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<Original Article>

Evaluations of vital signs and echocardiographic left ventricular function after the constant rate infusion of lidocaine and/or ketamine in Beagle dogs

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Abstract : Cardiopulmonary depression of long-term constant rate infusion (CRI) administration of multiple analgesic drugs is important, especially in critically ill dogs. Therefore, this study was conducted to evaluate the effects of lidocaine, ketamine or combined lidocaine-ketamine combination CRI treatment on vital signs and left ventricular (LV) function in healthy dogs. Six adult Beagle dogs were administered either ketamine (initial loading dose of 0.5 mg/kg followed by 10 μg/kg/min CRI), lidocaine (initial loading dose of 2 mg/kg followed by 0.025 mg/kg/min CRI), or combined lidocaine-ketamine intravenously. Arterial blood pressure (BP), heart rate (HR), respiratory rate (RR), body temperature (BT) and echocardiographic LV dimensions were measured before administration of medications, immediately after administration of drugs, and then every 10 min for 2 h. There were no significant changes in HR, RR, BT and BP after the administration of either lidocaine CRI, ketamine CRI, or combined lidocaine and ketamine CRI. There were also no significant changes in LV dimensions and stroke volume. The results revealed that treatment with either lidocaine, ketamine or combined lidocaine-ketamine may not cause cardiopulmonary suppression in healthy dogs.

Keywords: analgesia, cardiopulmonary, combination, constant rate infusion, dog

Introduction

Pain control is a key success management in critically ill patients, because it improves an animal's overall well-being and affects positively on the speed and quality of recovery [7]. Several general drug classes for analgesia including opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), α_2-adrenergic agonists, local anesthetics, *N*-methyl-d-aspartate (NMDA) antagonists, benzodiazepines, and phenothiazines have been used in veterinary medicine [7]. Constant rate infusion (CRI) administration of analgesics has advantage of maintaining effective plasma concentrations in patients suffering continuous pain [9]. Several drugs including morphine, fentanyl, ketamine, and lidocaine have been used for CRI administration of analgesics [4, 8]. Furthermore the combination of analgesic drugs using CRI administration has been also used in dogs. However, the effect of CRI administration of multiple analgesic drugs on vital signs and left ventricular (LV) function has rarely been studied in dogs. Therefore this study evaluated the effect of either lidocaine, ketamine or lidocaine-ketamine combination CRI administration on vital signs echocardiographic LV function in healthy Beagle dogs.

Materials and Methods

Approval from the animal ethics committee of Kangwon National University was obtained for this experiment prior to the commencement of this study. Six adult Beagle dogs (three males and three females in mean body weight 8.3 ± 3.1 kg and mean age 4.1 ± 1.7 yr) were used for this study. All dogs were healthy based upon physical examination, an electrocardiogram (ECG), serum chemistry, hematologic analyses, and diagnostic imaging studies including thoracic radiography and echocardiography. To minimize the induction and maintenance effects of anesthetic agents, all dogs were not anesthetized. Before administration of drugs, a catheter (22 or 24 gauge, BD Angiocath; Becton, Dickinson and Company, USA) was placed in a cephalic vein in each dog. Dogs with awake state were administered with either lidocaine alone (LID; Lidocaine, initial loading dose of 2 mg/kg followed by 0.025 mg/kg/min CRI; Daehan, Korea), ketamine (KET; Ketara, initial loading dose of 0.5 mg/kg followed by 10 μg/kg/min CRI; Yuhan, Korea), or the combination of both drugs (LID + KET) with a syringe pump (NE-1000; New Era Pump Systems, USA) intravenously. Total doses of lidocaine and ketamine administered to each dog were 41.5 ± 15.7 mg

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and 14.1 ± 5.8 mg, respectively. Each experiment with single drug or combined drug was repeated after 2-day wash-out period based on metabolism of lidocaine and ketamine [6, 11]. Arterial blood pressure (BP), heart rate (HR), respiratory rate (RR), rectal temperature (BT) and echocardiographic LV dimensions were measured before administration of medications (T0), immediately after administration of drugs (T1), and then every 10 min for 2 h. Systolic arterial blood pressure was measured at right thoracic limb between carpal and elbow joints using Doppler flow detector (811B; Parks Medical Electronics, USA). Heart and respiratory rates were obtained manually. Rectal temperature was also measured using the multi-parameter monitor (VSM7; Votem, Korea). All echocardiographic measurements were performed by the same experienced operator. Echocardiographic LV indices were measured in all dogs using M-mode echocardiography (Teichholz method) at the right parasternal short axis of left ventricular papillary muscle level with an ultrasound unit (SonoAce 8000; Medison, Korea) equipped with 3.0 to 8.5 MHz phased-array transducers. Left ventricular internal diameter in systole (LVIDs), left ventricular internal diameter in diastole (LVIDd), % fractional shortening (%FS), % ejection fraction (%LVEF) and stroke volume (SV) were measured.

The statistical software used for data analysis was SPSS for Windows (ver. 15.0; IBM, USA). Normality was tested by the Kolmogorov–Smirnov test. One-way ANOVA repeated measures were performed with the same parameters between baseline and post-induction values, and between each test time point with Dunnett's test for post hoc analysis. Significance was set at $p < 0.05$.

Results

Tables 1 and 2 summarized the changes in vital signs and echocardiographic LV dimensions after lidocaine CRI, ketamine CRI and the combination of lidocaine and ketamine CRI. There were no significant changes in HR, RR and BP before and after the administration of lidocaine CRI, ket-

Table 1. Changes of body temperature (BT), respiration rate (RR), heart rate (HR) and systolic blood pressure (BP) before (T0) and after the constant rate infusion of either lidocaine (LID), ketamine (KET) or the combination of ketamine and lidocaine (KET+LID) in Beagles (n = 6)

Time (min)		T0	T1	T10	T20	T30	T40	T50
BT (°C)	KET	38.4 ± 8.4	38.4 ± 8.4	38.5 ± 8.5	38.2 ± 8.2	38.5 ± 8.5	38.3 ± 8.3	38.3 ± 8.3
	LID	38.2 ± 8.2	38.1 ± 8.1	38.2 ± 8.2	38.0 ± 8.0	38.3 ± 8.3	38.2 ± 8.2	38.3 ± 8.3
	KET+LID	38.6 ± 8.6	38.6 ± 8.6	38.4 ± 8.4	38.4 ± 8.4	38.4 ± 8.4	38.3 ± 8.3	38.3 ± 8.3
RR (/min)	KET	32.3 ± 2.3	33.3 ± 3.3	37.7 ± 7.7	33.7 ± 3.7	42.0 ± 2.0	38.7 ± 8.7	39.0 ± 9.0
	LID	29.0 ± 9.0	31.7 ± 1.7	34.7 ± 4.7	36.7 ± 6.7	37.3 ± 7.3	32.0 ± 2.0	40.3 ± 0.3
	KET+LID	34.0 ± 8.7	32.0 ± 4.3	39.0 ± 3.5	33.3 ± 4.3	31.0 ± 2.3	39.0 ± 4.0	34.0 ± 7.1
HR (/min)	KET	112.7 ± 12.7	106.7 ± 06.7	112.7 ± 12.7	98.0 ± 8.07	86.7 ± 6.7	89.3 ± 9.37	89.3 ± 9.37
	LID	94.3 ± 4.37	94.0 ± 4.07	85.7 ± 5.77	84.0 ± 4.07	79.3 ± 9.37	77.0 ± 7.07	76.7 ± 6.7
	KET+LID	120.0 ± 20	112.0 ± 12.0	105.3 ± 5.0	82.7 ± 2.7	94.7 ± 4.73	89.3 ± 9.33	90.7 ± 7.3
BP (mmHg)	KET	160.0 ± 60.0	148.0 ± 48.0	154.0 ± 54.0	142.0 ± 42.0	158.0 ± 58.0	154.7 ± 54.7	154.7 ± 54.7
	LID	142.7 ± 42.0	137.3 ± 37.0	146.7 ± 46.7	150.0 ± 50.0	145.3 ± 45.0	144.0 ± 44.0	143.3 ± 43.3
	KET+LID	143.3 ± 43.3	145.3 ± 45.0	142.7 ± 42.0	135.3 ± 35.2	135.3 ± 35.3	140.7 ± 40.7	137.3 ± 37.0
Time (min)		T60	T70	T80	T90	T100	T110	T120
BT (°C)	KET	38.4 ± 0.3	38.4 ± 0.2	38.3 ± 0.3	38.2 ± 0.4	38.3 ± 0.4	38.1 ± 0.2	38.1 ± 0.3
	LID	38.1 ± 0.2	38.2 ± 0.1	38.1 ± 0.3	38.0 ± 0.3	38.0 ± 0.2	37.9 ± 0.2	38.1 ± 0.3
	KET+LID	38.2 ± 0.3	38.3 ± 0.3	38.2 ± 0.5	38.2 ± 0.3	38.1 ± 0.3	38.2 ± 0.3	38.2 ± 0.4
RR (/min)	KET	38.0 ± 19.3	35.3 ± 14.7	37.3 ± 13.1	36.7 ± 17.0	33.3 ± 17.2	39.0 ± 18.7	37.7 ± 15.9
	LIDO	36.3 ± 8.5	32.3 ± 5.9	32.0 ± 11.4	33.3 ± 12.9	28.3 ± 10.5	29.0 ± 11.4	33.7 ± 4.7
	KET+LID	41.3 ± 9.7	34.3 ± 5.1	31.7 ± 4.5	30.0 ± 5.2	34.0 ± 1.7	29.7 ± 2.5	30.0 ± 5.2
HR (/min)	KET	88.7 ± 18.1	87.0 ± 13.1	81.3 ± 12.2	79.7 ± 13.6	78.3 ± 15.9	80.3 ± 4.0	77.3 ± 8.3
	LID	77.3 ± 4.6	77.0 ± 2.6	71.0 ± 12.3	72.7 ± 7.0	73.3 ± 2.3	75.0 ± 6.6	76.0 ± 8.0
	KET+LID	90.7 ± 18.5	89.3 ± 23.4	85.3 ± 16.7	89.3 ± 26.6	85.3 ± 12.9	92.0 ± 20.8	96.0 ± 21.2
BP (mmHg)	KET	148.7 ± 20.2	142.0 ± 13.1	142.0 ± 12.5	139.3 ± 7.6	136.7 ± 3.1	140.0 ± 2.0	138.0 ± 10.4
	LID	146.0 ± 19.3	140.7 ± 14.2	138.0 ± 7.2	127.3 ± 7.0	138.0 ± 21.6	130.7 ± 14.0	144.7 ± 31.4
	KET+LID	134.7 ± 9.9	136.7 ± 8.3	134.7 ± 8.1	138.7 ± 5.0	130.7 ± 19.2	130.7 ± 11.4	132.7 ± 15.3

Table 2. Changes in echocardiographic left ventricular dimensions and stroke volume before (T0) and after the constant rate infusion of either lidocaine (LID), ketamine (KET) or the combination of ketamine and lidocaine (KET+LID) in in Beagles (n = 6)

Time (min)		T0	T1	T10	T20	T30	T40	T50
LVIDd (mm)	KET	28.4 ± 4.0	29.8 ± 4.2	29.2 ± 4.9	29.5 ± 4.0	29.6 ± 4.1	29.5 ± 3.8	29.8 ± 4.1
	LID	27.7 ± 3.6	29.1 ± 3.8	29.9 ± 4.2	28.9 ± 4.7	29.1 ± 4.0	28.9 ± 4.2	28.7 ± 3.8
	KET+LID	27.9 ± 3.8	30.2 ± 4.1	31.2 ± 4.5	29.9 ± 4.2	29.4 ± 3.8	29.9 ± 3.1	29.6 ± 4.1
LVIDs (mm)	KET	18.2 ± 3.3	21.2 ± 3.2	20.4 ± 5.1	21.4 ± 3.8	21.6 ± 3.8	22.2 ± 3.9	21.2 ± 4.2
	LID	17.7 ± 3.6	22.3 ± 5.1	21.1 ± 4.8	20.7 ± 4.5	20.8 ± 4.3	19.9 ± 4.1	19.7 ± 3.8
	KET+LID	18.1 ± 2.2	24.3 ± 3.9	23.5 ± 4.4	22.2 ± 5.4	21.8 ± 4.1	21.6 ± 4.8	20.3 ± 3.4
%FS	KET	35.9 ± 5.3	28.9 ± 7.3	30.1 ± 8.2	27.5 ± 5.6	27.0 ± 6.6	24.7 ± 8.4	28.9 ± 5.6
	LID	36.1 ± 6.6	23.4 ± 8.6	29.4 ± 9.3	28.4 ± 6.2	28.5 ± 8.1	31.1 ± 7.6	31.4 ± 5.8
	KET+LID	35.1 ± 6.3	19.5 ± 7.6	24.7 ± 7.0	25.8 ± 5.1	25.9 ± 9.7	27.8 ± 10.1	31.4 ± 8.9
%LVEF	KET	68.9 ± 9.6	59.4 ± 9.1	61.2 ± 15.9	57.4 ± 7.6	56.7 ± 9.4	53.4 ± 6.8	59.4 ± 8.9
	LID	69.2 ± 8.4	51.3 ± 7.9	60.2 ± 10.7	58.7 ± 9.6	58.9 ± 10.9	62.6 ± 8.8	64.9 ± 8.3
	KET+LID	67.9 ± 9.2	47.2 ± 13.2	53.3 ± 8.2	54.9 ± 7.3	55.1 ± 12.8	57.8 ± 6.6	62.9 ± 6.3
SV (mL)	KET	22.1 ± 6.3	21.4 ± 6.7	20.1 ± 7.8	22.1 ± 9.3	20.9 ± 8.9	18.1 ± 5.2	23.2 ± 6.7
	LID	18.9 ± 4.4	17.9 ± 6.2	18.1 ± 3.9	19.1 ± 6.4	18.4 ± 5.8	19.9 ± 6.4	18.9 ± 7.1
	KET+LID	20.1 ± 5.4	16.4 ± 6.9	18.7 ± 4.7	19.5 ± 7.2	18.3 ± 4.4	20.8 ± 7.6	19.5 ± 4.4

Time (min)		T60	T70	T80	T90	T100	T110	T120
LVIDd (mm)	KET	29.8 ± 4.2	30.2 ± 4.5	29.4 ± 5.1	29.9 ± 3.8	29.4 ± 4.0	29.5 ± 3.2	29.8 ± 4.3
	LID	29.7 ± 3.4	29.8 ± 3.3	28.9 ± 3.9	29.3 ± 4.9	29.1 ± 3.2	30.3 ± 3.9	29.7 ± 3.8
	KET+LID	29.6 ± 3.1	30.5 ± 4.2	30.2 ± 4.5	29.8 ± 4.2	28.8 ± 3.7	29.7 ± 2.7	28.6 ± 3.6
LVIDs (mm)	KET	19.8 ± 3.3	21.3 ± 3.9	20.8 ± 5.0	18.4 ± 3.1	21.2 ± 3.4	22.4 ± 3.8	19.2 ± 3.1
	LID	19.7 ± 4.3	22.5 ± 4.1	21.8 ± 5.4	19.7 ± 4.4	20.7 ± 4.1	19.9 ± 4.3	18.7 ± 2.8
	KET+LID	20.3 ± 3.4	24.3 ± 4.8	23.5 ± 5.3	22.0 ± 5.3	21.5 ± 4.2	21.3 ± 5.1	19.5 ± 2.7
%FS	KET	33.6 ± 5.7	29.5 ± 7.2	29.3 ± 5.1	38.5 ± 5.4	27.9 ± 9.1	24.1 ± 7.8	35.6 ± 4.7
	LID	33.7 ± 10.3	24.5 ± 9.6	24.6 ± 7.4	32.8 ± 6.4	28.9 ± 6.5	34.3 ± 4.3	37.0 ± 7.4
	KET+LID	31.4 ± 8.9	20.3 ± 7.8	22.2 ± 8.5	26.2 ± 4.5	25.3 ± 7.2	28.3 ± 8.3	31.8 ± 8.1
%LVEF	KET	65.9 ± 5.3	60.3 ± 5.7	59.9 ± 6.7	69.1 ± 11.8	58.0 ± 13.5	52.3 ± 14.3	66.8 ± 14.3
	LID	66.3 ± 10.6	52.9 ± 10.4	53.1 ± 11.3	62.8 ± 9.8	59.4 ± 9.5	64.8 ± 8.8	69.4 ± 6.5
	KET+LID	62.9 ± 6.5	46.5 ± 13.5	49.4 ± 9.4	55.5 ± 9.7	54.3 ± 9.6	58.6 ± 7.4	63.5 ± 11.4
SV (mL)	KET	23.1 ± 8.3	20.1 ± 7.8	19.8 ± 7.2	22.1 ± 7.4	21.7 ± 8.9	21.1 ± 7.2	22.9 ± 6.3
	LID	18.7 ± 4.1	17.1 ± 6.2	18.8 ± 6.7	17.3 ± 6.6	18.5 ± 3.8	19.9 ± 4.2	18.7 ± 4.4
	KET+LID	18.4 ± 9.4	16.9 ± 7.0	19.2 ± 4.3	20.5 ± 4.2	19.3 ± 5.3	20.1 ± 6.2	21.4 ± 9.6

LVIDs, left ventricular internal diameter in systole; LVIDd, left ventricular internal diameter in diastole; %FS, % fractional shortening; %LVEF, %ejection fraction; SV, stroke volume.

amine CRI, and the combination of lidocaine and ketamine CRI, although the HR in all study groups was reduced with each time point. There were also no significant changes in LVIDs, LVIDd, %FS, %LVEF, and SV after the administration of those drugs. Further statistical analyses on vital signs and echocardiographic LV dimensions in each time point after the administration of lidocaine CRI, ketamine CRI, and the combination of lidocaine and ketamine CRI also failed to reveal statistical difference.

Discussion

Combinations of multiple types of analgesics have been used for providing analgesia and for reducing the amount of inhalant required in dogs [8]. One recent study found morphine (3.3 μg/kg/min), lidocaine (50 μg/kg/min), and ketamine (10 μg/kg/min) administered through intravenous CRI in dogs provided sufficient analgesia with synergism and multiple receptor activation without cardiopulmonary depression [8]. Our study also revealed no cardiovascular and ventilatory

depressions during CRI administration of either lidocaine, ketamine or lidocaine and ketamine combination. Since anesthesia can be detrimental to dogs not tolerable with the hypotensive effects of inhalant anesthesia, the CRI administration of multiple analgesic drugs during surgery may be a good option for reducing dose of anesthetic drug for maintenance. One recent study found fentanyl in conjunction with propofol provided adequate and safe cardiovascular system–sparing anesthesia for critically ill cats that are poor anesthetic candidates [7].

NMDA receptor antagonist such as ketamine blocks multiple binding sites and induces analgesic, amnestic, and psychomimetic effects [5]. Ketamine can block signals from afferent pain neurons such as C-fibers [8, 13]. Unlike opioids, ketamine rarely causes cardiovascular and ventilatory depression, although it can induce muscle tremors and profound sedation along with increased sympathetic tone [13]. Low doses of ketamine have been used perioperatively to provide analgesia in dogs [13]. Minimal cardiopulmonary depression and isoflurane-sparing effects of lower dose of ketamine CRI along with other analgesic drugs have been found in dogs undergoing ovariohysterectomy [4]. Although the HR after administration of drugs were reduced in trend, lidocaine alone, ketamine alone and the combination of ketamine and lidocaine did not significantly affect BT, HR, RR and stroke volume measured by echocardiography. Furthermore, although there were changes in some vital signs after drug administration, clinically significant bradycardia (< 60 beats per min), hypotension (< 80 mmHg of systolic pressure) and hypothermia (32°C) were not observed in each experiment with sing or combined administration of the drugs, suggesting minimal cardiopulmonary effects in dogs.

Lidocaine is a common local anesthetic drug having a rapid onset of action and intermediate duration of efficacy and is widely used in infiltration, block, and surface anesthesia. Lidocaine can be used with CRI administration for pain control with or without other analgesic drugs [10, 12]. Recent study found lidocaine CRI along with fentanyl provided sufficient analgesia for dogs undergoing ovariohysterectomy, the lidocaine alone could not enhance the analgesia, although it did not adversely affect recovery [3]. One study reported lidocaine may attenuate the level of reperfusion injury by blocking the generation of free oxygen radicals and suppressing proinflammatory effect of granulocytes [2]. Adverse effects of lidocaine on cardiopulmonary system include hypotension, bradycardia, arrhythmias and respiratory depression. Some of cardiovascular adverse effects may be due to hypoxemia secondary to respiratory depression [2]. It has been also found that CRI administration of lidocaine could induce cardiopulmonary depression in critically ill cats [9]. However, in the present study, the CRI administration of either lidocaine alone or combination with ketamine did not depress cardiopulmonary function.

Although we revealed minimal cardiopulmonary depression in CRI administration of lidocaine, ketamine and lidocaine-ketamine combination in this study, there are several limitations when attempting to generalize the results of this study to clinical practice. The study population was limited to a small number of healthy colony dogs and was not capable of obtaining sufficient statistical power to prove minimal cardiovascular detrimental effects of each drug. The SV and %LVEF were measured by M-mode echocardiography, and this methodology has been associated with potential error in measurement of cardiac output [1]. Because the cardiopulmonary instability is more common in critically ill dogs, the effect of CRI administration of lidocaine, ketamine and lidocaine-ketamine combination on cardiopulmonary system of these dogs may be different from those of our study population. Despite these limitations, this study found the CRI administrations of lidocaine, ketamine and lidocaine-ketamine combination have rarely caused cardiopulmonary suppression in dogs.

References

1. **Atkins CE, Curtis MB, McGuirk SM, Kittleson MD, Sato T, Snyder PS.** The use of M-mode echocardiography in determining cardiac output in dogs with normal, low, and high output states: comparison to thermodilution method. Vet Radiol Ultrasound 1992, **33**, 297-304.
2. **Cassutto BH, Gfeller RW.** Use of intravenous lidocaine to prevent reperfusion injury and subsequent multiple organ dysfunction syndrome. J Vet Emerg Crit Care (San Antonio) 2003, **13**, 137-148.
3. **Columbano N, Secci F, Careddu GM, Sotgiu G, Rossi G, Driessen B.** Effects of lidocaine constant rate infusion on sevoflurane requirement, autonomic responses, and postoperative analgesia in dogs undergoing ovariectomy under opioid-based balanced anesthesia. Vet J 2012, **193**, 448-455.
4. **Gutierrez-Blanco E, Victoria-Mora JM, Ibancovichi-Camarillo JA, Sauri-Arceo CH, Bolio-González ME, Acevedo-Arcique CM, Marin-Cano G, Steagall PVM.** Evaluation of the isoflurane-sparing effects of fentanyl, lidocaine, ketamine, dexmedetomidine, or the combination lidocaine-ketamine-dexmedetomidine during ovariohysterectomy in dogs. Vet Anaesth Analg 2013, **40**, 599-609.
5. **Lamont LA, Tranquilli WJ, Mathews KA.** Adjunctive analgesic therapy. Vet Clin North Am Small Anim Pract 2000, **30**, 805-813.
6. **Lin HC.** Dissociative anesthetics. In: Tranquilli WJ, Thurmon JC, Grimm KA (eds.). Lumb and Jones' Veterinary Anesthesia and Analgesia. 4 ed. pp. 301-354, Blackwell, Ames, 2007.
7. **Mendes GM, Selmi AL.** Use of a combination of propofol and fentanyl, alfentanil, or sufentanil for total intravenous anesthesia in cats. J Am Vet Med Assoc 2003, **223**, 1608-1613.
8. **Muir WW 3rd, Wiese AJ, March PA.** Effects of morphine, lidocaine, ketamine, and morphine-lidocaine-ketamine drug combination on minimum alveolar concentration in dogs anesthetized with isoflurane. Am J Vet Res 2003, **64**, 1155-1160.
9. **Pypendop BH, Ilkiw JE.** Assessment of the hemodynamic effects of lidocaine administered IV in isoflurane-anesthetized cats. Am J Vet Res 2005, **66**, 661-668.
10. **Quandt JE, Lee JA.** Analgesia and constant rate infusions.

In: Silverstein DC, Hopper K (eds.). Small Animal Critical Care Medicine. 1 ed. pp. 710-716, Saunders, St. Louis, 2009.
11. **Skarda RT, Tranquilli WJ.** Local anesthetics. In: Tranquilli WJ, Thurmon JC, Grimm KA (eds.). Lumb and Jones' Veterinary Anesthesia and Analgesia. 4 ed. pp. 395-418, Blackwell, Ames, 2007.
12. **Smith LJ, Bentley E, Shih A, Miller PE.** Systemic lidocaine infusion as an analgesic for intraocular surgery in dogs: a pilot study. Vet Anaesth Analg 2004, **31**, 53-63.
13. **Wagnor AE, Walton JA, Hellyer PW, Gaynor JS, Mama KR.** Use of low doses of ketamine administered by constant rate infusion as an adjunct for postoperative analgesia in dogs. J Am Vet Med Assoc 2002, **221**, 72-75.