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Effects of Isoflurane/Remifentanil and Isoflurane/Fentanyl Anesthesia in Beagle Dogs

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Abstract : This study was performed to compare two opioid drugs with isoflurane and to determine the difference between isoflurane/remifentanil anesthesia and isoflurane/fentanyl anesthesia in terms of the anesthetic effects in beagle dogs. Isoflurane was maintained at 0.5 MAC, and the opioid drug was administered as a constant rate infusion. The anesthesia was maintained for 2 hours, and isoflurane and opioid drugs were discontinued 2 hours later. After discontinuing the anesthetics, the extremity movement time, eye global positioning time, gag reflex time, head up time, sternal recumbency time, standing time, walking time and complete recovery times were recorded for each dog. Both of the studied anesthetic protocols were suitable in beagle dogs because the anesthetic status was well maintained until the end of the procedure, and rapid recovery times were demonstrated in this experiment. And this study shows that the isoflurane/remifentanil group was more reliable than the isoflurane/fentanyl group because the recovery time CV was lower. Therefore, isoflurane/remifentanil combination anesthesia could be a better choice than isoflurane/fentanyl anesthesia if the patient is severely ill and stable recovery time is needed.

Key words **:** remifentanil, fentanyl, isoflurane, anesthesia, dog.

Introduction

Inhalation anesthetics are widely used for anesthetic management in mammals, reptiles, avians, and many other zoo animals. Inhalation anesthesia can be suitable for all species. If accurate doses are used, this method would be pharmacologically, physiologically, and chemically stable (12,16). The depth and duration of inhalation anesthesia are easily controlled by regulating the anesthetic concentration (3). Inhalation anesthetics provide optimal control of anesthesia, as well as rapid induction and recovery from anesthesia, and are associated with relatively few adverse effects (18,20).

Isoflurane has been widely used in veterinary medicine. It is a stable molecule that undergoes little metabolism and is, therefore, not toxic to the liver or kidney. Isoflurane does not induce cardiac arrhythmias and does not sensitize the heart to the action of catecholamines. However, similarly to other halogenated gases, it produces dose-dependent hypotension because of peripheral vasodilation (8). Therefore, when animals have blood pressure and respiratory rate problems or they have cardiovascular disease, it is difficult to maintain blood pressure and respiratory rates with isoflurane because it can suppress breathing and the cardiovascular system (7). There are various methods of preventing these effects by reducing the concentration of isoflurane. One of these methods is total intravenous anesthesia. This method could be an effective alternative anesthesia method. It does not involve the lung; therefore, it can maintain the stability of the cardiovascular status and analgesia. In addition, the postoperative status is stable compared with isoflurane anesthesia (15,21).

Another method of reducing the isoflurane concentration is by administering remifentanil or fentanyl, which are opioid drugs. It has already been shown that the administration of fentanyl can reduce the required concentration of isoflurane without remarkable side effects, and fentanyl has been long used in clinical cases in veterinary medicine (1).

Fentanyl is a potent, synthetic opioid analgesic with a rapid onset and short duration of action. Fentanyl is a strong agonist of μ-opioid receptors. It is approximately 100 times more potent than morphine, and its side effects include diarrhea, nausea, constipation, depression, dyspnea, hypoventilation, apnea, and urinary retention (13). Although there are side effects associated with fentanyl use, it has been used with isoflurane anesthesia in veterinary medicine worldwide because fentanyl can reduce the required concentration of isoflurane. Some studies have shown that fentanyl significantly reduced the isoflurane requirements during surgical procedures by 54% to 66% (1,19).

Remifentanil is a structural analog of fentanyl that was developed for use in human patients to create analgesics with a more rapid onset of action and a more predictable termination of opioid effects. Remifentanil infusion also reduces the isoflurane concentration required for surgical anesthesia, but it is metabolized differently in the body (2). Remifentanil is an esterase-metabolized opioid that was developed for use in anesthesia. The principal metabolite of remifentanil is considered to be less potent than fentanyl's (10). Fentanyl is considered to be a short-acting narcotic analgesic, but prolonged

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and recurrent ventilatory depression has been reported because it is metabolized through the liver (13). This effect of fentanyl could be exacerbated in cases involving hypoxemia or hypoperfusion of the liver, which might be followed by hepatic dysfunction (9).

Remifentanil has already gained popularity in human anesthesia because of its rapid onset and rapid offset characteristics, and it has been widely used in humans because of these characteristics (4,14). The interaction between opioids and volatile anesthetics has shown that opioids markedly reduce the concentration of the volatile anesthetic agents required to maintain anesthesia in a variety of species (5).

In addition, some human anesthesia reports have shown that remifentanil is more stable and predictable in surgery than fentanyl and that it has fewer post-surgical side effects (7). However, no veterinary medicine reports have compared these two opioid drugs with isoflurane inhalation anesthesia.

The aim of this study was to compare these two opioid drugs with isoflurane and to determine the difference between isoflurane/remifentanil anesthesia and isoflurane/fentanyl anesthesia in terms of the anesthetic effects in beagle dogs.

Materials and Methods

Animals

This study was approved by the Chungnam National University Animal Care and Use Committee. Eight healthy beagle dogs with an average weight of 7.83 ± 1.77 kg (female: 4, male: 4) were used.

Prior to the anesthesia, the health status of each dog was assessed based on a physical examination, a complete blood count, and serum biochemical analyses. All findings were within reference ranges. The experimental dogs were fed commercial dog food two times a day with ad libitum access to water. The dogs were fasted for 12 hours before the experiment, and water was withheld for 4 hours before anesthesia to prevent any possible adverse effects associated with anesthesia, such as vomiting during the anesthesia or recovery periods.

The dogs were randomly assigned to the isoflurane/remifentanil anesthesia group (I/R group, 4 dogs) and the isoflurane/fentanyl anesthesia group (I/F group, 4 dogs).

Procedure

Before inducing general anesthesia, venous catheterization was performed in both cephalic veins to inject opioid drugs and intravenous fluid administration. Premedication with anticholinergics, barbiturates, or benzodiazepines was not applied in this experiment because these drugs can influence cardiac parameters. ECG patches were placed on the both fore limbs pad and left hind limb pad of each dog for anesthesia monitoring (S-5 Anesthesia Monitor®, Datex-Ohmeda, Finland), followed by induction with propofol (Provive®, Myungmoon Pharm, Co, Korea, 6 mg/kg IV bolus).

Each dog was placed in a ventrodorsal recumbent position, and anesthesia was maintained through a semi-closed circle system with 1.5 MAC of isoflurane (Ifran liquid, Hana Pharm Co, Korea) under pure oxygen. A sterile 24-gauge arterial catheter (BD IV Catheter®, Becton Dickinson Korea Ltd, Korea) was inserted into the dorsal pedal artery of the left hind limb. A pressure transducer (Transpac® IV Monitoring Kit, 42587, Hospira Holdings De Costa Rica Ltd, Costa Rica) was connected to the catheter and the anesthesia monitor.

The anesthesia monitor was connected after inserting the catheter, and the isoflurane supply was decreased to 0.5 MAC, allowing the maintenance of the level of anesthesia until just before the dog awoke. Baseline cardiopulmonary parameters were measured, and arterial blood samples were drawn from the catheter and analyzed using a portable arterial blood gas analyzer (i-STAT®, HESKA Co, USA).

After the baseline values were recorded, each dog was simultaneously administered isoflurane and an opioid drug. Isoflurane was maintained at 0.5 MAC, and the opioid drug was administered as a constant rate infusion (CRI). For the isoflurane/remifentanil group, remifentanil (Ultiva® 2 mg/bottle, GlaxoSmithKline, UK) was prepared and infused at a rate of 13 μg/kg/hour. For the isoflurane/fentanyl group, fentanyl (Daihan Fentanyl injection water 500 μg/10 ml, Daihan Pharm Co, Korea) was prepared and infused at a rate of 25 μg/kg/hour. The anesthesia was maintained for 2 hours, and isoflurane and opioid drugs were discontinued 2 hours later.

Evaluation

Recovery times

After discontinuing the anesthetics, the extremity movement time, eye global positioning time, gag reflex time, head up time, sternal recumbency time, standing time, walking time and complete recovery times were recorded for each dog. Extremity movement time is the time period before which the dog tries to move his or her extremities. Eye global positioning time is the time period required for the dog's pupils to be normally positioned. Gag reflex time is the time period required for the dog to begin to chew the endotracheal tube. Head up time is the time period required for the dog to attempt to move its neck and head. Sternal recumbency time is the time period required for the dog to achieve sternal recumbency. Standing time is the time period required for the dog to stand for longer than 10 seconds without assistance. Walking time is the time period required for the dog to be able to walk without assistance. Finally, complete recovery time is the time period required for the dog to be able to walk without knuckling.

Cardiovascular parameters and rectal temperature

Cardiovascular parameters were measured and recorded at time 0 (before the drug injections) and every 20 minutes for 2 hours after the administration of the opioids. The heart rate (HR) and blood pressure (BP) [systolic arterial pressure (SAP), mean arterial pressure (MAP), and diastolic arterial pressure (DAP)] were measured using the anesthesia monitor. The rectal temperature (RT) was recorded every 20 minutes. Additional heating was not applied during the course of the experiment.

Respiratory parameters and arterial blood gas analysis

Respiratory parameters were also measured and recorded at time 0 (before the drug injections) and every 20 minutes until 2 hours after the drug administration. The respiratory

rate (RR) was measured using an anesthesia monitor. Arterial blood gas analysis was performed with a portable arterial blood gas analyzer. In this experiment, arterial oxygen partial pressure (PaO_2), carbon dioxide partial pressure ($PaCO_2$), bicarbonate (HCO_3), arterial oxygen saturation (SaO_2), total carbon dioxide (TCO_2), and arterial pH were measured.

Statistical analysis

Values were expressed as the means and standard deviation. Differences in the physiological parameters within the group were tested with one-way analysis of variance (ANOVA), and $p < 0.05$ was considered to be statistically significant. All statistical analyses were performed using statistical software (IBM SPSS Statistics 20.0, SPSS Inc., USA).

Results

Recovery time

For all dogs, the anesthesia was well maintained, and the recovery was uneventful. After all drugs were discontinued, the extremity movement time, eye global positioning time, gag reflex time, head up time, sternal recumbency time, standing time, walking time and complete recovery time were recorded in Table 1. The times in all categories were shorter in the isoflurane/remifentanil group than in the isoflurane/fentanyl group. Although this result shows that the isoflurane/remifentanil group tended to recover somewhat earlier than the isoflurane/fentanyl group, no significant difference between the groups was observed.

However, comparing the coefficient of variation (CV), the isoflurane/remifentanil group's values were lower than those of the isoflurane/fentanyl group in all categories (Table 1). In particular, the CVs for the isoflurane/remifentanil group's sternal recumbency time, standing time, walking time, and complete recovery time were much lower than those of the isoflurane/fentanyl group.

Table 1. Recovery times and coefficients of variation following isoflurane/remifentanil or isoflurane/fentanyl anesthesia in beagle dogs

		Time (Seconds)	CV (%)
Extremity movement	I/R	194.0 ± 67.9	34.98
	I/F	215.3 ± 90.1	41.86
Eye global positioning	I/R	201.3 ± 48.7	24.21
	I/F	228.8 ± 89.6	37.12
Gagging reflex	I/R	213.0 ± 52.9	24.85
	I/F	229.3 ± 85.1	39.92
Head up time	I/R	218.8 ± 59.9	27.36
	I/F	240.3 ± 95.9	39.16
Sternal recumbency time	I/R	299.3 ± 17.3	5.78
	I/F	444.0 ± 245.3	55.26
Standing time	I/R	361.3 ± 46.7	12.09
	I/F	583.8 ± 295.4	50.59
Walking time	I/R	375.5 ± 47.9	12.75
	I/F	632.3 ± 361.1	57.11
Complete recovery time	I/R	542.0 ± 78.6	14.49
	I/F	773.5 ± 322.1	41.63

I/R: isoflurane/remifentanil group; I/F: isoflurane/fentanyl group; CV: coefficient of variation (Mean ± SD, n = 4)

Cardiovascular parameters and rectal temperature

Data related to heart rate, systolic arterial pressure, mean arterial pressure and diastolic arterial pressure are summarized in Table 2. Changes in the cardiovascular parameters during isoflurane/remifentanil and isoflurane/fentanyl anesthesia were similar for 2 hours. Except for DAP, there were no significant differences in the cardiovascular parameters compared to the baseline values or between the groups. In DAP, a significant difference was observed only at the 20-minute time point in both groups ($p < 0.05$).

However, the heart rate of the isoflurane/remifentanil group was relatively more constant, while that of the isoflurane/fentanyl group tended decrease in the early period of anesthesia and at the end of anesthesia.

Rectal temperature decreased relative to baseline after the administration of anesthetics and did not change significantly at all time points in both groups. The rectal temperature of the isoflurane/remifentanil group decreased from 37.9°C to 36.7°C, and that of the isoflurane/fentanyl group decreased from 37.8°C to 36.8°C. This result is considered to be a general variation during anesthesia.

Respiratory parameters and arterial blood gas analysis

The RR, SpO_2, and $EtCO_2$ data are shown in Table 3. Changes in the respiratory parameters during isoflurane/remifentanil and isoflurane/fentanyl anesthesia were similar for 2 hours. There were no significant differences in RR, $PaCO_2$, HCO_3, SO_2, and TCO_2. Significant differences in SpO_2 were shown at 40 minutes ($p < 0.05$). In the isoflurane/remifentanil group, SpO_2 value was greater than that in the isoflurane/fentanyl group. In addition, there were significant differences in $EtCO_2$ at 100 minutes ($p < 0.05$). In the isoflurane/fentanyl group, the $EtCO_2$ value was lower than the other group. However, there were no significant differences at other time points. The arterial pH decreased smoothly until 100 minutes in both groups, but the last measurement of the isoflurane/remifentanil group's pH at 120 minutes increased nearly to baseline. There was a significant difference in the pH at 60 minutes ($p < 0.05$). PaO_2 in the isoflurane/remifentanil group was significantly lower than in the isoflurane/fentanyl group at 80 minutes ($p < 0.05$). However, there were no significant differences in other categories of the arterial blood gas analysis.

Discussion

The combinations of isoflurane/remifentanil and isoflurane/fentanyl produce a clinically relevant reduction in the anesthetic requirement of isoflurane concentration. Both groups (isoflurane/remifentanil and isoflurane/fentanyl) required reduced concentrations of isoflurane at 0.5 MAC, which allowed the cardiovascular suppression to be minimized. The cardiovascular system effects were similar with both drugs.

However, the remifentanil group's recovery time was more

Table 2. Heart rate (HR), blood pressure [systolic arterial pressure (SAP), mean arterial pressure (MAP), and diastolic arterial pressure (DAP)] and rectal temperature (RT) following the administration of isoflurane/remifentanil or isoflurane/fentanyl in Beagle dogs (Mean ± SD, n = 4)

	Group	Pre	20 minutes	40 minutes	60 minutes	80 minutes	100 minutes	120 minutes
HR (Beats/minute)	I/R	93.8 ± 29.1	75.3 ± 14.2	74.8 ± 14.2	87.8 ± 35.2	86.0 ± 24.1	89.5 ± 25.8	86.3 ± 23.2
	I/F	107.3 ± 35.5	63.3 ± 12.4	59.8 ± 9.3	62.8 ± 12.6	70.0 ± 16.2	75.0 ± 15.4	77.5 ± 15.3
SAP (mmHg)	I/R	133.5 ± 21.5	94.8 ± 2.4	112.5 ± 12.4	120.8 ± 21.8	116.0 ± 17.3	114.3 ± 21.3	118.8 ± 14.9
	I/F	124.3 ± 34.2	132.3 ± 44.8	117.5 ± 14.2	127.5 ± 17.2	118.0 ± 25.5	116.3 ± 11.5	136.5 ± 36.4
MAP (mmHg)	I/R	100.5 ± 6.2	61.3 ± 5.4	69.5 ± 19.7	78.3 ± 23.5	78.5 ± 21.0	77.8 ± 23.4	82.3 ± 21.9
	I/F	90.0 ± 19.5	80.5 ± 16.1	77.3 ± 5.1	87.0 ± 16.8	82.0 ± 15.9	89.8 ± 11.6	85.3 ± 10.7
DAP (mmHg)	I/R	81.3 ± 4.9	43.8 ± 4.9*	53.5 ± 15.6	56.5 ± 21.5	57.5 ± 19.2	57.3 ± 19.8	60.3 ± 21.1
	I/F	72.5 ± 15.5	58.5 ± 10.5*	55.5 ± 7.4	66.0 ± 13.7	58.0 ± 9.8	66.0 ± 9.0	62.0 ± 11.4
RT (°C)	I/R	37.90 ± 0.59	37.35 ± 0.85	37.35 ± 0.61	37.13 ± 0.63	36.93 ± 0.71	36.83 ± 0.65	36.73 ± 0.71
	I/F	37.78 ± 0.81	37.58 ± 0.79	37.28 ± 0.93	37.08 ± 0.74	37.00 ± 0.70	36.90 ± 0.70	36.78 ± 0.74

*Significantly different from the baseline ($p < 0.05$); I/R: isoflurane/remifentanil group; I/F: isoflurane/fentanyl group

Table 3. Respiratory rate (RR), saturated oxygen (SpO_2), end-tidal carbon dioxide ($EtCO_2$), and arterial blood gas analysis following the administration of remifentanil or fentanyl in beagle dogs (Mean ± SD, n = 4)

	Group	Pre	20 minutes	40 minutes	60 minutes	80 minutes	100 minutes	120 minutes
RR (breaths/minute)	I/R	16.0 ± 4.1	9.5 ± 3.1	11.5 ± 3.7	19.0 ± 15.5	20.5 ± 17.8	15.5 ± 6.8	19.25 ± 13.4
	I/F	16.8 ± 5.7	12.5 ± 5.8	10.3 ± 4.4	13.0 ± 7.8	15.0 ± 8.8	10.0 ± 4.1	10.5 ± 2.9
SpO_2 (%)	I/R	97.8 ± 1.0	97.5 ± 0.6	98.0 ± 0.8*	97.3 ± 1.0	97.3 ± 1.0	97.0 ± 0.8	97.3 ± 1.0
	I/F	97.3 ± 1.7	96.5 ± 0.6	96.8 ± 0.5*	96.8 ± 1.0	97.0 ± 0.9	96.5 ± 1.0	96.5 ± 1.0
$EtCO_2$ (mmHg)	I/R	41.0 ± 6.1	49.0 ± 5.4	50.5 ± 4.2	47.3 ± 5.4	48.0 ± 4.7	49.0 ± 5.3*	47.5 ± 5.6
	I/F	36.0 ± 6.7	44.8 ± 11.0	48.5 ± 14.7	52.8 ± 19.4	52.5 ± 14.3	59.5 ± 3.3*	56.3 ± 5.0
pH	I/R	7.340 ± 0.044	7.241 ± 0.023	7.222 ± 0.034	7.219 ± 0.025*	7.196 ± 0.060	6.991 ± 0.488	7.235 ± 0.030
	I/F	7.361 ± 0.045	7.205 ± 0.037	7.184 ± 0.078	7.161 ± 0.038*	7.197 ± 0.045	7.156 ± 0.037	7.159 ± 0.065
pCO_2 (mmHg)	I/R	35.43 ± 4.16	53.98 ± 2.75	59.90 ± 3.63	59.05 ± 4.93	59.65 ± 4.81	57.68 ± 5.99	60.25 ± 3.62
	I/F	38.63 ± 9.08	58.23 ± 14.05	64.80 ± 20.35	65.15 ± 13.59	61.78 ± 14.6	64.98 ± 7.30	68.40 ± 9.28
pO_2 (mmHg)	I/R	91.5 ± 22.1	508.3 ± 35.8	513.0 ± 42.3	502.0 ± 69.2	501.8 ± 23.1*	540.3 ± 5.6	527.3 ± 31.3
	I/F	88.5 ± 5.3	416.75 ± 85.9	512.8 ± 51.4	486.3 ± 45.3	550.8 ± 30.0*	475.3 ± 69.2	490.0 ± 29.6
HCO_3 (mmol/L)	I/R	18.85 ± 1.59	23.28 ± 2.19	24.68 ± 2.03	24.20 ± 2.74	24.75 ± 2.54	25.13 ± 2.82	25.53 ± 2.58
	I/F	22.30 ± 2.57	22.60 ± 3.81	23.53 ± 3.38	22.83 ± 2.98	23.50 ± 3.92	22.80 ± 3.41	23.98 ± 2.12
SO_2 (%)	I/R	97.0 ± 3.6	100.0 ± 0	100.0 ± 0	100.0 ± 0	100.0 ± 0	99.75 ± 0.5	100.0 ± 0
	I/F	97.8 ± 1.5	100.0 ± 0.1	100.0 ± 0	100.0 ± 0	100.0 ± 0	100.0 ± 0.1	100.0 ± 0.1
TCO_2 (mmol/L)	I/R	20.0 ± 1.6	25.0 ± 2.5	26.5 ± 2.1	26.0 ± 2.9	26.5 ± 2.9	26.8 ± 2.9	26.5 ± 1.7
	I/F	23.8 ± 2.9	23.3 ± 4.6	25.6 ± 3.5	24.4 ± 3.9	25.4 ± 4.4	24.7 ± 3.5	26.1 ± 2.0

*Significantly different from the baseline ($p < 0.05$); I/R: isoflurane/remifentanil group; I/F: isoflurane/fentanyl group

stable, according to the CV. The CV shows the statistical change in the size obtained from a sample; a smaller value indicates less variation and increased stability.

The CV for the isoflurane/remifentanil group is much lower than that of the isoflurane/fentanyl group. It could be suggested that the CV for the isoflurane/fentanyl group was significantly high; therefore, the isoflurane/remifentanil group would exhibit a relatively stable effect. In particular, the isoflurane/remifentanil group was remarkably more stable than the isoflurane/fentanyl group in terms of the sternal recumbency time, standing time, walking time, and complete recovery time. Therefore, in the isoflurane/remifentanil group, if the variation in the recovery time is small, then the recovery time can be reliably predicted. This result demonstrated that remifentanil could be a more suitable opioid drug than fentanyl in isoflurane inhalation anesthesia for hyposthenia patients with severe cardiovascular or respiratory disease because remifentanil's rapid onset of action allows it to be utilized more easily by a veterinarian who is performing surgery on a severely ill patient.

Remifentanil was successfully used as part of an anesthetic regimen that included propofol induction followed by isoflurane maintenance. Remifentanil appeared to be pharmacologically similar to fentanyl and other potent μ-opioid ago-

nists. Decreased heart rate was common, and hypotension and bradycardia after opioid administration are well-known side effects (2,6). Based on predominant metabolism by nonspecific esterases, remifentanil is first in the class of esterase-metabolized opioids (within the 4-anilidopiperidine drug series). Because of its rapid systemic elimination (i.e., a half-life of 8-10 minutes), remifentanil should have pharmacokinetic advantages in clinical situations that require a predictable termination of effect (4).

Historically, fentanyl has been used to treat pain and is commonly used as a pain reliever prior to procedures and as an anesthetic in combination with other drugs, such as isoflurane. Fentanyl can also reduce the amount of anesthetic agents required to maintain anesthesia in a variety of species. Therefore, it has been widely used in veterinary medicine (19). However, the hepatic oxygen delivery and consumption were calculated from the measured hepatic blood flow and oxygen content in hepatic arterial, portal venous, and hepatic venous blood during fentanyl metabolism. The hepatic energy charge was assessed by measuring the arterial ketone body ratio (AKBR), which is considered to be an indicator of the mitochondrial energy charge level. Hepatic blood flow and oxygen metabolism did not change after the administration of a small amount of fentanyl (3 μg/kg), but the mean arterial blood pressure, cardiac output, hepatic arterial blood flow, portal venous blood flow, and hepatic oxygen delivery were significantly suppressed by a large amount of fentanyl (30 μg/kg). This result suggests that the significant decrease in hepatic oxygen delivery during the administration of 30 μg/kg of fentanyl could be exacerbated by a combination with hypoxemia or liver hypoperfusion, and this administration might be followed by hepatic dysfunction (9,11). This result shows that remifentanil is a better choice than fentanyl for surgery in patients with hepatic disease.

It is known that opioid drugs may produce some bradycardia as a side effect (19), but no significant changes in heart rate were observed when using opioid drugs in this experiment. Fentanyl suppressed the heart rate more than remifentanil. Therefore, remifentanil and isoflurane combination could be a better choice for patients with cardiovascular disease. In addition, there was a significant difference in the respiratory rate and other arterial blood gas analysis categories during the procedure. There were significant differences in SpO_2 at 40 minutes and in $EtCO_2$ at 100 minutes after administering the drugs. There were also significant differences in pH at 60 minutes and pO_2 at 80 minutes. However, these changes were temporary, and few changes in respiration and arterial blood gases were observed during the entire anesthesia procedure.

One study reported that intravenous opioids, such as remifentanil, may affect presynaptic neurons that project to the pre-Bötzinger complex region and are involved with the control of respiratory phase timing; therefore, it does not appear that clinical doses of intravenous opioids act directly on these neurons to produce bradypnea *in vivo* (17). However, no bradypnea was observed in this experiment.

Conclusions

Both of the studied anesthetic protocols were suitable in beagle dogs because the anesthetic status was well maintained until the end of the procedure, and rapid recovery was observed. Suppression of heart rate or blood pressure were observed in both groups, but they were minimal.

The isoflurane/remifentanil group was more reliable than the isoflurane/fentanyl group, because the CVs of all recovery parameters in isoflurane/remifentanil group was lower than those of the other group.

This study showed that isoflurane/remifentanil combination anesthesia produced adequate anesthesia and is a better choice than isoflurane/fentanyl in severely ill patients because the recovery time in the isoflurane/remifentanil group was more constant and predictable compared to that in the isoflurane/fentanyl group. Therefore, isoflurane/remifentanil combination anesthesia could be a better choice than isoflurane/fentanyl anesthesia if the patient is severely ill and rapid recovery is needed. However, the analgesic effect will quickly disappear, and an additional post-operative analgesic treatment may help patients.

Acknowledgements

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비글견에서 아이소플루란/레미펜타닐 및 아이소플루란/펜타닐 조합의 마취 효과

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요 약 : 본 연구는 비글견에서의 마취 효과에 있어서 isoflurane과 병용시에 두가지 opioid 약물을 비교, 아이소플루란/레미펜타닐과 아이소플루란/펜타닐 조합의 마취간의 차이를 알아보기 위하여 실시하였다. Isoflurane은 0.5 MAC으로 유지하고, opioid 약물은 등속으로 정맥 주입하였다. 각 개체에서 마취를 2시간 동안 유지한 뒤, isoflurane과 opioid 약물을 중단하고서 안구가 제 위치를 찾는 시간(eye global positioning time), 연하 반사가 나타나는 시간(gag reflex time), 머리를 드는 시간(head up time), 엎드림 자세가 나타나는 시간(sternal recumbency time), 서는 시간(standing time), 걷는 시간(walking time), 그리고 마취에서 완전히 회복된 시간(complete recovery time)을 기록하였다. 두가지 조합 모두 전 과정에 걸쳐 양호한 마취상태를 유지함과 동시에 빠를 회복 시간을 보여 비글견의 마취에 적합하였다. 한편, 회복 시간에 있어 아이소플루란/레미펜타닐 조합은 아이소플루란/펜타닐 조합에 비해 그 변동 계수가 낮아 좀 더 신뢰할 만한 것으로 나타났다. 따라서, 환자의 중등도가 높고, 안정적인 회복이 요구될 때에는 아이소플루란/레미펜타닐 조합의 마취가 더 좋은 선택일 것으로 생각된다.

주요어 : 레미펜타닐, 펜타닐, 아이소플루란, 마취, 개