCO_2$ levels were determined using a capnometer attached to the intubation tube and the side-stream technique.

The oxygen saturation of haemoglobin was obtained from the buccal mucosa in a medium where the animal was breathing atmospheric air using a pulse oximeter probe (Advisor V9212 AR; Surgivet, Waukesha, USA).

Blood gas values were obtained from the blood samples withdrawn from the v. jugularis. Blood pH values, venous partial pressures of carbon dioxide ($PvCO_2$) and bicarbonate (HCO_3^-) concentrations were also evaluated.

Rectal body temperature was monitored during anaesthesia using a digital thermometer (Omron, The Netherlands).

Following relaxation of the jaw muscles, the dogs were intubated using endotracheal intubation tubes (Rusch, Germany) of suitable sizes. Induction of general anaesthesia for performing the operations was achieved with an initial concentration of 5% isoflurane together with 100% O_2 until protrusion occurred in the eyes and was maintained at a concentration of 2.5% isoflurane in all dogs. Isoflurane concentration was adjusted by a vaporizer.

Sedation levels in terms of behavioural parameters were scored by the same anaesthetist.

Statistical analysis. Prior to the statistical evaluation, the assumption of normality and homogeneity of the variances were tested using the Shapiro-Wilk test and Levene's test, respectively. Differences among anaesthesia groups (XK, MK and DK) in terms of the effects of anaesthesia on heart rate, respiratory rate, $EtCO_2$ level, SpO_2, blood gas parameters and body temperature were assessed using the Repeated Measures Analysis of Variance (Repeated Measures ANOVA) method in SPSS software, version 13.0. A contrast test was conducted to analyse the significance of comparisons among the treatment groups. The statistical model considered anaesthesia groups (XK, MK and DK), referred to as "between-subject factor", measurement time (T_0, immediately before sedation onset; T_1, five minutes after sedation onset and T_2, five minutes after endotracheal intubation following ketamine injection) and anaesthesia group-x measurement time interaction referred to as "within-subject factor".

The effect of the anaesthesia group-x measurement time interaction was found to be significant. One way variance analysis and Duncan's test were conducted to compare the anaesthesia groups at each measurement time point and repeated measures analysis of variance and the contrast test were applied to compare the measurement time points within each group.

RESULTS

Rapid general anaesthesia was achieved following drug injection without any complication in all animals in the xylazine – XK, medetomidine – MK and dexmedetomidine – DK anaesthesia groups. None of the patients had apnoea. Intubation was performed without any difficulties once the swallowing reflex disappeared and jaw muscle tone was lost.

Findings with respect to HR, *f*R, SpO_2 and body temperature in the dogs belonging to all three groups are shown in Table 1.

Heart rates decreased below 60 beats/minute after *i.v.* administration of medetomidine and dexmedetomidine. As average heart rate was 63.60 ± 4.00 in the XK group at T_1, the dogs in this group were evaluated as having bradycardia.

When the whole data set was evaluated according to heart rate, the effect of group on heart rate was not significant while the effect of measurement time was significant ($P < 0.001$). The difference between groups at T_0 and T_2 measurement time points was insignificant, whereas the heart rate of dogs in the MK group was lower than those of other two groups at T_1. When compared with T_0 in all groups, heart

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Table 1. Means and standard errors for heart rate (HR), respiration rate (*f*R), pulse oximeter (SpO_2) and body temperature for xylazine/ketamine (XK), medetomidine/ketamine (MK) and dexmedetomidine/ketamine (DK) groups at different measurement times (MT)

Parameter	Measurement time (mean ± SE)			*P*-value[e]	Significance of main effects[f]		
	T0	T1	T2		G	MT	G × MT
HR (beats/minute)							
XK	122^{x} ± 17.4	$64^{a,y}$ ± 4.0	107^{x} ± 8.4	0.003			
MK	133^{x} ± 6.9	$44^{b,y}$ ± 3.3	121^{x} ± 9.6	< 0.001	0.879	< 0.001	0.102
DK	144^{x} ± 9.5	$56^{a,z}$ ± 4.3	104^{y} ± 3.2	< 0.001			
P-value[d]	0.451	0.006	0.275				
***f*R** (breaths/minute)							
XK	$33^{b,x}$ ± 3.3	18^{y} ± 1.8	12^{z} ± 1.4	< 0.001			
MK	$55^{a,b,x}$ ± 10.9	21^{y} ± 2.7	13^{z} ± 1.5	< 0.001	0.018	< 0.001	0.019
DK	$79^{a,x}$ ± 15.8	34^{y} ± 8.7	14^{y} ± 3.9	< 0.001			
P-value[d]	0.022	0.460	0.907				
SpO_2 (%)							
XK	94^{x} ± 0,7	$89^{b,y}$ ± 1.6	88^{y} ± 1.4	0.012			
MK	95^{x} ± 0.6	$94^{a,x,y}$ ± 1.3	87^{y} ± 2.9	0.012	0.026	< 0.001	0.086
DK	95 ± 0.8	94^{a} ± 0.5	93 ± 0.9	0.186			
P-value[d]	0.477	0.022	0.104				
Body temperature (°C)							
XK	39 ± 0.09	39 ± 0.09	39 ± 0.1	0.784			
MK	39 ± 0.16	39 ± 0.16	39 ± 0.2	0.851	0.457	0.356	0.927
DK	39 ± 0.13	39 ± 0.14	39 ± 0.1	0.627			
P-value[d]	0.637	0.275	0.627				

G = group (XK, MK or DK), MT = measuring time, G × MT = interaction effects of group and measuring time

[a,b,c]Differences between the means of measurement times with different letters in the same row are significant ($P < 0.05$)

[d]Significance level of differences between groups for the same measurement time according to One-way ANOVA

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

[f]Significance of main effects according to repeated measurements ANOVA

[x,y,z]Differences between the means of groups with different letters in the same column are significant ($P < 0.05$)

rate decreased significantly at T_1 and increased again at T_2. In XK and MK groups, heart rate at T_2 returned to the levels of T_0, while there was no return to the baseline levels in the DK group.

The effects of group ($P < 0.05$), measurement time ($P < 0.001$) and the group-x measurement time interaction ($P < 0.05$) on respiratory rate were found to be significant. The respiratory rate of the DK group was higher ($P < 0.05$) than that of the XK group at T_0, while the difference among groups at T_1 and T_2 measurement time points was insignificant. All groups exhibited a statistically significant decrease ($P < 0.001$) in *f*R values compared to baseline values.

The effects of group ($P < 0.05$) and measurement time ($P < 0.001$) on SpO_2 levels were found to be significant. The difference among groups at T_0 and T_2 measurement time points was insignificant, while the XK group had lower SpO_2 levels at T_1 when compared with the other two groups ($P < 0.05$). There was a substantial decrease in pulse oximetry values at T_1 in comparison to T_0 in the XK group. Likewise, a statistically significant decrease in SpO_2 levels was observed in the MK group at T_2 when compared with T_0 ($P < 0.05$).

There was no statistically significant difference among groups with regards to body temperature at the different time points.

Findings with respect to pH, HCO_3^- and $PvCO_2$ values of all dogs in each group are presented in Table 2.

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Table 2. Means and standard errors for pH, HCO_3^- and venous partial pressures of carbon dioxide ($PvCO_2$) for xylazine/ketamine (XK), medetomidine/ketamine (MK) and dexmedetomidine/ketamine (DK) groups at different measurement times (MT)

Parameter	Measurement time (mean ± SE)			*P*-value[e]	Significance of main effects[f]		
	T0	T1	T2		G	MT	G × MT
pH							
XK	7.37 ± 0.01	7.37 ± 0.02	7.36^{b} ± 0.02	0.915			
MK	7.33^{y} ± 0.03	7.41^{x} ± 0.01	$7.41^{a,x}$ ± 0.01	0.009	0.054	0.043	0.024
DK	7.41 ± 0.01	7.41 ± 0.01	7.42^{a} ± 0.01	0.324			
P-value[d]	0.061	0.168	0.012				
HCO_3^-							
XK	21.19 ± 0.43	20.70 ± 0.72	21.85 ± 0.57	0.198			
MK	21.26 ± 0.59	21.31 ± 0.60	20.80 ± 0.54	0.472	0.448	0.637	0.183
DK	20.36 ± 0.57	20.41 ± 0.46	20.56 ± 0.42	0.822			
P-value[d]	0.426	0.563	0.187				
$PvCO_2$ (mm Hg)							
XK	$39.97^{a,b}$ ± 1.58	39.19 ± 1.72	42.57^{a} ± 2.41	0.324			
MK	$44.48^{a,x}$ ± 3.51	$36.90^{x,y}$ ± 1.33	$35.13^{b,y}$ ± 1.24	0.034	0.002	0.106	0.015
DK	34.79^{b} ± 1.02	34.50 ± 0.54	34.35^{b} ± 0.94	0.914			
P-value[d]	0.022	0.052	0.003				

G = group (XK, MK or DK), MT = measuring time, G × MT = interaction effects of group and measuring time

[a,b,c]Differences between the means of measurement times with different letters in the same row are significant ($P < 0.05$)

[d]Significance level of differences between groups for the same measurement time according to One-way ANOVA

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

[f]Significance of main effects according to repeated measurements ANOVA

[x,y]Differences between the means of groups with different letters in the same column are significant ($P < 0.05$)

When overall data were evaluated, the effects of measurement time and group-x measurement time interaction on pH were found to be significant ($P < 0.05$), and the effect of group exhibited a tendency to be significant ($P < 0.1$). Differences among groups in terms of pH values at T_0 and T_1 were found to be insignificant. Blood pH values of the XK group were lower than those of the other two groups at T_2 ($P < 0.05$). While no statistically significant difference was noted in pH values between different measurement time points in both XK and DK groups, there was a statistically significant increase in the MK group at T_1 in comparison to T_0, which rose again at T_2 ($P < 0.01$).

The effects of group, measurement time and group-x measurement time interaction on bicarbonate levels were found to be insignificant.

The effects of group ($P < 0.01$) and group-x measurement time interaction ($P < 0.05$) on $PvCO_2$ were found to be statistically significant. $PvCO_2$ levels in the MK group were higher than in the DK group at T_0, while the XK group exhibited higher values of $PvCO_2$ at T_2 when compared with the other groups.

The end-tidal CO_2 concentration values of all dogs in each group are presented in Table 3. The MK group had higher mean values for $EtCO_2$ than the other groups ($P < 0.01$).

The sedation scores of all dogs are shown in Table 4. Differences among groups in terms of certain behavioural parameters such as posture

Table 3. $EtCO_2$ for xylazine/ketamine (XK), medetomidine/ketamine (MK) and dexmedetomidine/ketamine (DK) groups at five minutes after endotracheal intubation following ketamine injection

	XK	MK	DK	*P*-value[d]
$EtCO_2$	28.60^{b} ± 2.66	41.60^{a} ± 3.01	33.80^{b} ± 1.91	0.005

[a,b]Differences between the means of groups with different letters in the same row are significant ($P < 0.05$)

[d]Significance level of differences between groups according to One-way ANOVA statistics

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Table 4. Mean scores for behaviours in xylazine/ketamine (XK), medetomidine/ketamine (MK) and dexmedetomidine/ketamine (DK) groups (mean ± SE)

Behaviour	XK	MK	DK	*P*-value[d]
Posture	2.60[b] ± 0.22	3.70[a] ± 0.15	3.30[a,b] ± 0.34	< 0.001
Resistance	2.70[b] ± 0.26	3.50[a] ± 0.22	2.80[a,b] ± 0.33	0.028
Response to sound	3.20 ± 0.36	3.50 ± 0.27	3.10 ± 0.38	0.553
Jaw relaxation	1.90 ± 0.23	2.50 ± 0.17	1.80 ± 0.20	0.062
General appearance	2.50[b] ± 0.17	3.00[a] ± 0.15	2.60[a,b] ± 0.22	0.042

[a,b]Differences between the means of groups with different letters in the same row are significant ($P < 0.05$)
[d]Significance level of differences between groups according to One-way ANOVA

($P < 0.001$), resistance ($P < 0.05$) and general appearance ($P < 0.05$) were found to be significant. The dogs which received medetomidine had higher scores for these three parameters than those which received xylazine. The difference in the scores obtained with dexmedetomidine administration was found to be insignificant when compared with the other anaesthetic premedication agents. The parameters evaluated for sedation scores (Tamura et al. 2015) are shown in Table 5.

Similar findings were obtained in each group in terms of quality of recovery and extubation time in the awakening period following anaesthesia.

DISCUSSION

Enabling the survival of the patient during anaesthesia and minimizing the potential complications due to anaesthesia is of paramount importance. Currently, α_2-agonists are used in combination with general anaesthetics such as ketamine, propofol and isoflurane particularly in healthy dogs in order to provide balanced anaesthesia and thus enable sedation, muscle relaxation and analgesia (Murrell and Hellebrekers 2005; Silva et al. 2010). In the present study, the α_2-agonists xylazine, medetomidine and dexmedetomidine were administered for premedication in dogs aged between one and six years that met the criteria of ASA 1 and ASA 2. This experimental setup contributed to uniformity in the parameters that were assessed. Ketamine HCl was selected as the general anaesthetic agent so as to diminish the adverse effects of α_2-agonists such as bradycardia, decreased respiratory rate and hypotension (Changmin et al. 2010).

The effects of these three combinations on HR, *f*R, SpO_2, blood gas parameters, $EtCO_2$ levels and body temperature were evaluated in all cases. The patients were provided with room air and did not receive any oxygen support, since it was our aim to assess the effects of α_2-agonists on the above-mentioned parameters.

The doses of the administered drugs were determined in accordance with relevant previous studies (Sinclair 2003; Quiros-Carmona et al. 2014; Webb et al. 2014; Pascoe 2015).

It was reported that the α_2-agonist agents xylazine and medetomidine caused vomiting in 50% and 8–20% of patients, respectively (Sinclair 2003). In the present study, vomiting was not observed in any of the patients in the evaluated anaesthesia groups.

Bradycardia was noted following the intravenous administration of α_2-agonists in all three groups, which was an anticipated finding (Murrell and Hellebrekers 2005; Cardoso et al. 2014; Kellihan et al. 2015). A significant decrease in heart rate occurred following premedication (T_1) in all groups (Sinclair 2003; Carter et al. 2010; Pascoe 2015). However, the decrease was determined to be most prominent in the MK group (Lamont et al. 2012; Webb et al. 2014; Lee et al. 2015). The decrease observed at T_2 following ketamine injection and endotracheal intubation in XK and MK groups later

Table 5. Sedation scores taken from Tamura et al 2015

	Posture	Resistance to displacement	Response to noise	Jaw relaxation	General appearance
0	standing	strong resistance	jumping	weak	excited
1	tired and standing	modest resistance	hearing and movement	slight	awake and normal
2	lies but can stand	slight resistance	hearing and ear movement	good	sedation
3	lies but can difficulty stand	unresisting	low perception		sleeping
4	can not stand		no answer		

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returned to T_0 levels, whereas no reversion was noted in the DK group, which we consider to be associated with the more marked depressive effect of dexmedetomine on HR than in the other two groups despite the stimulatory effects of ketamine and endotracheal intubation (Changmin et al. 2010).

One of the most important complications of α_2-agonist administrations is respiratory depression, which depends on the dose of the drug and the rate of administration (Lamont et al. 2012; Guzel et al. 2013a; Lee et al. 2015). In the present study, while respiratory rate decreased over time in all groups, apnoea, which has been associated with a slow rate of *i.v.* administration of drugs, did not develop in any of the patients. While the decrease in respiratory rate was found to be consistent with previous reports (Murrell-Hallebrekers 2005; Restitutti et al. 2017) no significant difference was observed among groups in terms of this parameter.

Pulse oximetry is a non-invasive monitoring method that provides information about lung ventilation and can be used to evaluate patient oxygenation and perfusion (Hackett 2002; Thawley and Waddell 2013). In the present study, SpO_2 values were found to be lower in the XK group at T_1 than in the other groups, whereas SpO_2 values in the MK group at T_2 were much lower than at T_1 despite the stimulatory effect of ketamine injection and endotracheal intubation (Changmin et al. 2010; Guzel et al. 2013a). This finding might reflect the suppressive effect of medetomidine on the cardiovascular system, as a marked decrease in heart rate and oxygen ventilation/perfusion were observed at T_1.

Atelectasis resulting from general anaesthesia leads to hyperventilation during spontaneous breathing, which consequently causes hypercapnia, hypoxemia and impaired acid-base balance (Sereno 2006; Haskins 2007; Cecen et al. 2009; Celebioglu 2011; Guzel et al. 2013b). Blood gas analyses are important in determining a patient's ventilation and oxygenation. Especially, venous blood analyses give information about tissue perfusion, ventilation (pCO_2) and acid-base balance. Venous blood can be collected from the jugular vein easily and serially (Proulx 1999; Day 2002; Irizarry and Reiss 2009). In the present study, blood samples were taken from the jugular vein, and, thus, complications (Kemler et al. 2009; Pang et al. 2009) that might have had occurred during arterial blood collection were prevented and repeated blood collection was easily performed.

No significant difference was noted among groups in terms of blood pH levels following administration of α_2-agonists, which is consistent with the literature (Lemke 2007). Blood pH values are usually reduced during general anaesthesia (Quiros-Carmona et al. 2017). However, in the present study, no significant difference was observed in blood pH levels, since the measurements were conducted within a short term.

The partial pressure of carbon dioxide is a parameter which always reflects the respiratory status of the patient. Hypoventilation and hypercapnia usually do not cause any problems if adequate oxygen is provided to the patient during short-term anaesthesia (45 to 60 min) (Sereno 2006; McDonell and Kerr 2007). We observed an increase in $PvCO_2$ values at T_2 in the XK group compared to the MK and DK groups. On the other hand, no significant difference was noted among groups in terms of HCO_3^- levels. Likewise, the differences between time points within the groups were statistically insignificant. However, increased levels of carbon dioxide in the blood leads to an increase in bicarbonate concentrations to compensate for the condition (Guzel et al. 2012; Guzel et al. 2013b). The increase in $PvCO_2$ levels in the XK group did not result in a significant alteration in blood HCO_3^- levels, which we consider to be associated with the short duration of the anaesthesia.

End-tidal carbon dioxide measurements provide essential information about respiratory functions, gas exchange and ventilation. Obtained measurements are considered to be equal to arterial CO_2 values (Hackett 2002; Thawley and Waddell 2013). The end-tidal CO_2 concentration levels obtained in the study were higher in the MK group than in the other two groups, and yet SpO_2 levels in the same group were found to be lower than in the others. This finding underlines the more prominent suppressive effect of medetomidine on lung ventilation and perfusion in comparison with the other agents.

No statistically significant difference was noted among either groups or time points within the groups in terms of body temperature, which is likely to be due to the relatively short duration of the anaesthesia. Thus, hypothermia, which has been associated with long-term anaesthesia (Guzel et al. 2013a; Guzel et al. 2013b), did not occur in any of the cases.

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Based on evaluation of behavioural sedation scores, all dogs in each group (XK, MK, DK) were considered to be in a state of clinical sedation. The scores for posture, resistance and general appearance were higher in the MK group. This might have been associated with the higher specificity of medetomidine towards α_2 receptors (Murrell and Hellebrekers 2005; Lamont et al. 2012), which results in a marked decrease in the heart rate causing sudden hypotension (Lemke 2007). No statistically significant difference was noted among groups in terms of response to voice and jaw muscle relaxation.

In conclusion, no anaesthetic drug alone has excellent properties. On the basis of our findings, we conclude that none of the α_2-agonists, i.e., xylazine, medetomidine or dexmedetomidine, had superior properties over the others. All three may thus be recommended for premedication in healthy patients. However, the use of medetomidine should be carefully controlled because of the rapid decrease in heart rate.

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