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Cardiopulmonary and propofol-sparing effects of dexmedetomidine in total intravenous anesthesia in cats undergoing ovariohysterectomy

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Abstract

Objectives This study aimed to assess the effect of dexmedetomidine on the propofol-based anesthesia of cats subjected to ovariohysterectomy.

Methods Twenty-eight cats were randomly allocated to four groups (seven cats in each) and premedicated with either 5 µg/kg dexmedetomidine (groups Dex 1, Dex 3 and Dex 5) or 0.05 ml saline (Prop group) intramuscularly. After the induction of anesthesia with propofol, total intravenous anesthesia was initiated with 300 µg/kg/min propofol plus 3 ml/kg/h NaCl 0.9% (Prop), or 200 µg/kg/min propofol plus dexmedetomidine at the rates of 1 µg/kg/h (Dex 1), 3 µg/kg/h (Dex 3) or 5 µg/kg/h (Dex 5). Cardiorespiratory variables were assessed 5 mins after induction and every 10 mins thereafter, until the end of anesthesia. The propofol infusion rate was adjusted every 10 mins (± 50 µg/kg/min) to maintain anesthetic depth. The times to extubation, sternal recumbency, ambulation and total recovery were recorded. Pain scoring was performed 1, 2, 4, 8, 12 and 24 h after the end of anesthesia.

Results Dexmedetomidine produced a propofol-sparing effect of 72.8%, 71.1% and 74.6% in the Dex 1, Dex 3 and Dex 5 groups, respectively. Cats in the Prop group maintained higher heart rate values than the other groups, and the mean arterial pressure remained higher in the Dex 3 and Dex 5 groups. Rescue intraoperative analgesia (fentanyl bolus) was most frequent in the Prop group. There was no significant difference in the time of extubation. Cats in the Dex 1 and Dex 3 groups had a faster anesthetic recovery, with shorter times to achieving sternal recumbency, regaining ambulation and reaching full recovery. Cats in the Dex 1 and Dex 5 groups presented the best recovery quality scores, with 4 (range 4–5) and 4 (range 3–5), respectively, while the Prop group scored 1 (range 1–3), the worst anesthetic recovery score among the groups.

Conclusions and relevance The use of dexmedetomidine as a total intravenous anesthesia adjuvant, especially at doses of 1 and 3 µg/kg/h, reduces propofol consumption and improves cardiorespiratory stability and intraoperative analgesia, while promoting a better and quicker recovery from anesthesia.

Keywords: Alpha$_2$ adrenergic agonist; analgesia; anesthesia; sedation

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Introduction

Inhalation anesthesia is currently the most common technique for anesthetic maintenance in cats.[1] However, the advantages offered by inhalation anesthetics, such as allowing for rapid changes in the depth of anesthesia and shorter recovery times, may be offset by important undesirable effects (eg, the decrease in systemic vascular resistance from peripheral vasodilation).[2–5] Total intravenous (IV) anesthesia (TIVA) with propofol is an alternative, since it can provide similar cardiovascular stability to, or

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in some cases better than, halogenated drugs.[5–7] However, cats slowly metabolize phenolic compounds owing to the lack of functional glucuronosyltransferase (UGT1A6) enzymes. Hence, TIVA in this species using propofol as the sole anesthetic agent should be avoided,[8] in order to prevent cumulative effects and delayed recovery.[8,9]

Anesthetic adjuvants are used to minimize the impact of propofol TIVA in cats. Fentanyl and its congeners have been shown to reduce the propofol dose required to maintain anesthesia, while also providing better intraoperative analgesia and cardiorespiratory stability, and shorter recovery times.[10] Ketamine has also improved propofol TIVA in cats submitted to non-surgical procedures, by lowering the dosage required for anesthetic maintenance and, in turn, the depressant effects on the cardiovascular and respiratory systems.[11]

Another drug frequently considered in feline anesthesia is dexmedetomidine.[12–14] As a preanesthetic, dexmedetomidine can reduce the requirement for propofol in the induction of anesthesia, as well as improve anesthetic recovery and decrease postoperative analgesic requirements.[15,16] When used as an adjunct to inhalation anesthesia in cats, dexmedetomidine considerably reduces isoflurane requirement, decreases the heart rate (HR) and increases blood pressure.[17] Regarding the quality of recovery, dexmedetomidine has been shown to reduce vocalization, tremors and other involuntary reactions in the postanesthetic period.[18–21] However, few studies have investigated the effect of dexmedetomidine on propofol infusion requirements and on postoperative analgesia in cats.

The aim of this study was to assess the effect of dexmedetomidine in cats anesthetized with propofol in a continuous rate infusion (CRI) and subjected to ovariohysterectomy. We hypothesized that dexmedetomidine would reduce the propofol requirement while improving cardiorespiratory stability, as well as the time and quality of anesthetic recovery.

Materials and methods

All procedures were approved by the Animal Care and Use Committee of the host institution, under application number 5126090818. Written and informed owner consent was obtained for every animal and procedure involved. The study population comprised 28 cats of varying breeds. Cats that did not allow handling were excluded from the study. Animals were considered healthy after physical examination, complete blood count, and liver and kidney function tests, with body condition scores of 3–4/9.[22] Prior to the procedure, the cats were fasted for 8 h, with no water restriction. The team responsible for scoring remained blinded to the treatments throughout the study period.

The animals were randomly distributed into four groups: Dex 1, Dex 3, Dex 5 and Prop. Animals in the Dex 1, Dex 3 and Dex 5 groups received 5 µg/kg dexmedetomidine (Dexdomitor; Zoetis) as a preanesthetic medication; animals in the Prop group received 0.05 ml saline intramuscularly (IM). After 20 mins, the degree of sedation was evaluated using a simplified scale, with scores ranging from 0 (no sedation) to 4 (maximum sedation).[12] A 24 G catheter was placed in the cephalic vein to allow induction of anesthesia, with propofol (Propovan; Cristália) administered to effect at 1 mg/kg every 10 s until endotracheal intubation was possible. Subsequently, TIVA was started, with 300 µg/kg/min propofol and 3 ml/kg/h NaCl 0.9% (Prop), or 200 µg/kg/min propofol and 1 µg/kg/h (Dex 1), 3 µg/kg/h (Dex 3) or 5 µg/kg/h (Dex 5) dexmedetomidine diluted in 3 ml/kg/h NaCl 0.9% (SR8x; Digicare 670, RZ Equipamentos Veterinários). All animals received 100% oxygen at a flow rate of 200 ml/kg/min through a Mapleson D system throughout the anesthesia procedure.

Total anesthesia time was standardized as 100 mins: the first 60 mins were reserved for allowing the animal to stabilize under the CRI, and the remaining 40 mins were reserved for the surgery. The dexmedetomidine CRI for each group was kept constant throughout the anesthesia procedure, while the propofol infusion rate was adjusted every 10 mins (± 50 µg/kg/min) to maintain anesthetic depth, which was assessed through palpebral reflex, and physiological and cardiovascular variables (Table 1).[23] At the end of the procedure, the total volume of propofol administered during the 60- and 100-min periods was calculated.

Table 1 Variables used to assess anesthetic depth in cats subjected to propofol-based total intravenous anesthesia alone or combined with dexmedetomidine at 1 µg/kg/h (Dex 1), 3 µg/kg/h (Dex 3) or 5 µg/kg/h (Dex 5) infusion rates (seven cats per group)

Variables	Superficial anesthesia	Surgical anesthesia	Deep anesthesia
Movement	Possible	No	No
Jaw tone	Mild to strong	Relaxed	Relaxed
Eye position	Central	Rotated	Central
Palpebral reflex	Positive	Negative	Negative
Heart rate	Usually increased	Normal	May be decreased
Respiratory rate	Usually increased	Normal	Usually decreased
Sympathetic response	Present	Usually absent	Absent

Cardiorespiratory variables were assessed 5 mins after induction and every 10 mins thereafter until the end of anesthesia (Life Window light LW8; Digicare). The HR and rhythm were monitored with a lead II electrocardiography configuration. Pulsatile oxygen saturation (SpO_2) was assessed by a pulse oximetry probe placed on the tongue. The systolic, mean (MAP) and diastolic arterial pressures were measured as a single reading, by inflating an appropriately sized occlusion cuff (width of approximately 40% of the limb circumference) over the pedal dorsal artery, and the respiratory rate (*f*) and end-tidal carbon dioxide ($ETCO_2$) were obtained from a side-stream capnograph, with the tubing connected between the endotracheal tube and the breathing system. An esophageal probe allowed for continuous monitoring of the body temperature and a thermal mattress was used to prevent hypothermia (Styllus term; Ortovet).

During surgery, a single bolus of fentanyl (2.5 µg/kg [Fentanest; Cristália]) was provided as rescue analgesia whenever *f*, HR or MAP increased by >20% of the 60-min timepoint, repeated whenever necessary. In any event of hypotension (MAP <60 mmHg), propofol CRI was reduced by 50 µg/kg/min. If the episode persisted for >5 mins, 10 µg/kg/min dopamine was initiated. A 0.4 ml arterial blood sample was collected from the coccygeal artery by a 22 G needle and a previously heparinized 1 ml syringe, at 5 and 60 mins after induction of anesthesia, to obtain the pH, partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide ($PaCO_2$), arterial oxygen saturation, base excess, bicarbonate, and glucose concentration (CG8+; Abbott).

At the end of the propofol infusion, 0.1 mg/kg meloxicam (Maxicam; Ouro Fino) was administered subcutaneously to all animals, and the times to extubation, sternal recumbency, ambulation and total recovery were logged. The quality of anesthetic recovery was evaluated on a five-point subjective scale,[9] ranging from poor (many attempts to stand, falling over repeatedly, marked ataxia) to excellent (the animal remains calm and rolls into sternal recumbency, gets up without falling and shows minimal ataxia). Pain scoring was performed using the UNESP-Botucatu multidimensional composite pain scale.[12] Animals scoring ⩾4 received 0.2 mg/kg morphine (Dimorf; Cristália) IM as rescue analgesia. Assessments were performed immediately before preanesthetic medication and 1, 2, 4, 8, 12 and 24 h after the end of anesthesia.

A sample size calculation indicated that seven cats per group would be required to confirm a reduction in the propofol CRI (alpha error of 0.05; beta error of 0.20; effect size of 30%; standard deviation of 0.05 – pilot study). The data were verified for distribution normality with the Shapiro–Wilk test. Propofol CRI, HR, MAP, $ETCO_2$, SpO_2, blood gas values and body temperature were compared by a two-way ANOVA with a post-hoc Tukey test for between-group comparisons and a post-hoc Dunnett test for within-group comparisons. Sedation score, *f*, requirement of a fentanyl bolus, time to extubation, time to sternal recumbency, time to ambulation, time to total recovery and quality recovery were compared by a Kruskal–Wallis test with a post-hoc Dunn test, and Friedman test. Parametric values were expressed as mean ± SD, whereas non-parametric values were expressed as median (range). Differences were considered to be statistically significant at a 5% level.

Results

No statistically significant differences in animal weight and age were observed between groups. Animals from the Prop group weighed 2.4 ± 0.6 kg and were 10 ± 4 months of age, whereas those from the Dex 1, Dex 3 and Dex 5 groups were 3.1 ± 0.9 kg and 14 ± 10 months, 2.5 ± 0.7 kg and 10 ± 4 months, and 2.9 ± 0.6 kg and 14 ± 10 months, respectively.

All cats that received dexmedetomidine as a preanesthetic presented with mild sedation, with a score of 1 (range 1–2), when compared with cats in the Prop group (P <0.01). Vomiting after premedication occurred in one animal in the Dex 1 group, two in the Dex 3 group and three in the Dex 5 group. Cats in the Prop group required a higher dose of propofol for the induction of anesthesia (13.4 ± 1.6 mg/kg) than for cats in the Dex 1 (6.7 ± 0.8 mg/kg), Dex 3 (7.4 ± 1.4 mg/kg) and Dex 5 (6.9 ± 0.7 mg/kg) groups. Cats in the Dex 1, Dex 3 and Dex 5 groups did not significantly differ from each other regarding the requirement of propofol for anesthesia induction (P <0.01).

Throughout the anesthetic period, the cats that received dexmedetomidine required a lower propofol CRI than cats in the Prop group. At the end of the stabilization period, the mean propofol rates administered were 93 ± 53 µg/kg/min in the Dex 1 group, 129 ± 76 µg/kg/min in the Dex 3 group, 86 ± 48 µg/kg/min in the Dex 5 group and 486 ± 80 µg/kg/min in the Prop group (P <0.01). At the end of the ovariohysterectomy procedure, the mean rates were 86 ± 60 µg/kg/min in the Dex 1 group, 100 ± 60 µg/kg/min in the Dex 3 group, 64 ± 20 µg/kg/min in the Dex 5 group and 500 ± 170 µg/kg/min in the Prop group (P <0.01; Figure 1). Thus, the addition of dexmedetomidine had a significant propofol-sparing effect, as it reduced the propofol CRI by 72.8%, 71.1% and 74.6% in the Dex 1, Dex 3 and Dex 5 groups, respectively (P <0.01).

In general, cats in the Prop group had higher HRs than all other groups throughout the anesthetic period (Table 2). MAP in cats in the Dex 3 and Dex 5 groups was considerably higher than in cats in the Prop group, at virtually all assessment points (Table 2). Episodes of hypotension (MAP <60 mmHg) were observed 21 times in the Prop group, three times in the Dex 1 group, once in the Dex 3 group and on no occasions in the Dex 5 group, and episodes of hypertension (MAP >130 mmHg) were observed

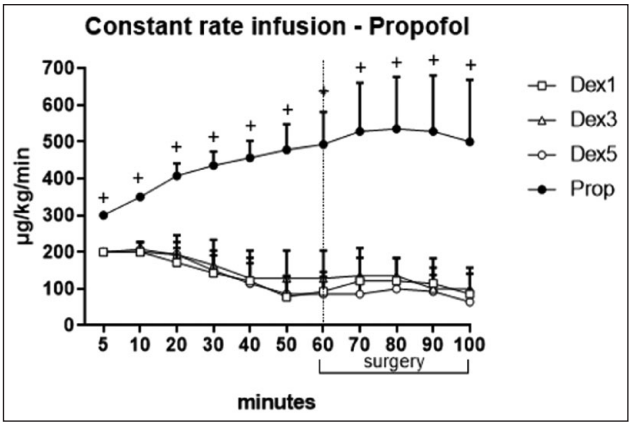

Figure 1 Propofol infusion rate (µg/kg/min) in cats (n = 7) subjected to propofol-based total intravenous anesthesia alone or combined with dexmedetomidine at 1 µg/kg/h (Dex 1), 3 µg/kg/h (Dex 3) or 5 µg/kg/h (Dex) infusion rates. Values expressed as mean ± SD. A cross (+) indicates a significant difference among the Prop group compared with the Dex 1, Dex 3 and Dex 5 groups ($P < 0.05$)

twice in the Prop group, 31 times in the Dex 1 group, 29 times in the Dex 3 group and 31 times in the Dex 5 group. All animals that presented with episodes of hypotension responded positively to a reduction in the propofol CRI within the subsequent 5-min assessment interval.

Group comparison did not reveal significant difference in $ETCO_2$ values, but an increase was observed in the Prop group from 20 mins onward. A similar increase occurred in the Dex 1 and Dex 3 groups, but only after 80 mins of anesthesia (Table 2). The *f* was higher in the Dex 3 group than in the Prop group at the 70-, 90- and 100-min assessment points. Group comparison did not reveal significant difference in temperature values. No significant differences in blood gases were observed between groups (Table 3). However, the serum glucose concentration was lowest in the Prop group ($P < 0.05$; Table 3).

During anesthesia, animals in the Prop group required rescue analgesia (fentanyl bolus) 35 times, which was statistically significantly more often than in the Dex 1 (22 times; $P = 0.04$), Dex 3 (21 times; $P = 0.017$) and Dex 5 (20 times; $P = 0.0058$) groups. No rescue analgesia was required for cats in any group during the postoperative period. Time to extubation did not differ significantly between groups (17 mins in the Prop group [range 11–28]; 13 mins in the Dex 1 group [range 3–20]; 12 mins in the Dex 3 group [range 5–23]; 16 mins in the Dex 5 group [range 4–23]). Cats in the Dex 1 and Dex 3 groups had a quicker anesthetic recovery than cats in the Prop and Dex 5 groups, with shorter times needed to achieve sternal recumbency, regain ambulation and reach full recovery (Table 4). The quality of anesthetic recovery was considered to be best in the Dex 1 and Dex 5 groups vs the Prop group, with scores of 4 (range 4–5; $P = 0.005$) and 4 (range 3–5; $P = 0.0018$), respectively, while cats in the Prop group had the worst anesthetic recovery score of 1 (range 1–3). Cats in the Dex 3 group scored 3 (range 3–4) and did not differ significantly from any other group regarding quality of recovery ($P = 0.188$).

Discussion

The use of dexmedetomidine as an adjuvant to propofol-based TIVA produced a propofol-sparing effect, along with bradycardia and hypertension. An improvement in intraoperative analgesia, a shorter recovery time and a better quality of recovery were also observed. The doses of dexmedetomidine premedication reported for cats range from 2 to 75 µg/kg, with a dose-dependent sedation.[13,24,25] All animals included in this study had a docile nature, and the dexmedetomidine dose of 5 µg/kg, chosen for mild-to-moderate sedation, was enough to allow for smooth, easy handling and venipuncture of the animals. Of all cats premedicated with dexmedetomidine, 28.6% (n = 6/21) vomited, highlighting the action of this drug on the chemoreceptor trigger zone in the vomiting center.[26,27] A sparing effect of 47.8% in propofol dose required for endotracheal intubation was also observed with the administration of dexmedetomidine, which is explained by the anxiolytic and sedative effects of this drug.[15,16] However, the dexmedetomidine-sparing effect on the propofol dose to permit endotracheal intubation could be higher, considering the speed of propofol injection used in this study.[28]

During the 60-min stabilization period, the animals in the dexmedetomidine groups had lower HRs than cats in the Prop group. This was an expected outcome, as dexmedetomidine decreases sympathetic tone, and the stimulation of peripheral adrenergic receptors in the vascular smooth muscle results in increased systemic vascular resistance and reflex bradycardia.[21,29] This effect was also observed in blood pressure values, particularly in cats in the Dex 3 and Dex 5 groups, which had higher MAPs than the cats in the Prop group. Although MAP was considered within the range of anesthetized cats, hypertension (MAP >130 mmHg) must be considered when propofol–dexmedetomidine CRIs were used in this species.

It is likely that the rate of 1 µg/kg/h dexmedetomidine can promote vasoconstriction to the point of counterbalancing the vasodilator effect of propofol, without significantly increasing vascular resistance.[30,31] A similar result was found in cats subjected to inhalation anesthesia that showed no relevant alterations on blood pressure under the same rate of dexmedetomidine.[21] It is important to note, however, that the use of inhalation agents results in peripheral vasodilation, reducing vascular resistance and leading to hypotension,[32] which explains the absence of dexmedetomidine effects on MAP. The increased MAP values in cats in the Dex 1 group at the beginning of the surgical procedure can be explained by the activation of the sympathetic system as a response to the surgical stimulus.[33,34]

Table 2 Heart rate (HR), mean arterial pressure (MAP), end-tidal carbon dioxide ($ETCO_2$), respiratory rate (*f*), pulsatile oxygen saturation (SpO_2) and temperature of cats subjected to propofol-based total intravenous anesthesia alone (Prop) or combined with 1 µg/kg/h (Dex 1), 3 µg/kg/h (Dex 3) and 5 µg/kg/h (Dex 5) dexmedetomidine (seven cats per group)

Variables	Group	Min							
		5	20	40	60	70	80	90	100
HR (bpm)	Prop	158 ± 28[a]	147 ± 31[a]	138 ± 24[a]	140 ± 28[a]	154 ± 27[a]	142 ± 25[a]	154 ± 30[a]	150 ± 36
	Dex 1	105 ± 17[b]	95 ± 9[b]	93 ± 13[bc]	89 ± 14[bc]	106 ± 13[b]	117 ± 16[ab]	116 ± 17[ab]	121 ± 24
	Dex 3	112 ± 12[b]	106 ± 6[b]	100 ± 10[b]	104 ± 12[ab]	120 ± 20[ab]	125 ± 21[ab]	129 ± 26[ab]	124 ± 31
	Dex 5	102 ± 15[b]	97 ± 14[b]	86 ± 5[c]	85 ± 8[c]	90 ± 19[b]	105 ± 20[b]	108 ± 22[b]	110 ± 17
MAP (mmHg)	Prop	68 ± 19[a]	69 ± 13[a]	74 ± 18[a]	72 ± 17[a]	79 ± 22[a]	82 ± 25	84 ± 27	73 ± 18[a]
	Dex 1	98 ± 18[b]	95 ± 20[b]	94 ± 20[ab]	97 ± 15[ab]	108 ± 10[ab]	115 ± 12	106 ± 26	104 ± 16[b]
	Dex 3	105 ± 25[b]	113 ± 25[b]	111 ± 23[b]	114 ± 14[b]	129 ± 23[b]	104 ± 33	102 ± 21	102 ± 21[ab]
	Dex 5	118 ± 20[b]	118 ± 24[b]	115 ± 18[b]	111 ± 15[b]	119 ± 19[b]	109 ± 10	99 ± 10	97 ± 15[ab]
$ETCO_2$ (mmHg)	Prop	33 ± 4	40 ± 8	40 ± 6*	40 ± 6	44 ± 5*	47 ± 6*	50 ± 9*	47 ± 9
	Dex 1	32 ± 7	38 ± 5	38 ± 6	36 ± 12	40 ± 9	42 ± 9*	47 ± 11*	42 ± 7*
	Dex 3	33 ± 7	37 ± 7	37 ± 6	38 ± 6	39 ± 7	44 ± 9	43 ± 6*	40 ± 5
	Dex 5	34 ± 8	35 ± 5	36 ± 5	36 ± 7	37 ± 6	42 ± 8	44 ± 7	42 ± 4
f (breaths/min)	Prop	16 (6–35)	17 (10–31)	14 (9–28)	15 (7–28)[a]	10 (8–25)[a]	6 (4–40)	7 (3–27)[a]	8 (5–19)[a]
	Dex 1	17 (6–41)	17 (14–37)	19 (8–35)	17 (10–26)[a]	18 (7–32)[ab]	16 (5–29)	11 (7–24)[ab]	16 (11–26)[ab]
	Dex 3	26 (22–28)	24 (19–32)	23 (19–36)	28 (24–37)[b]	20 (13–33)[b]	22 (11–27)	19 (14–32)[b]	22 (13–34)[b]
	Dex 5	26 (12–31)	22 (12–32)	22 (11–37)	23 (11–36)[ab]	24 (10–39)[ab]	18 (7–32)	19 (12–30)[ab]	17 (11–34)[ab]
SpO_2 (%)	Prop	99 ± 2	97 ± 2	98 ± 1	98 ± 1	98 ± 1	99 ± 1	98 ± 1	99 ± 1
	Dex 1	99 ± 1	99 ± 1	99 ± 1	100 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1
	Dex 3	99 ± 1	99 ± 2	99 ± 2	99 ± 2	98 ± 3	99 ± 1	98 ± 2	98 ± 2
	Dex 5	98 ± 2	98 ± 2	99 ± 1	98 ± 1	98 ± 2	98 ± 1	99 ± 1	98 ± 2
Body temperature (°C)	Prop	37.8 ± 0.5	37.8 ± 1.3	37.5 ± 1.0	37.4 ± 1.0	37.5 ± 0.9	37.5 ± 0.7	37.5 ± 0.8	37.5 ± 0.6
	Dex 1	38.0 ± 0.6	38.0 ± 0.9	38.0 ± 0.9	38.0 ± 0.8	37.9 ± 0.9	37.9 ± 0.8	37.9 ± 0.9	37.9 ± 0.7
	Dex 3	37.8 ± 0.4	37.8 ± 0.5	37.7 ± 0.7	37.8 ± 0.8	37.9 ± 0.7	37.9 ± 0.6	37.9 ± 0.5	37.8 ± 0.5
	Dex 5	37.9 ± 0.4	37.8 ± 0.8	37.7 ± 0.6	37.7 ± 0.8	37.9 ± 0.5	37.8 ± 0.6	37.7 ± 0.5	37.8 ± 0.7

Data are presented as mean ± SD or median (range). Different superscript letters indicate a significant difference between groups ($P < 0.05$)
*Differences at the 5-min time point
bpm = beats/min

Table 3 pH, partial pressure of carbon dioxide ($PaCO_2$), partial pressure of oxygen (PaO_2), bicarbonate (HCO_3^-), base excess (BE), arterial oxygen saturation (SaO_2) and glucose of cats subjected to propofol-based total intravenous anesthesia alone (Prop) or combined with 1 µg/kg/h (Dex 1), 3 µg/kg/h (Dex 3) and 5 µg/kg/h (Dex 5) dexmedetomidine (seven cats per group)

Variables	Group	Min	
		5	60
pH	Prop	7.24 ± 0.04	7.27 ± 0.06
	Dex 1	7.31 ± 0.08	7.29 ± 0.06
	Dex 3	7.27 ± 0.08	7.26 ± 0.06
	Dex 5	7.29 ± 0.04	7.32 ± 0.06
$PaCO_2$ (mmHg)	Prop	42 ± 9.1	41 ± 8.9
	Dex 1	39 ± 12.2	45 ± 13.9
	Dex 3	42 ± 14.2	44 ± 9.1
	Dex 5	37 ± 9.5	36 ± 6.4
PaO_2 (mmHg)	Prop	285 ± 87	271 ± 55
	Dex 1	275 ± 39	329 ± 60
	Dex 3	313 ± 82	338 ± 74
	Dex 5	316 ± 83	310 ± 35
HCO_3^- (mEq/l)	Prop	18.0 ± 2.82	18.6 ± 2.00
	Dex 1	18.9 ± 3.42	21.0 ± 2.48
	Dex 3	17.9 ± 2.55	20.2 ± 3.18
	Dex 5	18.3 ± 2.51	18.5 ± 1.13
BE (mEq/l)	Prop	–9 ± 3	–9 ± 2
	Dex 1	–8 ± 3	–7 ± 5
	Dex 3	–8 ± 2	–6 ± 3
	Dex 5	–8 ± 2	–8 ± 2
SaO_2 (%)	Prop	100 ± 0	100 ± 0
	Dex 1	99 ± 1	100 ± 0
	Dex 3	100 ± 0	100 ± 0
	Dex 5	99 ± 1	99 ± 1
Glucose (mg/dl)	Prop	89 ± 13[a]	92 ± 30[a]
	Dex 1	165 ± 49[ab]	236 ± 87[b]*
	Dex 3	182 ± 53[b]	265 ± 66[b]
	Dex 5	189 ± 69[b]	220 ± 78[b]

Data are presented as mean ± SD or median (range). Different superscript letters indicate a significant difference between groups ($P < 0.05$)
*Differences at the 56-min time point

The lower f and higher $ETCO_2$ values found for the cats in the Prop group can be explained by the higher propofol infusion rates required for maintenance of anesthesia, which results in an important depressant effect on the respiratory center.[30,35] However, the addition of dexmedetomidine to the protocol decreased propofol requirements, minimizing its respiratory depressant effects. After 60 mins, rescue analgesia with fentanyl was necessary owing to nociceptive stimuli, which led to a decreased f, thus explaining the $ETCO_2$ values above physiological levels for the species found in cats in the Prop group. However, the use of a non-rebreathing circuit could have underestimated $ETCO_2$ owing to the possible gas flow dilution, which must be considered. Thus, it is best to consider only $PaCO_2$, which showed no difference between the groups. However, $PaCO_2$ levels were considered higher than the reference interval for cats.[36] This could be due to the hypoventilation, which is also reflected in the far-from-expected PaO_2 values, considering that these cats received 100% oxygen. Another explanation for the low PaO_2 levels could be that dorsal recumbency, leading to atelectasis, may have worsened gas exchange.[37]

A reduction in anesthesia dose requirements when using dexmedetomidine has been reported previously.[38] Thus, we decided to start with a lower propofol infusion rate in the dexmedetomidine groups than in the Prop group, avoiding deep anesthesia. The dexmedetomidine rates of 1, 3 and 5 µg/kg/h reduced total propofol consumption by 72.83%, 71.11% and 74.56%, respectively. Continuous infusions from 1 to 2 µg/kg/h dexmedetomidine in dogs reduced the propofol requirement by approximately 36%, also providing cardiovascular stability.[18] Although the reduction in the propofol CRI is mainly caused by the presence of dexmedetomidine, the use of intraoperative fentanyl may have influenced the results. However, it is important to note that a propofol-sparing effect was still observed for the first 60 mins of anesthesia, when no fentanyl was administered. Furthermore, dexmedetomidine promoted analgesia, as shown by the lower fentanyl requirement for the animals in the

Table 4 Times to extubation, sternal recumbency, ambulation and recovery of cats subjected to propofol-based total intravenous anesthesia alone (Prop) or combined with 1 µg/kg/h (Dex 1), 3 µg/kg/h (Dex 3) and 5 µg/kg/h (Dex 5) dexmedetomidine (seven cats per group)

	Prop	Dex 1	Dex 3	Dex 5
Extubation (mins)	17 (11–28)	13 (3–20)	12 (5–23)	16 (4–23)
Sternal recumbency (mins)	102 (75–117)[a]	51 (33–65)[b]	48 (25–91)[b]	63 (11–78)[ab]
Ambulation (mins)	124 (85–128)[a]	60 (56–103)[b]	62 (27–95)[b]	79 (41–112)[ab]
Recovery time (mins)	165 (135–180)[a]	129 (122–134)[b]	127 (70–139)[b]	130 (88–155)[ab]

Data are presented as median (range). Different superscript letters indicate significant difference between groups ($P < 0.05$)

dexmedetomidine groups vs those in the propofol group, albeit without eliminating the need for rescue analgesia, especially at times of ovarian and cervical traction.

While the dexmedetomidine doses of 1 and 3 µg/kg/h shortened anesthetic recovery time, the same was not observed with the 5 µg/kg/h dose. Most likely, the increasing dose deepened postanesthetic sedation, a known dose-dependent effect of alpha$_2$ adrenergic agonists.[24,39] Furthermore, recovery from anesthesia was worse in cats in the Prop group, with cases of hyperreflexia, ataxia and opisthotonos absent in animals that received dexmedetomidine. These effects may have been exacerbated due to the antagonistic propofol effect on glycine receptors, concentrated in the spinal cord and brainstem, which play a key role in motor neuron regulation.[40]

As expected, rescue analgesia was not required by any animals in the postoperative period, as meloxicam reduces the inflammatory response and the primary hyperalgesia of the procedure.[41–43] Although it is possible that the administration of meloxicam interfered with the postoperative analgesic evaluation of the treatments, such an approach was elected for animal welfare reasons and to simulate a real clinical situation.

This study had some limitations, such as the use of a CRI instead of a target-controlled infusion, which would have enabled better assessment of the necessary doses, analgesia and sedation in a plasma concentration-dependent manner. Furthermore, the postoperative analgesia produced by dexmedetomidine may have been overshadowed by the effects of meloxicam.

Conclusions

The use of dexmedetomidine, especially at doses of 1 and 3 µg/kg/h, reduces propofol consumption, and improves cardiorespiratory stability and antinociception, while promoting better and quicker recovery from anesthesia.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognized high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (either experimental or non-experimental animals, including cadavers) for all procedure(s) undertaken (either prospective or retrospective studies). No animals or people are identifiable within this publication, and therefore additional informed consent for publication was not required.

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