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Anesthetic Effect of Different Ratio of Ketamine and Propofol in Dogs

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Abstract : Use of ketamine and propofol combination (so-called Ketofol) anesthesiain a fixed ratio (1:1 mg/ml) was reported in dogs. The use of ketofol reduced cardiovascular suppression, but respiratory-related side effects was not significantly different from propofol alone. In this study, we evaluated the quality of ketofol anesthesia and changes in cardiopulmonary function according to the ratio of ketamine to propofol. The experimental groups were divided into three groups: propofol alone (P group), 3:7 ketofol group (PK1 group) and 1:1 ketofol group (PK2). For each group, the dose of 0.8 ml/kgwas administered intravenously at a constant rate until the tracheal intubation was possible and anesthesia was maintained with isoflurane for 120 minutes after induction of anesthesia. There was no significant difference in the anesthetic quality among three groups. Also, there was no difference in respiratory rate, tidal volume, end-tidal carbondioxide, and oxygen saturation. In group P, heart rate was not changed significantly during anesthesia, but arterial blood pressure decreased, while heart rate and arterial blood pressure increased significantly in group PK2. In the PK1 group, heart rate and arterial blood pressure during anesthesia remained similar to pre-anesthetic values. In conclusion, ketofol might be used as induction agent, and 3:7 ratioof ketofol showed more safe and effective anesthetic effect in dogs. Additionally, 1:1 ketofol may be used in patients with severe bradycardia orhypotension with close monitoring during anesthesia.

Key words **:** ketamine, propofol, ketofol, dog.

Introduction

Propofol is a phenol-derivate sedative-hypnotic agent, commonly used for induction agent of anesthesia in dogs. It provides quick onset, smooth induction, short duration of action, and smooth recovery (23). Although there are many advantages, use of propofol is limited by its dose dependent adverse effect such as hypotension and respiratory depression (7,18). Premedication can reduce the incidence of these adverse effects by decrease the dose of propofol required for induction of anesthesia, but cannot eliminate the adverse effects (21).

Ketamine is a phencyclidine derivate with dissociative anesthetic and analgesic effects produced by N-methyl-D-aspartate receptor antagonism. The unique effect on cardiovascular system of ketamine is maintenance or increase of heart rate and arterial blood pressure by stimulation of sympathetic efferent activity, which mask the direct depression of myocardial contractility (25). Transient respiratory depression can occurs but is minimal at clinically effective doses. Ketamine is also associated with reactions during recovery such as psychomimetic effects and a long recovery period, and it is not used as a sole anesthetic agent in dogs owing to its tendency to potentiate seizures (9).

In human medicine, the combination of ketamine with propofol has been shown to reduce the dose of propofol required to induce anesthesia, and is believed to result in less toxicity than each drug alone by complementary effects that reduce the doses of each drug (1,24). Administering ketamine and propofol mixed in the same syringe (so-called ketofol) has been shown to be efficacious in the emergency department and pediatric patients (12,19). Physical and chemical stability of ketofol was demonstrated (7). The potential advantages of ketofol over propofol alone in human include the provision of deep sedation with lower doses of propofol, thus potentially limiting propofol-associated adverse effects (8). The potential advantages of ketofol over ketaminealone in human include shorter recovery time and a lower incidence of ketamine-associated emesis and recovery agitation (2).

An early attempt in dogs, treatment with ketamine and propofol using separate syringes showed less cardiovascular depression but more respiratory depression compared to propofol alone (13). Also in previous study of ketofol, the dogs treated with ketofol resulted in higher pulse rate and mean arterial pressure than when propofol was used, but lower respiratory rate. Quality of induction and tracheal intubation were consistently good with ketofol, but more variable when using propofol (16). Total intravenous anesthesia in healthy dogs with ketamine and propofol in a 1:1 mg/ml combination resulted in significant propofol dose reduction, higher heart rate, improved mean arterial pressure, no difference in recovery quality, but more significant respiratory depression compared to propofol alone (11).

To alleviate the respiratory depression for example elongation of apnea period and lower respiratory rate, it is thought essential to adjustment of ketamine versus propofol ratio.

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There are some studies performed about variable ratio of ketamine versus propofol to compare the cardiopulmonary effects in human (4,10). But in dogs, most of the study about ketamine-propofol combination deal with sole ratio of each drugs (6,11,13,20).

To the authors' knowledge, there is no comparative study of ketofols with different ketamine-propofol ratio. Although there is one study about relatively small dose of ketamine (0.25 mg/kg, 0.5 mg/kg) as a co-induction agent of propofol, the concept is different that ketamine is injected one minute prior to induction of anesthesia (14).

This study was aimed to compare the cardiorespiratory variables and quality of induction, intubation and recovery in dogs induced anesthesia with propofol alone andtwo different ratio of ketofol.

Materials and Method

Experimental animals

This study was approved by Chungnam National University Animal Care and Use Committee. Nineteen healthy intact male beagle dogs in weight range from 7.5 to 13.2 kg (mean body weight of 9.8 kg) were used. All dogs were considered to be healthy by physical examination, complete blood count, electrolyte analysis and serum biochemistry. Dogs were fasted for 10 hours before anesthesia. Water was available before the experiment.

Each dog was allocated randomly to receive following agent to induce anesthesia: group P received propofol (Provive®, Myungmoon Pharm Co LTD, Korea) alone, group PK1 received 3:7 ketofol (adding 43 mg of ketamine (Ketamine 50®, Yuhan Co, Korea) and 0.57 ml of normal saline to a 100 mg vial of propofol), group PK2 received 1:1 ketofol (mix 100 mg of ketamine and 100 mg of propofol) (Table 1).

Anesthetic procedure

Before the anesthesia, baseline physiological parameters were measured including heart rate, respiratory rate, indirect arterial blood pressure and rectal temperature. Then 22 gauge intravenous catheter was placed percutaneously in a cephalic vein and 0.9% normal saline was administered through the catheter at a rate of 10 ml/kg/h. Any premedication were not applied because it can influence to the cardiorespiratory parameters.

Each dog was administered 0.8 ml/kg of allocated induction agent intravenously at a rate of approximately 10% of the total calculated dose every 10 seconds by hand over until tracheal intubation could be achieved (decreased jaw tone, no reaction to tongue base depression with a laryngoscope) and the total given amount of drug was recorded. A single blinded investigator, who was unable to know the drug in the syringe, assessed loss of jaw tone and ability to intubate the trachea then record the induction quality score. The size of endotracheal tube was chosen by palpation of cervical trachea and according to the body size of the dog. Using laryngoscope, intubation was performed confirming the rima glottidis as able to not stimulate the laryngeal cartilage as possible and the intubation score was assessed. The cuff of endotracheal tube was inflated but not checked for leakage between cuff and trachea. After tracheal intubation, the dog was positioned in left lateral recumbency and the endotracheal tube was connected to a rebreathing circle system delivering a flow of 200 ml/kg/min of pure oxygen with 2% of isoflurane (Ifran Liq®, Hana Pharm Co, Korea) for the remainder of the anesthetic episode. If the SpO_2 dropped below 92% or no spontaneous breath for longer than 1 minute, one manual ventilation was given every 30 seconds. The time from tracheal intubation to the first spontaneous breath (TTFB) was measured and recorded. Post-intubation apnea was defined as a period of 60 seconds without a spontaneous breath after tracheal intubation.

After 120 minutes from intubation, the dog is disconnected from the breathing circle system. Extubation of endotracheal tube was performed when the dog appears adequate laryngeal reflex and the time from end of anesthesia to extubation was recorded. The time from end of anesthesia to head lift, sternal recumbency, standing, and walk without ataxia were also recorded, respectively. Overall recovery quality was assessed and recorded.

Table 1. Experimental groups

Group	Treatment	n
P	Propofol 8 ml/kg	7
PK1	Propofol 7.28 ml/kg with ketamine 3.12 ml/kg	7
PK2	Propofol 7.28 ml/kg with ketamine 7.28 ml/kg	7

Evaluation

Anesthetic quality score

The quality of anesthetic induction and intubation were assessed using the classification according previously study (21) (Table 2, 3). The quality of recovery was assessed using the classification according previous study (15) (Table 4).

Physiological parameters

Heart rate in beats/minute was measured by auscultation with a stethoscope. Respiratory rate was counted the number of breath/minute by visual inspection of the movement of abdomen and chest. Blood pressure were measured at right dorsal pedal artery by noninvasive method using oscillometric blood pressure monitor. Rectal temperature in degrees Celsius (°C) was measured by using a commercial digital thermometer. From induction of anesthesia, additionally to physiologic parameter measured at baseline, end-tidal carbon dioxide, tidal volume and oxygen saturation at tongue were measured. All parameters were recorded at 1, 3, 5 minutes after the tracheal intubation, 5 minutes intervals from 10 minutes to 30 minutes after intubation, and then 10 minutes intervals until the end of anesthesia. Electrocardiogram, spirometry, and capnogram were monitored by multi-parameter monitor (S/5™ Anesthesia Monitor, Datex Ohmeda, Finland). Arterial blood pressure monitoring and pulse oximetry were performed by diagnostic monitor (Cardell® 9402, Sharn Veterinary Inc, USA).

Table 2. Induction quality scoring system

0	Smooth	Without excitement
1	Fair	Slight excitement, muscle twitching or movement of limbs
2	Poor	Marked excitement, muscle twitching, paddling of limbs, head movement
3	Very poor	Severe excitement with vocalization

Table 3. Intubation scoring system

0	Smooth	No swallowing, coughing, tongue or jaw movement
1	Fair	Some tongue movement, slight cough
2	Poor	Marked tongue/jaw movement and swallowing or coughing
3	Very poor	As 2 but requiring additional dose and second attempt at intubation

Table 4. Recovery scoring system

0	Excellent	Smooth, calm, uncomplicated
1	Good	Minimal vocalization and/or struggling
2	Fair	Moderate vocalization and/or struggling
3	Poor	Marked vocalization and/or struggling

Statistical analysis

Statistical analysis was performed using statistical software (IBM SPSS Statistic 22.0, SPSS Inc, USA).

Physiological variables were compared within group using paired t test, among groups using one-way analysis of variance (ANOVA) with Tukey post hoc tests where significance was found.

Chi-squared test and Fisher's exact test were used to compare the induction, intubation and recovery quality score and incidence of post-induction apnea.

For all analysis, a value of $p < 0.05$ was considered as statistically significant.

Results

There were seven dogs allocated to each groups. The dose of propofol administered to achieve intubation was decreased according to increase of ketamine ratio, but there was no statistical significance (Table 5). All of the dogs were intubated without additional dose of induction agent. No significant difference was observed among groups in the induction, intubation and recovery quality score (Table 6). Recovery time was also not significantly different among groups (Table 7). Some side effects were observed during anesthesia such as muscle twitching (2 of group P, 2 of group PK1), paddling (2 of group P, 2 of group PK1), panting (1 of group P, 2 of group PK1, 1 of group PK2), apnea (2 of group P, 2 of group PK2). These reaction were lasted less than 1 minute and resolved spontaneously.

Data of HR and BP are shown in Table 8 and 9, respectively. Because the baseline values of HR among groups were significantly different, the variation of the HR at time

Table 5. The doses of propofol and ketamine (mg/kg) administered to achieve intubation

(mean ± SD)

Group	P	PK1	PK2
Propofol	5.64 ± 1.09	5.01 ± 1.11	4.75 ± 0.66
Ketamine		2.15 ± 0.47	4.75 ± 0.66

Table 6. Induction quality, intubation, recovery quality score for three groups are exressped as median (range)

Group	P	PK1	PK2
Induction score	0 (0-1)	0 (0-1)	0 (0-1)
Intubation score	0 (0-2)	0 (0-1)	0
Recovery score	1 (0-2)	2 (0-2)	1 (0-2)

Table 7. Recovery time (seconds) followingthe administration of propofol, 1:1 or 3:7 ketofol in beagle dogs

(mean ± SD)

Group	P	PK1	PK2
Time to extubation	155 ± 100	280 ± 208	222 ± 145
Head lift	504 ± 526	393 ± 288	386 ± 77
Sternal recumbency	562 ± 544	452 ± 262	482 ± 109
Stand up	634 ± 517	658 ± 358	683 ± 226
Walking without ataxia	1294 ± 331	1340 ± 327	1274 ± 177

Table 8. Heart rate (beats/min) following the administration of propofol, 1:1 or 3:7 ketofol in beagle dogs

(mean ± SD)

Group	Base	1 min	3 min	5 min	10 min	15 min	20 min	25 min	30 min
P	124 ± 16	114 ± 20[a]	116 ± 11[a]	124 ± 17	132 ± 20	122 ± 18	122 ± 17	129 ± 17	125 ± 17
PK1	108 ± 17	129 ± 36	119 ± 18	130 ± 19*	127 ± 19	121 ± 13	118 ± 13	119 ± 10	127 ± 19*
PK2	104 ± 9	155 ± 39*[a]	131 ± 23*[a]	134 ± 26*	129 ± 10*	129 ± 10*	126 ± 14*	126 ± 10*	130 ± 18*
Group	40 min	50 min	60 min	70 min	80 min	90 min	100 min	110 min	120 min
P	122 ± 17	124 ± 18	128 ± 15	130 ± 16	133 ± 22	131 ± 22	131 ± 20	138 ± 21	133 ± 20
PK1	120 ± 11	121 ± 12	119 ± 10	123 ± 15	121 ± 11	123 ± 15	124 ± 16	124 ± 17	124 ± 16
PK2	130 ± 10*	136 ± 13*	138 ± 14*	136 ± 15*	134 ± 11*	136 ± 13*	134 ± 9*	132 ± 9*	132 ± 10*

* Significantly different from the baseline ($p < 0.05$).

a Variation of parameter from baseline is significantly different between groups ($p < 0.05$).

Table 9. Arterial blood pressure (mmHg) following the administration of propofol, 1:1 or 3:7 ketofol in beagle dogs

(mean ± SD)

	Group	Base	1 min	3 min	5 min	10 min	15 min	20 min	25 min	30 min
SAP	P	146 ± 14	130 ± 22[a]	134 ± 16*	119 ± 15*[a]	107 ± 10*[a]	103 ± 15*	100 ± 12*	98 ± 16*	99 ± 18*
	PK1	137 ± 19	147 ± 14	142 ± 33	131 ± 18	129 ± 25	119 ± 27	119 ± 26	123 ± 28	123 ± 30
	PK2	137 ± 23	168 ± 15*[a]	154 ± 17	147 ± 26[a]	140 ± 26[a]	123 ± 26	122 ± 30	123 ± 31	118 ± 31
MAP	P	110 ± 11	98 ± 18*	98 ± 14	88 ± 14*	78 ± 14*	72 ± 12*	69 ± 8*	67 ± 16*	66 ± 10*
	PK1	110 ± 15	107 ± 13	108 ± 15	94 ± 10	90 ± 15*	83 ± 16*	82 ± 15*	84 ± 17*	87 ± 20
	PK2	106 ± 24	124 ± 18	106 ± 13	106 ± 18	101 ± 25	83 ± 26	83 ± 25	83 ± 26	80 ± 23
	Group	40 min	50 min	60 min	70 min	80 min	90 min	100 min	110 min	120 min
SAP	P	100 ± 19*	98 ± 19*	98 ± 18*	98 ± 13*	101 ± 15*	101 ± 13*	97 ± 13*	101 ± 18*	100 ± 15*
	PK1	120 ± 34	113 ± 23	106 ± 10*	107 ± 13*	107 ± 18*	106 ± 15*	105 ± 12*	100 ± 10*	103 ± 11*
	PK2	117 ± 27	124 ± 28	125 ± 26	116 ± 20	114 ± 20	114 ± 17	114 ± 19	121 ± 17	115 ± 17
MAP	P	65 ± 12*	66 ± 11*	67 ± 8*	67 ± 8*	69 ± 8*	70 ± 10*	71 ± 11*	72 ± 16*	72 ± 13*
	PK1	82 ± 21*	80 ± 18*	74 ± 7*	76 ± 9*	77 ± 12*	75 ± 10*	72 ± 7*	70 ± 8*	70 ± 9*
	PK2	80 ± 22	87 ± 24	89 ± 22	80 ± 15	78 ± 17	79 ± 11	79 ± 15	81 ± 11	75 ± 10

* Significantly different from the baseline ($p < 0.05$).
a Variation of parameter from baseline is significantly different between groups ($p < 0.05$).

Table 10. Respiratory rate (breaths/min) following the administration of propofol, 1:1 or 3:7 ketofol in beagle dogs

(mean ± SD)

Group	Base	1 min	3 min	5 min	10 min	15 min	20 min	25 min	30 min
P	26 ± 4	2 ± 4*	7 ± 7*	12 ± 10*	15 ± 6*	18 ± 16	15 ± 8*	16 ± 4*	16 ± 5*
PK1	30 ± 4	1 ± 4*	8 ± 6*	12 ± 7*	20 ± 11*	20 ± 12	21 ± 12	23 ± 11	22 ± 10
PK2	26 ± 4	2 ± 5*	5 ± 5*	10 ± 9*	12 ± 5*	18 ± 20	19 ± 19	17 ± 13	15 ± 13
Group	40 min	50 min	60 min	70 min	80 min	90 min	100 min	110 min	120 min
P	16 ± 4*	20 ± 8*	24 ± 10	21 ± 7	24 ± 11	20 ± 8	22 ± 8	25 ± 12	22 ± 8
PK1	20 ± 7*	20 ± 7*	20 ± 9	21 ± 5*	20 ± 6*	20 ± 5*	20 ± 5*	21 ± 6*	21 ± 6*
PK2	20 ± 13	22 ± 14	22 ± 14	21 ± 14	23 ± 12	24 ± 16	21 ± 13	21 ± 15	20 ± 14

*Significantly different from the baseline ($p < 0.05$).

Table 11. Tidal volume (ml/kg) and end-tidal carbon dioxide (mmHg) following the administration of propofol, 1:1 or 3:7 ketofol in beagle dogs

(mean ± SD)

	Group	1 min	3 min	5 min	10 min	15 min	20 min	25 min	30 min
Tidal volume (ml/kg)	P	2 ± 4	9 ± 6	11 ± 5	13 ± 3	14 ± 3	14 ± 4	15 ± 5	14 ± 3
	PK1	2 ± 5	8 ± 6	9 ± 5	11 ± 3	12 ± 4	13 ± 4	12 ± 5	13 ± 4
	PK2	1 ± 2	8 ± 6	10 ± 5	14 ± 7	14 ± 8	14 ± 6	15 ± 5	12 ± 7
EtCO2 (mmHg)	P	8 ± 20	32 ± 22	38 ± 18	40 ± 11	44 ± 6	45 ± 6	42 ± 6	42 ± 5
	PK1	8 ± 21	35 ± 24	42 ± 19	47 ± 7	45 ± 9	46 ± 9	45 ± 9	44 ± 10
	PK2	8 ± 20	35 ± 24	40 ± 18	45 ± 3	43 ± 3	43 ± 6	42 ± 5	36 ± 17
	Group	40 min	50 min	60 min	70 min	80 min	90 min	100 min	110 min	120 min
Tidal volume (ml/kg)	P	13 ± 2	12 ± 2	13 ± 3	12 ± 3	12 ± 3	12 ± 2	14 ± 5	13 ± 3	13 ± 3
	PK1	13 ± 5	13 ± 5	12 ± 3	14 ± 4	12 ± 3	12 ± 3	11 ± 2	12 ± 2	13 ± 2
	PK2	13 ± 5	12 ± 3	12 ± 3	13 ± 4	12 ± 4	13 ± 4	12 ± 4	13 ± 4	12 ± 3
EtCO2 (mmHg)	P	41 ± 7	40 ± 8	41 ± 8	40 ± 7	39 ± 6	42 ± 6	41 ± 7	40 ± 7	43 ± 6
	PK1	45 ± 5	45 ± 5	46 ± 5	48 ± 8	43 ± 4	45 ± 4	44 ± 4	43 ± 4	47 ± 9
	PK2	43 ± 6	43 ± 8	43 ± 8	43 ± 7	43 ± 6	40 ± 9	42 ± 8	42 ± 9	42 ± 10

Table 12. SpO_2(%) following the administration of propofol, 1:1 or 3:7 ketofol in beagle dogs

Group	1 min	3 min	5 min	10 min	15 min	20 min	25 min	30 min
P	97 ± 1	97 ± 2	97 ± 1	97 ± 1	97 ± 1	97 ± 2	97 ± 2	98 ± 2
PK1	95 ± 3	97 ± 2	96 ± 2	96 ± 1	97 ± 1	97 ± 1	97 ± 2	97 ± 1
PK2	97 ± 2	97 ± 3	98 ± 2	97 ± 2	97 ± 2	97 ± 2	97 ± 2	97 ± 2
Group	40 min	50 min	60 min	70 min	80 min	90 min	100 min	110 min	120 min
P	97 ± 1	98 ± 1	97 ± 1	97 ± 1	97 ± 1	97 ± 1	97 ± 1	97 ± 0	97 ± 1
PK1	97 ± 1	97 ± 1	97 ± 2	97 ± 1	97 ± 1	97 ± 1	97 ± 1	97 ± 1	97 ± 1
PK2	97 ± 2	97 ± 2	97 ± 2	97 ± 2	97 ± 2	97 ± 2	97 ± 2	97 ± 2	97 ± 2

points from the baseline was compared between groups. In group P, the HR was maintained during overall anesthesia. In group PK2, the HR was significantly high from 1 minute after intubation to the end of the experiment compared to baseline. HR of group PK1 was increased at the time point of 5 and 30 minute. The variation of HR from baseline between group P and PK2 appearedsignificant difference at 1 and 3 minutes.

The SAP from 5 minutes of group P and 60 minutes of group PK1 to the end of the study were decreased. Significant increase in SAP was observed at 1 minute in group PK2. There were significant differences of SAP variation between group P and PK2 at 1, 5, 10 minutes.

The variation of MAP was significantly different only at 1 minute between group P and PK2. The MAP of group P was decreased at 1 minute and from 5 minutes to the end. Group PK1 showed decreased in MAP from 10 minutes to the end.

TTFB were 120 ± 107 seconds in group P, 159 ± 108 seconds in group PK1, 140 ± 104 in group PK2. Post-intubation apnea occurred in four dogs in group P and six dogs each of group PK1 and PK2. There were no significant differences in TTFB and occurrence in post-intubation apnea among groups. Respiratory rate was significantly decreased after the administration of each induction agents, then return to around the baseline values in all groups at 10 minutes (Table 10). There was no significant difference in tidal volume and $EtCO_2$ values among the groups at all-time points (Table 11). SpO_2 in all groups appeared normal range during the overall anesthesia and no significant difference among groups (Table 12).

Discussion

In previous studies in human, ketamine was used to reduce the dose-dependent side effects of propofol, such as hypotension and respiratory depression. However against the expectation, although cardiovascular effects were satisfactory with ketofol treatment, respiratory adverse effects were not diminished, rather tend to be worsen according to increase the ketamine ratio (3). On the other hand, there are some reports that ketofol with relatively lower ketamine ratio is a reasonable alternative to propofol alone for higher risk for respiratory depression (22).

In veterinary medicine, ketofol did not appear to induce respiratory depression in cats (26). But in dogs, although minimal respiratory depression of ketamine-propofol combination compared to propofol alone were observed in some studies, there are several evidences of considerable respiratory depression with addition of ketamine (11,20). One report suspected that the greater decrease of respiratory rate compared to other species may be due to a different and/or inadequate rate of administration, although a particular sensitivity of dogs to ketamine cannot be totally ruled out (16).

In this study, end-tidal carbon dioxide, respiratory rate and tidal volume were measured and no statistically significant difference was shown. Though it was not mentioned above, minute volume was also not different among groups. In fact, two ratio of ketofol was judged from the consideration for substantial respiratory depression of prior studies with 1:1 ratio ketofol (11,16). It is considered that lower ketamine ratio alleviate the respiratory depression. In the present study, both ketofol groups showed similar respiratory effect with propofol groups. It is suspected that the difference of the anesthetic method or relatively small size of present study had an effect on the results. The injection speed of induction agent was different and most of the previous studies used ketofol for maintenance of anesthesia, as total intravenous anesthesia (TIVA). Further studies should be investigated about TIVA using different ratio of ketofol to ensure the respiratory effect of ketofol in dogs.

In the present study, the quality of anesthesia was similar among three groups. While previous study showed better intubation and induction qualities with ketofol (16). These differences may be due to small scale of this study or variation of individual standard of assessment. Recovery quality and time were similar between groups in previous studies (11,13,14). These results seem to agree with that result of this study.

In cardiovascular parameters, group PK2 showed significant increase of HR and arterial blood pressure at early stage of experiment. The increment of HR value was 50 beats/min at 1 minute after tracheal intubation. The arterial blood pressure was also quite increased at 1 minute, about 30 mmHg in SAP, 20 mmHg in MAP. Although the changes were transient in this study, these increases are thought to be too severe. In group PK1, HR and arterial blood pressure was maintained well around the baseline values, comparatively. Group P showed consistent value of HR and decreased arterial blood pressure. The decline of blood pressure was got worsen with the course of time at early stage of anesthesia, and then maintained lower about after 30 minutes of tracheal intubation. The rate of decline of SAP was approximately 40% at 30 minutes in group P. The decrease of SAP may be

due to the use of isoflurane as a maintenance agent, SAP of group PK1 and PK2 remain around the baseline value until 50 minutes although they also was maintained anesthesia with isoflurane.

There are several limitations of this study. The small size of study, only 7 anesthetic procedures was included in each group. It may blunted the difference among the groups. Secondly, the parameters were not measured immediately after induction of anesthesia. The incidence of post-induction apnea was considerably high in previous studies (13). Thus, tracheal intubation was performed immediately after the induction of anesthesia to prepare an occasion that requires free air way and manual ventilation, just in case. Finally, direct arterial blood pressure measurement was not performed in this study. Although indirect blood pressure measurement using oscillometric device and method which were used in this case have demonstrated reasonable bias and precision compared to direct blood pressure monitoring for the range of MAP, the golden standard of measurement of blood pressure is direct invasive method (5).

Conclusion

Ketofol (3:7 and 1:1) provided satisfactory quality of anesthesia as good as propofol. However, both ketofol (3:7 and 1:1) required respiratory support and monitoring because of respiratory depression as propofol.

In this study, 3:7 ketofol showed minimal change of HR and arterial blood pressure, so this could be safe and effective anesthetic induction agent in dogs. However, 1:1 ketofol should be used with caution because it cause an excessive increase in heart rate and arterial blood pressure during the course of anesthesia. For this reason, this could be an alternative for the anesthesia of dogs with severe bradycardia or hypotension with a close monitoring.

In conclusion, 3:7 ketofol might be used as compatible anesthetic induction agent in dogs.

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