Kafkas Univ Vet Fak Derg
19 (Suppl-A): A33-A40, 2013
DOI: 10.9775/kvfd.2012.7548

Journal Home-Page: http://vetdergi.kafkas.edu.tr
Online Submission: http://vetdergikafkas.org

RESEARCH ARTICLE

Comparison of Propofol-Remifentanil and Propofol-Fentanyl Anesthesia During Ovariohysterectomy in Dogs [1] [2]

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[1] *This research was supported by the Scientific Research Project Unit of Kirikkale University (2007/30)*
[2] *This study was previously presented at a scientific meeting of XI. Veterinary Surgery Congress, 19-22 May, Belek, Antalya, TURKEY, 2010*

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Makale Kodu (Article Code): KVFD-2012-7548

Summary

The aim of the study was to evaluate the cardiorespiratory and clinical effects of propofol and remifentanil anesthesia compared to propofol and fentanyl anesthesia during ovariohysterectomy in dogs. Sixteen healthy dogs were randomly assigned to two groups. After premedication with atropine, anesthesia was induced with propofol and maintained with the infusion of propofol at a dose of 0.5 mg/kg/min. Once stable anesthesia was achieved, 1 µg/kg remifentanil or 2 µg/kg fentanyl was administered intravenously, and infusion was begun at a dose of 0.6 µg/kg/min and 0.5 µg/kg/min, respectively. Cardiorespiratory variables were recorded after propofol administration combined with remifentanil or fentanyl at 10-min intervals, and the quality of anesthesia, return of spontaneous ventilation, head lift and sternal position were also recorded. Apnea was observed after remifentanil and fentanyl administration in all dogs. Heart rate, systolic and mean arterial blood pressures tended to decrease rapidly after remifentanil and fentanyl administration, and during the first 20 min, in both groups. Although the difference between times was significant, the difference between groups was statistically insignificant. Recovery periods were longer in the fentanyl group than in the remifentanil group. The administration of propofol with remifentanil or fentanyl provides a stable haemodynamic state and depth of anesthesia with a constant infusion, and remifentanil could be preferred to fentanyl when aiming a rapid recovery period.

Keywords: *Propofol, Remifentanil, Fentanyl, Anesthesia, Cardiorespiratory, Recovery, Dog*

Köpeklerde Ovariohisterektomi Operasyonunda Propofol-Remifentanil ve Propofol-Fentanil Anestezisinin Karşılaştırılması

Özet

Bu çalışmanın amacı köpeklerde ovariohysterektomi operasyonunda propofol-remifentanil ile propofol-fentanil anestezisinin etkinliğini ve kardiyorespiratorik etkilerini karşılaştırmaktır. Bu amaçla 16 adet yetişkin, dişi köpek rastgele iki gruba (n=8) ayrıldı. Anesteziye atropin ile premedikasyon yapılarak başlandıktan sonra propofol ile indüksiyon yapıldı ve 0.5 mg/kg/dk dozunda propofol infüzyonuna başlandı. Stabil anesteziden sonra ilk gruba 1 µg/kg remifentanil, ikinci gruba 2 µg/kg fentanyl bolus olarak uygulandı. Remifentanil ve fentanil infüzyonu sırasıyla 0.6 µg/kg/dk ve 0.5 µg/kg/dk dozunda devam edildi. Kardiyovasküler değişiklikler propofol sonrası, remifentanil veya fentanil sonrası ve operasyon süresince 10 dakika aralıklarla kaydedildi. Anestezinin derinliği, spontan ventilasyonun başlama, kafayı kaldırma ve sternal pozisyona gelme zamanları kaydedildi. Tüm olgularda remifentanil ve fentanil uygulamasından sonra apnea oluşumu gözlendi. Her iki grupta da kalp atım hızı, sistolik (SAP) ve ortalama arteriyel basınç (MAP) değerlerinin remifentanil ve fentanil uygulanmasından sonra hızla düştüğü ve ilk 20 dakikada düşmeye devam ettiği görüldü. Bu değerlerde zaman içindeki farklılıklar istatistiksel olarak anlamlı olarak kaydedilirken, gruplar arasında istatistiksel açıdan anlamlı olmadığı saptandı. Fentanil grubundaki uyanma süresinin remifentanilden daha uzun olduğu tespit edildi. Sonuç olarak, köpeklerde ovariohisterektomi operasyonlarında sabit hızla uygulanan propofol-remifentanil veya propofol-fentanil infüzyonunun stabil hemodinamik parametreleri sağladığı, uyanma süreleri değerlendirildiğinde ise remifentanilin tercih edilebileceği kanısına varılmıştır.

Anahtar sözcükler: *Propofol, Remifentanil, Fentanil, Anestezi, Kardiopulmoner, Uyanma, Köpek*

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INTRODUCTION

Propofol is a short-acting, nonbarbiturate sedative drug, which is rapidly metabolized in dogs [1-4]. Minimal accumulation on repeated or constant administration makes propofol suitable for both the induction and maintenance of anesthesia [5-7]. Total intravenous (IV) anesthesia with propofol has been widely investigated in dogs, however, due to the lack of analgesic properties this drug is considered inadequate to provide anesthesia during surgery [5-9].

Remifentanil and fentanyl are potent synthetic μ-opioid agonists. Both drugs are administered to achieve intraoperative analgesia. Fentanyl has been widely investigated in veterinary anesthesia for many years. Fentanyl is metabolized mainly in the liver, and its half life is 2 to 3 h [10]. After prolonged infusions, its side effects continue because of its cumulative effect [2,7,11]. Its ultra-short action, rapid control of the depth of anesthesia, and lack of dependence on organ functions for breakdown and clearance make remifentanil more advantageous than fentanyl. Remifentanil does not accumulate in the body even after prolonged infusion, and its terminal half-life has been reported to be less than 6 minutes [5,12,13]. These properties make remifentanil ideal as part of a total IV anesthesia technique [8,14,15]. Although vagally mediated bradycardia often occurs, cardiovascular stability remains even when remifentanil or fentanyl are combined with propofol [7,9,16].

Remifentanil has gained popularity in human medicine in recent years. Although several pharmacokinetic and pharmacodynamic studies have demonstrated its distribution and clearance, there are only a few reports published on its clinical use in dogs [6,8,13-15,17].

Although the bolus administration of fentanyl is frequently used in veterinary practice, to the authors' knowledge, this is the first clinical study on the use of remifentanil given as a bolus administration in dogs [18].

The aims of this study were to evaluate the cardiorespiratory and clinical effects of propofol and remifentanil anesthesia compared to propofol and fentanyl anesthesia during ovariohysterectomy in dogs. The length of the recovery period was also recorded.

MATERIAL and METHODS

Sixteen client-owned, adult female dogs, aged between 8 months and 5 years (mean 1.7 years), and weighing between 14 and 36 kg (mean 23.2 kg), which were admitted for elective ovariohysterectomy, were studied. Each animal was randomly assigned to one of two groups of eight. They were considered to be healthy based on physical and haematological examination. The study was approved by the local Ethics Committee (Approvel number: 08/48). All dogs were fasted overnight and water was withheld for 2 h prior to anesthesia. All dogs were anesthetized by an anesthetist who was unaware of the treatment groups (ZP). Atropine (0.05 mg/kg, Atropin, Vetas, Turkey) was administered to all dogs subcutaneously (SC) 45 min before the induction of anesthesia. Following the placement of a catheter in both cephalic veins, propofol (Pofol, Sandoz, Turkey) was administered within 90-120 seconds as an IV bolus to induce anesthesia. Incremental doses were administered until a suitably sized, cuffed endotracheal tube could be inserted into the trachea. Postinduction apnea was defined as a period of >30 sec without spontaneous ventilation, and in such cases intermittent positive pressure ventilation (IPPV) was initiated manually until spontaneous ventilation resumed. Immediately after intubation, an IV infusion of propofol was started to maintain anesthesia. Propofol was administered using an infusion pump (Accumate 2300, Woo Young Medical, Korea), and the initial infusion rate of propofol was 0.5 mg/kg/min. The dogs were placed in dorsal recumbency and connected to a semiclosed circle rebreathing system (TMS Maxi 2200; Turkey). The fresh gas flow was 2 l/min. Lactated Ringer's solution (Ringesol, Vilsan, Turkey) was administered intravenously at a rate of 10 ml/kg/h throughout anesthesia.

A 20 G cannula was placed in the femoral artery per cutaneously to monitor arterial blood pressure and obtain samples for blood gas and acid-base analysis (Gastat Mini, Techno Medica, Germany). Heart rate (HR), systolic (SAP), diastolic (DAP) and mean (MAP) arterial blood pressures, end-tidal carbon dioxide ($PE'CO_2$), oxygen saturation (SpO_2), and body temperature were recorded before the infusion of propofol and during anesthesia at 10-min intervals with a multiparameter monitor (Petas, KMA 800, Turkey). Anesthesia was considered stable in terms of no changes in the blood pressure and heart rate for 5 min, no palpebral reflexes and no tone of the jaw muscle. Once a stable plane of anesthesia was maintained, a bolus of 1 μg/kg remifentanil (Ultiva, GlaxoSmithKline, Turkey) or 2 μg/kg fentanyl (Fentanyl Citrate, Antigen Pharmaceuticals, Germany) was administered intravenously to the remifentanil and fentanyl groups, respectively, and infusion was begun at a dose of 0.6 μg/kg/min and 0.5 μg/kg/min, respectively. Following the depression of spontaneous ventilation, manual IPPV with a respiratory rate of 14 breaths/minute was initiated with 100 percent oxygen and continued to maintain $PE'CO_2$ between 35-45 mm Hg. To ensure that pH, arterial O_2 (PaO_2) and arterial bicarbonate (HCO_3) values were within the reference ranges, arterial blood gases were measured by blood gas analyzers at 15-min intervals.

The dose of propofol infused was changed according to the clinical assessment of the depth of anesthesia based on the observation of changes in blood pressure and heart rate, presence of palpebral reflex, increases in jaw and abdominal muscle tone during traction on the ovaries, as evaluated by the surgeon. Deviations of more than 20% in heart rate and blood pressure, during the incision and traction of the ovaries, without palpebral reflex or increase in the muscle tone, were

assumed to indicate inadequate analgesia, and 1 µg/kg fentanyl or 0.5 µg/kg remifentanil was administered intravenously. A heart rate less than 60 beats/min for 5 min with the presence of hypotension (MAP<60) was treated with atropine (0.02 mg/kg, IV).

Ovariohysterectomy was performed via a midline abdominal incision using a standard technique by the same surgeon.

Carprofen (2 mg/kg, IV, Rimadyl, Pfizer, Turkey) [19] and morphine (0.2 mg/kg, intramuscularly (IM), Morphine, Galen Ilac, Turkey) were administered 20 and 10 minutes before the end of the operation, respectively. Propofol, remifentanil or fentanyl infusions were stopped once surgery was completed. Manual ventilation was continued until spontaneous ventilation resumed, and the time to the first spontaneous ventilation, head lift and sternal recumbency were also recorded.

Pain scores were recorded at 0, 1, 2, 3, 4, 8, 12 and 24 h after recovery. Postoperative analgesia was provided with 0.2 mg/kg morphine administered intramuscularly every four hours for the first 24 h after surgery. Each dog received 4 mg/kg carprofen orally each day for three days after the operation. Pain was scored using a multifactorial scoring system [20]. The subjective and objective variables were recorded to assess the pain score. A score of 0 to 16 was possible, with increased scores indicative of greater pain. During the observation period, analgesia was considered inadequate if the total pain score was ≥ 8, and morphine (0.2 mg/kg, IM) was administered as a rescue analgesic postoperatively [20].

Statistical analysis: Statistical analyses were performed with commercial software (SPSS, USA). All data were reported as mean ± standard deviations (SD). The normality check of the variables was performed by the Shapiro-Wilk test, and according to these test results, between- and within-group differences in heart rate, SAP, MAP, DAP and temperature were analyzed by analysis of variance (ANOVA) for repeated measures. Also, the differences in recovery periods between groups were tested by the independent sample *t*-test. All differences were considered significant for P<0.05.

RESULT

The mean dose of propofol required to allow intubation was 5.7±0.7 mg/kg (ranged from 4.9 to 7.1) in the remifentanil group and 5.9±1.4 mg/kg (ranged from 4.5 to 7.9) in the fentanyl group. The differences between the groups for the required dose of propofol were not statistically significant. No apnea was recorded after propofol administration, and respiratory rates ranged from 10 to 16 breaths/min. Therefore, there was no need to initiate IPPV after anesthetic induction with propofol.

Mean surgical times for the remifentanil and fentanyl groups were 45.0±5.3 min and 43.75±5.2 min, respectively, and did not differ statistically between the groups.

The mean heart rate of the dogs was 143±16 beats per minute (bpm) (ranged from 111 to 170) in the remifentanil group and 140±18 bpm (ranged from 114 to 168) in the fentanyl group before remifentanil and fentanyl administration. No arrhythmias were recorded during anesthesia. Heart rate tended to decrease significantly after remifentanil and fentanyl administration (P=0.0004), and during the first 20 min in both groups but not different between groups *(Fig. 1)*. Although heart rate decreased, bradycardia was not recorded and atropine was not readministered to any of the dogs.

MAP was 85.25±20.84 mmHg in the remifentanil group and 84.86±12.95 mmHg in the fentanyl group after propofol administration, and it was decreased to 66.85±18.99 mmHg and 65.50±15.22 mmHg after remifentanil and fentanyl administration, respectively *(Fig. 2)*. In both groups, the highest values for SAP, MAP, and DAP were recorded after propofol administration alone and the lowest values were recorded after remifentanil or fentanyl administration prior to the operation. The decrease in SAP, MAP and DAP was significant between times (P<0.047) but not significant between groups. Although SAP, DAP, and MAP were approximately the same between groups for most time points, SAP and MAP were transiently higher 30 min after fentanyl administration compared to the remifentanil group (*Fig. 2, 3* and *4*).

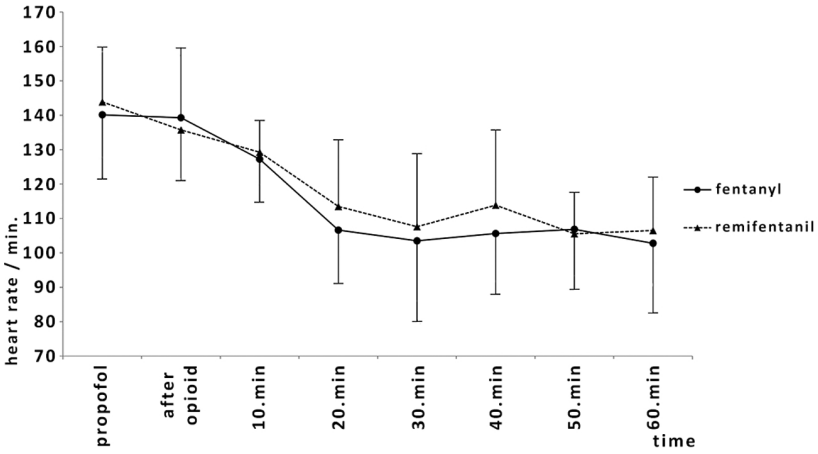

Fig 1. The heart rate of the dogs (mean±SD) during ovariohysterectomy (OH). The heart rates of the two groups did not differ significantly. The 0. minute time point shows the time at which remifentanil or fentanyl was administered

Şekil 1. Köpeklerin ovariohisterektomi (OH) sırasındaki kalp ritmleri (ortalama±SD). İki grup arasındaki kalp ritm farklılığı istatistiksel açıdan önemli bulunmamıştır. "0" zamanı fentanil veya remifentanilin uygulanmaya başlandığı zamandır

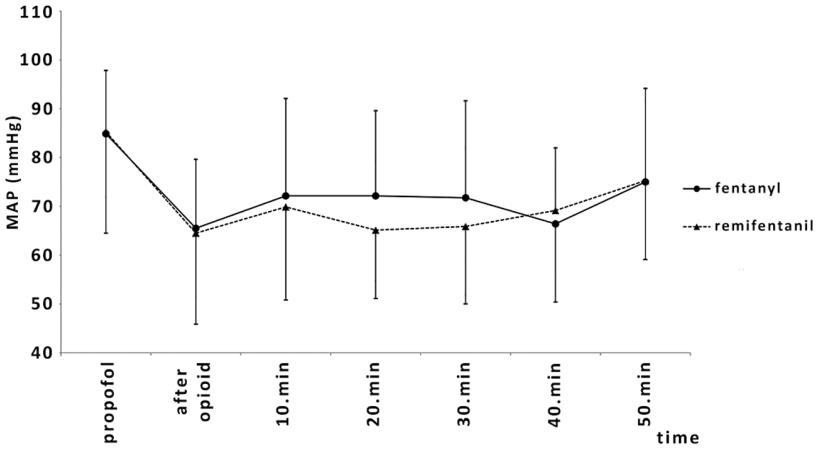

Fig 2. The mean arterial blood pressure (MAP) of the dogs (mean±SD) during ovariohysterectomy. The MAP of the two groups did not differ significantly. The 0. minute time point shows the time at which remifentanil or fentanyl was administered

Şekil 2. Köpeklerin OH sırasındaki ortalama arteriyel kan basınçları (ortalama±SD). İki grup arasındaki ortalama arteriyel kan basınç değerleri istatistiksel açıdan önemli bulunmamıştır. "0" zamanı fentanil veya remifentanilin uygulanmaya başlandığı zamandır

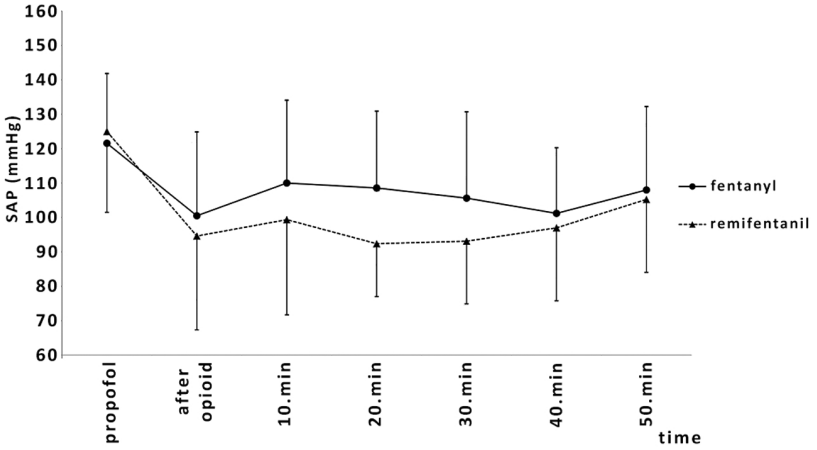

Fig 3. The systolic arterial blood pressure (SAP) of the dogs (mean±SD) during ovariohysterectomy. The SAP of the two groups did not differ significantly. The 0. minute time point shows the time at which remifentanil or fentanyl was administered

Şekil 3. Köpeklerin OH sırasındaki sistolik arteriyel kan basınçları (ortalama±SD). İki grup arasındaki sistolik arteriyel kan basınç değerleri istatistiksel açıdan önemli değildir. "0" zamanı fentanil veya remifentanilin uygulanmaya başlandığı zamandır

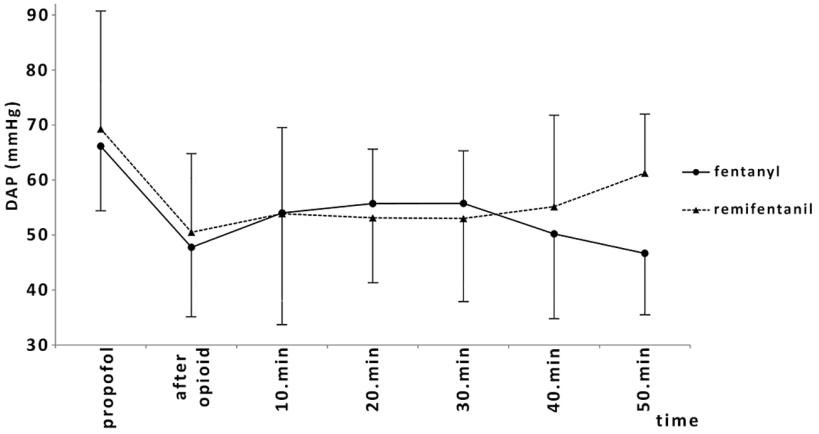

Fig 4. The diastolic arterial blood pressure (MAP) of the dogs (mean±SD) during ovariohysterectomy. The DAP of the two groups did not differ significantly. The 0. minute time point shows the time at which remifentanil or fentanyl was administered

Şekil 4. Köpeklerin OH sırasındaki diyastolik arteriyel kan basınçları (ortalama±SD). İki grup arasındaki diyastolik arteriyel kan basınç değerleri istatistiksel açıdan önemli bulunmamıştır. "0" zamanı fentanil veya remifentanilin uygulanmaya başlandığı zamandır

Apnea was recorded immediately after remifentanil and fentanyl administration in all dogs, therefore manual IPPV was continued throughout the operation. Mean times to return of spontaneous respiration, head lift and sternal position were shorter in the remifentanil group than in the fentanyl group *(Fig. 5)*. They were 17.5±6.85 min, 33.3±16.3 min and 50.8±17.1 min in the remifentanil group, and 22.7±11.04, 37.0±15.9, 66.25±35.9 min in the fentanyl group, respectively. However, the difference was statistically not significant.

There was no significant difference between the groups for mean arterial blood pH (reference range 7.35-7.45), PaO_2 (above 500 mmHg when an animal is breathing 100% O_2) and HCO_3 (reference range 18-25 mmol/l) values. The blood gas values were given in *Table 1*.

None of the dogs were given supplemental intraoperative analgesics. One dog in the remifentanil group and two dogs in the fentanyl group whined immediately after extubation, however, it only lasted 10 min. They did not appear to be in pain and supplemental analgesia was not given. The multimodal pain scale was not greater than 7/16. All dogs recovered without postoperative complications.

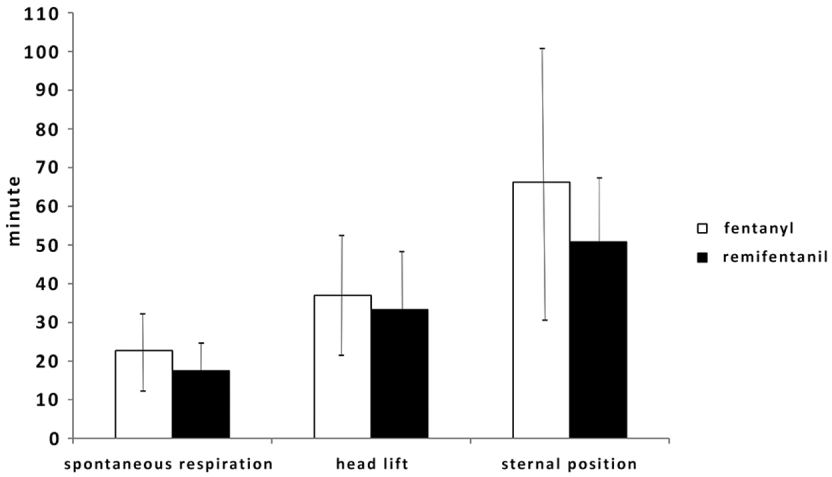

Fig 5. Mean times (mean±SD) to return of spontaneous respiration, head lift and sternal position after ovariohysterectomy in dogs. The times of the two groups did not differ significantly

Şekil 5. OH operasyonu sonlandıktan sonra köpeklerin spontan solunumlarının başladığı, kafalarını kaldırabildikleri ve sternal pozisyona geçtikleri zamanların ortalaması (mean±SD). İki grup arasındaki zamanlar açısından fark istatistiksel olarak önemli bulunmamıştır

Table 1. *Blood gas values of the dogs. The 0. min time point shows the time at which remifentanil or fentanyl was administered*
Tablo 1. *Köpeklerin kan gazı değerleri. "0" zamanı fentanil veya remifentanilin uygulanmaya başlandığı zamandır*

Parameter	Drug	0. minute	15. minute	30. minute	45. minute
pH	Remifentanil Fentanyl	7.4±0.05 7.42±0.02	7.39±0.04 7.41±0.06	7.38±0.09 7.4±0.02	7.38±0.09 7.39±0.04
PaO_2 (mmHg)	Remifentanil Fentanyl	488±20 492±60	490±15 520±74	515±45 545±32	532±20 567±38
HCO_3 (mmol/l)	Remifentanil Fentanyl	22.0±08 22.8±0.4	21.4±0.9 22.4±0.4	20.9±0.4 21.1±0.9	20.5±1.5 18.94±0.7

DISCUSSION

Propofol alone has proved to be unsatisfactory for major surgical procedures as it has no analgesic properties and the dose required to suppress responses to surgical manipulations induces severe cardiovascular and respiratory adverse effects [1,6,8,12,21]. Thus, it may be combined with some opioids like remifentanil or fentanyl. In this study, both drugs are considered as ideal analgesics for continuous infusion when combined with propofol [2,5,7,17,22,23].

The mean induction dose of propofol in this study was the same with that reported for unpremedicated dogs in several studies [24,25]. Apnea was a frequent adverse effect after rapid bolus propofol administration for induction [25-28]. Musk et al.[29] investigated 4 different doses of propofol and recorded a higher incidence of apnea with higher doses. There are also studies, in which propofol was administered slowly for induction and no adverse effects associated with respiratory depression were reported [7,8,22]. In this study, none of the animals exhibited apnea after induction with propofol, which may have resulted from slow IV administration and the discontinuation of injections after a satisfactory depth of anesthesia was achieved for intubation [5,6,9,21].

Propofol is a negative inotrope and reduces systemic vascular resistance, causing dose-dependent hypotension. Marked decreases in systemic blood pressure were reported previously [3,27]. Although the dose of propofol administered was higher than in some studies, mean SAP, MAP and DAP after propofol administration were similar to those reported in studies in which lower propofol doses were administered. It was confirmed in previous studies that hypotension is less pronounced when propofol is administered slowly [5,8,25].

The remifentanil and fentanyl infusion rates used in our study were extrapolated from published data [7,8,14]. A dose-dependent adverse effect frequently associated with the use of opioids is bradycardia [2,7,17,30]. Allweiler et al.[15] administered two different doses of remifentanil to dogs without anticholinergic injections, and reported a need for glycopyrrolate injections because of severe bradycardia related to the dose of remifentanil. In another study conducted by Murrell et al.[8], although the administered doses of remifentanil were the same as those administered in this study, atropine was re-administered during the operation because of the decrease in heart rate and blood pressure in two among 15 dogs. The bradycardia expected after the bolus administration of remifentanil or fentanyl not having been observed was attributed to the use of atropine for preanesthesia. Heart rate was not recorded below 80 beats/min during any of the procedures. It was determined that premedication with 0.05 mg/kg atropine was enough to prevent remifentanil or fentanyl-induced bradycardia.

Steagall et al.[16] administered atropine to ameliorate bradycardia, associated with a reduction in MAP, in other words, atropine was not administered as a premedicant to prevent opioid-induced cardiovascular side effects. In this study, 3 dogs in the remifentanil group exhibited low MAP (<60 mmHg) after bolus injections, but these values increased to the reference range of the anesthesia within five minutes.

During this period, atropine was not administered to any of the animals because bradycardia was not recorded and MAP increased spontaneously. It was thought that the reason for the decrease in MAP in the remifentanil group could be related to the bolus injection. In previous studies, remifentanil was not administered as a bolus for induction, and this is the first research on the use of a bolus dose of remifentanil for induction.

There are discrepancies between studies. Some researchers reported bradycardia and hypotension during remifentanil or fentanyl infusions because of the stimulation of μ-opioid receptors and the central vagotonic effect [7,17,30]. On the contrary, some other researchers observed stabilized haemodynamic variables during remifentanil or fentanyl infusions resulting from no effect on myocardial contractility, no histamine release and preserved arterial baroreflex integrity [5,9,12]. Hatschbach et al.[17] used propofol and remifentanil during ovariohysterectomy operations in bitches. These researchers reported slight decrease in blood pressure before the operation and an increase in blood pressure during the traction of the ovaries and uterus. Consequently, they reported that 0.3 μg/kg/min remifentanil was not enough to eliminate the surgical stimulus. In the same study, it was emphasized that hypotension could be observed after propofol administration. However, in our study, neither bradycardia nor hypotension was observed after propofol administration. It was considered that the hypotension recorded by Hatschbach et al.[17] prior to remifentanil administration may have arisen from the hypotensive effect of methotrimeprazine, which was used as a premedicant with propofol. The result of this study is in agreement with the report of Gimenes et al.[6], suggesting that 0.5 μg/kg/min remifentanil was enough to eliminate surgical nociception.

Grimm et al.[31] reported slight decrease in SAP, DAP and MAP after fentanyl administration alone within 60 min. Andreoni and Hughes [7] administered propofol and fentanyl with various operations in dogs. They administered atropine immediately after fentanyl to counteract anticipated bradycardia and made reductions in the rate of propofol infusions on the basis of the decrease in blood pressure Ethier et al.[23] administered fentanyl and propofol during a 24-h period without a surgical stimulation, and reported that the cardiovascular variables were slightly lower than the reference values. Furthermore, Beier et al.[9] compared propofol and propofol-remifentanil anesthesia and recorded a significant decrease in DAP and slight increase in SAP in the propofol-remifentanil group. Murrell et al.[8] administered propofol and remifentanil and reported a biphasic increase in blood pressure during surgery as the administration dose of propofol was altered according to the signs of the depth of anesthesia. When the depth of anesthesia was found to be inadequate for surgery, especially during the traction of the ovaries, an additional dose of propofol and/or remifentanil was given to the dogs. In the present study, in both groups, the lowest arterial pressures were recorded within 10 min after opioid administration, and slight increases were recorded immediately after the operation had begun in both groups. As these increases were below 20% and no muscle tone contraction was felt, they were not considered clinically important. It was suggested that the combination of propofol with remifentanil or fentanyl in these dose ranges provided good anesthesia with small individual variations in SAP, DAP and MAP.

In a recent study, a 0.3 μg/kg/min constant rate infusion of remifentanil was administered in conjunction with a target-controlled infusion of propofol, which reduced the required propofol dose by as much as 55% [9]. In the present study, the administered doses of propofol and remifentanil were approximately twice as much as that administered in the study by Beier et al.[9], and SAP, DAP and MAP were lower than those reported in the recent study. It was considered that blood pressures would have been higher if a lower dose of propofol had been administered after remifentanil or fentanyl infusion.

The arterial blood pressures were reduced after remifentanil or fentanyl administration. The decrease in SAP in the remifentanil group was clinically more pronounced than in the fentanyl group, and continued until the 40th min. The reason for the decrease in SAP in the remifentanil group could be the administration of a bolus of 1 μg/kg remifentanil, as remifentanil infusion was administered without bolus injections in previous studies [8,9,18].

Adequate anesthesia can be maintained using different doses of propofol and remifentanil [9,17]. O'Hare et al.[18] investigated the effects of different doses of propofol and remifentanil on recovery times in people. They reported shorter recovery times when the maintenance of anesthesia was achieved using a higher dose of remifentanil and lower dose of propofol instead of a lower dose of remifentanil and higher dose of propofol. It was not aimed to demonstrate a propofol-sparing effect of remifentanil or fentanyl, so the doses administered were not changed unless the depth of anesthesia was too deep or unsatisfactory. The dogs could have recovered earlier if the dose of propofol was lower and the dose of remifentanil was higher.

Mean times to return of spontaneous respiration, head lift and sternal position were similar to those reported in other studies. Hughes and Nolan [2] administered propofol and fentanyl without surgery, and recorded the first spontaneous respiration in 26±7 min and head lift in 59±12 min. In this study, although mean times to return of spontaneous respiration were similar to those reported by Hughes and Nolan [2], the mean time of head lift was shorter. The reason for a shorter period of head lift in this study could be surgery, as in the study conducted by Hughes and Nolan [2], there was no surgery or painful procedures and the dogs lay down for longer periods. Furthermore, Murrell et al.[8] administered propofol and remifentanil during ovariohysterectomy and recorded the time to return of

spontaneous respiration as 11.1 min and head lift time as 16.7 min. As higher doses of propofol and remifentanil were administered in the present study, mean times to return of spontaneous respiration and head lift were longer than those reported in the previous study. When the two groups were compared, it was observed that the mean times were longer in the fentanyl group than in the remifentanil group. The differences between the two groups throughout the recovery period can be explained by the cumulative effect of fentanyl [2], which extends the recovery period.

Due to the rapid metabolism of fentanyl and remifentanil, it is important to give an analgesic before the end of remifentanil and fentanyl administration to ensure a gradual transition of intraoperative to postoperative analgesia [8,15,20]. In the present study, carprofen and morphine were administered for postoperative analgesia prior to the end of remifentanil and fentanyl infusion. All dogs made an uneventful recovery, and none of the dogs showed signs of pain.

As the semi-conscious period during recovery is a high-risk period, it is important to select a short-acting anesthetic drug [8]. With respect to the recovery period, remifentanil could be preferred to fentanyl because of the rapid return of spontaneous respiration, consciousness and full awakening [5,8,17].

The quality of anesthesia and analgesia was judged to be satisfactory and it was concluded that a constant rate infusion of propofol combined with remifentanil or fentanyl was efficient for ovariohysterectomy in bitches. In conclusion, propofol with remifentanil or fentanyl provides haemo-dynamic stability and a stable depth of anesthesia with a constant rate of infusion during ovariohysterectomy in dogs. Remifentanil could be preferred to fentanyl when aiming a rapid recovery period. However, careful monitoring of heart rate, blood pressure and respiration is essential during remifentanil and fentanyl administration. Further studies to optimize the dose ratios are considered worthwhile.

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