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Cardiopulmonary Effects of Enflurane Combined with Propofol in Dogs

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Abstract : This study was performed to evaluate cardiopulmonary depressant effects of enflurane (1.0 vol%) combined with propofol(0.25 mg/kg/min) compared with enflurane inhalation, and propofol infusion, respectively, in 18 healthy dogs premedicated with acepromazine and atropine. After bolus injection of propofol 5 mg/kg for induction and tracheal intubation, they were randomly assigned to 3 groups: propofol 0.5 mg/kg/min infusion (Group I, n = 6), enflurane 2.5 vol% (Group II, n = 6) and enflurane 1.0 vol% combined with propofol 0.25 mg/kg/min (Group III, n = 6). Mean arterial Pressure (MAP), systolic arterial pressure (SAP) and diastolic arterial pressure (DAP) were depressed significantly in all groups, especially in Group II. MAP, SAP and DAP values of Group IIIwere higher than those of Group II, but lower than those of Group I. The changes of PaO_2, $PaCO_2$ and pHa were similar in all groups. Respiration rates were decreased in all groups 5 minutes after induction but maintained in normal range. Those of Group I were less depressant than those of Group II and Group III. Concentrations of Na^+ and Cl^- were increased and those of K^+ were decreased in all groups, but their values were quitely similar. Heart rate was changed in small range and the value of Group I was higher than those of Group II and Group III. Body temperature was decreased significantly in all groups. Adverse effects like as muscle rigidity, nausea or vomiting and shivering were not appeared and apnea at induction was occured 6 dogs. From the these results, enflurane 1.0 vol% combined with propofol 0.25 mg/kg/min also could be applied for anesthesia in dogs.

Key words **:** anesthesia, enflurane, propofol, cardiopulmonary effects, dog

Introduction

Enflurane (CHF2-O-CF2-CHFCl; 1,1,2-trifluoro-2-chloroethyl difluoromethyl ether) is a clear, colorless, non-flammable inhalation anesthetic that produces rapid and smooth induction and recovery, not irritating the respiratory membranes and stable cardiac rhythm, and undergoes minimal biotransformation (2 to 5%) to toxic metabolites compared with halothane and methoxyflurane[14,28,29]. The minimal alveolar concentration (MAC) of enflurane that pre-vented movement in response to a standard painful stimulus is 2.06 vol% in dogs. The average end-tidal enflurane concentration that produces at least 60 seconds of apnea is 5.29 ± 0.8% and the resultant respiratory anesthetic index (apneic concentration/MAC) for enflurane is 2.57 ± 0.08%[39].

In veterinary practice, anesthesia is usually maintained by admistration of the potent inhalant anesthetic agents such as halothane, enflurane, isoflurane or sevoflurane. These agents, as well as induce progressive depression of the central nervous system, induce cardiovascular and respiratory depression in dose dependent fashion[18,25]. Cardiovascular and respiratory effects of enflurane are greater than those of halothane, isoflurane and sevoflurane. Respiratory rate was significantly lower and arterial carbon dioxide higher during maintenance anesthesia with enflurane than with halothane[12]. Enflurane induces muscle twitches, tonic-clonic convulsions and grand-mal type convulsions in dogs, cats and humans. These characteristics may be exaggerated by hypocapnia and these actions of enflurane seem to be the biggest disadvantage to its use in clinical practice. Enflurane-induced convulsions are facilitated by an increase in concentration and hypocapnia[14]. Enflurane should not be selected for intracranial surgery or for a patient with a history of seizures, cranial trauma, or cerebrovascular diesase, but these are reduced by hypercapnea[15]. Because opioids induce minimal changes in cardiovascular dynamics in human beings, opioids and sedative hypnotics are often administered with low concentrations of inhalant anesthetics and muscle relaxants as a technique called "balanced anesthesia"[24].

Propofol(2,6-diisopropylphenol, Diprivan) is formulated as a 1% aqueous emulsion contaning 10% soybean oil, 1.2% egg lecithin, and 2.25% glycerol. It could be used either as a single injection for anesthetic procedures of short duration, or as an induction agent with anesthesia being maintained by incremental injections of propofol given to effect or as an induction agent with anesthesia being maintained by gaseous agents[24]. Propofol is a modified phenol that is largely metabolized in the liver by glucuronidation. Cats are deficient in glucuronide synthetase, and although they recover rapidly from a single dose, it is likely that recovery from an infusion of propofol may be prolonged[42].

The median effective dosage (ED50) of propofol for induction of anesthesia were about 3 mg/kg in premedicated and 5 mg/kg in unpremediacted dogs[17,41]. The infusion rate for anesthetic maintenance is 0.3 to 0.5 mg/kg/min, and this produces a satisfactory anesthetic plane in the dog with minimal effects on arterial blood pressure and ventilation. The

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cardiovascular depressant effects of propofol; myocardial depression, peripheral vasodilation and ventilation have been reported to cause the arterial hypotension[6,8,32,38].

There are many studies on cardiovascular and respiratory effects of enflurane and propofol, but those on the effects of enflurane combined with propofol are none. The purpose of this study was to evaluate the practical influences of cardiopulmonary effects of enflurane at light concentration (1.0 vol%) combined with propofol infusion (0.25 mg/kg/min), compared with enflurane inhalation (2.5 vol%) and propofol infusion (0.5 mg/kg/min).

Materials and Methods

1. Animals

Eighteen mixed-breed dogs of both sex, weighing 2.2 to 5.4 kg (mean, 3.89 kg), were used in this study. The dogs were vaccinated against distemper, parvovirus and parainfluenza (Vanguard® Plus, Pfizer Inc., USA), leptospirosis (Leptoferm C-1®, Pfizer Inc., USA) and coronavirus (First Dose® CV, Pfizer Inc., USA) and treated vermicide (Rintal® tabs, Bayer Korea Ltd., Korea). They were determined to be in good health by physical examination, routine biochemical and hematological screening. Food was withheld at least 12 hours before experiments. They were alloted to 3 groups and each groups were composed of 6 dogs.

2. Premedication

All dogs were premedicated with acepromazine maleate (KOMI CERASTRESS Inj.® Korea Microbiological Laboratories Ltd., Korea) 0.05 mg/kg, given IM one hour before induction of anesthesia and atropine sulfate (Dai Han Pharm. Co., Korea) 0.05 mg/kg, given IM fifteen minutes before induction. The right cephalic vein was cannulated (Insyte® 24 G × 3/4". Becton Dickinson Infusion Therapy Systems Inc., USA) for propofol infusion (STC-523, TERUMO Co., Japan) and for the administration of lactated Ringer's solution (10 ml/kg/h). The femoral artery was cannulated with FEP TEFLON cannular (ACCUCATH® 20 G × 11/4", B. Braun Melsungen AG., Malaysia) after local anesthesia and small incision, for continuous monitoring of the blood pressure and for obtaining arterial blood. The cannular was connected with extension catheter (HS-T-25, Hyup Sung Medical Co. Ltd., Korea) and 3-way valve (1 DISCOFIX®-3, B. Braun Melsungen AG., Belgium), then linked physiograph's pressure tranducer (P23XL, SPECTRAMED. USA). Venous and arterial catherization were made within 5 minutes.

Anesthesia were induced in all groups with an IV bolus injection of propofol (Diprivan®, ZENECA Ltd., UK) 5 mg/kg, over 60 seconds for tracheal intubation to supply O_2 and enfluran (Gerolan® soln. Choongwae Pharma Co., Korea) was vaporized with a commercial vaporizer (Enfluratec 5, Ohmeda. USA). As soon as possible, the trachea was intubated with a cuffed tracheal tube(Matrx ID® 5.0, Murphy Eye. Matrx Medical Inc., USA). After anesthesia was induced, all dogs were delivered O_2 at a flow rate of 200 ml/kg/min during 10 minutes and 50 ml/kg/min during 50 minutes for maintenance.

3. Experimental design

After propofol induction, they were treated as follows; 0.5 mg/kg/min of propofol infusion rate in Group, 2.5 vol% of enflurane inhalation at Group, and 0.25 mg/kg /min of propofol infusion rate combined with 1.0 vol% of enflurane inhalation at Group .

4. Determination of cardiopulmonary and adverse effects, and vital signs

Mean arterial pressure(MAP), systolic arterial pressure (SAP), and diastolic arterial pressure(DAP) were measured every 5 minutes by physiograph(GRASS MODEL 79 POLYGRAPH, Grass Instrument Co., USA). Arterial oxygen(PaO_2), and carbon dioxide ($PaCO_2$) tensions and arterial pH(pHa) were measured in 10, 20, 40 and 60 minutes using a blood gas analyzer(AVL COMPACT 1 Blood Gas Analyzer, AVL LIST GmbH Medizintechnik. Austria) and they were corrected for patient temperature(38.5). Serum K^+, Na^+ and Cl^- levels were also checked at that time(AVL 9180 Electrolyte Analyzer, AVL Scientific Corporation. USA). Body temperature(BT) was checked 10 minutes interval, heart rate(HR) and respiratory rate(RR) were recorded every 5 minutes. Safety was monitored(5250 RGM, Ohmeda. USA) by the recording of all adverse events occurring throughout the study and for up to one hour after the end of anesthesia. Muscle rigidity at induction, nausea or vomiting and postoperative shivering were also recorded as adverse effect.

5. Statistical analysis

Data are expressed as the mean± SD and statistically analyzed by Student's *t*-test (comparisons within groups). *P* values of less than 0.05 were considered significant.

Table 1. Experimental groups used in this study

Group	Number of dogs	Anesthetic maintenance
Group I	6	0.5 mg/kg/min propofol infusion
Group II	6	2.5 vol% enflurane inhalation
Group III	6	0.25 mg/kg/min propofol infusion + 1.0 vol% enflurane inhalation

Results

1. Arterial blood pressure

The MAP decreased significantly from the base line in Group II and III (Table 2). Simialr changes occured in SAP and DAP(Table 3, 4). Blood pressure were decreased in all groups, especially into 20 minutes after induction. The MAP, SAP and DAP values of Group III were higher than those of Group II and lower than those of Group I.

2. Respiratory effects

The PaO_2 during anesthesia was high because of O_2 supply, the $PaCO_2$ also increased from the base(awake), and the pH decreased(Table 5, 6, 7). Some changes were occured in all three groups, but they were in normal ranges.

3. Electrolytes in serum

Arterial value of Na^+ and Cl^- were increased from the awake values, but those of K^+ was decreased for 10 minutes then gradually increased(Table 8, 9, 10). Their values were in normal ranges.

4. Physical examination and adverse effects

BT decreased in all anesthetic periods and groups. Although BT in Group II and Group III more decreased that in Group I, they were all in normal ranges(Table 11). HR was not changed significantly in all groups(Table 12). RR of Group II and Group III were lower than that of Group I (Table 13).

Muscle rigidity at induction, nausea or vomiting during maintenance were not discovered in all dogs. Apnea during

Table 2. The changes of MAP (Mean ± SD, mmHg) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time(minute)	Group I	Group II	Group III
Awake(0)	174.72 ± 22.03	131.67 ± 29.36	141.8 ± 25.66
5	159.33 ± 34.04	101.65 ± 21.37**	125.8 ± 22.88§§
10	161.12 ± 29.49	93.88 ± 13.73**	113.9 ± 22.9§§
15	157.78 ± 26.75	88.05 ± 6.37**	107.2 ± 19.95§§
20	144.88 ± 37.64	85 ± 9.06**	108.9 ± 15.9§§
25	147.87 ± 37.54	85.28 ± 10.86**	104.2 ± 22.17§§
30	144.43 ± 35.39	83.43 ± 12.77**	106.1 ± 24.16§
35	146.12 ± 39.01	81.65 ± 11.46**	104.2 ± 24.19§§
40	144.7 ± 34.02	86 ± 12.94*	104.5 ± 25.16§
45	151.38 ± 36.34	82.5 ± 11.88**	107.8 ± 28.75§
50	152.5 ± 38.36	80.27 ± 12.45**	106.1 ± 30.35§
55	153.6 ± 37.24	81.95 ± 12.86**	107.5 ± 30.23§
60	155.55 ± 36.81	83.6 ± 14.92*	110 ± 29.72§

*,**Significantly (*P<0.05, **P<0.01) different from the awake value for 2.5 vol% enflurane
§,§§Significantly (§P<0.05, §§P<0.01) different from the awake value for 1.0 vol% enflurane combined with 0.25 mg/kg/min propofol infusion

Table 3. The changes of SAP(Mean ± SD, mmHg) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time (minute)	Group I	Group II	Group III
Awake (0)	200 ± 20.74	155 ± 27.02	167.1 ± 23.79
5	190.83 ± 34.27	128.33 ± 18.35*	155.8 ± 18.55§
10	190.83 ± 27.82	125 ± 12.25**	148.3 ± 20.89§
15	188.33 ± 23.8	120.8 ± 36.65*	145 ± 16.43§
20	177.33 ± 35.36	118.3 ± 36.83*	143.3 ± 18.35§
25	180.33 ± 34.91	119.17 ± 8.01*	144.2 ± 18.28§
30	178.33 ± 31.89	115.33 ± 11.52**	146.7 ± 22.73
35	180.83 ± 35.97	115 ± 10.95**	144.2 ± 20.35§
40	182.5 ± 33.28	118 ± 10.29*	145 ± 21.45§
45	185.83 ± 33.68	115.83 ± 13.19*	145 ± 21.45
50	187.5 ± 37.52	114.17 ± 15.3*	145 ± 24.69§
55	187.5 ± 36.57	114.17 ± 14.29**	145.8 ± 23.11§
60	190 ± 36.47	115.83 ± 15.63*	148.3 ± 26.58

*,**Significantly (*P<0.05, **P<0.01) different from the awake value for 2.5 vol% enflurane
§Significantly (§P<0.05) different from the awake value for 1.0 vol% enflurane combined with 0.25 mg/kg/min propofol infusion

Table 4. The changes of DAP (Mean ± SD, mmHg) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time (minute)	Group I	Group II	Group III
Awake (0)	162.08 ± 23.15	120 ± 31.14	129.6 ± 27.13
5	143.33 ± 35.45	88.33 ± 23.38**	110.8 ± 25.18§§
10	146.67 ± 31.41	78.33 ± 14.72**	96.67 ± 24.01§§
15	142.5 ± 28.59	71.67 ± 7.53**	88.33 ± 22.29§§
20	128.67 ± 39.09	68.33 ± 11.25**	91.67 ± 15.38§§
25	131.67 ± 39.07	68.33 ± 13.29**	84.17 ± 24.38§§
30	127.5 ± 37.38	65 ± 14.83**	85.83 ± 25.38§
35	129.17 ± 40.17†	65 ± 14.14**	85.83 ± 27.64§
40	125.83 ± 34.84†	70 ± 16.43*	84.17 ± 27.82§
45	134.17 ± 38	65.83 ± 13.93**	88.33 ± 32.04§
50	135 ± 38.99	63.33 ± 14.02**	86.67 ± 33.41§
55	136.67 ± 37.9	65.83 ± 14.63**	88.33 ± 34.01§
60	138.33 ± 37.37	67.5 ± 16.36*	90.83 ± 31.53§

†Significantly (†P<0.05) different from the awake value for 0.5 mg/kg/min propofol infusion

*,**Significantly (*P<0.05, **P<0.01) different from the awake value for 2.5 vol% enflurane

§,§§Significantly (§P<0.05; §§P<0.01) different from the awake value for 1.0 vol% enflurane combined with 0.25 mg/kg/min propofol infusion

Table 5. The changes of PaO_2 (Mean ± SD, mmHg) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time (minute)	Group I	Group II	Group III
Awake(0)	111.23 ± 22.65	98.18 ± 24.13	111.48 ± 25.22§§
10	178.32 ± 28.56†	183.07 ± 41.76*	203.15 ± 25.39§§
20	167.47 ± 45.36	175.77 ± 32.99**	187.35 ± 30.14§§
40	155.85 ± 36.59	171.73 ± 30.54**	171.68 ± 30.05§
60	159.65 ± 22.39	164.68 ± 32.24	171.58 ± 22.92

†Significantly (†P<0.05) different from the awake value for 0.5 mg/kg/min propofol infusion

*,**Significantly (*P<0.05, **P<0.01) different from the awake value for 2.5 vol% enflurane

§,§§Significantly (§P<0.05, §§P<0.01) different from the awake value for 1.0 vol% enflurane combined with 0.25 mg/kg/min propofol infusion

propofol induction appeared in 2 dogs(18 and 25 seconds, respectively) in Group I, one dog(35 seconds) in Group II and 3 dogs(15, 27 and 34 seconds, respectively) in Group III.

Discussion

Enflurane and propofol depress cardiopulmonary functions, however, enflurane seems more depressing than propofol and enflurane combined with propofol. Enflurane depressed

Table 6. The changes of $PaCO_2$ (Mean ± SD, mmHg) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time (minute)	Group I	Group II	Group III
Awake (0)	36 ± 5.23	37.7 ± 6.37	35.32 ± 4.29
10	40.22 ± 7.67	40.82 ± 6.14	38.62 ± 4.09
20	38.55 ± 9.13	38.63 ± 6.24	38.62 ± 8.51
40	44.67 ± 15.4	41.72 ± 7.35*	42.63 ± 7.95§
60	39.58 ± 9.96	38.9 ± 3.62	42.6 ± 8.39

*Significantly (*P<0.05) different from the awake value for 2.5 vol% enflurane

§Significantly (§P<0.05) different from the awake value for 1.0 vol% enflurane combined with 0.25 mg/kg/min propofol infusion

Table 7. The changes of pHa (mean ± SD) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time (minute)	Group I	Group II	Group III
Awake (0)	7.28 ± 0.05	7.26 ± 0.09	7.31 ± 0.05
10	7.27 ± 0.07	7.26 ± 0.03	7.26 ± 0.04
20	7.23 ± 0.11	7.26 ± 0.05	7.26 ± 0.05
40	7.25 ± 0.11	7.24 ± 0.05	7.27 ± 0.04
60	7.25 ± 0.09	7.25 ± 0.05	7.26 ± 0.06

Table 8. The changes of arterial Na^+ level (Mean ± SD, mEq/L) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time (minute)	Group I	Group II	Group III
Awake (0)	144.67 ± 4.84	142.83 ± 5.04	145 ± 2.53
10	145.33 ± 4.93	146.67 ± 3.01	146.67 ± 2.07
20	146.17 ± 5.12	146.33 ± 3.61	146.33 ± 2.07§
40	146.5 ± 4.76†	145.5 ± 3.73	145.83 ± 1.94
60	146 ± 4.6‡	148.5 ± 3.45	145.5 ± 2.17

†,‡Significantly (†P<0.05, ‡P<0.01) different from the awake value for 0.5 mg/kg/min propofol infusion

§Significantly (P<0.05) different from the awake value for 1.0 vol% enflurane combined with 0.25 mg/kg/min propofol infusion

Table 9. The changes of arterial K^+ level (Mean ± SD, mEq/L) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time (minute)	Group I	Group II	Group III
Awake (0)	3.6 ± 0.29	3.83 ± 0.63	3.57 ± 0.33
10	3.08 ± 0.22‡	2.93 ± 0.14*	2.87 ± 0.36§§
20	3.1 ± 0.25†	2.92 ± 0.49	2.95 ± 0.29§§
40	3.05 ± 0.3†	3.13 ± 0.34	3.07 ± 0.14§
60	3.15 ± 0.28†	3.12 ± 0.31	3.37 ± 0.35

†,‡Significantly (P<0.05, P<0.01) different from the awake value for 0.5 mg/kg/min propofol infusion

*Significantly (*P<0.05) different from the awake value for 2.5 vol% enflurane

§,§§Significantly (§P<0.05, §§P<0.01) different from the awake value for 1.0 vol% enflurane combined with 0.25 mg/kg/min propofol infusion

Table 10. The changes of arterial Cl^- level(Mean ± SD, mEq/L) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time(minute)	Group I	Group II	Group III
Awake(0)	112.83 ± 2.79	106.5 ± 9.91	113.17 ± 2.04
10	113.67 ± 3.56	112.67 ± 3.56	115 ± 3.29
20	114.5 ± 5.01	112.83 ± 4.92	114.83 ± 2.71
40	115.17 ± 3.82	111.83 ± 2.93	114.67 ± 2.07
60	114.83 ± 4.31	113.83 ± 4.12	113 ± 2

‡Significantly(‡P<0.05) different from the awake value for 0.5 mg/kg/min propofol infusion

Table 11. The changes of body temperature(Mean ± SD, °C) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time(minute)	Group I	Group II	Group III
Awake(0)	38.15 ± 0.85	38.17 ± 0.29	38.27 ± 0.92
10	37.57 ± 0.81	37.2 ± 0.79*	36.83 ± 1.65‡
20	37.4 ± 0.84	36.77 ± 1.2	36.67 ± 1.86
30	37.32 ± 0.83	36.65 ± 1.39	36.6 ± 1.79
40	37.2 ± 0.84	36.45 ± 1.58*	36.48 ± 1.74

*Significantly(*P<0.05) different from the awake value for 2.5 vol% enflurane
‡Significantly(‡P<0.05) different from the awake value for 1.0 vol% enflurane combined with 0.25 mg/kg/min propofol infusion

Table 12. The changes of heart rate(Mean ± SD, beats/min) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time (minute)	Group I	Group II	Group III
Awake (0)	136 ± 27.54	115 ± 30.22	141 ± 18.49
5	142 ± 21.01	130 ± 24.79	128 ± 15.49‡
10	148 ± 20.58	119 ± 26.94	124 ± 22.02
15	148 ± 20.32	116 ± 26.74	123 ± 25.67
20	145 ± 25.29	114 ± 26.83	119 ± 27.73
25	143 ± 23.82	110 ± 27.54	118 ± 28.31
30	138 ± 25.17	111 ± 28.59	119 ± 30.46
35	140 ± 25.08	112 ± 27.80	121 ± 29.98
40	140 ± 25.08	110 ± 27.01	119 ± 31.16
45	139 ± 22.90	110 ± 30.54	116 ± 22.34
50	138 ± 23.08	112 ± 32.13	118 ± 24.79
55	138 ± 21.80	111 ± 32.81	117 ± 21.72
60	140 ± 20.32	111 ± 32.81	116 ± 22.02

‡Significantly(‡P<0.05) different from the awake value for 1.0 vol% enflurane combined with 0.25 mg/kg/min propofol infusion

the sympathetic activity accompanied with a decrease of blood pressure in a dose-dependent manner[19,33,35]. The result that enflurane produced a dose-dependent decrease of blood pressure is consistent with the previous studies in humans[4], and cats[37].

Table 13. The changes of respiratory rate(Mean ± SD, breaths/min) in dogs anesthetized with enflurane, propofol or enflurane/propofol combination

Time (minute)	Group I	Group II	Group III
Awake(0)	29 ± 11.44	19.67 ± 7.94	16.67 ± 5.75
5	20.67 ± 6.02	15.33 ± 7.12	14.17 ± 6.21
10	20.50 ± 8.71	12.5 ± 7.89	14 ± 6.07
15	19.67 ± 6.98	11.33 ± 6.06	13 ± 5.62
20	22.33 ± 7.53	11.33 ± 6.25	10.83 ± 5.04
25	20 ± 5.06	11.83 ± 7.03	11.67 ± 4.63
30	20.17 ± 5.19	11.67 ± 5.99	14 ± 6.72
35	20 ± 3.85	11.5 ± 6.72	14.33 ± 5.85
40	21.83 ± 5.88	11.83 ± 6.99	14.33 ± 8.07
45	23.83 ± 7.11‡	11.17 ± 6.46	14.17 ± 7.39
50	23.33 ± 8.16	11 ± 5.93	14.83 ± 8.5
55	23.67 ± 8.02	12 ± 5.51*	14.17 ± 7.7
60	24.67 ± 7.89	11.17 ± 5.88	14.17 ± 7.6

‡Significantly(‡P<0.05) different from the awake value for 0.5 mg/kg/min propofol infusion
*Significantly(*P<0.05) different from the awake value for 2.5 vol% enflurane

Enflurane anesthesia is associated with epileptiform cortical and motor activity[3,13], enhanced by hypocarbia[21,30]. Thus enflurane may be used to provoke a quiescent epileptic focus into activity during the investigation of seizure disorders. When the patients is already anesthetized, it may be the drug of choice for this purpose. Hypoventilation will increase the likelihood of the focus becoming active and reduce the concentration of enflurane needed to induce spiking activity[7]. Caution will be necessary when the patient has a disorder involving abnormally low intracranial compliance. Abnormal muscle twitching occuring with enflurane has been previously reported for the dog[18] and man[30], but in this study, it was not obseved. The twitching can be related to grand mal seizure-like activity in the electroencephalogram of dogs anesthetized with enflurane, it can be prevented by narcotic premedication or thiopental induction. In the cat, enflurane produces bursts of high-voltage spikes seperated by periods of total electrical silence[18].

Enflurane produces concentration-dependent biphasic effects on perforant path to dentate granule evoked field potentials. Low concentrations(0.5 to 2 vol%) help facilitate transmission in the dentate granule, whereas higher concentrations(2.5 to 4 vol%) produce depression[20].

Enflurane-induced reduction in myocardial contractility was not due to ischemia, it likely reflected a direct negative inotropic effect. Enflurane anesthesia was associated with more AV nodal depression, only at faster heart rates than either halothane or isoflurane. These rate-related effects are important in the genesis of supraventricular reentrant tachyarrhythmias. Enflurane has more depressant effects on AV

nodal recovery properties than halothane or isoflurane; however, there were no difference demonstrated on slow AV nodal conduction[11]. Enflurane produce dose-dependent negative inotropic effects in the intact dog, accompanied by equivalent decreases in cardiac oxygen demand[22]. Halothane induce a concentration-dependent lengthening of RR interval and bradycardia, whereas enflurane did not. Both agents slowed longitudinal and transverse ventricular conduction velocity with no anisotropic change. Both anesthetics induced a decrease in the coronary perfusion pressure that was significant from 1 vol%, but that was not concentration-dependent.

Volatile anesthetics affect conduction and refractoriness *via* the modulation of various ionic currents flowing through the myocardial cell membrane. Arterial blood gas tensions and plasma concentrations of Na^+ and K^+ did not change significantly during the entire course of anesthesia in enflurane and isoflurane[40]. In this study, Na^+ and Cl^- were little increased and K^+ was decreased significantly in all groups at 10 minutes after induction, then increased progressively. Their values were changed manifoldly, but in normal ranges.

Enflurane produced dose-related decreases in cardiac output by 24% and 52% at 1.7% and 3.4% enflurane, respectively and end-systolic pressure-volume relation by 31% and 57% at 1.7% and 3.4% enflurane, respectively. The mean arterial blood pressure(MAP) and heart rate decreased at 1.7% and 3.4% enflurane[34]. Halothane and enflurane decreases total hepatic blood flow and hepatic O_2 supply to various degrees[2,31]. Respiratory rate was significantly lower and arterial carbon dioxide was higher during maintenance anesthesia with enflurane than with halothane.

Enflurane causes concentration-dependent increases in coronary blood flow, and in myocardial oxygen consumption and myocardial segmental shortening accompanied by equivalent decreases in cardiac oxygen demand. Enflurane produces dose-dependent negative inotropic effects and direct coronary vasodilating effect in the intact dog. In healthy dogs, an anesthetic technique utilizing fentanyl/enflurane offers considerable cardiovascular sparing compared to enflurane alone, provided an anticholinergic is administered to prevent bradycardia[39]. The opioid/inhalant anesthetic techniques were less depressant on cardiovascular function than standard inhalant techniques. To prevent hypoventilation, respiration is usually controlled to maintain arterial carbon dioxide at about 40 mmHg, but decrease in heart rate may not be treated if arterial blood pressure is well maintained[15].

Central nervous system depressants and narcotic analgesics such as morphine, butorphanol, nalbuphine, fentanyl and remifentanyl reduce the minimum alveolar concentration (MAC) of volatile anesthetics[10,23,26,27,36] and propofol[5,16]. Narcotic analgesics are frequently used as supplements to nitrous oxide or potent inhalational agents and have even used in high doses as anesthetics[26], especially fentanyl have been advocated as primary or sole anesthetic agent[27]. The use of high dose of narcotic analgesics as anesthetics is based primarily on their lack of cardiovascular depression, however, respiratory depression is a significant problem in the postoperative period.

Propofol is a novel nonbarbiturate, IV administered anesthetic agent that has recently been introduced into medical anesthetic practice. The anesthesia induced by this compound is reported to be distinguished by rapid onset, prompt recorvery, lack of cumulation, and absence of excitatory phenomena on induction of recovery[41,42]. Induction of anesthesia with propofol is accompanied by a decrease in arterial pressure in association with decreases in cardiac output and systemic vascular resistance[1,9]. Respiratory depression associated with propofol administration should be anticipated and may necessitate assisted ventilation.

In anesthetic concentration of enflurane and propofol, propofol depressed respiratory rate less than that of enflurane. Both enflurane and propofol had cardiopulmonary depression effects, but in this study, enflurane depressed SAP, DAP, MAP, BT, HR and RR values more than that of popofol.

In conclusion, the arterial blood pressure effects of enflurane(1.0 vol%) combined with propofol(0.25 mg/kg/min) were greater than those of propofol(0.5 mg/kg/min) alone but less than those of enflurane(2.5 vol%) alone. The other values were in similar patterns and normal ranges. Thus, results of this study suggested that enflurane(1.0 vol%) combined with propofol(0.25 mg/kg/min) can be used as a anesthetics in dogs.

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개에서 Enflurane과 Propofol의 병용이 심폐기능에 미치는 영향

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요 약 : 일반적인 마취용량에서의 enflurane과 propofol 단독 투여와 두 마취제의 병용 투여가 심혈관계에 미치는 영향을 비교하기 위해 본 실험을 수행하였다. 진정제(acepromazine 0.05 mg/kg) 투여 후 atropine(0.05 mg/kg)으로 전처치한 실험견 18두를 3개군으로 무작위 분류하고 각 군에 propofol infusion 0.5 mg/kg/min(Group I), enflurane 2.5 vol%(Group II), enflurane 1.0 vol%와 propofol infusion 0.25 mg/kg/min(Group III)을 각각 1시간 동안 산소공급하에서 투여하였다. 대퇴동맥에 설치한 카테터를 통하여 전 실험기간에 걸쳐 Physiograph로 MAP(Mean Arterial Pressure), SAP(Systolic Arterial Pressure), DAP(Diastolic Arterial Pressure)를 기록하고 동맥혈을 채취하여 Na^+, K^+, Cl^- 등 전해질 농도와, PaO_2(arterial oxygen tension), $PaCO_2$(arterial carbon dioxide tension), pHa(arterial pH)를 측정하였다. 마취 전후의 체온, 심박수, 호흡수를 측정하였다. 특히 심혈관계와 관계된 검사(MAP, SAP, DAP, 체온)에서 마취유도 후 20분 동안은 모든 group에서 감소가 뚜렷하였다. Group II와 Group III에서 유의적인 감소($p<0.05$, 0.01)를 보였으며 Group III는 Group I보다는 낮았으나 Group II보다는 높은 수치를 기록하였다. 산소공급과 관련하여 PaO_2의 증가($p<0.05$, 0.01)가 있었으며 전해질 검사에서는 Na^+와 K^+의 유의적인 변화($p<0.05$, 0.01)가 나타났다. 실험결과 유의성있는 변화가 나타났지만 모든 결과들이 정상범위내에 있었고 뚜렷한 부작용이 나타나지 않았으므로 enflurane 1.0 vol%와 propofol 0.5 mg/kg/min 병용투여는 개 마취에 있어서 적용가능한 방법이라 생각된다.