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Anesthetic and Cardiopulmonary Effects of Medetomidine, Midazolam and Ketamine Combination in Beagle Dogs

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Abstract : This study was performed to examine the anesthetic and cardiopulmonary effects of medetomidine, midazolam and ketamine (MMK) combination in ten beagle dogs. Dogs were randomly allocated to two groups. Treatment group MMK-L received 0.015 mg/kg medetomidine followed by 0.3 mg/kg midazolam and 5 mg/kg ketamine by intramuscular injection. Treatment group MMK-H received 0.02 mg/kg medetomidine followed by 0.3 mg/kg midazolam and 5 mg/kg ketamine by intramuscular injection. Induction, anesthesia, sternal recumbency, standing, walking time, heart rate, arterial blood pressure, rectal temperature, respiratory rate and arterial blood gases were measured. Mean anesthesia time was significantly different between MMK-L group (52.4 ± 11.08 minutes) and MMK-H group (78.2 ± 20.72 minutes). Sedative scores and noxious stimuli were raised to the maximum value at 5 minutes after administration of the test dose and maintained until 40 minutes in both groups. In both groups, the heart rate significantly decreased after MMK administration. The blood pressures (MAP, SAP and DAP) increased after MMK administration but there were no significant differences in blood pressures between two groups. In conclusion, intramuscular administration of medetomidine followed by intramuscular injection of midazolam and ketamine in beagle dogs, leads immediate and sufficient anesthesia and proper doses of medetomidine for minimal adverse effects in intramuscular MMK combination will be 0.015 mg/kg in dogs.

Key words **:** medetomidine, midazolam, ketamine, anesthesia, dog.

Introduction

The combination of sedative/dissociative drugs has been widely used in veterinary medicine but a single dose may be inefficient. Based on this fact, the combination of different agents has been suggested, especially drugs with a higher specificity for α_2-receptors (14).

Medetomidine and other α_2-adrenoceptor agonists are frequently used in veterinary medicine for both their sedative and analgesic properties (2,12). Medetomidine is a highly selective α_2-adrenoceptor agonist ($\alpha_2 : \alpha_1$ selectivity is 1620 : 1) that activates both pre- and post-synaptic α adrenergic receptors in the peripheral nervous system and pre-synaptic α_2 receptors in the central nervous system (2,18). Unfortunately, the negative cardiovascular effects of earlier α_2-agonists, including bradycardia and associated arrhythmias, hypertension or hypotension, and reduced cardiac output, are still observed with medetomidine and cause concern among clinicians with respect to their use as premedication or sedative agents (2,15). Currently, xylazine and medetomidine are used relatively low doses, alone or in combination with other drugs (benzodiazepine, opioids), to induce sedation for minor diagnostic and surgical procedures, and as adjuncts to injectable and inhalational anesthetics (10).

Ketamine, a dissociative anesthetic, is an N-methyl-D-aspartate (NMDA) antagonist that acts by blocking pre- and post-synaptic NMDA receptors. Ketamine anesthesia is characterized by a relatively short duration of action and comparatively mild cardiorespiratory effects when used as the sole anesthetic (18). Medetomidine-ketamine combinations have helped to reduce the dose required to produce anesthesia thereby shortening the duration of recovery and enhancing muscle relaxation. Also, many clinical procedures and minor surgical operations could be performed after administration of a combination of medetomidine-ketamine (7,11,18).

Midazolam is water-soluble, well absorbed following intramuscular administration and rapidly eliminated injectable benzodiazepine that is used as an anxiolytic in human medicine (17,19). Midazolam in combination with ketamine it shows only limited cardiopulmonary effects and to be able to minimize the dose of the third drug was chosen to be added (3). Combinations of medetomidine, ketamine and midazolam were tested in ferrets, rabbits, cats and small hedgehog tenrec (3,5,12,13). However, there is little information available on the effects of medetomidine/midazolam/ketamine (MMK) combination in dogs.

The purpose of this study was to examine the anesthetic and cardiopulmonary effects of MMK combination in beagle dogs. Furthermore, this study can establish the recommended

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dose of MMK combination anesthesia for minor diagnostic and surgical procedures in dogs.

Materials and Methods

Experimental animals

Ten adult male healthy beagles with a mean body weight of 8.5 ± 0.78 kg were used in this study. All dogs were raised in appropriate animal management facilities and fed standard commercial dry canine food. Routine hematological tests were performed before the experiment commenced. All values were within the normal physiological range. This experiment was conducted under the supervision of the Chungnam National University Animal Care and Use Committee (CNU-00054). The dogs were fasted for 6 hours before each experiment, and water was withheld for 2 hours before anesthesia in order to prevent any possible adverse effects, such as vomiting during anesthesia or recovery periods.

Instrumentation and drug administration

Before the experiment, a sterile 24-gauge arterial catheter (BD IV Catheter®, Becton Dickinson Korea Ltd, Korea) was inserted percutaneously into the dorsal pedal artery of each dog masked down by isoflurane (Forane®, Choongwae Pharmaceutical Corp, Korea). After endotracheal intubation anesthesia was maintained lighly for few minutes. The catheter was flushed with heparinized saline, secured in place, and connected to a pressure transducer (TranStar Single Monitoring Kit, MX9504, A Furon Company, USA) with a noncompliant tube. The transducer was attached to anesthetic patient monitor (S-5 Anethesia Monitor®, Datex-Ohmeda, Finland). After measurement of baseline values and collecting arterial blood samples, isoflurane was discontinued, and only 100% oxygen was given, waiting to recover from anesthesia. To comply with a crossover study design, each of the five dogs received two different treatments with 14 days of withdrawal time, in a randomized order. Treatment group MMK-L received 0.015 mg/kg medetomidine (Domitor®, Orion Pharma, Finland) followed by 5 mg/kg ketamine (Ketamine 50®, Yuhan Co, Korea) and 0.3 mg/kg midazolam (Midazolam®, Bukwang Pharm Co, Korea) by intramuscular injection. Treatment group MMK-H received 0.02 mg/kg medetomidine followed by 5 mg/kg ketamine and 0.3 mg/kg midazolam by intramuscular injection. After administration of the test drug, animals were positioned in lateral recumbency, and anesthesia and cardiopulmonary data were determined and recorded.

Measurement of parameters

Anesthesia and recovery

Onset time, anesthesia time, sternal recumbency time, standing time, walking time and recovery time were recorded for each dog. Onset time was the time from MMK administration to complete immobilization, defined as a lack of response to being handled. Anesthesia time was the time interval between complete immobilization and the first attempt made by the animal to lift its head a few centimeters above the ground. Sternal recumbency time was the time from MMK administration to when the dog achieved sternal recumbency. Standing time was the time from MMK administration to when the dog stood up without assistance for longer than 10 seconds. Walking time was the time from the injection of MMK administration to when the dog was able to walk without knuckling. Recovery time was the time from the first attempt made by the animal to lift its head to when the dog was able to walk without knuckling.

Evaluation of sedation and analgesia

The levels of sedation (spontaneous posture) and analgesia (pedal withdrawal) were assessed each designated times during anesthesia according to the criteria of Table 1. The scores of sedation and response to noxious stimuli were assigned to each animal by one observer who was unaware of the dose of

Table 1. Subjective criteria used to score levels of sedation and response to noxious stimulus in dogs treated with medetomidine/midazolam/ketamine

Sedative score Spontaneous posture (0-5)	
0	Normal
1	Being able to stand or sit on their hind legs
2	Keeping the position of ventral recumbency
3	Lateral recumbency with apparent spontaneous movement (head lifting or struggling)
4	Lateral recumbency with subtle spontaneous movement (ear and nose twitching or blink)
5	Lateral recumbency without spontaneous movement
Score of response to noxious stimulus Pedal withdrawal response to pinching of a digit or interdigital web (0-3)	
0	Hypersensitive or normal
1	Slightly impaired
2	Clearly weak
3	Absent

medetomidine used.

Heart rate, blood pressures and rectal temperature

The heart rate (HR), blood pressure and rectal temperature (RT) were measured at time 0 (before injection of the drugs) and at 5, 10, 20, 30, 40, 50 and 60 minutes after the administration of the drugs. The HR was measured by a patient monitor. The mean arterial pressure (MAP), systolic arterial pressure (SAP) and diastolic arterial pressure (DAP) were measured by using a patient monitor and were recorded. Calibration of blood pressure device was done in each experiment for the accurate measurement of blood pressure. The left scapulohumeral joint was used as the zero reference point for MAP measurement. RT was continuously recorded using a digital thermometer (MT 1681®, Microlife, Switzerland) that was placed deep into the rectum.

Respiratory rate and arterial blood gases

The respiratory rate (RR) was also measured at time 0, 5, 10, 20, 30, 40, 50 and 60 minutes after administration of the drugs and blood gases were measured at time 0 and at 10, 20 and 40 minutes after administration of the drugs. The respiratory rate was measured on the basis of the thoracic movements of the animal. Arterial blood samples were collected anaerobically and analyzed immediately using a portable arterial blood gas analyzer (i-STAT® Portable Clinical Analyzer, HESKA, USA). The analyzer measured sample arterial pH, carbon dioxide partial pressure ($PaCO_2$), oxygen partial pressure (PaO_2) and oxygen saturation (SaO_2).

Statistical analysis

Values were expressed as means and standard deviation. Kruskal-Wallis analysis of variance was used for group comparison. Between-group differences were compared by Mann-Whitney U-test. Differences in cardiopulmonary parameters within groups were tested with one-way analysis of variance (ANOVA) and Duncan's post hoc test. Wilcoxon signed rank's test was used to compare the differences in the scores of sedation and response to noxious stimuli within group. $P < 0.05$ was considered statistically significant. All statistics were performed using a computer statistical package (Statistics Package for the Social Sciences, version 18.0; SPSS Inc, IL, USA).

Results

Anesthesia and recovery

Onset, anesthesia, sternal recumbency, standing and walking times were shown in Table 2. Mean onset times were not significantly different between MMK-L and MMK-H groups. Mean anesthesia time was significantly different between MMK-L group (52.4 ± 11.08 minutes) and MMK-H group (78.2 ± 20.72 minutes) ($p < 0.05$).

Mean sternal recumbency times were not significantly different between MMK-L and MMK-H groups. Mean standing time in the MMK-L group (69.6 ± 12.97 minutes) was significantly shorter than that in the MMK-H group (94.4 ± 19.71 minutes) ($p < 0.05$). Mean walking time in the MMK-L group (70.6 ± 12.97 minutes) was significantly shorter than that in the MMK-H group (95.4 ± 19.71 minutes) ($p < 0.05$). Mean recovery time was not significantly different between MMK-L and MMK-H groups.

Evaluation and sedation and analgesia

Sedative scores and noxious stimuli were raised to the maximum value at 5 minutes after administration of the test dose and maintained until 40 minutes in both groups.

There were no significant differences in the scores of sedation and response to noxious stimuli between two groups (Table 3).

Heart rate, blood pressures and rectal temperature

Data of heart rate, blood pressures and rectal temperature were shown in Table 4. In both groups, the heart rate significantly decreased after MMK administration ($p < 0.05$). In the MMK-L groups, the heart rate significantly decreased within 20 minutes after MMK administration and remained consistently below the baseline value for 40 minutes ($p < 0.05$). In the MMK-H groups, the heart rate decreased significantly at 5 minutes after administration of the drugs and remained consistently below baseline for 40 minutes ($p < 0.05$). The heart rate was significantly high in MMK-L group at 5 minutes after administration ($p < 0.05$).

In both groups, the blood pressures (MAP, SAP and DAP) increased after MMK administration. In the MMK-L group, SAP was significantly higher than baseline at 10 minutes after administration ($p < 0.05$). MAP was significantly higher than baseline at 5, 10, 20 and 30 minutes after administration ($p < 0.05$). DAP was significantly higher than baseline at 5 minutes after administration ($p < 0.05$). In the MMK-H group, SAP was significantly higher than baseline at 5 minutes after administration, MAP and DAP were significantly higher than baseline at 10 minutes after administration ($p < 0.05$). There were no significant differences in blood pressures between two groups.

Table 2. Onset time, duration of anesthesia and recovery times in beagle dogs after administration of medetomidine/midazolam/ketamine (MMK)

	MMK-L(min)	MMK-H(min)
Onset time	1.0 ± 0.0	1.0 ± 0.0
Anesthesia time	52.4 ± 11.08[a]	78.2 ± 20.72[a]
Sternal recumbency time	63.6 ± 12.44	80.6 ± 21.48
Standing time	69.6 ± 12.97[a]	94.4 ± 19.71[a]
Walking time	70.6 ± 12.97[a]	95.4 ± 19.71[a]
Recovery time	18.2 ± 8.17	17.2 ± 5.26

Data are expressed as mean ± SD (n = 5)
[a]Significantly different between groups ($p < 0.05$)

Table 4. Heart rate, blood pressure and rectal temperature in beagle dogs after administration of medetomidine/midazolam/ketamine (MMK)

	Group	0 min	5 min	10 min	20 min	30 min	40 min	50 min	60 min
HR (beats/min)	MMK-L	120.4 ± 18.66	87.8 ± 9.26[a]	83.4 ± 18.88	65.0 ± 14.53[*]	59.6 ± 16.58[*]	58.0 ± 18.96[*]	57.3 ± 11.37	68.7 ± 15.70
	MMK-H	113.4 ± 33.41	65.6 ± 16.82[*a]	67.8 ± 23.05[*]	58.0 ± 10.30[*]	51.0 ± 3.74[*]	46.6 ± 4.83[*]	46.8 ± 11.21	44.0 ± 6.78
SAP (mmHg)	MMK-L	128.6 ± 4.98	152.2 ± 12.48	162.6 ± 15.65[*]	146.4 ± 12.60	145.0 ± 15.43	139.4 ± 17.14	140.0 ± 14.80	134.3 ± 15.01
	MMK-H	121.8 ± 35.32	153.2 ± 23.26[*]	164.0 ± 27.82	165.6 ± 27.94	156.4 ± 9.21	152.2 ± 11.37	145.2 ± 2.49	145.0 ± 3.67
MAP (mmHg)	MMK-L	91.4 ± 9.18	125.0 ± 8.40[*]	122.0 ± 14.63[*]	114.8 ± 6.76	115.4 ± 11.15[*]	105.0 ± 9.14	102.3 ± 10.26	101.3 ± 3.51
	MMK-H	82.4 ± 25.95	113.4 ± 21.96	129.6 ± 26.85[*]	119.6 ± 22.37	113.2 ± 12.68	106.4 ± 11.15	104.8 ± 5.72	105.2 ± 6.50
DAP (mmHg)	MMK-L	74.4 ± 11.70	111.4 ± 12.78[*]	101.0 ± 14.53	99.0 ± 8.86	101.0 ± 12.75	87.2 ± 8.44	82.7 ± 8.02	74.0 ± 2.31
	MMK-H	63.8 ± 21.52	95.0 ± 21.73	112.4 ± 24.83[*]	97.2 ± 19.06	92.6 ± 12.74	88.6 ± 11.59	85.4 ± 5.41	85.0 ± 8.63
RT (°C)	MMK-L	37.2 ± 0.80	37.2 ± 0.90	37.1 ± 0.94	37.0 ± 1.00	36.8 ± 1.04	36.7 ± 1.10	36.4 ± 0.85	36.3 ± 0.85
	MMK-H	36.6 ± 0.75	36.7 ± 0.73	36.6 ± 0.78	36.5 ± 0.75	36.5 ± 0.75	36.3 ± 0.82	36.1 ± 0.89	36.0 ± 0.80

Data are expressed as mean ± SD (n = 5)
[*]Significantly different from the base line ($p < 0.05$)
[a]Significantly different between groups ($p < 0.05$)

Table 5. Respiratory rates and blood gases in beagle dogs after administration of medetomidine/midazolam/ketamine (MMK)

	Group	0 min	5 min	10 min	20 min	30 min	40 min	50 min	60 min
RR (breath/min)	MMK-L	20.4 ± 5.13	13.8 ± 4.92	11.4 ± 7.50	12.6 ± 4.34	15.0 ± 4.47	14.2 ± 5.89	15.0 ± 7.81	23.0 ± 14.18
	MMK-H	16.6 ± 5.81	10.2 ± 5.22	8.2 ± 5.89	11.2 ± 4.38	13.2 ± 2.77	16.4 ± 2.61	14.2 ± 2.68	18.4 ± 4.28
pH	MMK-L	7.3 ± 0.05	N.E	7.2 ± 0.08	7.3 ± 0.05	N.E	7.3 ± 0.05	N.E	N.E
	MMK-H	7.3 ± 0.03	N.E	7.1 ± 0.07	7.2 ± 0.07	N.E	7.3 ± 0.04	N.E	N.E
$PaCO_2$ (mmHg)	MMK-L	47.0 ± 8.93	N.E	55.1 ± 8.25	50.2 ± 6.33	N.E	42.8 ± 6.06	N.E	N.E
	MMK-H	47.3 ± 3.64	N.E	58.5 ± 12.01	56.4 ± 16.55	N.E	50.3 ± 11.76	N.E	N.E
PaO_2 (mmHg)	MMK-L	491.4 ± 30.07	N.E	524.2 ± 43.55	523.2 ± 18.23	N.E	521.8 ± 37.11	N.E	N.E
	MMK-H	505.4 ± 72.63	N.E	518.4 ± 27.92	514.2 ± 72.12	N.E	549.2 ± 67.12	N.E	N.E
SaO_2 (%)	MMK-L	100.0 ± 0.00	N.E	100.0 ± 0.00	100.0 ± 0.00	N.E	100.0 ± 0.00	N.E	N.E
	MMK-H	100.0 ± 0.00	N.E	100.0 ± 0.00	100.0 ± 0.00	N.E	100.0 ± 0.00	N.E	N.E

Data are expressed as mean ± SD (n = 5), N.E: Not examined

Rectal temperature didn't change significantly at all times points in both groups.

Respiratory rate and arterial blood gases

Respiratory rate (RR) and blood gas analysis were shown in Table 5. RR was decreased after MMK administration, but there were no significant differences over times and between groups. In both groups, the arterial pH decreased during the first 10 minutes and then gradually increased. In both groups, the $PaCO_2$ increased during the first 10 minutes and then decreased. The PaO_2 increased within 10 minutes following MMK administration and remained consistently above the baseline value for 40 minutes in both groups. There were no significant differences in terms of RR and blood gases between two groups.

Discussion

This study compared two anesthetic combinations containing medetomidine, midazolam and ketamine given by dosage of medetomidine 0.015 mg/kg and medetomidine 0.02 mg/kg in dogs. MMK administration provided rapid induction time and adequate durations of immobilization time and no response to noxious stimuli in dogs.

Medetomidine leads sedation and analgesia in the dog, but it also induces the negative cardiovascular effects including bradycardia and associated with arrhythmias, hypertension or hypotension and reduced cardiac output (1,2,15). Increases in arterial blood pressure are typically dose related with the administration of medetomidine and the route of administration also plays a role on the extent of increased systemic vascular resistance. The initial hypertension is greater when the

α_2-agonist is intravenously administered, than when it is intramuscularly administered (15). Based on these findings, it is recommended that lower doses of medetomidine will be intramuscularly administered to avoid extremes of blood pressure. In this study, intramuscular doses of medetomidine were determined as 0.015 and 0.02 mg/kg for minimal cardiovascular effects. In our pilot study, MMK administration with the dose of 0.01 mg/kg medetomidine could not produce sufficient anesthesia in dogs.

α_2-agonists have proved very effective as sedative-analgesic adjuncts when co-administered with dissociative, benzodiazepins or opioids (16). Also, co-administering with other agents has helped to reduce the dose required to produce anesthesia thereby minimizing the side effects and enhancing sedation and analgesia (4,8). The cardiovascular actions of ketamine include increases in heart rate and cardiac output which are attributed to prevent negative cardiovascular effects of medetomidine. Also, midazolam was added to be able to reduce the dosage of medetomidine and ketamine. A combination of medetomidine with midazolam has been reported to enhance the sedative analgesic actions and to produce deep sedation in dogs (4,17). In the present study, a constant low dose of 0.3 mg/kg midazolam was combined with changing doses of medetomidine to decrease undesirable behavioral effects.

This study showed that MMK at the given doses produced sufficient anesthesia and analgesia for 60 minutes in dogs. The dogs in both MMK-L and MMK-H groups remained in lateral recumbency and showed no response to noxious stimuli for more than 40 minutes. These result revealed that both anesthetic combinations provide an adequate duration for minor procedure.

A decrease in HR was recorded in all of the dogs during the period of anesthesia in both groups. A significant decrease in HR was seen within 5 minutes of administration of MMK with higher dose of medetomidine (0.02 mg/kg). However, decrease in heart rate was observed at 20 minutes after administration of MMK with lower dose of medetomidine (0.015 mg/kg). Decreased heart rate is due to α_2-adrenergic agonist induced a decrease in sympathetic activity by inhibition of noradrenaline release from sympathetic nerves and noradrenergic neurons in the central nervous system (CNS) (14,18).

Alpha$_2$ agonists may allow for better maintenance of body temperature due to the peripheral vasoconstriction and central redistribution of blood (15). In the present study, the rectal temperatures showed gradually but not significantly decreased tendency in both groups after anesthesia. In previous study with α_2-adrenergic agonist, hypothermia might be caused by the ambient air temperature and vasoconstriction (9).

The action of the peripheral α_2-adrenoreceptors accounts for the dramatic increase in systemic vascular resistance, which will be recognized clinically as an increase in arterial blood pressure (15). In the present study, the blood pressure in both groups increased with time. The arterial blood pressure increased from baseline for 40 minutes in the both groups. There were no significant differences in blood pressures between groups.

Respiratory depression occur secondary to the CNS depression produced by α_2-adrenoreceptor stimulation and the degree and significance of respiratory depression produced with any α_2-agonist will be increased when the drug is given with other sedatives (15). In the present study, respiratory rates in all dogs decreased (but not significantly) following MMK administration and respiratory patterns become more regular. In a previous study, the development of significant tachypnea and hypoxemia following the administration of MMK combination was identified. They administered MMK to dogs with higher dosages (medetomidine 0.04 mg/kg) (6). However, in the present study, the PaO_2 in both groups increased and remained consistently above baseline for 40 minutes. This might be due to the pure oxygen supply through the endotracheal tube until the end of the study. In conclusion, intramuscular administration of medetomidine (0.015 mg/kg or 0.02 mg/kg), followed by intramuscular injection of midazolam (0.3 mg/kg) and ketamine (5 mg/kg) in dogs, leads immediate and sufficient anesthesia but produce significant changes in cardiopulmonary parameters compared with baseline values. But the cardiovascular effects are acceptable based upon normal values for heart rate, arterial blood pressure and body temperatures in dogs.

Therefore, we recommend that dogs with no cardiovascular or circulatory disorder can be anesthetized with medetomidine-midazolam-ketamine combination to minor surgical or diagnostic procedures and proper doses of medetomidine for minimal adverse effects in intramuscular MMK combination will be 0.015 mg/kg in dogs.

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Reference

1. Carter JE, Campbell NB, Posner LP, Swanson C. The hemodynamic effects of medetomidine continuous rate infusions in the dog. Vet Anesth Analg 2010; 37: 197-206.
2. Cullen LK. Medetomidine sedation in dogs and cats: a review of its pharmacology, antagonism and dose. Br Vet J 1996; 152: 519-535.
3. Ebner J, Wehr U, Busch R, Erhardt W, Henke J. A comparative clinical study of three different dosages of intramuscular midazolam-medetomidine-ketamine immobilization in cats. J Vet Med A Physiol Pathol Clin Med 2007; 54: 418-423.
4. Fabio L, Barbara S, Maria MF, Stefano Z, Teresa S, Paolo B. Clinical comparison of medetomidine-butorphanol, medetomidine-midazolam and midazolam-butorphanol for intramuscular premedication in the English bulldog. Ann Fac Med Vet di Parma 2007; 27: 131-142.
5. Henke J, Reinert J, Preissel AK, Radtke-Schuller S. Partially antagonisable anaesthesia of the small hedgehog tenrec

(Echinops telfairi) with medetomidine, midazolam and ketamine. J Experi Ani Sci 2007; 43: 255-264.
6. Hwang HK, Lee JY, Jeong SM, Kim MC. Antagonistic effects of atipamezole and yohimbine on medetomidine-midazolam-ketamine anesthesia in Beagle dogs. J Vet Clin 2011; 28: 211-218.
7. Jalanka H, Skutnabb K, Damsten Y. Preliminary results on the use of medetomidine-ketamine combinations in the dog. Acta Vet Scand 1989; 85: (Suppl) 125-127.
8. Ko JCH, Fox SM, Mandsager RE. Sedative and cardiorespiratory effects of medetomidine, medetomidine-butorphanol, and medetomidine-ketamine in dogs. J Am Vet Med Assoc 2000; 216: 1578-1583.
9. Lee JY, Jee HC, Jeong SM, Park CS, Kim, MC. Comparison of anaesthetic and cardiorespiratory effects of xylazine or medetomidine in combination with tiletamine/zolazepam in pigs. Vet Rec 2010; 167: 245-249.
10. Lemke KA. Perioperative use of selective alpha-2 agonists and antagonists in small animals. Can Vet J 2004; 45: 475-480.
11. McLaren GW, Thornton PD, Newman C, Buesching CD, Baker SE, Mathews F, Macdonald DW. The use and assessment of ketamine-medetomidine-butorphanol combinations for field anaesthesia in wild European badgers (Meles meles). Vet Anesth Analg 2005; 32: 367-372.
12. Orr HE, Roughan JV, Flecknell PA. Assessment of ketamine and medetomidine anaesthesia in the domestic rabbit. Vet Anesth Analg 2005; 32: 271-279.
13. Schernthaner A, Lendl CE, Hartmann K, Pragst I, Preissel A, Henke J. Medetomidine/midazolam/ketamine anaesthesia in ferrets: effects on cardiorespiratory parameters and evaluation of plasma drug concentrations. Vet Anesth Analg 2011; 38: 439-450.
14. Silva FC, Hatschbach E, Carvalho YK, Minto BW, Massone F, Junior PN. Hemodynamics and bispectral index (BIS) of dogs anesthetized with midazolam and ketamine associated with medetomidine or dexmedetomidine and submitted to ovariohysterectomy. Acta Cir Bras 2010; 25: 181-189.
15. Sinclair MD. A review of the physiological effects of α_2-agonists related to the clinical use of medetomidine in small animal practice. Can Vet J 2003; 44: 885-896.
16. Tranquilli WJ, Benson GJ. Advantages and guidelines for using alpha-2 agonists as anesthetic adjuvants. Vet Clin North Am Small Anim Pract 1992; 22: 289-293.
17. Ueoka N, Hikasa Y. Antagonistic effects of atipamezole, flumazenil and 4-aminopyridine against anaesthesia with medetomidine, midazolam and ketamine combination in cats. J Feline Med Surg 2008; 10: 47-54.
18. Ueyema Y, Waselau AC, Wiese AJ, Muir WW. Anesthetic and cardiopulmonary effects of intramuscular morphine, medetomidine, ketamine injection in dogs. Vet Anesth Analg 2008; 35: 480-487.
19. Yamashita K, Wijayathilaka TP, Kushiro T, Umar MA, Taguchi K, Muir WW. Anesthetic and cardiopulmonary effects of total intravenous anesthesia using a midazolam, ketamine and medetomidine drug combination in horses. J Vet Med Sci 2007; 69: 7-13.

비글견에서 medetomidine-midazolam-ketamine 합제의 마취효과와 심폐기능에 미치는 영향

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요 약 : 본 연구는 비글견에서 medetomidine-midazolam-ketamine 병용 마취 시 마취효과와 심혈관계 및 호흡기계에 미치는 영향을 평가하였다. Medetomidine 0.015 mg/kg (MMK-L군) 또는 medetomidine 0.02 mg/kg (MMK-H군)을 근육 주사한 후에 midazolam (0.3 mg/kg) 및 ketamine (5 mg/kg)을 근육 주사하였다. 마취유도 및 회복시간, 진정 및 진통점수, 심박수, 혈압, 직장 온도 및 호흡수 측정 및 동맥혈액가스분석을 실시하였다. 평균 마취 시간은 MMK-L군 (52.4 ± 11.08분)과 MMK-H군(78.2 ± 20.72분)이 유의성 있게 달랐다. 두 군 모두에서 MMK 투여로 인해 개에서 만족스런 진정 및 진통을 얻을 수 있었다. 두 군 모두에서 심박수는 유의적인 감소를 보였으며 MMK-H군은 투여 후 5분부터 MMK-L군은 투여 후 20분부터 유의적인 심박수의 저하가 확인되었다. MMK 투여 후 두 군 모두에서 혈압은 증가하였으나 두 군사이의 유의적인 차이는 확인되지 않았다. 실험 결과 비글견에서 medetomidine-midazolam-ketamine 병용마취는 양호한 마취효과를 나타냈으며, 개의 MMK 병용마취에서 부작용을 최소화 하면서 만족할 만한 마취효과를 얻을 수 있는 medetomidine의 용량은 0.015 mg/kg 인 것으로 생각된다.

주요어 : medetomidine, midazolam, ketamine, 마취, 개.