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Comparison between Propofol/Remifentanil and Ketamine/Remifentanil for TIVA in Beagle Dogs

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Abstract : The cardiopulmonary responses during total intravenous anesthesia (TIVA) between remifentanil/propofol infusion and remifentanil/ketamine infusion in dogs were compared. Fourteen healthy adult beagle dogs were premedicated with acepromazine (0.1 mg/kg, SC) and medetomidine (20 μg/kg, IV), and anesthetized for 3 hr with remifentanil (0.5 μg/kg/min)/propofol (loading dose: 1 mg/kg, CRI: 0.3 mg/kg/min) CRI (group 'P') or remifentanil/ketamine (loading dose : 5 mg/kg, CRI: 0.1 mg/kg/min) CRI (group 'K'), respectively. Hemodynamics, blood gas analysis and behavioral changes during recovery were measured. The level of anesthesia was determined by toe-web clamping test. The level of surgical anesthesia was maintained throughout the experiment in both groups. Systolic arterial pressure, mean arterial pressure, PaO_2 and SpO_2 in group 'K' were significantly higher than in group 'P', and were maintained near the normal ranges. In addition, $PaCO_2$ in group 'K' was significantly lower than in group 'P'. However, diastolic arterial pressure, heart rate and respiratory rate were not significantly differed. Mean extubation time from the end of infusion was significantly reduced in group 'K', but mean sitting time was significantly reduced in group 'P'. Mean head-up time and mean walking time were not significantly differed. In group 'K', brief muscle rigidity, head waving and licking during recovery were observed. In conclusion, infusion rate of ketamine (0.1 mg/kg/min) with remifentanil (0.5 μg/kg/min) is an appropriate for obtaining the surgical plane of anesthesia. These results showed that group 'K' had better cardiopulmonary function than group 'P'. That is, remifentanil/ketamine CRI is better TIVA protocol than remifentanil/propofol CRI for 3 hr surgery.

Key words **:** remifentanil, propofol, ketamine, TIVA, dog.

Introduction

Total intravenous anaesthesia (TIVA) is a relatively new method for maintaining anaesthesia using intravenous anaesthetics injection, and is widely used for an alternative to inhalation anaesthesia in humans and animals (27,30). TIVA has been able to provide better cardiorespiratory performance and alleviated the hormonal stress response observed during halothane anaesthesia (22,25).

Propofol infusion becomes known to general method of TIVA, and has been widely evaluated in dogs (29,30,32). Generally, propofol (2,6-diisopropylphenol) is used for the induction and maintenance of anaesthesia, and is characterized by rapid onset, short duration of action and fast recovery from anaesthesia (16,23,35). However, well-known adverse effects are decrease in arterial blood pressure, apnoea and hypoventilation (39). Hypoventilation caused by direct inhibition of central inspiratory drive leads to hypercarpnoea (17). Dose-dependent reduction in arterial blood pressure following propofol administration may be caused by suppression of myocardial contractility and a decrease in systemic vascular resistance (34,46). To avoid side effects during induction, such as hypotension and transient apnoea, a reduced dose of propofol administration by premedication and reduction of propofol infusion rate have been investigated (12,16,31), and slowing propofol administration rate both is usually acceptable to prevent an overdose and to minimize cardiopulmonary depression (16,19,42).

Because propofol has few analgesic effects, even if it has some analgesic properties (48), TIVA with propofol is needs of co-administration of analgesics for making sure of producing the level of surgical anaesthesia (29). The combination infusion of remifentanil and propofol is taken increasingly interested in providing general anaesthesia in humans (31,33) and dogs (15,29,30).

Remifentanil is a synthetic 4-anilidopiperidine and ultra-short acting opioid analgesics and a potent μ-opioid receptor agonist (6). Remifentanil has a methyl ester side chain which renders it to undergo a rapid hydrolysis by blood and tissue non-specific esterase (5,7). In dogs, remifentanil is rapidly eliminated with a terminal elimination half-life of 5.59 min and 7.71 min (15,18). Unlike with other opioids, because of its extrahepatic biotransformation, hepatic dysfunction minimally affects pharmacokinetic properties of remifentanil (1). In addition, remifentanil gives rapid onset of action, that is, quickly penetrates the blood-brain barrier and rapidly arrives to the equilibration across the plasma-effect compartment (1,9). Remifentanil infusion has been known to be able to reduce the minimum alveo-

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lar concentration of isoflurane in dogs, cats and rats (4,8,26).

Ketamine is a non-competitive *N*-methyl-D-aspartate (NMDA) receptor antagonist with analgesic and anaesthetic properties and is commonly used for induction and maintenance of anaesthesia (27,47). Ketamine also reduces the requirements of inhalants during anaesthesia (28,44), but not in target-controlled infusion of propofol in dogs (23). Previous reports showed that constant-rate-infusion (CRI) at sub-anaesthetic doses of ketamine is an effective means for perioperative analgesia (2,3,36), but one reports demonstrated that a low-dose CRI of ketamine in conscious dogs was not satisfied as a sole analgesic (2). Ketamine administration usually results in increases of heart rate and arterial blood pressure causing by an activated sympathetic tone (45). Because muscle rigidity and convulsion during recovery are common side effects of ketamine in dogs, this drug should be combined with other anaesthetics (11,13). However, although many studies evaluated the analgesic effects of ketamine infusion, method for maintaining the level of surgical anaesthesia using ketamine infusion is rare.

In the present study, we were aimed to compare the cardiopulmonary function and the effect of each method on anaesthetic recovery in dogs anaesthetized with remifentanil/propofol and remifentanil/ketamine CRI.

Materials and methods

Animals

Fourteen adult male beagle dogs were used in this experiment. All dogs were clinically healthy based on physical examination, complete blood count and serum biochemistry performed prior to the experiment. All dogs were vaccinated and heart worm infection negative. Dogs were housed individually, and fed a commercial diet and were given water *ad libitum.* Food, but not water, was withheld for 12 hrs before experiment. The dogs weighed 7.9 ± 1.0 kg and were 20.1 ± 2.3 months of age. The dogs were divided into 2 groups, and each group contained 7 dogs. The dogs in Group 'K' were administered loading dose of ketamine (5 mg/kg, IV) followed by ketamine (0.1 mg/kg/min) and remifentanil (0.5 μg/kg/min) infusion. The dogs in Group 'P' were administered loading dose of propofol (1 mg/kg, IV) followed by propofol (0.3 mg/kg/min, Provive 1%, Claris Lifesciences Ltd., India) and remifentanil (0.5 μg/kg/min).

Experimental procedures

The experiments were approved by the Kyungpook National University Institutional Animal Care and Use Committee (KNU-2010-7). Twenty-four hr, at least, before experiment, under isoflurane/oxygen anaesthesia and lidocaine regional anaesthesia, a catheter was inserted into the right external carotid artery in the carotid sheath about 5 cm forwarded to the aorta. The catheter was placed in a tunnel through the subcutis and exited on the dorsal surface of the neck, and it filled with heparinized saline (50 IU/ml). The arterial catheter was used for measuring arterial blood pressure, heart rate and collecting blood sample. To prevent blood coagulation, the catheter was flushed with heparinized saline for three times a day.

On the day of experiment, acclimation time (over 1 hr) was given to dogs in experimental room, and then an arterial catheter was connected to a polygraph (Model 7P1, Grass Instrument Co., USA). Pre-administration state (baseline) values were measured in setting position after acclimation, and, after that, each animal were placed a 24 gauge cephalic vein catheter for drug administration, and a normal saline was infused at a rate of 5 ml/kg/hr. All dogs were premedicated with acepromazine (0.1 mg/kg, subcutaneously) and medetomidine (20 μg/kg, intravenously [IV]); 20 min after acepromazine injection, medetomidine was administered. Another 10 min after medetomidine injection later, loading dose of ketamine followed by ketamine infusion was initiated. Endotracheal intubation was simultaneously done with ketamine infusion. The dog's body temperature was maintained > 37°C throughout the experiment with an electric heating bed and an electronic heating instrument. Anaesthesia was continued for 3 hr. The level of anaesthesia and test items was evaluated at 10, 20, 40, 60, 90, 120, 150 and 180 min after the initiation of CRI. After the cessation of CRI, behavioral changes during recovery were monitored.

Evaluations

Pedal withdrawal reflex test was performed to evaluate the level of surgical anaesthesia. Each tow-web regions in the hindlimbs were alternatively clamped with crile forceps to the first-rachet-lock for 30 seconds. If the dogs showed purposeful movements, such as head, body or non-affected limb movements, the level of anaesthesia was not the level of surgical anaesthesia. The pedal withdrawal reflex test would be stopped immediately if the dog showed a positive response. Pedal withdrawal reflex test was performed after the completion of other test items.

Systolic, diastolic and mean arterial blood pressures (SAP, DAP and MAP, respectively) were measured using polygraph (Model 7P3, Grass instrument Co., USA). Heart rate was calculated from the pulse wave of arterial blood pressure. Respiratory rate was measured using movement of chest wall for 60 sec. Arterial blood sample was collected through the external carotid arterial catheter and pH, PaO_2, $PaCO_2$ and SpO_2 were measured with a portable blood gas analyzer (I- STAT® Analyzer MN300, Abbott Point of Care Inc., USA) and test cartridges (I- STAT® G3+ Cartridge, Abbott Point of Care Inc., USA). Arterial blood was collected by 0.5 ml and catheter was flushed with 0.5 ml of heparinized saline following each sampling. The analyses were done within 30 seconds, at least, after blood sampling.

Time latency to extubation (MET), head-up movement (MHT), sitting (MST) and walking (MWT) after the cessation of infusion were measured to evaluate recovery time from the anesthesia.

Statistical analysis

All data were expressed as mean ± SD. Variables of arterial blood pressures, heart rate, respiratory rate and blood gas analysis were analyzed by two factor repeated measures ANOVA with time and treatment, and a Student's *t*-test test was used to

analyze variables with time between groups (SPSS 14.0K; Datasolution, Seoul, Korea). Statistical differences of behavioral changes between groups were analyzed using a Student's *t*-test. If a p value was less than 0.05, it was considered as statistically significant.

Results

Zero mortality was obtained from this experiment. All dogs included in this experiment were not shown positive PWR, and were determined to get a surgical level of anesthesia.

Arterial Blood Pressure

SAP

SAP after CRI was 116 ± 14.4 mmHg in Group 'K', and 98 ± 18 mmHg in Group 'P'.

SAP of Group 'K' decreased until 40 min after CRI and then increased before end of infusion. That of Group 'P' decreased until 90 min, increased in 120, 150 min and decreased slightly in 180 min.

Repeated measures ANOVA revealed that treatment (F = 6.48, p = 0.026) was significant. Student's *t*-test indicated that SAPs in group 'K' from 60 to 180 min were significantly higher than in group 'P'.

DAP

DAP was 73 ± 13 mmHg in Group 'K', and 69 ± 14 mmHg in Group 'P' after CRI.

DAP in Group 'K' increased at 10 min, but value decreased in Group 'P' at same time. DAP in Group 'K' significantly decreased after 10 min, and was lowest at 40 min and then increased until the end of CRI. DAP in Group 'P' decreased before 60 min.

DAP of 1 dog in Group 'P' was lower than 50 mmHg from 60 to 180 min after CRI. Other values were within the normal range.

Repeated measures ANOVA revealed that treatment (F = 0.63, p = 0.444) was not significant.

MAP

MAP after CRI was 88 ± 12 mmHg in Group 'K', and 77 ± 14 mmHg in Group 'P', respectively.

MAP in Group 'K' increased at 10 min, even if Group 'P' decreased. In Group 'K', decease of values was observed until 40 min. In Group 'P', the lowest value was detected at 90 min.

Repeated measures ANOVA revealed that treatment (F = 4.87, p = 0.048) was significant. Student's *t*-test indicated that MAPs in group 'K' from 60 to 180 min were significantly higher than in group 'P'.

Heart rate

Heart rate was 80 ± 16 beats/min in Group 'K', and 92 ± 16 beats/min in Group 'P' after CRI.

Both of Group 'K' and Group 'P' decreased at 10 min, but value of Group 'P' were lower than that of Group 'K'. After 20 min, value of Group 'P' was higher than that Group 'K' and this pattern was maintained to cessation of infusion.

Repeated measures ANOVA revealed that treatment (F = 1.67, p = 0.22) was not significant.

Respiratory rate

Respiratory rate after CRI was 11 ± 3 breaths/min in Group 'K' and 9 ± 3 breaths/min in Group 'P'

Values in all groups deceased before 40 min. Those of Group 'K' increased until the end of anesthesia. In Group 'P', values increased during 50 mins after 40 min but decreased subsequently.

Repeated measures ANOVA revealed that treatment (F = 1.77, p = 0.208) was not significant.

pH

pH of arterial blood after CRI were 7.233 ± 0.044 in Group 'K', and 7.201 ± 0.049 in Group 'P', respectively.

Values of pH declined before 40 min in Group 'K', but afterwards increased slightly. In Group 'P', value decreased at the time of CRI cessation.

Repeated measures ANOVA revealed that treatment (F = 3.24, p = 0.097) was not significant.

PaO_2

PaO_2 was 67 ± 16 mmHg in Group 'K', and 48 ± 7.8 mmHg in Group 'P' after CRI.

Concentrations of PaO_2 in Group 'K' and Group 'P' were lowest at 20 min (Group 'K'; 53 ± 10, Group 'P'; 38 ± 3).

Repeated measures ANOVA revealed that treatment (F = 8.27, p = 0.014) was significant. Student's *t*-test indicated that values in group 'K' at 20 min and from 60 to 180 min were significantly higher than in group 'P'.

$PaCO_2$

$PaCO_2$ after CRI was 57.5 ± 8.82 mmHg in Group 'K', and 63.8 ± 8.99 in Group 'P'

$PaCO_2$ increased throughout experiment in Group 'P'. In Group 'K', increased to 60 min, but decreased until the time of CRI cessation.

Repeated measures ANOVA revealed that treatment (F = 4.94, p = 0.046) was significant. Student's *t*-test indicated that values in Group 'K' from 90 to 180 min were significantly lower than those in Group 'P'.

SpO_2

SpO_2 after CRI were 84 ± 11 mmHg in Group 'K', and 72 ± 10 mmHg in Group 'P', respectively.

Concentration of SpO_2 was lowest at 20 min in both Groups (77 ± 14 in Group 'K' and 60 ± 6.1 in Group 'P')

Repeated measures ANOVA revealed that treatment (F = 7.86, p = 0.016) was significant. Student's *t*-test indicated that values in Group 'K' at 20 min and from 90 to 180 min were significantly higher than those in Group 'P'.

Table 1. Systolic arterial blood pressures, diastolic arterial blood pressures, mean arterial blood pressures, heart rates, respiratory rates, arterial blood pH, PaO_2, $PaCO_2$, SpO_2 in dogs anaesthetized with constant rate infusion of ketamine (0.1 mg/kg/min)/remifentanil (0.5 μg/kg/min) (group 'K') or propofol (0.3 mg/kg/min)/remifentanil (group 'P')

	Group	Baseline	10 min	20 min	40 min	60 min	90 min	120 min	150 min	180 min
SAP (Hg)	K	151 ± 8.86	130 ± 12.3$^{\#}$	112 ± 11.1$^{\#\#}$	108 ± 14.1$^{\#\#}$	110 ± 12.6$^{*,\#\#}$	114 ± 15$^{*,\#\#}$	116 ± 15$^{**,\#\#}$	121 ± 13.7$^{**,\#\#}$	122 ± 13.8$^{**,\#\#}$
	P	145 ± 13.8	119 ± 20$^{\#}$	105 ± 21$^{\#\#}$	96 ± 18$^{\#\#}$	91 ± 16$^{\#\#}$	90 ± 16$^{\#\#}$	93 ± 13$^{\#\#}$	96 ± 14$^{\#\#}$	95 ± 14$^{\#\#}$
DAP (Hg)	K	88 ± 6.4	99 ± 7.9$^{\#}$	77 ± 9.9$^{\#}$	65 ± 9.1$^{\#\#}$	68 ± 7.0$^{\#\#}$	67 ± 7.0$^{\#\#}$	69 ± 6.7$^{\#\#}$	70 ± 7.1$^{\#\#}$	71 ± 11$^{\#}$
	P	91 ± 6.1	90 ± 13	79 ± 14	67 ± 11$^{\#\#}$	61 ± 11$^{\#\#}$	61 ± 11$^{\#\#}$	64 ± 11$^{\#\#}$	66 ± 9.0$^{\#\#}$	66 ± 12$^{\#\#}$
MAP (Hg)	K	109 ± 6.82	110 ± 9.1	89 ± 9.7$^{\#\#}$	79 ± 9.6$^{\#\#}$	82 ± 7.2$^{*,\#\#}$	83 ± 7.5$^{*,\#\#}$	85 ± 7.8$^{*,\#\#}$	87 ± 8.0$^{*,\#\#}$	88 ± 11$^{*,\#\#}$
	P	107 ± 8.8	97 ± 13	86 ± 15$^{\#}$	76 ± 12$^{\#\#}$	71 ± 12$^{\#\#}$	69 ± 11$^{\#\#}$	72 ± 11$^{\#\#}$	75 ± 9.5$^{\#\#}$	74 ± 11$^{\#\#}$
Heart Rates (beats/min)	K	93 ± 23	84 ± 18	89 ± 19	81 ± 16	77 ± 14	80 ± 18	78 ± 13	76 ± 16	76 ± 12
	P	89 ± 26	70 ± 17	98 ± 15	94 ± 12	94 ± 10	93 ± 11	91 ± 12	96 ± 14	99 ± 18
Respiratory rates (breaths/min)	K	19 ± 4.9	11 ± 4$^{\#}$	9 ± 3$^{\#\#}$	8 ± 3$^{\#\#}$	10 ± 3$^{\#\#}$	11 ± 3$^{\#}$	12 ± 3$^{\#}$	12 ± 4$^{\#}$	13 ± 3$^{\#}$
	P	16 ± 3.1	10 ± 3$^{\#}$	9 ± 3$^{\#\#}$	8 ± 3$^{\#\#}$	9 ± 3$^{\#}$	9 ± 3$^{\#}$	9 ± 4$^{\#}$	8 ± 3$^{\#\#}$	8 ± 3$^{\#\#}$
Arterial blood pH	K	7.398 ± 0.029	7.280 ± 0.040$^{\#\#}$	7.226 ± 0.037$^{\#\#}$	7.202 ± 0.023$^{\#\#}$	7.219 ± 0.047$^{\#\#}$	7.230 ± 0.040$^{\#\#}$	7.227 ± 0.043$^{\#\#}$	7.233 ± 0.042$^{\#\#}$	7.249 ± 0.050$^{\#\#}$
	P	7.419 ± 0.038	7.287 ± 0.033$^{\#\#}$	7.234 ± 0.022$^{\#\#}$	7.201 ± 0.020$^{\#\#}$	7.193 ± 0.026$^{\#\#}$	7.176 ± 0.035$^{\#\#}$	7.177 ± 0.031$^{\#\#}$	7.174 ± 0.039$^{\#\#}$	7.163 ± 0.036$^{\#\#}$
PaO_2 (Hg)	K	89 ± 6.2	62 ± 23$^{\#}$	53 ± 10$^{**,\#\#}$	56 ± 11$^{\#\#}$	66 ± 15$^{*,\#}$	72 ± 16$^{**,\#}$	70 ± 15$^{*,\#}$	69 ± 14$^{*,\#}$	73 ± 13$^{*,\#}$
	P	90 ± 6.1	44 ± 5.9$^{\#\#}$	38 ± 3.0$^{\#\#}$	48 ± 6.7$^{\#\#}$	51 ± 7.4$^{\#\#}$	49 ± 8.2$^{\#\#}$	54 ± 6.8$^{\#\#}$	51 ± 7.7$^{\#\#}$	50 ± 6.2$^{\#\#}$
$PaCO_2$ (Hg)	K	34.9 ± 3.46	49.3 ± 7.9$^{\#}$6	58.3 ± 5.00$^{\#\#}$	60.4 ± 11.1$^{\#\#}$	61.5 ± 8.87$^{\#\#}$	59.4 ± 8.26$^{*,\#\#}$	58.8 ± 8.71$^{*,\#\#}$	58.5 ± 8.45$^{*,\#\#}$	52.9 ± 8.46$^{**,\#\#}$
	P	33.2 ± 2.25	48.1 ± 4.92$^{\#\#}$	57.0 ± 3.95$^{\#\#}$	62.6 ± 4.79$^{\#\#}$	64.1 ± 5.07$^{\#\#}$	68.2 ± 6.65$^{\#\#}$	67.7 ± 5.54$^{\#\#}$	69.8 ± 5.92$^{\#\#}$	72.9 ± 4.74$^{\#\#}$
SpO_2 (%)	K	97 ± 0.95	81 ± 14$^{\#}$	77 ± 14$^{*,\#}$	79 ± 11$^{\#\#}$	84 ± 13$^{\#}$	88 ± 9.3$^{*,\#}$	88 ± 7.9$^{*,\#}$	87 ± 8.8$^{**,\#}$	90 ± 8.3**
	P	97 ± 0.58	73 ± 7.9$^{\#\#}$	60 ± 6.1$^{\#\#}$	71 ± 8.1$^{\#\#}$	74 ± 9.1$^{\#\#}$	76 ± 15$^{\#}$	76 ± 6.3$^{\#\#}$	73 ± 8.2$^{\#\#}$	71 ± 6.8$^{\#\#}$

Data are expressed as mean ± SD, * and ** indicates a significant difference from group P ($p < 0.05$ and $p < 0.01$, respectively), $^{\#}$ and $^{\#\#}$ indicates a significant difference from baseline ($p < 0.05$ and $p < 0.01$, respectively).

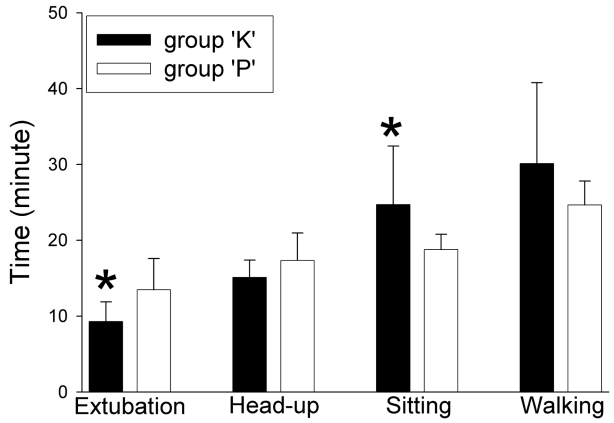

Fig 1. Behavioral changes during recovery from anaesthesia in dogs anaesthetized with constant rate infusion of ketamine (0.1 mg/kg/min)/remifentanil (0.5 μg/kg/min) (group 'K') or propofol (0.3 mg/kg/min)/remifentanil (group 'P'). Time latencies to extubation, head-up movement, sitting and walking from the cessation of infusion were measured. Data were analyzed by a Student's *t*-test. * indicates a significant difference from group 'P'($p<0.05$).

Behavioral changes (Fig 1.)

MET in Group 'K' was significantly shorter than that in Group 'P' ($p = 0.042$), and MST in Group 'K' was significantly longer than that in Group 'P' ($p = 0.042$). However, MHT and MWT did not significantly different between groups.

Discussion

The present results demonstrated that remifentanil/ketamine infusion not only can produce the surgical level of anaesthesia, but also provide more stable maintenance of cardiopulmonary function than remifentanil/propofol infusion. Especially, there were remarkable differences on pulmonary function between two groups. Even though hemodynamics in Group 'K' was significantly higher than that in Group 'P', SAP and MAP in Group 'P' were also not beyond the acceptable ranges during anaesthesia.

Unlike other anaesthetics, ketamine administration increases heart rate and (mean) arterial blood pressure and cardiac output while peripheral vascular resistance remains unchanged (20,45). Based on the present results, ketamine infusion may affect the changes of SAP. That is, ketamine/remifentanil CRI in this experiment significantly increased arterial blood pressures both in MAP and SAP, and did not induce a hypertension. Actually, MAP, which is used for determining hypotension during anaesthesia, did not demonstrate hypotension in any groups. However, because no groups in the present study indicated the hypertension, we considered as CRI protocol which has higher values of arterial blood pressures would provide better anaesthetic condition.

Ketamine anesthesia significantly increased survival rate of hemorrhaged rats when compared to halothane anesthesia (21), and has been recommended for critically ill patients in which there is a risk of cardiac depression and hypotension (20). However, other studies demonstrated cautious use of ketamine in patients with valvular heart disease or critically ill patients (20, 38,40,43). Actually, increase in myocardial oxygen consumption by tachycardia resulted from ketamine is a hazard in geriatric patients. In the present study, marked tachycardia was not observed in Group 'K'. Additionally, heart rate in Group 'K' was not significantly different from Group 'P', and even more the mean values were less than in Group 'P'. That is, ketamine/remifentanil CRI may not be cause of workload burden of heart by tachycardia, and may be applicable to geriatric patients.

Significant differences between two groups were mostly appeared after a lapse of anaesthesia of, at least, 60 min. That is, cardiopulmonary function with remifentanil/ketamine infusion will be more available than remifentanil/propofol CRI for long period of surgery.

Effect of ketamine on the respiratory system has been known to differ from other anaesthetics; well maintains arterial blood oxygenation by maintenance or increase the skeletal muscle (including respiratory muscles) tone (10,20,24,37). In dogs, ketamine has been induced initial decreases in respiratory rate and min volume, followed by return to baseline values within 15 min (13). The present study described similar pattern with above stated results. Significantly higher value of PaO_2 and lower value of $PaCO_2$ in group 'K' represented a less depressant effect of ketamine on ventilatory response, especially on tidal volume. Because we were aimed to evaluate the characteristics of each combination protocol on pulmonary reaction, manipulation for control of blood gas was not intervened. Additionally, in further study comparison of each CRI protocol with cardiovascular depression under mechanical ventilation (14,41) will be needed.

The depth of anaesthesia is able to affect the cardiopulmonary function. However, the depth of anaesthesia in Group 'P' and Group 'K' would be similar, based on preliminary study. Preliminary data looking for titration of the infusion rate showed the dogs in both groups were begun to a negative PWR response from these infusion rates of the present study.

Behavioral changes during recovery were not remarkable in both experiments. Remifentanil and propofol are known to their rapid onset and minimal effect on recovery time. Additionally, even high doses or prolonged infusion of remifentanil did not extend a recovery time (1,29,33). The dogs in Group 'K' showed a significantly shorter MET than in Group 'P', but MST was *vice versa*. These might be caused by muscle rigidity or tremor by ketamine. Side effects of ketamine infusion, such as from salivation to emergence phenomena has been reported (2). Eventful recovery from ketamine anaesthesia, such as muscle rigidity and head weaving are obviously unpleasant phenomenon to patients, practitioners and owners. However, adverse effect of ketamine during recovery is seemed to be not able to avoid only by reduction of ketamine dose. Adverse effect of ketamine in Group 'K' did not significantly affect the total recovery time, MWT.

In conclusion, remifentanil (0.5 μg/kg/min)/ketamine (0.1 mg/kg/min) CRI can produce a surgical level of anaesthesia,

and provide better cardiopulmonary responses than remifentanil/propofol CRI. Therefore, it will be a suitable and relatively safe TIVA method for a long time surgery under intubation, oxygen administration and cardiorespiratory monitoring.

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비글견에서 Propofol/Remifentanil과 Ketamine/Remifentanil을 사용한 완전 정맥 내 마취법의 비교

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요 약 : 비글견에서 remifentanil/ketamine 점적 투여 병용마취법과 remifentanil/propofol 점적 투여 병용마취법이 심폐 기능에 미치는 영향에 대하여 비교평가하였다. 14 마리의 비글견을 이용하였다. 실험견은 acepromazine (0.1 mg/kg, 피하)과 medetomidine (20 μg/kg, 정맥내)으로 전처치하고, Group P는 정맥 내 propofol 1 mg/kg, Group K는 정맥 내 ketamine 5 mg/kg으로 마취 유도 하고, 이 후 실험군별로 고정된 용량의 remifentanil (0.5 μg/kg/min)과 ketamine 0.1 mg/kg/min 또는 propofol 0.3 mg/kg/min을 3 시간 동안 투여하였다 (Group K와 Group P). 동맥혈압, 심박수, 호흡수, 혈액가스분석과 마취회복기 동안의 행동변화를 측정하였다. 또한 toe-web clamping 검사를 통해 마취 깊이를 평가하였다. 외과적 마취기는 두 군 모두에서 전 시간 동안 유지가 되었다. Group K의 수축기 동맥혈압, 평균 동맥혈압, 동맥산소 분압, 동맥 산소 포화도는 Group P에 비해 정상 범위 내에서 현저히 높았으며 Group K의 이산화 탄소 분압은 Group P에 비해 현저히 낮았다. 그러나 이완기 동맥혈압, 심박수, 호흡수에서는 현저한 차이가 없었다. 점적투여 중단 시점부터 발관까지의 평균시간은 Group K에서 현저히 감소되었지만, 평균 sitting time은 Group P에서 현저히 감소되었다. 평균 head-up time과 평균 walking time은 현저한 차이가 없었다. Group K에서는 약간의 근강직, 머리 흔듬, 혀로 핥는 동작이 회복기에 관찰되었다. 결론적으로, Group K가 Group P보다 심폐 기능에서 더 좋았다. 즉, remifentanil/ketamine을 이용한 점적투여 병용마취법이 remifentanil/propofol을 이용한 점적투여 병용마취법 보다 3 시간의 마취 유지에서 보다 나은 방법으로 판단되었다.

주요어 : remifentanil, propofol, ketamine, TIVA, 개