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The Effect of Doxapram on Cardiopulmonary Function in Dogs under Total Intravenous Anesthesia with Remifentanil and Propofol

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Abstract : We investigated the effect of constant rate infusion (CRI) with doxapram on cardiopulmonary function during total intravenous anesthesia (TIVA) with remifentanil and propofol CRI in dogs. Fifteen male Beagle dogs were randomly divided into 3 groups. All groups were premedicated with medetomidine (20 μg/kg, IV) and anesthetized by remifentanil/propofol CRI for one and half hour. At the initiating of the anesthesia, different doses of doxapram for each group were administrated as the followings; D1 group - doxapram 0.25 mg/kg bolus followed by doxapram 8.33 μg/kg/min, D2 group - doxapram 2 mg/kg bolus followed by doxapram 66.66 μg/kg/min, control group - normal saline. The anesthetic depth for surgery was well maintained in all groups throughout the anesthetic periods. The respiratory rate was significantly higher in D2 group than that of control group ($p < 0.05$). The values of PaO_2 and SaO_2 were significantly increased in both D1 and D2 groups compared with control group ($p < 0.05$). High dose of doxapram (D2 group) significantly decreased the level of $PaCO_2$ compared with control group ($p < 0.05$). The values of systolic, mean and diastolic arterial pressure were significantly increased in doxapram 2 group ($p < 0.05$). There were no significant differences in the values of heart rate and pH of arterial blood. Therefore, doxapram CRI may be useful to alleviate the suppression of cardiopulmonary function including hypoxia and hypotension during TIVA with remifentanil and propofol in dogs.

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

Introduction

Total intravenous anesthesia (TIVA) is an anesthetic method that is maintained only using intravenous anesthetics injection. It is used in veterinary and human medicines as an alternative of inhalation anesthesia (8,18). TIVA has no hazard of atmospheric pollution, allows easy control over the depth of anesthesia and has complete and fast awakening. Furthermore, TIVA does not require specialized, costly and bulky equipment, such as, vaporizer or oxygen delivery system. It requires just a simple IV pump.

Rapid onset of action and short half-life are essential in ideal drugs for TIVA. Nowadays, the combination of remifentanil and propofol is considered as the most adequate agent.

Propofol is a most commonly used agent for TIVA, because of smooth induction, rapid onset and clearance, short duration of action and rapid recovery (7). Propofol has antiemetic effects, and, its use results in a lower incidence of postoperative nausea and vomiting compared with volatile anesthesia agent (17). But propofol has only minimal analgesic effect, it need concurrent administration of proper analgesic agent (24). Vascular pain on venous injection has been also reported in human (7). The most popular combination of TIVA is propofol with an opioid such as fentanyl, alfentanil, or remifentanil. Remifentanil has the most short recovery time in opioids until now (14).

Remifentanil is an ultra-short acting phenylpiperidine opioid analgesic, and a potent μ-opioid receptor agonist. It is rapidly hydrolyzed by blood and tissue esterases. Therefore, remifentanil has excellent properties for TIVA such as rapid onset, short latency to its peak effect, high clearance, short elimination half-life, low accumulation effect and rapid recovery. Such unique characteristics make remifentanil suitable for long surgical procedures (4,5).

When propofol is coadministrated with remifentanil, in order to add analgesic effect, propofol reduces remifentanil dose in synergistic manner (11). However, propofol has some adverse effects in cardiovascular and respiratory system (13, 19). Respiratory depression and apnea are most common side effects of propofol. It also induces hypotension by arteriolar vasodilation, especially in hypovolemic dogs. Similarly to propofol, remifentanil dose-dependently causes respiratory depression and hypotension (10,20). While propofol has minimal alteration of heart rate, remifentanil can cause bradycardia. It was reported that synergistic respiratory depression occurred when remifentanil and propofol were co-administrated (15).

Doxapram is a respiratory stimulant that synthesized in the 1960s. It indirectly but selectively stimulated medullary respiratory neurons at low dose, and non-selectively, directly activated respiratory and non-respiratory medullary neurons

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(9). Doxapram is usually used as a stimulant in respiratory failure such as chronic obstructive pulmonary disease, and apnea of the new born. It is also used for stimulating central nervous system in drug-induced central nervous system depression (21). Doxapram is metabolized very rapidly when given intravenously and has short duration of action (3). In postanesthesia, doxapram improve oxygenation, shorten recovery time and prevent from shivering during recovery period (25). Side effects of doxapram are relatively minor. Most common side effects are cough, dyspnea, tachypnea, headache, dizziness, nausea, vomiting, hypertension, flushing and urinary retention (2,22). Doxapram is contraindicated in patients with specific disorders such as mechanical physical obstructed respiratory tract, severe hypertension, and epilepsy (26).

It was reported that doxapram reversed the morphine-induced respiratory depression without alteration of analgesia and morphine requirements (6). Doxapram induced release of cathecolamines, such as epinephrine and dopamine, and it increase systemic blood pressure and heart rate by cardiac contractility increase (1).

In this study, we investigated the effect of doxapram constant rate infusion (CRI) on cardiopulmonary function during TIVA with remifentanil and propofol CRI in dogs. Using doxapram CRI, we expected the possibility to increase the safety of anesthesia with remifentanil and propofol CRI.

Materials and Methods

Animals

Fifteen adult beagle dogs (8.53 ± 1.00 kg in weight, 17.5 ± 1.4 months of age) were used in the study. Each dog was housed individually, and fed commercial dry pellet food and water *ad libitum*. Food, but not water, was withheld for 12 hours before each experiment. All animals were clinically healthy, based on physical examination, complete blood count and serum biochemistry done before experiment.

The dogs were randomly assigned to 3 groups, and each group consisted of 5 dogs.

Procedures

This study was approved by the Kyungpook National University Animal Ethics Committee (KNU-2010-8). One day before experiment, an arterial catheter (pediatric jugular catheterization set®, arrow international, Inc., USA) was inserted into the right femoral artery. The catheter was used for measuring arterial blood pressure, heart rate, and blood collecting. For inserting of the arterial catheter, anesthesia was inducted by propofol and maintained by isoflurane/oxygen. 2% lidocaine (JEIL Lidocaine HCL Inj®, Jeil Pharmaceutical Co., Ltd, Korea) was subcutaneously injected into the incision site for infiltrated anesthesia. The catheter tip was inserted into the femoral artery about 5 cm forwarded to the aorta, and the catheter, through a tunnel beneath of the subcutis, was exited on the median sacral crest. It filled with saline diluted heparin (10 IU/ml) as an anticoagulant. The arterial catheter was flushed with saline diluted heparin two times a day.

The dogs were placed in experimental room at least 1 hour before experiment for acclimation. The arterial catheter was connected to a polygraph (Model 7P1, Grass Instrument Co., USA). Following measurement of baseline values in setting position, a 22 gage cephalic catheter was placed for drug administration.

All dogs were premedicated with medetomidine (Domitor®; Orion Corporation ANIMAL HEALTH, Finland, 20 μg/kg) 10 min before CRI and anesthetized with remifentanil and propofol CRI for one and a half hour.

Normal saline (control group), doxapram 0.25 mg/kg loading followed by doxapram 8.33 μg/kg/min (D1 group), and doxapram 2 mg/kg loading followed by doxapram 66.66 μg/kg/min (D2 group) were co-administrated.

Loading dose of porpofol (2 mg/kg, IV) was administrated and, concurrently, infusion of propofol (Provive 1%®, Claris Lifesciences Ltd., India, 0.3 mg/ kg/min) and remifentanil (Ultiva®, GlaxoSmithKline, Italy, 0.5 μg/kg/min) was followed.

All dogs were positioned in right lateral recumbency after the induction of general anesthesia.

Evaluation Items

Heart rate and systolic/diastolic pressure were measured with the polygraph. Values of heart rate were recorded at a speed of 25 mm/s and were calculated from the mean of 10 s arterial pulse wave records in each period. Systolic and diastolic pressures were recorded at a speed of 50 mm/min and were calculated from the mean of 1 min records in each period. Respiratory rate was measured at times 5, 10, 20, 40, 60, and 90 min after CRI.

Arterial blood sample was collected through the right femoral arterial catheter. A mount of blood sample in each period was 0.5 ml and catheter flushing with 0.5 ml heparinized saline was followed just after each blood sampling. pH, PaO_2, SaO_2, $PaCO_2$ were measured by an portable blood gas analyzer (i-STAT® Analyzer MN300, i-STAT Co. Ltd, USA) with test cartridges (i-STAT® G3+ cartridge, Abbott Point of Care Inc., USA). The analysis was carried out within 10 s after blood sampling.

Pedal withdrawal reflex test was performed to determine the clinical level of surgical anesthesia. Interdigital regions in the forelimbs were pinched with a crile forceps to first-rachet-lock for 10 s. The pedal withdrawal reflex test was immediately stopped if the dog showed a positive response. The tests were evaluated at 10, 20, 40, 60, 90 min after CRI initiation.

After the cessation of CRI, the mean times of latency to first head up movement (MHT), to taking the posture of sternal recumbency (MST) and to walking (MWT) were measured as behavioral changes. The walking was defined to walk at least 5 steps.

All data were expressed as mean ± standard deviation, and the statistical analysis was carried out using SPSS (version 12.0, spss Inc, USA).

Arterial blood pressures, heart rates, respiratory rates, blood gas analysis were statistically analyzed by two-way repeated measure analysis of variance (ANOVA), and if there was interaction effect, bonferroni test was followed as post-hoc test.

Kruskal-Wallis test (nonparametric method) and one-way ANOVA (parametric method) were used to analyze behavioral changes. Difference from control or between groups were considered statistically significant when $p < 0.05$.

Results

Heart rate

The two-way repeated measure ANOVA showed that neither the treatment group factor nor the time course was significantly different. The interaction of two factors was not significant (Table 1).

Mean heart rates of control group were higher than those of doxapram treatment groups throughout anesthetic period (Fig 1).

Table 1. Statistical analysis result of heart rates in control and experiment groups. Data were analyzed by two-factor repeated measures ANOVA followed by a Bonferroni test

Heart rate	F-value	p-value
Tests of between-subjects effects of group	0.457	0.644
Tests of within-subjects contrasts of time	0.852	0.374
Tests of within-subjects contrasts of group*time interaction effect	2.866	0.096

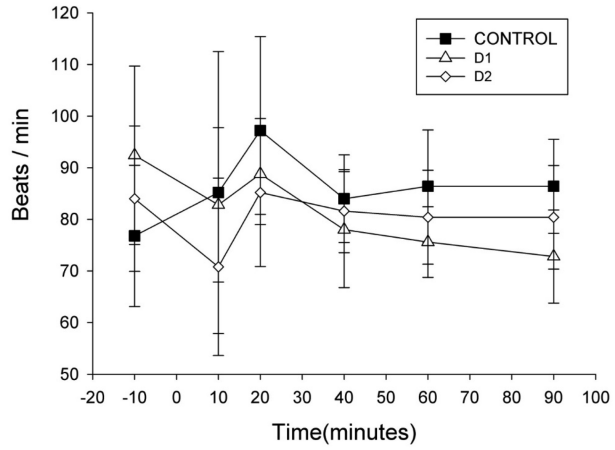

Fig 1. The change of heart rates in control and experiment groups. Data were expressed as mean ± standard deviation, and $n = 5$/group.

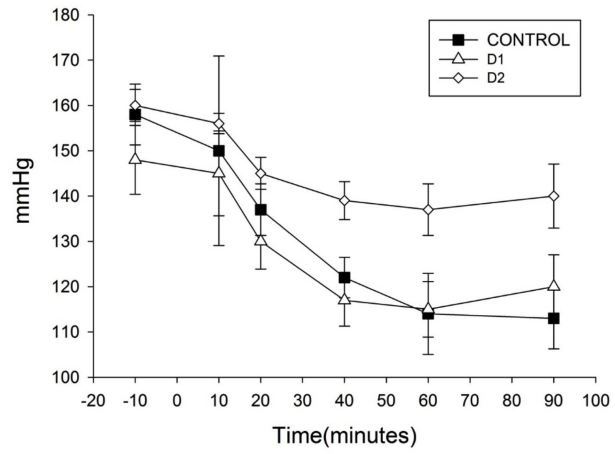

Fig 2. The change of SAP values in control and experiment groups. Data were expressed as mean ± standard deviation, and $n = 5$/group.

Arterial pressure

After anesthesia, systolic arterial pressure (SAP) was decreased in all groups compare with each baseline. In D2 group, just after doxapram injection, a little increase of blood pressure was observed. As shown in Fig 2, mean SAP of control group was continuously decreased but those of doxapram treatment groups were increased after 60 min.

In systolic blood pressures, two-way repeated measure ANOVA revealed that a difference over time ($p < 0.001$), and a difference over treatment ($p < 0.001$) was significant, and the interaction between treatment and time was also significantly different ($p < 0.05$). In Bonferroni test, there was significant difference between control group and D2 group (Table 2).

Diastolic arterial pressures (DAP) were increased at 10 min in all groups but it became to be lower than each baseline after 40 min in all groups. DAP was sequentially de-

Table 2. Statistical analysis result of systolic arterial pressure in control and experiment groups. Data were analyzed by two-factor repeated measures ANOVA followed by a Bonferroni test. *, ** indicates a significant differences ($p < 0.05$, $p < 0.001$)

Systolic arterial pressure	F-value	p-value
Tests of between-subjects effects of group	16.655	0.000**
Tests of within-subjects contrasts of time	216.413	0.000**
Tests of within-subjects contrasts of group*time interaction effect	9.831	0.003*

Table 3. Statistical analysis result of diastolic arterial pressure in control and experiment groups. Data were analyzed by two-factor repeated measures ANOVA followed by a Bonferroni test. *, ** indicates a significant differences ($p < 0.05$, $p < 0.001$)

Diastolic arterial pressure	F-value	p-value
Tests of between-subjects effects of group	7.369	0.008*
Tests of within-subjects contrasts of time	353.783	0.000**
Tests of within-subjects contrasts of group*time interaction effect	13.341	0.001**

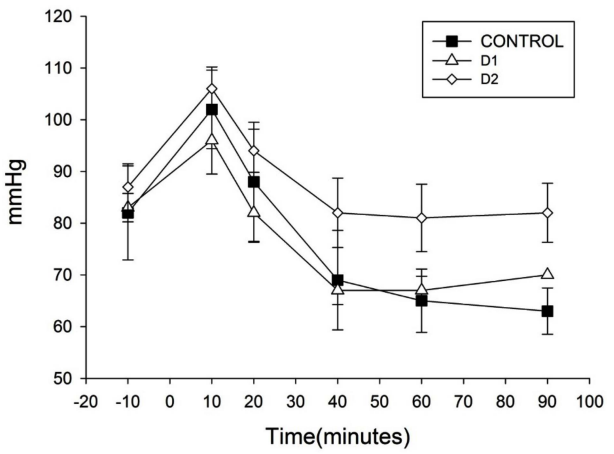

Fig 3. The change of DAP values in control and experiment groups. Data were expressed as mean ± standard deviation, and $n = 5$/group.

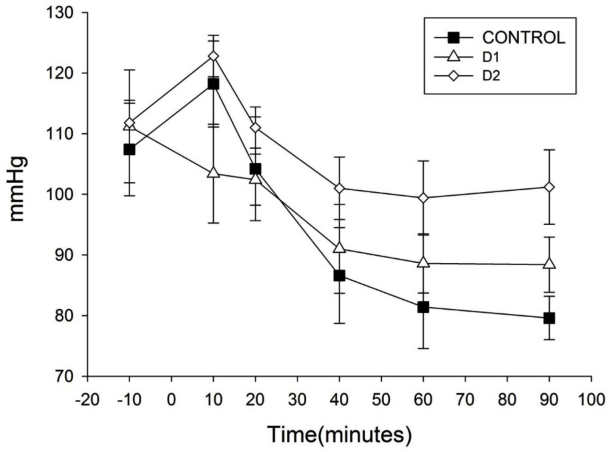

Fig 4. The change of MAP values in control and experiment groups. Data were expressed as mean ± standard deviation, and $n = 5$/group.

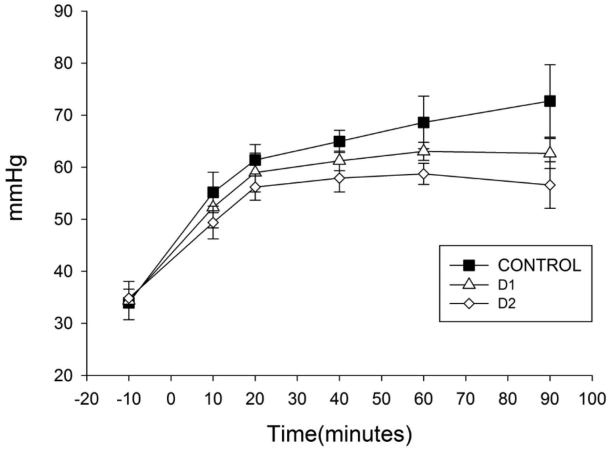

Fig 5. The change of $PaCO_2$ values in control and experiment groups. Data were expressed as mean ± standard deviation, and $n = 5$/group.

Table 4. Statistical analysis result of mean arterial pressure in control and experiment groups. Data were analyzed by two-factor repeated measures ANOVA followed by a Bonferroni test. *, ** indicate a significant differences ($p < 0.05$, $p < 0.001$)

Mean arterial pressure	F-value	p-value
Tests of between-subjects effects of group	8.547	0.005*
Tests of within-subjects contrasts of time	177.407	0.000**
Tests of within-subjects contrasts of group*time interaction effect	7.833	0.007*

creased until the end of CRI only in control group, it was increased after 40 min and 60 min in D1 and D2 groups, respectively.

As shown in Table 3, the analysis showed that the time course ($p < 0.001$) and the treatment factor ($p < 0.05$) were significantly different, and their interaction was significant ($p < 0.001$).

The post-hoc analysis using Bonferroni test revealed that there was significant difference between control group and D2 group, and between D1 group and D2 group.

Mean arterial pressure (MAP) was in normal range in all groups. Two-way repeated measure ANOVA revealed that a difference over time ($p < 0.001$), a difference over treatment ($p < 0.05$), and the interaction between treatment and time were significant ($p < 0.05$). There were significant differences between control group and D2 group and also between D1 group and D2 group in Bonferroni test.

$PaCO_2$

After anesthesia, $PaCO_2$ was increased in all groups compare with each baseline. As shown in Fig 5, mean value of $PaCO_2$ was continuously increased throughout anesthesia in control group but decreased in doxapram treatment groups after 60 min.

Range of $PaCO_2$ after anesthesia was 55.16 ± 3.88 to 72.72 ± 6.96 in control group, 52.28 ± 3.92 to 63.04 ± 1.74 in D1 group, and 49.36 ± 3.14 to 58.72 ± 2.04 in D2 group (Fig 5).

Statistical analysis reveal that time course ($p < 0.001$), treatment group factor ($p < 0.05$) were significantly different,

Table 5. Statistical analysis result of $PaCO_2$ in control and experiment groups. Data were analyzed by two-factor repeated measures ANOVA followed by a Bonferroni test. *, ** indicate a significant differences ($p < 0.05$, $p < 0.001$)

$PaCO_2$	F-value	p-value
Tests of between-subjects effects of group	11.159	0.002*
Tests of within-subjects contrasts of time	395.627	0.000**
Tests of within-subjects contrasts of group*time interaction effect	9.778	0.003*

Table 6. Statistical analysis result of PaO_2 in control and experiment groups. Data were analyzed by two-factor repeated measures ANOVA followed by a Bonferroni test. *, ** indicate a significant differences ($p < 0.05$, $p < 0.001$)

PaO_2	F-value	p-value
Tests of between-subjects effects of group	17.796	0.000**
Tests of within-subjects contrasts of time	25.319	0.000**
Tests of within-subjects contrasts of group*time interaction effect	3.274	0.073

and time*group interaction ($p < 0.05$) was significant (Table 5). There was significant difference between control group and D2 group in Bonferroni test.

PaO_2

Range of PaO_2 after anesthesia was 35.6 ± 0.89 to 47 ± 11.38, 45.6 ± 5.94 to 59.4 ± 6.27, and 48.4 ± 8.62 to 70.8 ± 7.36 in control group, D1 group and D2 group, respectively (Fig 5).

As shown in Table 6, the analysis showed that the time course ($p < 0.001$) and the treatment factor ($p < 0.001$) were significantly different, but their interaction effect was not significant (Table 5).

SaO_2

After anesthesia, mean SaO_2 values had range of 57.4 ± 3.21 to 71 ± 9.77 in control group, 71 ± 8.51 to 84 ± 6.28 in D1 group, and 73.8 ± 11.14 to 90 ± 2.83 in D2 group (Fig 7).

The analysis revealed that time course ($p < 0.05$) and treat-

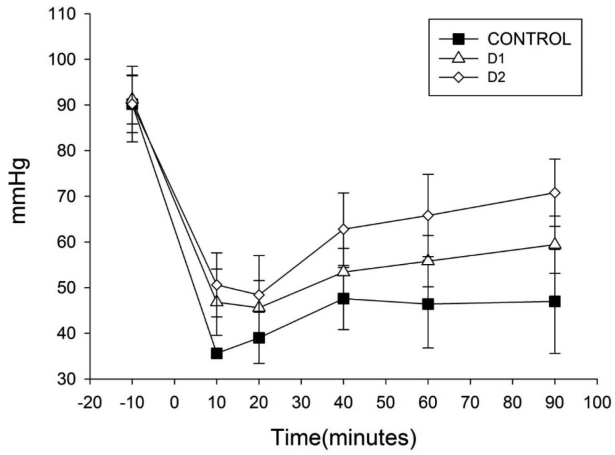

Fig 6. The change of PaO_2 values in control and experiment groups. Data were expressed as mean ± standard deviation, and n = 5/group.

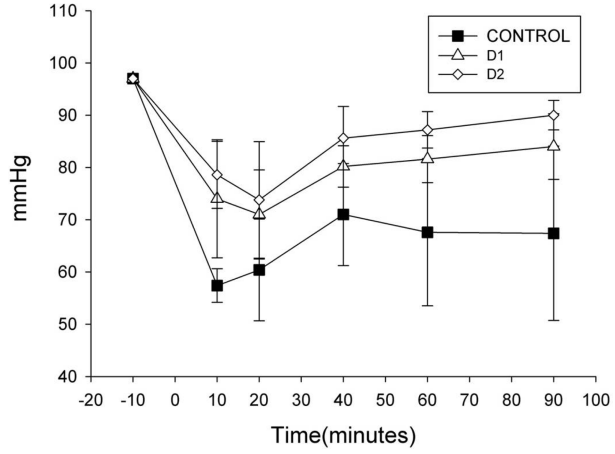

Fig 7. The change of SaO_2 values in control and experiment groups. Data were expressed as mean ± standard deviation, and n = 5/group.

Table 7. Statistical analysis result of PaO_2 in control and experiment groups. Data were analyzed by two-factor repeated measures ANOVA followed by a Bonferroni test. * indicates a significant difference ($p < 0.05$)

SaO_2	F-value	p-value
Tests of between-subjects effects of group	9.963	0.003*
Tests of within-subjects contrasts of time	4.933	0.046*
Tests of within-subjects contrasts of group*time interaction effect	2.448	0.128

ment group factor ($p < 0.05$) were significantly different, whereas interaction effect was not significant (Table 7).

pH

In control group, values of pH were continuously decreased until cessation of CRI, while they were increased after 40 min in D1 group. D2 group has increase aspect at 90 min (Fig 8).

As shown in Table 8, difference over the time course was

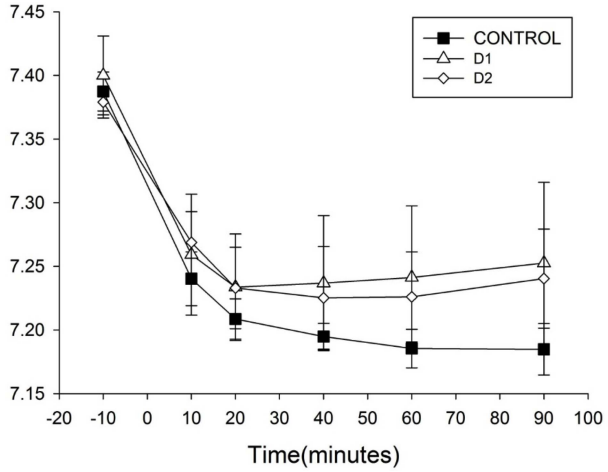

Fig 8. The change of pH values in control and experiment groups. Data were expressed as mean ± standard deviation, and n = 5/group.

Table 8. Statistical analysis result of pH in control and experiment groups. Data were analyzed by two-factor repeated measures ANOVA followed by a Bonferroni test. *, ** indicate a significant differences ($p < 0.05$, $p < 0.001$)

pH	F-value	p-value
Tests of between-subjects effects of group	2.200	0.153
Tests of within-subjects contrasts of time	112.231	0.000**
Tests of within-subjects contrasts of group*time interaction effect	2.103	0.165

Table 9. Statistical analysis result of respiratory rate values in control and experiment groups. Data were analyzed by two-factor repeated measures ANOVA followed by a Bonferroni test. *, ** indicate a significant differences ($p < 0.05$, $p < 0.001$)

respiratory rate	F-value	p-value
Tests of between-subjects effects of group	8.502	0.005*
Tests of within-subjects contrasts of time	42.725	0.000**
Tests of within-subjects contrasts of group*time interaction effect	1.175	0.342

significant ($p < 0.05$), but difference between groups and interaction effect of time*group were not significant.

Respiratory rate

In D2 group, steep increase of mean respiratory rate was observed at 5 min. whereas, in control group, steep decrease of mean respiratory rate was observed at the same time.

Mean respiratory rate of control group was lower than that of D2 group through anesthetic period.

The two-way repeated measure ANOVA analysis revealed that difference between groups ($p < 0.05$) and difference in time course ($p < 0.001$) was significant, but time*group interaction was not significant (Table 9).

Behavioral parameter

Although Fig 10 showed that, comparing with control group, there were a little reductions of behavioral changing

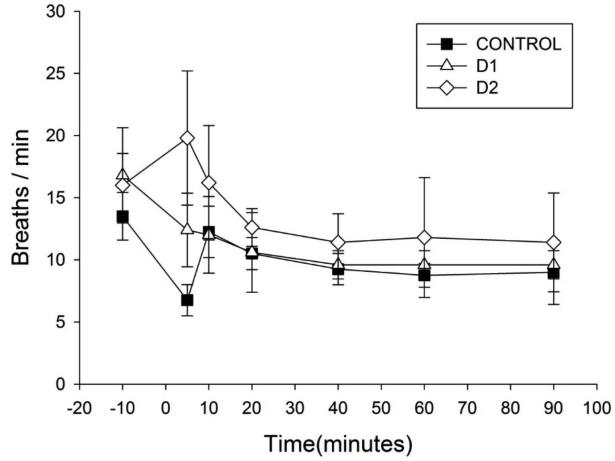

Fig 9. The change of respiratory rate values in control and experiment groups. Data were expressed as mean ± standard deviation, and $n = 5$/group.

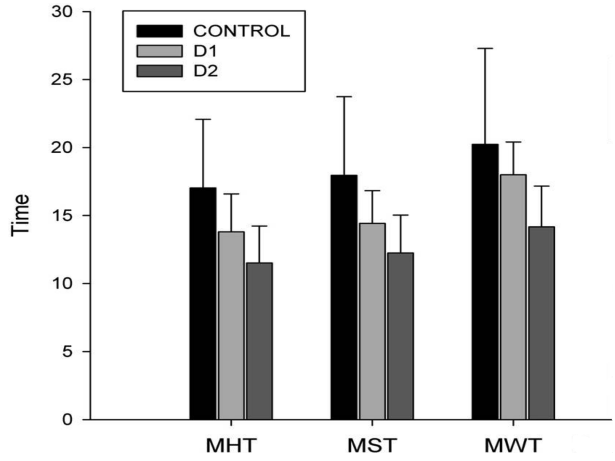

Fig 10. The change of behavioral parameters in control and experiment groups. Data were expressed as mean ± standard deviation, and n = 5/group.

Table 10. Statistical analysis result of behavioral parameters in control and experiment groups. Data were analyzed by one-way ANOVA

	F-Value	P-Value
MHT	2.839	0.098
MST	2.650	0.111
MWT	2.188	0.155

times in doxapram treatment groups, Kruskal-Wallis test (non-parametric method) and one-way ANOVA (parametric method) analyses revealed that difference between groups were not significant (Table 10).

The level of anesthesia

There were no positive responses to toe-web pinching test in all groups throughout the experiment procedure.

Discussion

As propofol induces greater cardiovascular depression than remifentanil, the use of a high-dose opioid and low-dose hypnotic combination can provide optimal cardiovascular stability (23), and an anesthetic regimen with high-dose remifentanil and low-dose propofol has shorter recovery time than a regimen with low-dose remifentanil and high-dose propofol. Although it has many benefits, high dose remifentanil induce respiratory depression.

When using combination of remifentanil and propofol in human, 0.025 to 0.05 μg/kg/min of remifentanil is regarded to provide adequate respiration, and remifentanil infusion rate over 0.5 μg/kg/min is strictly recommended to supply adequate oxygen in human (20). O'Hare *et al*. also used controlled ventilation for patients (16).

In veterinary medicine, Murrell *et al*. used remifentanil 0.6 μg/kg/min and mean propofol infusion rate 0.33 mg/kg/min in dogs and manual intermittent positive-pressure ventilation was used for adequate respiratory function (14).

Moerman *et al*. (12) reported that remifentanil in combination with propofol showed significantly decrease in blood pressure and respiratory function and, as long as patient maintained spontaneous ventilation, the addition of remifentanil to propofol offered no benefits compared with the use of propofol alone.

The purpose of this experiment was to resolve the problem of respiratory depression and hypotension in combination of remifentanil and propofol by co-infusion of doxapram as adjuvants.

In our experiment, the values of blood gas analysis were improved in doxapram co-infusion groups. PaO_2 and SaO_2 in the anesthetic periods were significantly increased by doxapram treatment. $PaCO_2$ was significantly decreased by doxapram infusion, and as time goes on, differences became more significant.

Baseline values of arterial pressure were slightly high, it seems to be implied that the dogs were not completely acclimated. After infusion, arterial blood pressures were increased in D2 group compared with control group within normal range.

Respiratory rate was measured for evaluating ventilation and it regarded as hypoventilation when respiratory rate was under the 8 breath per min. In contrast with control group, states of hypoventilation were not seen in doxapram treated groups. Respiratory rates of doxapram treated groups were higher than that of control group throughout anesthesia.

Respiratory rates were closely correlated with tidal volume. Following changes in tidal volume, respiratory rate concurrently altered. So, respiratory rate did not seem to be proper indicator for hypoventilation alone, it was considered to be more suitable that, if possible, measurement should be carried out in respiratory rate and tidal volume, concurrently.

In behavioral parameters, MHT, MST and MWT tended to decrease by doxapram infusion, dose-dependently, but statistical differences between groups were not significant. According to the literature (25), if doxapram infusion were not ceased with the end of anesthesia and were continuously infused, arousal effect of doxapram might be efficacious.

Although possibilities of doxapram CRI were seen as anti-hypotension effect and anti-hypoxia effect in TIVA with remifentanil and propofol, further studies for titration of

proper dose of each drugs seems to be needed.

Conclusions

In this study, doxapram CRI could alleviate the suppression of cardiopulmonary function, such as apnea, dyspnea, hypoxia, acidosis and hypotension, during general anesthesia with remifentanil/propofol CRI, without altering of analgesia and hypnosis. But it considered that doxapram might not have enough effect to substitute positive ventilation, even at highest dose in this study.

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개에서 Remifentanil과 Propofol에 의한 완전 정맥 내 마취 시 Doxapram 투여가 심폐기능에 미치는 효과

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요 약 : 개에서 remifentanil과 propofol을 사용한 완전 정맥내 마취에서 doxapram의 점적투여가 심폐기능에 미치는 영향에 대해 평가해 보았다. 수컷 비글견 15마리를 사용하였으며 무작위로 5마리씩 3군으로 나누었다. 모든 군에서 전마취제로 medetomidine을 20 μg/kg 정맥주사 하였고 remifentanil과 propofol의 점적 투여로 1시간 30분 동안 마취하였다. 마취 시작 시, 각 그룹 별로 지정된 용량의 doxapram을 병용 투여하였다. D1 군은 doxapram 0.25 mg/kg을 투여한 후 8.33 μg/kg/min의 속도로 점적 투여했다. D2 군은 doxapram 2 mg/kg을 투여한 후 66.66 μg/kg/min의 속도로 점적 투여했다. 대조군은 생리 식염수를 투여하였다. 외과적 마취기를 평가하고, 혈액 가스 분석, 호흡수, 심박수, 동맥혈압을 측정하였으며 마취회복기 동안의 행동변화를 관찰 기록하였다. 외과적 마취기는 마취기 전반에 걸쳐 모든 군에서 잘 유지되었다. 대조군에 비해 D2 군에서 호흡수의 유의적인 상승이 있었으며 ($p < 0.05$), 동맥혈 산소 분압과 산소 포화도에서는 doxapram 처치군 모두에서 대조군에 비해 유의적인 상승을 보였다($p < 0.05$). 동맥혈 이산화탄소 분압은 고농도 처치 군인 D2군에서 유의적인 감소를보였다($p < 0.05$). 수축기 동맥혈압, 이완기 동맥혈압, 평균 동맥혈압은 D2군에서 유의적인 증가를 보였다. 심박수와 pH는 유의적인 변화가 관찰되지 않았다. 따라서 본 실험을 통해 개에서 remifentanil과 propofol을 사용한 완전 정맥내 마취에서 일어날 수 있는 저산소증이나 저혈압과 같은 심폐 기능 저하를 doxapram의 점적 투여가 진통 작용에 경감 없이 완화 시키는 것을 알 수 있었다.

주요어 : 개, doxapram, propofol, remifentanil, 완전 정맥내 마취