Ankara Üniv Vet Fak Derg, **65**, 313-322, 2018

The comparison of clinical and cardiopulmonary effects of xylazine, medetomidine and detomidine in dogs*

Rahime YAYGINGÜL, Ali BELGE

Adnan Menderes University, Faculty of Veterinary Medicine, Department of Surgery, Aydın, Turkey.

Summary: This study intended to evaluate the effects of α_2-adrenoceptor agonists (xylazine, medetomidine and detomidine) on clinical status and cardiopulmonary system in dogs. A total of 30 dogs were randomly assigned to 3 different groups. Following fasting period of 12 hours, xylazine (1 mg/kg IM), medetomidine (25 µ/kg IM) and detomidine (20 µg/kg IM) were administered to groups I, II and III, respectively. Body temperature, heart rates, and respiratory rates were recorded at predetermined times before and after injections. Serum electrolyte, biochemical parameters, blood gases were also evaluated in the blood samples before and after injection. ECG was recorded before, during and after sedation. Decrease in heart rate was found significant in all of the groups. Decrease in the respiration rate was statistically significant ($P<0.001$) for groups I and II, but not for group III. The decrease in body temperature was statistically significant ($P<0.01$) only in medetomidine group. Regarding to the biochemical parameters, the increase in blood glucose level was only statistically significant ($P<0.05$) in group I. Bradycardia, sinoatrial block, 2^0 Mobitz Type I, and 2^0 Mobitz Type II block were observed in all groups according to the ECG. Only in medetomidine group, heart rhythm disorders such as escape beat and escape rhythm were observed.

Keywords: Cardiopulmonary effect, detomidine, dog, medetomidine, xylazine.

Köpeklerde xylazine, medetomidine ve detomidine'nin klinik ve kardiopulmoner etkilerinin karşılaştırılması

Özet: Bu çalışmada, köpeklerde α_2-adrenoreseptör agonistlerinin (xylazine, medetomidine ve detomidine) klinik ve kardiopulmoner sistem üzerindeki etkilerinin değerlendirilmesi amaçlandı. Toplam 30 adet köpek rastgele olarak 3 farklı gruba ayrıldı. 12 saatlik açlığı takiben I. gruptaki köpeklere xylazine (1 mg/kg İM), medetomidine (25 µg/kg İM), detomidine (20 µg/kg İM) dozunda uygulandı. Enjeksiyon öncesi ve sonrası belirli zaman beden ısısı, kalp atım ve solunum sayıları kaydedildi. Enjeksiyon öncesi ve sonrası alınan kan örneklerinde serum elektrolitleri, biyokimyasal parametreler ve kan gazları değerlendirildi. Sedasyon öncesi, sırası ve sonrası EKG kaydedildi. Kalp atım sayısındaki azalma bütün gruplarda anlamlı bulundu. Solunum sayısındaki azalma I. ve II. grupta anlamlı iken ($P<0.001$), III. grupta anlamlı değildi. Beden ısısında sadece medetomidine grubunda önemli azalma ($P<0.01$) belirlendi. Biyokimyasal parametrelerde sadece I. grupta glikoz değerinde artma istatiksel olarak anlamlı idi. Yapılan EKG değerlendirmelerinde bütün gruplarda bradikardi, sinoatrial blok, 2 derece Mobitz Tip I, 2 derece Mobitz Tip II bloklar görülürken, sadece medetomidine grubunda escape vuru, escape ritim gibi kalp ritm bozukluklarına rastlandı.

Anahtar sözcükler: Detomidine, kardiyovasküler etki, köpek, medetomidine, xylazine.

Introduction

In veterinary medicine, commonly used α_2-adrenoceptor agonists are xylazine, detomidine, medetomidine (23, 24, 27). Xylazine was the first α_2-adrenoceptor agonist which is used as a sedative analgesic in veterinary practice (13, 24, 27). In the 1980s, two new α_2-adrenoceptor agonists, that is detomidine and medetomidine, were introduced as sedative analgesic agents for large and smalls animals (7, 32). Medetomidine is a more selective and specific α_2-adrenoceptor agonist than xylazine and detomidine. The α_2/α_1 selectivity ratios are 1/620, 260 and 160 for medetomidine, detomidine and xylazine respectively (14, 38).

In spite of this difference, the 3 agents can be used similarly in practice. This study aimed to evaluate the effects of alpha-2 adrenoceptor agonists (xylazine, medetomidine and detomidine) on clinical status and cardiopulmonary system of dogs.

Materials and Methods

Animals: The researchers obtained the approval by of Adnan Menderes University's Institutional Animal Care

* This study was prepared from PhD thesis of first author and were presented as an oral presentation at the 14. National Veterinary Surgery Congress, (Antalya, 2014).

and Use Committee. The study was carried out using a total of 30 dogs of both sexes, between 1 and 4 years-old, 10 and 28 kg BW. The dogs were divided randomly into three groups which consisted 10 animals. Following fasting period of 12 hours, xylazine at dose rate of 1 mg/kg IM (xylazine hydrochloride, 23.32 mg/ml, Rompun® Bayer), medetomidine at dose rate of 25 µ/kg IM (medetomidine hydrochloride 1 mg/ml, Domitor® Pfizer) and detomidine at dose rate of 20 µg/kg IM (Detomidine Hydrochloride 10 mg/ml, Domesedan® Pfizer) were administered to groups I, II and III, respectively. Body temperature (BT, ^{o}C), heart rate (HR, beats/per min) and respiratory rate (RR, beats/per min) of the three groups were recorded before and 5, 10, 15, 20, 25, 30, 45, 60, 90, 120, 150 minutes, 6 and 24 hours after the injection.

Analysis: Serum electrolyte [sodium (Na), ionised calcium (Ca^{++}), potassium (K), magnesium (Mg)] and blood gases [arterial pH (pH), arterial carbon dioxide tension (pCO_2), arterial oxygen tension (pO_2), bicarbonate concentration (HCO3), total carbon dioxide (TCO_2), haematocrit (HCT) oxyhaemoglobin saturation (O_2Sat)] were evaluated in the blood samples which were taken before and 15, 30, 45, 60, 120, 6 and 24 h after the injection. Before and 15, and 120 min, 6, and 24 h after the injection, the researchers took blood samples and analyzed the biochemical parameters [glucose, urea, creatinin, alanine aminotranferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT), alkaline phosphatase (ALP), total protein, albumine]. ECG was recorded before, during and after sedation. The researchers also assessed the duration and amplitude of P and T waves, duration and amplitude of QRS complex, duration of PQ and QT intervals. The second derivation, durations and amplitudes of the P, T waves, durations and amplitudes of the QRS complex, durations of PQ and QT intervals were analyzed. Electrical axises of the heart at the 1st and 3rd derivations were also measured.

Statistical analysis: Statistical analyses were performed using SPSS software programme. The study datas were assessed using means and standard deviations (mean ± SD). In the repeated measurements, analysis of variance was applied for the statistical evaluation of all the obtained numerical datas. Tukey HSD test for Post-Hoc comparisons were used. Values with a P value under 0.05 were considered to be statistically significant

Results

Findings related to physiological parameters, biochemical analysis, electrolytes values and blood gas values are shown in Tables 1, 2, 3 and 4, respectively. Durations, and amplitudes of the waves, electrical axis values and electrocardiographic changes of xylazine, medetomidine and detomidine groups are presented in Tables 5. Bradycardia, sinoatrial block, 2^0 Mobitz Type I, and 2^0 Mobitz Type II block were observed in all groups in the evaluation of ECG. Only in medetomidine group, heart rhythm disorders such as escape beat, escape rhythm were observed. Bradycardia related to sinoatrial block was seen in five dogs in the xylazine group, eight in the medetomidine group and one in the detomidine group. In the xylazine group, seven dogs have experienced a second-degree Mobitz type II atrioventricular block. Four dogs in the medetomidine group presented a second-degree Mobitz type II block, escape beats combined with second-degree Mobitz type II block were seen in two dogs and two other dogs had both Mobitz type I and type II blocks, and one dog had escape beats only. In the detomidine group, three dogs had a second-degree Mobitz type II atrioventricular block, one dog had a Mobitz I and II combination and one other dog had a wondering pacemaker.

Discussion and Conclusion

Due to sedative and analgesic properties, α_2-adrenoceptor agonists are often used as pre-anaesthetic drugs for examination of the patient, radiographic imaging and simple clinical interventions. The major advantages of α_2-adrenoceptor agonists as pre-anaesthetic drugs is that they reverse the effects of these processes completely. In this study, we aimed to examine the possible effects of α_2-adrenoceptor agonists when used as a single pre-anesthetic agent.

The sedative effects were observed 8.3 ± 0.09, 7.2 ± 0.07 and 8.4 ± 0.11 minutes after the administration of xylazine, medetomidine and detomidine, respectively. The sedation levels were sufficient for minor interventions and examinations (ear examination, radiologic interventions, abscess, drainagei scaling of teeth). The sedative effect duration was longer in the medetomidine group compared to the xylazine and detetomidine groups. Dogs in the detomidine group recovered earlier than the others.

Past studies have reported possible side effects of α_2 agonists including vomiting, excitation, defecation and urination (14, 23, 35). Vomiting and defecation were not seen in the xylazine and detomidine groups. Ambrisko and Hikasa (1) reported that vomiting seen in 60% of the dogs sedated with medetomidine at a dose rate of 25 µg/kg intramusculary. Uevena et al. (36) reported that vomiting was not observed in the dogs sedated with medetomidine at a dose rate of 20 µg/kg intramusculary. In present study, vomiting in two dogs and defecation in three dogs in the medetomidine groups was detected. Our finding was consistent with Ambrisko and Hikasa (1), whereas it was different from the findings of Uevena et al. (36).

Table 1: Heart rate (HR), respiratory rate (RR), body temperature (BT) values of the xylazine, medetomidine, detomidine groups.
Tablo 1: Ksilazin, medetomidin, detomidin gruplarına ait kalp atım sayısı (HR), solunum sayısı (RR), beden ısısı (BT).

Time	Xylazine (1 mg/kg)			Medetomidine (25 µ/kg)			Detomidine (20 µ/kg)		
	BT $\overline{X}$ ± SD	RR $\overline{X}$ ± SD	HR $\overline{X}$ ± SD	BT $\overline{X}$ ± SD	RR $\overline{X}$ ± SD	HR $\overline{X}$ ± SD	BT $\overline{X}$ ± SD	RR $\overline{X}$ ± SD	HR $\overline{X}$ ± SD
Baseline	39.1±0.13	34.5±4.75^{a}	108.7±6.82^{a}	39.1±0.16^{ab}	44.4±5.78^{a}	103.7±6.14^{a}	39.4±0.16	26.7±4.36	108.6±4.84^{a}
5 min	39.2±0.12	26.4±4.81^{abcde}	75.30±7.64^{bc}	39.2±0.14^{a}	28.1±5.87^{bcd}	56.0±4.28^{c}	39.2±0.18	21.8±4.75	86.1±5.55^{bc}
10 min	39.2±0.11	16.50±2.82^{cde}	60.8±4.95^{c}	39.2±0.13^{a}	20.1±2.42^{d}	54.3±3.47^{c}	39.2±0.13	19.0±4.65	77.6±3.70^{bc}
15 min	39.2±0.12	14.9±2.18^{de}	63.0±7.00^{c}	39.2±0.13^{a}	17.8±2.38^{d}	56.00±4.28^{c}	39.1±0.13	17.8±4.76	75.3±4.31^{c}
20 min	39.2±0.13	14.0±1.71^{e}	64.2±6.23^{c}	39.2±0.16^{a}	17.4±1.85^{d}	55.2±4.19^{c}	39.0±0.14	16.8±3.46	73.6±4.37^{c}
25 min	39.1±0.12	14.8±1.78^{de}	64.7±6.86^{c}	39.1±0.16^{ab}	15.4±1.42^{d}	52.7±4.33^{c}	39.0±0.15	15.9±2.58	72.4±4.33^{c}
30 min	39.1±0.10	15.7±1.86^{cde}	66.4±6.94^{c}	39.2±0.15^{a}	18.2±2.85^{d}	52.6±3.82^{c}	38.9±0.14	14.3±1.75	71.2±3.94^{c}
45 min	39.0±0.14	16.5±2.21^{cde}	67.0±6.30^{c}	39.2±0.15^{a}	20.7±4.22^{cd}	53.5±5.16^{c}	38.8±0.15	15.3±1.47	71.3±4.73^{c}
60 min	38.9±0.21	21.1±3.28^{bcde}	67.7±6.67^{c}	39.1±0.16^{ab}	18.6±2.96^{d}	52.4±4.74^{c}	38.6±0.20	14.4±1.10	72.9±4.53^{c}
90 min	38.7±0.21	28.0±5.45^{abc}	74.70±7.21^{bc}	39.1±0.20^{ab}	19.8±3.32^{d}	56.4±5.63^{c}	38.6±0.22	15.4±1.62	83.8±5.92^{bc}
120 min	38.6±0.23	27.6±5.06^{abcd}	79.2±7.13^{bc}	38.7±0.17^{abc}	21.6±3.26^{cd}	61.2±7.81^{c}	38.7±0.23	19.0±3.52	84.1±3.57^{bc}
150 min	38.8±0.20	31.5±5.65^{ab}	90.2±8.61^{ab}	38.6±0.21^{bc}	26.9±4.73^{bcd}	62.4±7.59^{c}	38.8±0.15	19.8±3.31	92.6±7.58^{ab}
6 h	38.8±0.16	36.7±4.55^{a}	104.1±6.76^{a}	38.4±0.20^{c}	33.1±6.68^{abc}	86.4±7.92^{b}	39.0±0.22	19.2±2.54	102.6±7.63^{a}
24 h	39.0±0.14	36.0±5.80^{a}	102.1±7.51^{a}	38.9±0.13^{abc}	37.6±4.05^{ab}	93.8±3.66^{ab}	38.9±0.13	23.6±4.47	108.1±7.66^{a}
P values		***	***	**	***	***			***

***: P<0.001 **: P<0.01
a-e: There is statistical difference between baseline value in the same column with different letters (P<0.01, P<0.001).
a-e: Aynı sütunda farklı harf taşıyan ortalama değerler arası fark istatistiksel olarak önemlidir (P<0.01, P<0.001).

Table 2: Blood biochemical values of the xylazine, medetomidine, detomidine groups.
Tablo 2: Ksilazin, medetomidin, detomidin gruplarına ait kan biyokimyasal değerleri.

	Groups	Baseline $\overline{X}$ ± SD	15 min $\overline{X}$ ± SD	120 min $\overline{X}$ ± SD	6 h $\overline{X}$ ± SD	24 h $\overline{X}$ ± SD
Glucose (mg/dl)	Xylazine	108.04±6.7^{b}	115.55±7.75^{b}	136.50±8.38^{a}	114.33±5.84^{b}	107.86±3.23^{b}
	Medetomidine	108.74±7.06	107.51±7.91	143.10±10.51	130.70±18.26	112.31±4.77
	Detomidine	106.14±7.49	110.34±6.99	122.47±8.96	103.91±7.18	94.98±4.63
ALT (U/I)	Xylazine	35.63±6.49	36.30±6.58	35.03±5.70	35.92±6.29	39.93±8.18
	Medetomidine	27.27±3.32	29.35±3.36	30.06±3.53	25.14±3.85	21.52±3.28
	Detomidine	27.74±6.27	29.04±7.41	31.42±6.72	28.99±6.07	23.55±2.99
AST (U/I)	Xylazine	28.92±2.56	28.86±2.15	27.81±2.05	29.20±2.80	29.95±3.41
	Medetomidine	43.80±13.14	45.39±14.91	40.11±12.83	37.84±9.24	31.08±5.33
	Detomidine	36.88±8.10	40.95±7.60	41.16±7.48	38.68±8.48	34.96±6.15
GGT (U/I)	Xylazine	4.82±0.70	4.89±0.54	4.33±0.45	4.0±0.58	5.01±0.74
	Medetomidine	4.72±0.37	5.25±0.29	4.76±0.23	5.13±0.51	5.44±0.72
	Detomidine	8.80±2.57	7.45±1.79	7.27±1.69	5.92±1.65	6.78±1.83
ALP (U/I)	Xylazine	77.25±12.90	70.82±12.77	74.72±13.64	86.43±15.77	76.76±17.36
	Medetomidine	66.20±13.69	75.88±13.49	61.43±11.45	61.88±10.14	62.80±12.53
	Detomidine	115.15±12.43	107.38±11.07	101.74±10.51	96.74±10.65	105.99±14.9
T. Protein (g/dl)	Xylazine	6.89±0.52	6.45±0.61	6.74±0.60	7.20±0.72	6.44±0.53
	Medetomidine	6.24±0.27	7.14±0.30	6.51±0.29	6.30±0.25	6.23±0.33
	Detomidine	5.47±0.38	5.35±0.39	5.84±0.42	5.20±0.47	5.57±0.33
Albumin (g/dl)	Xylazine	2.48±0.23	2.26±0.19	2.18±0.14	2.39±0.20	2.61±0.20
	Medetomidine	2.54±0.14	2.67±0.16	2.52±0.18	2.87±0.25	2.63±0.13
	Detomidine	2.17±0.21	2.12±0.22	2.16±0.19	2.24±0.23	2.15±0.18
Creatinine (mg/dl)	Xylazine	0.96±0.07	0.93±0.05	1.00±0.06	1.00± 0.07	0. 94±0.08
	Medetomidine	1.15±0.07	1.15±0.07	1.08±0.07	1.07±0.06	1.10±0.06
	Detomidine	0.90±0.04	0.92±0.05	0.94±0.06	0.85±0.07	0.96±0.06
Urea (mg/dl)	Xylazine	43.85±12.08	39.94±11.82	37.10±11.76	41.61±9.87	36.12±5.76
	Medetomidine	41.32±4.65	47.45±6.63	42.97±6.49	46.87±6.99	35.11±4.41
	Detomidine	29.76±5.54	31.14±5.00	34.52±5.20	34.0±4.85	23.52±3.31

a-b: There is statistical difference between baseline value in the same line with different letters (P<0.05).
a-b: Aynı satırda farklı harf taşıyan ortalama değerler arası fark istatistiksel olarak önemlidir (P<0.05).

Table 3: Blood electrolytes values of the xylazine, medetomidine, detomidine groups.
Tablo 3: Ksilazin, medetomidin, detomidin gruplarına ait kan elektrolit değerleri.

n =10	Groups	Baseline $\overline{X}$ ± SD	15 min $\overline{X}$ ± SD	120 min $\overline{X}$ ± SD	6 h $\overline{X}$ ± SD	24 h $\overline{X}$ ± SD
K^{+} (mmol/L)	Xylazine	4.92±0.21	4.42±0.12	4.95±0.08	4.70±0.16	4.93±0.17
	Medetomidine	4.77±0.17^{ab}	4.55±0.17^{ab}	5.05±0.12^{a}	5.05±0.20^{a}	4.58±0.14^{ab}
	Detomidine	4.60±0.18	4.79±0.16	5.15±0.11	5.03±0.14	4.80±0.13
iCa^{++} (mmol/L)	Xylazine	1.46±0.02	1.45±0.04	1.46±0.02	1.43±0.01	1.39±0.06
	Medetomidine	1.35±0.05	1.39±0.06	1.48±0.03	1.38±0.05	1.42±0.03
	Detomidine	1.63±0.20	1.48±0.02	1.43±0.06	1.45±0.05	1.48±0.03
Na^{+} (mmol/L)	Xylazine	156.08±1.89	155.54±2.19	155.01±1.63	152.08±1.04	155.13±1.48
	Medetomidine	155.63±1.77	153.86±1.35	155.14±1.33	155.33±3.60	152.90±2.18
	Detomidine	155.32±2.14	158.31±2.17	155.35±1.39	155.96±2.15	154.27±2.12
Mg (mmol/dl)	Xylazine	0.41±0.03^{B}	0.39±0.04^{B}	0.37±0.03^{B}	0.33±0.01^{C}	0.35±0.02^{C}
	Medetomidine	1.02±0.19^{A}	1.03±0.18^{A}	1.09±0.19^{A}	1.09±0.17^{A}	0.93±0.13^{A}
	Detomidine	0.67±0.08^{AB}	0.64±0.05^{B}	0.70±0.09^{B}	0.66±0.06^{B}	0.62±0.06^{B}

A-C: There is statistical difference between groups in the same column with different letters (P<0.001).
A-C: Aynı sütunda farklı harf taşıyan ortalama değerler arası fark istatistiksel olarak önemlidir (P<0.001).
a-b: There is statistical difference between baseline value in the same column with different letters (P<0.05).
a-b: Aynı sütunda farklı harf taşıyan ortalama değerler arası fark istatistiksel olarak önemlidir (P<0.05).

Table 4: Blood gases values of the xylazine, medetomidine, detomidine groups.
Tablo 4: Ksilazin, medetomidin, detomidin gruplarına ait kan gazı değerleri.

	Groups	Baseline $\overline{X} \pm SD$	15 min $\overline{X} \pm SD$	30 min $\overline{X} \pm SD$	45 min $\overline{X} \pm SD$	60 min $\overline{X} \pm SD$	120 min $\overline{X} \pm SD$	6 h $\overline{X} \pm SD$	24 h $\overline{X} \pm SD$	P
pH	Xyl	7.37±0.04	7.38±0.05	7.38±0.04	7.34±0.04	7.41±0.06	7.37±0.03	7.42±0.05	7.35±0.02	
	Med	7.32±0.01	7.30±0.01	7.36±0.05	7.34±0.05	7.32±0.01	7.35±0.04	7.32±0.01	7.39±0.03	
	Det	7.33±0.27	7.34±0.02	7.36±0.29	7.33±0.01	7.35±0.03	7.334±0.03	7.31±0.01	7.37±0.04	
pCO_2 (mmHg)	Xyl	44.55±3.66	43.87±4.12	45.12±3.58	48.43±4.28	42.37±4.73	45.27±4.28	43.43±4.03	44.54±2.34	
	Med	45.45±1.61	49.33±1.87	46.05±4.62	47.57±3.97	48.05±2.10	47.31±3.61	46.53±1.23	39.99±2.48	
	Det	47.89±3.10	47.73±2.36	45.88±2.80	48.28±1.43	47.86±2.92	49.29±3.21	49.75±1.22	43.42±4.26	
pO_2 (mmHg)	Xyl	63.24±4.79	52.18±3.30	52.36±3.47	54.37±3.343	55.05±1.68	55.54±1.85	53.42±3.12	56.37±3.01	
	Med	65.11±3.9^{a}	44.14±2.35^{c}	44.53±1.65^{bc}	46.40±1.78^{bc}	48.56±2.59^{bc}	49.37±1.78^{bc}	48.95±2.88^{bc}	54.26±5.61^{b}	***
	Det	50.64±3.54	45.58±1.69	46.04±2.72	44.69±1.90	41.72±3.40	41.55±3.82	42.31±2.85	50.44±4.61	
HCT (%)	Xyl	40.17±1.49^{a}	36.16±1.50^{ab}	34.20±1.87^{b}	33.06±1.66^{b}	31.16±2.04^{b}	32.64±2.12^{b}	36.89±1.53^{ab}	34.24±2.07^{b}	*
	Med	39.77±1.98	38.24±0.95	36.80±1.43	35.97±1.08	36.28±0.89	36.24±1.20	37.81±1.87	35.63±1.37	
	Det	35.15±3.16	29.51±3.00	29.42±2.93	30.99±3.70	31.70±3.53	31.62±2.05	31.74±2.63	33.13±2.60	
O_2Sat (%)	Xyl	84.74±2.73	78.64±4.42	78.57±4.10	77.70±4.03	83.63±2.43	83.63±2.19	81.80±3.43	81.25±2.94	
	Med	85.49±2.40^{a}	64.73±3.48^{c}	68.02±4.49^{c}	70.84±3.35^{bc}	72.29±3.06^{bc}	75.61±3.24^{abc}	75.60±2.75^{abc}	79.22±4.59^{ab}	**
	Det	72.37±4.23	70.09±2.91	71.75±4.22	69.73±2.34	66.07±5.54	62.42±5.84	63.85±4.05	73.53±4.99	
TCO_2 (mmol/L)	Xyl	25.63±0.94	25.60±0.76	26.38±0.86	25.72±0.90	25.85±0.68	26.51±1.05	27.64±0.89	25.35±0.78	
	Med	24.34±0.58	24.70±0.51	24.78±0.60	25.12±0.68	25.37±0.87	25.93±0.95	25.64±1.07	24.77±0.69	
	Det	25.45±0.84	26.38±0.96	26.23±0.79	26.27±0.69	26.67±0.71	26.63±0.68	25.94±0.78	24.78±1.36	
HCO_3 (mmol/L)	Xyl	24.39±0.89	24.37±0.75	25.08±0.79	24.38±0.80	24.65±0.64	25.22±1.01	26.52±0.92	24.09±0.76	
	Med	23.04±0.56	23.37±0.51	23.53±0.54	23.81±0.62	24.04±0.85	24.59±0.95	24.30±1.06	23.62±0.71	
	Det	24.11±0.80	25.04±0.94	24.95±0.75	22.90±2.36	25.29±0.71	25.23±0.64	24.53±0.78	23.62±1.29	

*: P<0.05 **: P<0.01 ***: P<0.001
Xyl: Xylazine Med: Medetomidine Det: Detomidine
a-c: There is statistical difference between baseline value in the same line with different letters (P<0.05, P<0.01, P<0.001).
a-c: Aynı satırda farklı harf taşıyan ortalama değerler arası fark istatistiksel olarak önemlidir(P<0.05, P<0.01, P<0.001).

Table 5: The amplitude and period of the waves of the groups xylazine, medetomidine, detomidine.
Tablo 5: Ksilazin, medetomidin, detomidin gruplarına ait dalgaların süre ve amplitüdleri.

	Groups	Baseline $\overline{X}$ ± SD	5 min $\overline{X}$ ± SD	10 min $\overline{X}$ ± SD	15 min $\overline{X}$ ± SD	30 min $\overline{X}$ ± SD	45 min $\overline{X}$ ± SD	6 h $\overline{X}$ ± SD	24 h $\overline{X}$ ± SD
P-wave duration (s)	Xyl	0.051±0.001	0.058±0.002	0.063±0.003	0.063±0.003	0.059±0.003	0.059±0.003	0.054±0.001	0.055±0.002
	Med	0.052±0.002	0.052±0.002	0.054±0.003	0.054±0.003	0.058±0.003	0.057±0.003	0.054±0.002	0.051±0.004
	Det	0.054±0.002	0.050±0.002	0.050±0.001	0.047±0.002	0.113±0.059	0.54±0.001	0.053±0.002	0.052±0.002
P-wave amp. (mV)	Xyl	0.155±0.012	0.152±0.011	0.147±0.010	0.144±0.008	0.142±0.012	0.146±0.012	0.153±0.002	0.179±0.012
	Med	0.141±0.015	0.127±0.016	0.196±0.062	0.131±0.018	0.127±0.017	0.134±0.018	0.152±0.016	0.133±0.012
	Det	0.130±0.011	0.127±0.017	0.113±0.020	0.109±0.018	0.115±0.013	0.109±0.014	0.128±0.011	0.114±0.008
P-Q interval (s)	Xyl	0.127±0.012	0.138±0.006	0.142±0.008	0.145±0.007	0.138±0.007	0.135±0.008	0.124±0.007	0.118±0.007
	Med	0.121±0.005^{b}	0.132±0.003^{ab}	0.133±0.004^{ab}	0.137±0.003^{a}	0.138±0.003^{a}	0.140±0.004^{a}	0.131±0.004^{ab}	0.121±0.005^{b}
	Det	0.106±0.004^{d}	0.114±0.003^{bcd}	0.117±0.003^{bcd}	0.121±0.004^{abc}	0.127±0.004^{ab}	0.131±0.006^{a}	0.110±0.005^{cd}	0.109±0.004^{cd}
QRS complex duration (s)	Xyl	0.067±0.001	0.065±0.001	0.065±0.001	0.125±0.058	0.066±0.001	0.067±0.001	0.067±0.001	0.128±0.057
	Med	0.066±0.001	0.067±0.001	0.120±0.053	0.067±0.002	0.134±0.068	0.065±0.001	0.121±0.053	0.124±0.058
	Det	0.066±0.002	0.065±0.002	0.065±0.002	0.123±0.058	0.065±0.001	0.063±0.002	0.065±0.001	0.063±0.004
QRS complex amp. (mV)	Xyl	1.373±0.149	1.470±0.147	1.449±0.147	1.378±0.159	1.328±0.153	1.327±0.165	1.236±0.156	1.328±0.208
	Med	1.230±0.164	1.270±0.175	1.290±0.165	1.309±0.161	1.283±0.159	1.267±0.159	1.293±0.148	1.193±0.146
	Det	1.079±0.148	1.376±0.374	1.088±0.163	1.045±0.178	1.038±0.156	1.050±0.150	1.109±0.129	1.031±0.126
QT interval (s)	Xyl	0.204±0.006	0.221±0.003	0.225±0.004	0.229±0.004	0.221±0.009	0.231±0.004	0.228±0.011	0.214±0.007
	Med	0.204±0.005^{b}	0.225±0.004^{a}	0.223±0.002^{a}	0.225±0.004^{a}	0.226±0.004^{a}	0.228±0.005^{a}	0.223±0.009^{a}	0.213±0.005^{ab}
	Det	0.193±0.005	0.203±0.005	0.209±0.006	0.210±0.006	0.216±0.007	0.219±0.007	0.212±0.006	0.211±0.005
T-wave duration (s)	Xyl	0.071±0.009	0.084±0.009	0.093±0.009	0.092±0.010	0.089±0.009	0.092±0.010	0.150±0.083	0.069±0.007
	Med	0.083±0.010	0.094±0.008	0.093±0.010	0.094±0.008	0.098±0.009	0.098±0.010	0.084±0.012	0.089±0.007
	Det	0.076±0.007	0.072±0.007	0.075±0.007	0.080±0.008	0.078±0.008	0.078±0.009	0.083±0.008	0.076±0.011
T-wave amp. (mV)	Xyl	0.195±0.041^{bc}	0.342±0.044^{a}	0.348±0.049^{a}	0.358±0.053^{a}	0.322±0.038^{ab}	0.319±0.042^{ab}	0.180±0.026^{c}	0.198±0.035^{bc}
	Med	0.229±0.041	0.235±0.036	0.274±0.053	0.273±0.049	0.294±0.053	0.304±0.053	0.334±0.066	0.262±0.031
	Det	0.242±0.057	0.239±0.055	0.239±0.055	0.266±0.055	0.246±0.057	0.259±0.057	0.260±0.061	0.262±0.053
Electrical axis	Xyl	78.11±1.96	75.56±2.49	78.11±3.87	85.11±5.31	71.78±4.98	75.44±2.48	74.67±3.10	77.33±2.87
	Med	77.79±4.42	77.44±1.98	75.67±2.33	77.56±2.38	77.00±2.42	79.89±1.37	76.33±4.81	75.89±2.21
	Det	73.11±2.89	76.89±3.02	73.22±3.09	75.67±3.78	74.67±3.74	72.78±3.61	73.67±5.01	68.22±4.57

Xyl: Xylazine Med: Medetomidine Det: Detomidine
a-d: There is statistical difference between baseline values in the same line with different letters (P<0.05).
a-d: Aynı satırda farklı harf taşıyan ortalama değerler arası fark istatistiksel olarak önemlidir (P<0.05).

Some authors (10, 19, 25, 26, 29) reported a decrease in body temperature following α_2 agonist administration. It was caused by thermoregulatory failure as a result of the inhibition of limbic-hypothalamic centres and deterioration of homeostasis following reduced metabolic and muscular activity. Body temperature decreased from a baseline value of 39.1 ± 0.1 °C to 38.6 ± 0.17 °C at 150th minutes and 38.4 ± 0.21 °C at 6th hours following injection in the medetomidine group. This decrease was statistically significant (P<0.01). These findings were consistent with reports on decreased body temperature following medetomidine administration in dogs (10, 26, 29), cattle (19) and goats (25). However, no statistical significance was detected between xylazine and detomidine groups in terms of body temperature. This was also consistent with the reports by Yamashita et al. (39) in horses and Börkü et al. (5) in dogs.

Even though the effect on respiratory rate of α_2-adrenoceptor agonists is minimal, it was reported that the respiratory rate may decrease depending on type of drug, dose rate, the route of administration and the species of animal (7, 15, 19, 23). In this study the respiratory rate was depressed in all groups. While the time-dependent decrease of the respiratory rate following administration was statistically significant in the xylazine and medetomidine groups (P<0.001), a difference was not observed among the treatment groups. Recovery time of the respiratory rate to baseline value was earlier in the xylazine group than it was in the medetomidine group. A decrease in respiratory rate was observed in the detomidine group but it was not statistically significant. Börkü et al. (5) reported an important decrease in respiratory rate following the administration of xylazine. Yamashita et al. (39) indicated that xylazine, detomidine and medetomidine depressed the respiratory rate in horses and further, the least decrease was detected in the detomidine group. These findings were consistent with our findings. This situation seems to confirm that α_2 agonists lead to mild respiratory depression. The decrease of respiratory rate was not found statistically significant. It was thought that this was caused by the dose rate of the anesthetic agents was minimum.

Reports for the effects of α_2-adrenoceptors on blood gases are inconsistent (2, 7, 9, 21, 23). While Kurtdede et al. (21) and Atalan et al. (2) reported that the possible changes may be seen in pH, pO_2, O_2SaT, pCO2 and HCO3 values; Lemke (23), Cullen (7), Greene and Thurmon (9) observed no such changes. Kurtdede et al. (21) reported that xylazine did not alter venous blood pH or HCO3 values but increased pCO2 and reduced pO2 and O_2Sat. According to Atalan et al. (2), pCO2 increased and pO2 decreased by using xylazine. They did not observe statistically significant alterations of blood gas values in medetomidine sedation. Yamashita et al. (39) reported that high doses of detomidine or medetomidine did not alter pCO2 levels, but pO2 reduced markedly; they recorded no statistically significant change with xylazine in horses. However, no alteration in pH or HCO3 was observed any of the three groups of this study. A statistically significant alteration was noted in pO_2 (P<0.001) and O_2Sat (P<0.01) in the medetomidine group. No significant change was detected in the xylazine or the detomidine group. Our findings were different from the reports by Kurtdede et al. (21) and Atalan et al. (2). Their findings were similar to the observations by Yamashita et al. (39). Kurtdede et al. (21) stated that the changing of the blood gas analysis results caused by xylazine did not alter the blood pH. The finding of this study did not reveal a relationship between blood gas values and pH as well.

A statistically significant decrease in haematocrit was found in the xylazine group in our study in minutes 30, 45, 60 and 120 (P<0.05). Similar observations have been reported by Ünsüren et al. (37). No statistically significant changes were seen in hematocrit in medetomidine and detomidine groups in our study; there was no difference among groups. The researchers believe that this change, which remained within normal limits, may be due to fluid influx from the extracellular and extravascular compartments into the intravascular space as a result of decreased hydrostatic pressure because of the hypotensive effects which occurred during anesthesia.

In this study, time-dependent increase in serum glucose levels were statistically significant (P<0.001) in all three groups. The only significant difference was in the xylazine group between the level of baseline and in minute 120 (P<0.05). It was consistent with the reports on hyperglycemic effect of α_2 agonists in animal (1, 4, 8, 16). Ambrisko and Hikasa (1) observed an increased serum glucose following the administration of different doses of xylazine and medetomidine. This increase was dose-dependent in the case of xylazine. Burton et al. (6) reported that intravascularly medetomidine at doses of 10-20 µg/kg of body weight elevated the serum glucose. Kanda and Hikasa (16) indicated that the administration of different doses of medetomidine and xylazine resulted in increased serum glucose in all treatment groups. Our findings were similar to these studies. It has been reported that the hyperglycemic effect of these drugs might be related to the reduced level of insulin following the action on α_2-adrenoceptors in the pancreatic β cells (1, 4, 8).

The changes of urea, creatinine, ALT, AST, GGT, alkaline phosphatase, total protein and albumin levels were not significant in three groups. Simon et al. (34) determined three different dose rates of 20, 40 and 80 µg/kg body weight to 90 dogs in their study. They reported no change in serum AST, alkaline phosphatase, ure or creatinine levels. Our findings are consistent with those of Simon et al. (34).

Khan et al. (18) reported a reduction in serum potassium in the calves after administration of detomidine. The authors attributed this reduction to either increased urinary potassium excretion or to an intracellular transfer of potassium ions due to hyperglycemia and diuretic effect of detomidine following its administration. The serum potassium level was reduced in the xylazine and detomidine groups in our study, but decreases were noted in the detomidine group. There was also no difference in the animals treated with xylazine or medetomidine. These results have some similarities with those of Khan et al. (18).

It is known that α_2 agonists have depressant and arrhythmogenic effects on the cardiovascular system. Firstly, arterial hypertension develops, following by development of bradycardia, reduction in cardiac contractility and performance, and drop in blood pressure. Also, it was reported that sinus bradycardia, sinus arrhythmias or sinoatrial and atrioventricular block may occur (11, 31). In the presented study, a time-dependent reduction in heart rate was observed in all groups. The reduction in heart rate observed from 5^{th} minutes up to 120^{th} minutes and this was statistically significant ($P<0.001$ for all). While the heart rate was returned to normal limits after 150 minutes in the xylazine and detomidine groups, recovery was observed later in the medetomidine groups. These findings were similar to the earlier reports (9, 20). This property of α_2 agonist agents was reported to be a result of a depression of sympathetic activity coupled with an increase in parasympathetic effect which decreases heart rate (11, 31).

Rhythm disorders are formed as a result of abnormalities in impulse formation or transmission, or both. Pre-anesthesia and induction of drugs may affect impulse formation and transmission by modifying autonomic tonus. These effects lead to clinically significant or insignificant various types of arrhythmia (12, 30). Bradycardia related to sinoatrial block was seen in five dogs in the xylazine group, eight in the medetomidine group and one in the detomidine group. In the xylazine group, seven dogs have experienced a second-degree Mobitz type II atrioventricular block. Four dogs in the medetomidine group presented a second-degree Mobitz type II block, escape beats combined with second-degree Mobitz type II block were seen in two dog and two other dogs had both Mobitz type I and type II blocks, and one dog had escape beats only. In the detomidine group, three dogs had a second-degree Mobitz type II atrioventricular block, one dog had a Mobitz I and II combination and one other dog had a wondering pacemaker. Arrhythmias did not occur at life-threatening events in any dogs in the study.

Güzel (12) reported rhythm disorders such as bradycardia, atrial stagnation and first degree AV block in 26 of 56 cases following xylazine administration as sedative premedication. Seeler et al. (33) noted that sinus bradycardia is most frequently encountered arrhythmia in small animals intra-operatively. They indicated that xylazine is an important etiologic factor. Özaydın et al. (26) reported no abnormal findings, with exception of sinus bradycardia occuring within 5 minutes up to 60 minutes in all animals, on the ECG of dogs receiving medetomidine-ketamine-propofol anesthesia. These reports are consistent with our study.

Lele and Bhokre (22) established that the P-wave amplitude (in mV) varied, shortened its duration and PR interval was extended on the ECG of dogs given xylazine. Pişkin et al. (1999) reported reduced amplitude of the P-wave, prolonged P-wave and prolonged PR interval in guinea pigs given a combination of xylazine and ketamine. Belge et al. (3) indicated that the P-wave duration remained unchanged, while its amplitude was reduced during xylazine-ketamine anesthesia. In this study, increased duration and decreased amplitude of the P-wave were observed, yet they were not statistically significant. An insignificantly prolonged P-wave duration and reduction in amplitude were also observed in the medetomidine group. Shortening and amplitude loss in the P-wave were detected. While the findings in our study were similar to those of Pişkin et al. (28) and Belge et al. (3) for xylazine and medetomidine, those for the detomidine group were different. The overall observations may be explained by the cardiodepressant effect of even small doses of xylazine, detomidine and medetomidine, leading to a prolonged P-wave and PR interval.

Pişkin et al. (28) stated that the low potassium level may affect the T-wave amplitude, and reduction of the sodium and chloride levels may affect the R-wave amplitude by leading ventricular depolarization. The finding of increased T-wave amplitude concurrently decreased potassium level in the xylazine and medetomidine-treated animals in our study supports the report by Pişkin et al. (28). No T-wave elevation was recorded in the detomidine group.

The QT interval represents the time from the start of ventricular depolarization to the completion of repolarization. A QT increase is seen along with the prolongation of QRS or the T-wave or both. The duration of QT interval varies inversely to heart rate. Tachycardia causes an increase in the QT and bradycardia causes shortening (17, 22, 30). The increase of QT interval along with bradycardia was noted in all groups in our study. There was also an increase in the PQ interval and the T-wave duration. The slower heart rate could be explained with the increased the PR, QT and T-wave durations on the ECG. Belge et al. (3) and Sarchahi et al. (31) reported a reduced heart rate and prolonged QT interval in dogs sedated with xylazine. These reports showed similarities

to the findings in our study. Lele and Bhokre (22) indicated that xylazine did not change the duration of the QRS complex. Belge et al. (3) stated that the amplitude of the QRS complex reduced. No significant changes were recorded in the QRS duration in our groups. While our findings consistent with the findings of Lele and Bhokre (3), they did not correspond to the report by Belge et al. (3).

No significant changes were seen in any group in the electrical heart axis, an indicator of the electromotor force of cardiac activity. Belge et al. (3) measured an axis of 71.00 ± 1.10 and 77.50 ± 7.00, before and during anesthesia, respectively. The corresponding values in our study are consistent with those of Belge et al. (3). Additionally, a left shift of the axis was noted in one dog of each group, which is thought to be due to the dog's recumbency position.

We concluded that three α_2-adrenoceptors (xylazine, medetomidine and detomidine) are similar in terms of their clinical and cardiopulmonary effects, while the pre-anesthetic properties of medetomidine may make it more efficient than the other two.

Acknowledgement

This study supported by Adnan Menderes University, Scientific Research Foundation (Project No: VTF-10013). The authors would like to thank Adnan Menderes University for their support.

References

1. **Ambrisko TD, Hikasa Y** (2002): *Neurohormonal and metabolic effect of medetomidine compared with xylazine in beagle dogs.* Can J Vet Res, **66**, 42-49.
2. **Atalan G, Özba B, Erdoğan HM, et al.** (2001): *Comparison the clinical and cardiovaskular effects of the combination of xylazine-ketamine HCI with medetomidine-ketamine HCI.* Turk J Vet Surg, **7**, 21-27.
3. **Belge F, Çınar A, Yur F, et al.** (1998): The research on the effect of ketalar's utilization with different preedicant agents on ECG and some blood parameters. Turk J Vet Surg, **4**, 13-18.
4. **Benson GJ, Thurmon JC, Neff-Davis CA** (1984): Effect of xylazine hydrochloride upon plasma glucose and serum insulin concentrations in adult pointer dogs. J Am Anim Hosp Assoc, **20**, 791-794.
5. **Börkü MK, Özkanlar YE, Gürkan M, et al.** (2005): Xylazine ile sedasyon oluşturulan köpeklerde xylazine antagonisti yohimbine'in etkinliğinin araştırılması. Uludag Univ J Fac Vet Med, **1-2-3-4**, 27-32.
6. **Burton SA, Lemke KA, Ihle SL, et al.** (1997): *Effect of medetomidine on serum insulin and plasma glucose concentrations in clinically normal dogs*. Am J Vet Res, **58**, 1440-42.
7. **Cullen LK** (1999): *Xylazine and medetomidine in small animals: These drugs should be used carefully.* Aust Vet J, **77**, 112-116.
8. **Felberg W, Symonds HW** (1980): *Hyperglycaemic effect of xylazine.* J Vet Pharmacol Therap, **5**, 241-245.
9. **Greene SA, Thurmon JC** (1988): *Xylazine review of its pharmacology and use in veterinary medicine.* J Vet Pharmacol Therap, **11**, 295-313.
10. **Gülanber EG, Kaya U, Aktaş M, et al.** (2000): *The effects of medetomidine-ketamine anaesthesia on some physiological functions and blood in dogs*. Turk J Vet Surg, **6**, 5-9.
11. **Güzel Ö, Perk EC** (2002): *Diagnosis and treatment of cardiac rhythm disorders encountered during the general anaesthesia procedure and intraoperative period in dogs.* J Fac Vet Med Istanbul Univ, **28**, 381-401.
12. **Güzel Ö** (2003): *Effects of Anesthetic Agents used in cats and dogs on the heart.* J Fac Vet Med Kafkas Univ, **9**, 215–218.
13. **Hall LW, Clarke KW** (1991): *Anaesthesia in the dog*. 51-79, 92-97, 290-323. In: Veterinary Anaesthesia. Bailliere Tindall, Philadelphia.
14. **Hikasa Y, Takase K, Saito K, et al.** (1986): *Antagonism of the emetic action of xylazine by alpha-adrenoceptor blocking agents.* Eur J Pharmacol, **130**, 229-235.
15. **Jarvis N, England GCW** (1991): *Reversal of xylazine sedation in dogs.* Vet Rec, **128**, 323-325.
16. **Kanda T, Hikasa Y** (2008): *Neurohormonal and metabolic effect of medetomidine compared with xylazine in healthy cats*. Can J Vet Res, **72**, 278–286.
17. **Khan AM, Ashraf M, Pervez K, et al.** (2003): *Effect of detomidine on blood chemistry and electrolyte profile in buffalo calves*. Int J Agri Biol, **5**, 308-310.
18. **Khan MA, Ashraf M, Pervez K, et al.** (2004): *Comparative effects of detomidine and xylazine as sedative and analgesic agent in small ruminant.* Pakistan Vet J, **24**, 62–69.
19. **Kilic N** (2008): *Cardiopulmonary, biochemical and haematological changes after detomidine-midazolam-ketamine anaesthesia in calves*. Bull Vet Inst Pulawy, **52**, 453-456.
20. **Kramer S, Nolte I, Jochle W** (1996): *Clinical comparison of medetomidine with xylazine/l-methadone in dogs.* Vet Rec, **138**, 128-133.
21. **Kurtdede A, Börkü MK, Özlem MB, et al.** (1994): *Effects of xylazine and xylazine plus ketamine on blood gases and some hematological parameters in healthy dogs*. Vet J Ankara Univ, **41**, 327-335.
22. **Lele CM, Bhokre AP** (1985): *Evaluation of xylazine as an anaesthetics agent in combination with certain preanaesthetics drugs in dogs*. II. Electrocardiographic and biochemical study. India Vet J, **62**, 863-868.
23. **Lemke KA** (2004): *Perioperative use of selective alpha-2 agonists and antagonists in small animals*. Can Vet J, **45**, 475-480.
24. **Maze M, Tranquilli W** (1991): *Alpha-2 adrenoceptor agonist*: Defining the role in clinical anesthesia. Anesthesiology **74**, 581–605.
25. **Mohammad FK, Zangana IK, Al-Kassim NA** (1991): *Clinical observations in Shami goat kids sedated with medetomidine*. Small Rum Res, **5**, 149–153.
26. **Özaydın İ, Atalan G, Uzun M, et al.** (2001): *Assessment of anaesthetic properties and clinical, cardiovascular and*

respiratoric effects of medetomidine, propofol and ketamine combination in dogs. J Fac Vet Med Kafkas Univ, **7**, 71-76.
27. **Paddleford RR, Harvey RC** (1999): *Alpha-2 agonists and antagonists.* Vet Clin North Am Small Anim Pract, **29**, 737-745.
28. **Pişkin I, Şireli M, Sağmanlıgil V, et al.** (1999): *The effects of some anaesthetics on the electrocardiograms of guinea pigs.* Turk J Vet Anim Sci, **23**, 161-166.
29. **Pypendop BH, Verstegen JP** (1998): *Hemodynamic effects of medetomidine in the dog: A dose titration study*. Vet Surg, **27**, 612-622.
30. **Saraçoğlu A** (2008): *Drug-related cardivascular disorders*. Turkiye Klinikleri J Cardiovasc Sci, **20**, 107-123.
31. **Sarchahi AA, Vesal N, Nikahval B, et al.** (2009): Comparison of the effects of different doses of acepromazine- xylazine on the electrocardiogram in dogs. Iran J Vet Res, **10**, 208-215.
32. **Savole JM, Ruskoaho H, Puurunen J, et al.** (1986): *Evidence for medetomidine as a selective and potent agonist at alpha-2 adrenoceptors.* J Auton Pharmacol, **5**, 275-284.
33. **Seeler DC, Dodman NH, NormanWM, et al.** (1987): *Intraoperative cardiac dysrhythmias and their treatment*. Brit Vet J, **143**, 97-111.
34. **Simon F, Romvary A, Mora S** (1989) *Clinical investigations of medetomidine in dog*. Acta Vet Scand Suppl, **85**, 161-165.
35. **Sinclair DM** (2003): *A review of the physiological effect of α2- agonists related to the clinical use of medetomidine in small animal practice*. Can Vet J, **44**, 885-897.
36. **Ueyena Y, Waselau AC, Wiese AJ, et al.** (2008): *Anesthetic and cardipulmonary effect of intramuscular morphine, medetomidine, ketamine injection in dogs*. Vet Anaesth Analg, **35**, 480-487.
37. **Ünsüren H, Kurtdede A, Şeker Y, et al.** (1986): *Clinical, biochemical and haematological finding in dogs given Xylazine hydrochloride*. Vet J Ankara Univ, **33**, 373–380.
38. **Virtanen R** (1986): *Pharmacology of detomidine and other α2- adrenoreceptor agonists in the brain.* Acta Vet Scand, **82**, 35-46.
39. **Yamashita K, Tsubakishita S, Futaoka S, et al.** (2000): *Cardiovascular effect of medetomidine, detomidine, and xylazine in horse*s. J Vet Medi Sci, **62**, 1025-32.

Geliş tarihi: 12.12.2016 / Kabul tarihi: 24.07.2017

Address for correspondence:
Asst. Prof. Dr. Rahime YAYGINGÜL
Adnan Menderes University,
Faculty of Veterinary Medicine,
Department of Surgery, Işıklı, 09017 Aydın, Turkey.
e-mail: ryaygingul@hotmail.com