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Total intravenous anesthesia with propofol, ketamine, and lidocaine associated with dexmedetomidine or xylazine for ovariohysterectomy surgery in female dogs

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ABSTRACT: This study compared cardiovascular and respiratory effects of dexmedetomidine and xylazine in total intravenous anesthesia with propofol, ketamine, and lidocaine. Twenty-one female dogs were submitted to ovariohysterectomy, premedicated with acepromazine and anesthetized with propofol at a variable rate. The dogs were intubated and supplemented with 100% oxygen in a circuit without rebreathing gases in spontaneous ventilation. They were divided into three groups (n=21) after induction: control (CON) with ketamine (2 mg/kg + 0.6 mg/kg/h) and lidocaine (2 mg/kg + 3 mg/kg/h), DEX and XIL with the same drugs as CON, associated with dexmedetomidine (2 µg/kg + 1 µg/kg/h) or xylazine (0.2 mg/kg + 0.1 mg/kg/h). Propofol consumption, fentanyl analgesic rescue, and cardiorespiratory and blood gas parameters were evaluated during anesthesia. The DEX group had a lower consumption of propofol (0.16 ± 0.09 mg/kg/min) compared to CON (0.24 ± 0.09 mg/kg/min), both not differing from XIL (0.23 ± 0.09 mg/kg/min). The mean arterial pressure was higher after the initial *bolus* in DEX (107 ± 8 mmHg) and XIL (96 ± 11 mmHg) compared to the CON group (80 ± 10 mmHg). Higher accumulation of arterial carbon dioxide and a decrease in pH were observed in the CON group. The total number of fentanyl rescues did not differ between DEX (7) and XIL (6) and were lower than CON (16). Therefore, dexmedetomidine and xylazine reduced intraoperative fentanyl consumption compared to ketamine and lidocaine infusion alone. However, only dexmedetomidine promoted lower propofol consumption and higher blood pressure values.
Key words: infusion rate, alpha-2 adrenergic agonists, analgesia, sparing effect, neutering.

Anestesia total intravenosa com propofol, cetamina e lidocaína associados à dexmedetomidina ou xilazina para cirurgia de ovário-histerectomia em cadelas

RESUMO: Esse estudo comparou efeitos cardiovasculares e respiratórios da dexmedetomidina e xilazina na anestesia total intravenosa com propofol, cetamina e lidocaína. Foram submetidas a ovário-histerectomia 21 cadelas, pré-medicadas com acepromazina, anestesiadas com propofol em taxa variável. As cadelas foram intubadas e suplementadas com oxigênio 100% em circuito sem reinalação de gases em ventilação espontânea. Após a indução, foram distribuídas em três grupos (n=21): controle (CON) com cetamina (2 mg/kg + 0,6 mg/kg/h) e lidocaína (2 mg/kg + 3 mg/kg/h), DEX e XIL com os mesmos fármacos do CON, associados à dexmedetomidina (2 µg/kg + 1 µg/kg/h) ou xilazina (0,2 mg/kg + 0,1 mg/kg/h). Durante a anestesia, foram avaliados o consumo de propofol, resgate analgésico de fentanil, parâmetros cardiorepiratórios e hemogasométricos. O grupo DEX apresentou menor consumo de propofol (0,16 ± 0,09 mg/kg/min) comparado ao CON (0,24 ± 0,09 mg/kg/min), ambos sem diferir de XIL (0,23 ± 0,09 mg/kg/min). A pressão arterial média foi maior após o *bolus* inicial em DEX (107 ± 8 mmHg) e XIL (96 ± 11 mmHg) comparadas ao grupo CON (80 ± 10 mmHg). Houve maior acúmulo de gás carbônico arterial e diminuição do pH no grupo CON. O número total de resgates com fentanil não diferiram entre DEX (7) e XIL (6), e foram inferiores ao CON (16). Conclui-se que a dexmedetomidina e xilazina reduziram o consumo de fentanil transoperatório em comparação à infusão isolada de cetamina e lidocaína. Porém, nesse estudo apenas a dexmedetomidina promoveu menor consumo de propofol e maiores valores de pressão arterial.
Palavras-chave: infusão continua, agonistas alfa-2 adrenérgicos, analgesia, efeito poupador, castração.

INTRODUCTION

Total intravenous anesthesia (TIA) consists of administering anesthetic drugs exclusively intravenously (RAFFE, 2020). Propofol is the drug most used in TIA, but the association of adjuvant and analgesic drugs, promoting a balanced anesthesia, is necessary in order to work with the lowest possible doses to allow the suppression of the nociceptive reflex (AGUADO et al., 2019).

Opioids are analgesic drugs used in TIA in medicine and veterinary practice, but there is attention focused on rationalizing the use of opioids due to their side effects on the immune system and because they are used as a drug of abuse (WHITE et al., 2017). Therefore, reducing doses and using alternative drugs to the use of opioids, including ketamine, lidocaine, and alpha-2 adrenergic agonists, have been described in the literature (GUTIERREZ-BLANCO et al., 2013).

Among alpha-2 adrenergic agonists, dexmedetomidine is characterized by being highly liposoluble and selective, with 1600/1 alpha-2/alpha-1 binding ratio (VALVERDE & SKELDING,

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2019). In dogs, it is used under continuous infusion at rates ranging from 0.1 to 5.0 µg/kg/h with or without initial *bolus* (AKASHI et al., 2020). Another alpha-2 adrenergic agonist used in veterinary medicine is xylazine, which is more often used in dogs as a sedative or associated with dissociative anesthesia despite being frequently used under continuous infusion in horses. Xylazine is less liposoluble and has a selectivity 10 times lower than dexmedetomidine, with infusion rates ranging from 0.2 to 1.0 mg/kg/h being described in dogs (JENA et al., 2014; IBRAHIM, 2017). However, its analgesic effects at low doses are poorly studied.

This study evaluated the cardiorespiratory effects, the propofol infusion rate, and the need for rescue with fentanyl during continuous infusion of lidocaine, ketamine, and propofol associated or not with dexmedetomidine or xylazine in female dogs submitted to ovariohysterectomy. We believed that continuous infusion of xylazine could present cardiovascular and anesthetic effects similar to those of continuous infusion of dexmedetomidine.

MATERIALS AND METHODS

Twenty-one mixed-breed adult female dogs (1 to 5 years old) with an average weight of 18 ± 5 kg were used and referred to elective ovariohysterectomy. A general physical examination, electrocardiogram, blood count, and renal and hepatic biochemical profiles were performed before the surgical procedure.

The dogs were submitted to an eight-hour fast before preanesthetic medication, performed with acepromazine (1%, Vetnil®) at a dose of 0.03 mg/kg, intramuscularly. After 30 minutes, venous access was performed through the cephalic vein with a 20G venous catheter and the dogs were induced to general anesthesia with propofol *bolus* (1%, União Química) at a dose of 5 mg/kg, followed by orotracheal intubation and positioning in dorsal decubitus on a thermal mattress. Anesthetic maintenance was performed with propofol at an initial rate of 0.4 mg/kg/min (Universal Syringe Pump, model 400, PAQIN, China) and the dogs were maintained in spontaneous breathing, connected to a system without re-breathing gases type T Baraka with a 1-liter reservoir flask under continuous flow of 0.2 L/min/kg of 100% O_2. The propofol maintenance rate was altered at more or less 0.1 mg/kg/min, starting with the administration of adjuvants, to maintain an adequate anesthetic plane, characterized by rotation of the eyeball, decrease or absent eyelid reflex, and loss of mandibular tone.

The intraoperative evaluation included electrocardiogram, heart rate (HR) (InCardio, InPulse Animal Health), respiratory rate (RR), partial pressure of expired carbon dioxide ($ETCO_2$) with a side stream sensor, and esophageal temperature (RM1000 VET – RZvet). Arterial access was performed with a 20G catheter in the metatarsal artery for sample collection for blood gas analysis and measurement of mean arterial pressure (MAP) using an analog sphygmomanometer with the liquid column at the height of the right atrium.

The first parametric measurement (M1) was performed before starting adjuvant infusions. Then, the dogs were randomly distributed into three groups (n=7): control (CON), dexmedetomidine (DEX), and xylazine (XIL) groups. The CON group received an intravenous *bolus* of ketamine (10%, Syntec) and lidocaine (2%, Hypofarma), both at a dose of 2 mg/kg, followed by infusions of 0.6 mg/kg/h and 3 mg/kg/h, respectively. In the DEX group, dexmedetomidine (0.05%, Zoetis) was added to the same doses of ketamine and lidocaine, also intravenously and administered at a dose of 2 µg/kg, followed by an infusion of 1 µg/kg/h. Conversely, xylazine (2%, Syntec) was administered in the XIL group as a *bolus* at a dose of 0.2 mg/kg, followed by a continuous infusion of 0.1 mg/kg/h, intravenously, associated with the same doses of ketamine and lidocaine mentioned above. The initial boluses of lidocaine, ketamine, and dexmedetomidine or xylazine were administered in this sequence in separate syringes directly into the equipment at a rate of 600 mL/h with a peristaltic pump (Equipo Universal Infusion Pump, model 100VET, PAQIN, China), followed by infusion at a fixed rate of 5 mL/kg/h of a solution of 250 mL of 0.9% NaCl plus diluted drugs.

The parameters already described were measured again five minutes after the initial *bolus* of analgesics and before the beginning of the surgery (M2). Then, from the beginning of the surgery, the parameters were reassessed right after the skin incision (M3), after the linea alba incision and access to the abdominal cavity (M4), after the act of pinching the first and second ovarian pedicles (M5 and M6), uterine cervix (M7), and during laparorrhaphy (M8) and dermorrhaphy (M9). Blood gas collections and analyses were performed at M1 and M9.

Rescue with fentanyl (0.005%, Cristália) at a dose of 2 µg/kg in intravenous *bolus* was performed from the beginning of the surgery, when MAP and HR or RR increased above 20% of the value of the previous measurement under adequate

anesthesia. Moreover, manually assisted ventilation was instituted when $ETCO_2$ exceeded 60 mmHg. Ventilation was performed using the balloon of the anesthetic system, with a manual pressure of 15 mmHg measured by a sphygmomanometer attached to the system. Each ventilation lasted one second during inspiration and two seconds during expiration, with intervals of three seconds between breaths. $ETCO_2$ was evaluated at each cycle of three ventilation, which were interrupted when it showed values below 60 mmHg. All animals received 0.2 mg/kg meloxicam (2%, Ourofino) subcutaneously at the end of the procedure and the time until extubation was measured.

Among the measurements in each group, one-way ANOVA tests followed by Dunnett's test or Friedman's test followed by Dunn's test were performed for parametric and non-parametric variables, respectively. The analysis of measurements between groups was performed using two-way ANOVA tests, Tukey's and Dunnett's post-tests or Kruskal-Wallis tests, and Dunn'spost-tests for parametric and non-parametric data. The evaluation between two variables used the t-test and the Mann-Whitney test for parametric and non-parametric data. Statistical tests were performed using the GraphPad Prism 8.0 program under a 95% confidence interval, P-value less than 5% was considered significant.

RESULTS

No differences were observed in the parameters evaluated between groups after anesthetic induction (M1). The administration of treatments (M2) led to an increase in HR at M2, M3, and M4 (P = 0.01, 0.02, and 0.03, respectively) in the CON group relative to M1. In contrast, HR was lower in the DEX group than in the CON group at moments M2, M3, M4, M6, M7, M8, and M9 (P = 0.001, 0.004, 0.006, 0.02, 0.01, 0.03, and 0.01, respectively). HR in the XIL group was lower at M2, M3, and M4 (P = 0.004, 0.005, and 0.01, respectively) relative to the CON group, but subsequently higher relative to the DEX group at M6, M8, and M9 (P = 0.02, 0.01, and 0.03, respectively) (Figure 1).

MAP of the DEX and XIL groups at M2 showed higher values than the CON group (P = 0.001 and 0.04, respectively). However, MAP in the DEX group was higher from M2 to M9 compared to M1 (P = 0.003, 0.01, 0.02, 0.0006, 0.006, 0.005, 0.004, and 0.001, respectively), while the XIL group presented higher values only at M5, M6, and M7 (P = 0.0001, 0.001, and 0.008, respectively). In addition, MAP of the DEX group was higher than that of the CON group at M7 (P = 0.03) and that of the XIL group at M9 (P = 0.01) during the procedure.

The respiratory evaluation showed no differences between moments or between groups in the RR, and $ETCO_2$ of the CON group was higher only at M5 compared to the DEX and XIL groups (P = 0.03 and 0.02). In this sense, the arterial pressures of O_2 and CO_2 at M9 showed no differences between groups or in comparison to M1 in the groups (Table 1). However, $PaCO_2$ of the CON group showed higher values in the second evaluation (M9) compared to the first evaluation (M1) but with no statistical difference (P = 0.09), and for the DEX and XIL groups, but also with no statistical difference (P = 0.07 and 0.06, respectively). In addition, the pH of the CON group was lower at M9 compared to M1 (P = 0.03) and M9 in the DEX group (P = 0.03). The bicarbonate concentration in the XIL group decreased within reference values between the first and second collection (P = 0.04). No significant changes were observed in the other blood gas data.

The mean propofol infusion rate was lower in the DEX group compared to the CON group (P = 0.02) and both did not differ from the XIL group (Table 2). The frequency of fentanyl administration did not differ between the DEX and XIL groups and both were lower than in the CON group (P = 0.005 and 0.001, respectively). Episodes of sinus arrest were observed in the electrocardiogram of twelve dogs, that is, 86% of the DEX group (6/7) and 86% of the XIL group (6/7). Moreover, one dog from each of these groups had second-degree Mobitz type II atrioventricular blocks after boluses of dexmedetomidine and xylazine (M2). No statistical difference was observed between groups regarding the number of assisted ventilations (P = 0.09) during the procedure despite the numerical difference. Also, the time to extubation did not differ between groups (P = 0.7133).

DISCUSSION

Lidocaine and ketamine doses were taken from previous studies (ORTEGA & CRUZ, 2011; REED et al., 2015). The dexmedetomidine dose was also chosen from previous studies (SMITH et al., 2017). Xylazine under continuous infusion regimen was less studied in dogs and its dose was based on the lowest dose used in existing studies (SILVA et al., 2007; CASSU et al., 2014; IBRAHIM, 2017), the researchers' routine, and a pilot study with unpublished results.

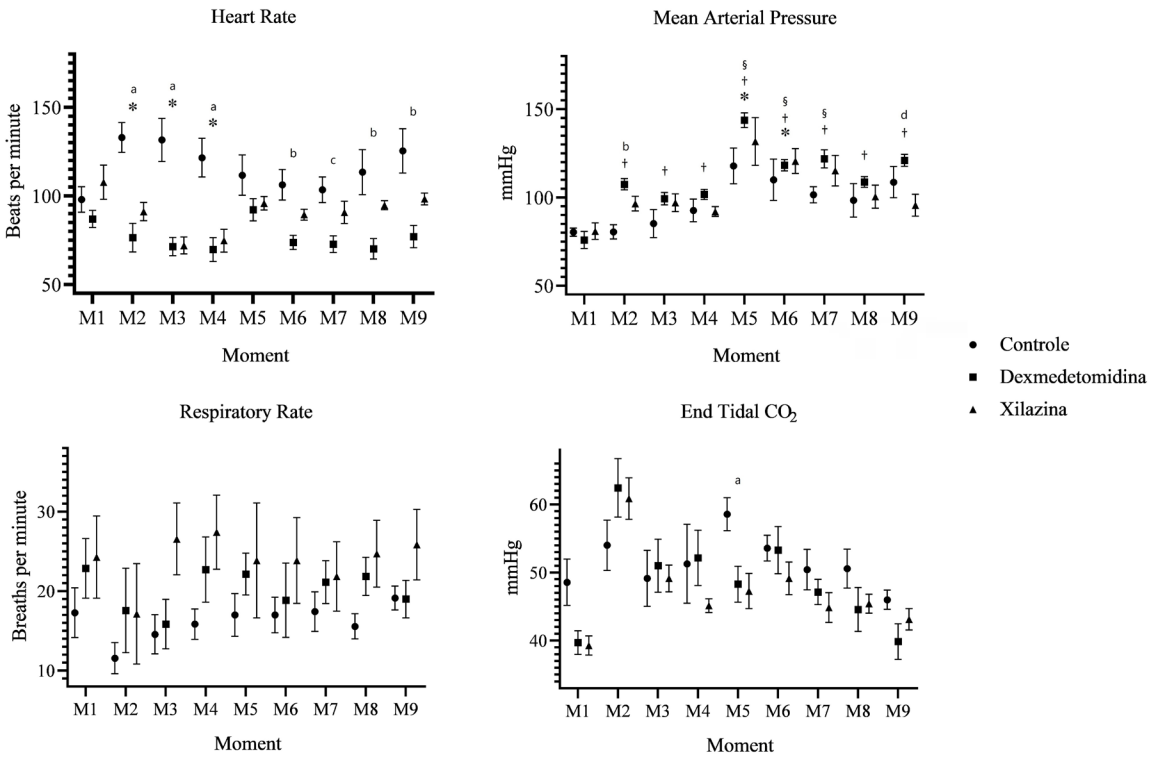

Figure 1 - Mean and standard error of heart rate (bpm), mean arterial pressure (mmHg), respiratory rate (rpm), and carbon dioxide at the end of expiration (mmHg) of female dogs submitted to ovariohysterectomy and anesthetized with continuous infusion of propofol, ketamine, lidocaine (CON), and dexmedetomidine (DEX) or xylazine (XIL) in spontaneous breathing. Measurements were performed after induction with propofol (M1), five minutes after the end of the initial *bolus* of analgesics and before the beginning of the surgery (M2), right after skin incision (M3), after access to the abdominal cavity (M4), after the act of clamping the first and second ovarian pedicles (M5 and M6), suture of the uterine cervix (M7), and laparotomy and dermorrhaphy (M8 and M9).

[a]Difference between CON compared to DEX and XIL; [b]Difference between CON and XIL compared to DEX; [c]Difference between CON compared to DEX, both without differing from XIL; [d]Difference between DEX compared to XIL, both without differing from CON; P-value less than 5% was considered significant.
[*]Difference compared to M1 in the CON group; [†]Difference compared to M1 in the DEX group; [§]Difference compared to M1 in the XIL group; P-value less than 5% was considered significant.

Higher MAP and lower HR values were observed after the *bolus* of dexmedetomidine and xylazine (M2) than the control group. However, a significant increase in MAP relative to the moment before the *bolus* (M1) was observed only in the DEX group. These effects are related to the action of alpha-2 adrenergic agonist drugs on the contraction of smooth muscles in blood vessels. This effect has been experimentally and clinically described in dogs that received continuous infusion of dexmedetomidine (PADDLEFORD & HARVEY, 1999; MURRELL & HELLEBREKERS, 2005; LI et al., 2016; VALVERDE & SKELDING, 2019; DENT et al., 2019). Continuous infusion of dexmedetomidine (0.1 to 5 µg/kg/h) causes an increasing and dose-dependent increase in blood pressure (AKASHI et al., 2020). Dexmedetomidine had more pronounced effects than xylazine on peripheral vasoconstriction considering the increase in MAP in the DEX group and the results of studies that used dexmedetomidine by continuous infusion (MURRELL & HELLEBREKERS 2005, LI et al., 2016; DENT et al., 2019). Thus, the doses used in the present study may not have been equipotent, especially due to the impossibility of comparison, as there are no studies in the literature that have also made this correlation or evaluated the effect of continuous infusion of xylazine at increasing doses in dogs.

The XIL group showed no increase in MAP after the initial *bolus* (comparison between M1 and M2), but it increased compared to CON.

Table 1 - Mean and standard deviation of pH, bicarbonate (HCO_3, mmol/L), arterial carbon dioxide pressure ($PaCO_2$, mmHg), and arterial oxygen pressure (PaO_2, mmHg) before (M1) and after (M9) continuous infusion of ketamine, lidocaine (CON), and dexmedetomidine (DEX) or xylazine (XIL) in dogs under general anesthesia with propofol in spontaneous breathing submitted to ovariohysterectomy.

Group	----------M1----------	----------M9----------
CON	7.326 ± 0.05*	7.268 ± 0.04*a
DEX	7.341 ± 0.03	7.325 ± 0.04a
XIL	7.334 ± 0.04	7.311 ± 0.03
	pH	
CON	23.2 ± 1.8	23.1 ± 1
DEX	21.6 ± 1.6	21.9 ± 1.7
XIL	23.4 ± 1.9*	22.2 ± 1.4*
	HCO3 (mmol/L)	
CON	46 ± 8	52 ± 4
DEX	41 ± 3	45 ± 8
XIL	45 ± 6	45 ± 3
	PaCO2 (mmHg)	
CON	431 ± 38	378 ± 93
DEX	420 ± 35	432 ± 56
XIL	407 ± 86	444 ± 60
	PaO2 (mmHg)	

*Difference between M1 and M2 in the CON, DEX, or XIL groups; aDifference between CON and DEX groups; P-value less than 5% was considered significant.

Nonetheless, an increase in blood pressure could be observed when xylazine was administered at higher doses than those in the present study (PADDLEFORD & HARVEY, 1999; SANTOS et al., 2006; SILVA et al., 2007; CASSU et al., 2014; SILVA et al., 2019). We believed that the xylazine dose was not enough to increase blood pressure significantly, but higher doses could possibly reach higher blood pressure values. The lower specificity and selectivity of xylazine for alpha-2 adrenergic receptors compared to dexmedetomidine is another factor that may be related to the lower increase in blood pressure in the XIL group (VALVERDE & SKELDING, 2019). Studies in rats indicated that different alpha-2 agonists have different selectivity to alpha-2 receptors, with medetomidine being 5–10 times more selective than the other agents, while xylazine has lower selectivity and specificity (VIRTANEN et al., 1988). We suggested the administration of xylazine in continuous infusion at higher doses, increasing the dose used in this study by up to three times to observe equivalent effects of dexmedetomidine administered at doses of 2 µg/kg in *bolus* and 1 µg/kg/h in continuous infusion.

Older studies reported that the administration of alpha-2 agonists causes a biphasic effect on blood pressure, characterized by an increase followed by a decrease (PADDLEFORD & HARVEY, 1999). However, this effect is mainly related to higher doses administered alone. In practice, low doses of alpha-2 agonists, especially associated with other drugs, lead to an increase in blood pressure, followed by a decrease to baseline values (CONGDON et al., 2011). These results were also observed in the present study.

The sinus blocks that occurred in the DEX and XIL groups after boluses (M2) are described in the literature and observed when there is an overlap of the parasympathetic nervous system over the sympathetic one (DETWEILER, 2010). Conversely, the arrhythmias ceased during the surgery, when HR increased. We know that arrhythmias were mediated by accentuated vagal tonus, a reflection of increased blood pressure associated with the sympatholytic effect of alpha-2 adrenergic agonist drugs. However, the association between ketamine and lidocaine possibly attenuated these effects (GÜZEL et al., 2018; VLERICK et al., 2020; TISOTTI et al., 2021).

HR remained within physiological values in the DEX and XIL groups instead of the expected bradycardia, characteristic of alpha-2 adrenergic agonists. It is due to the surgical stimulus that ends up raising HR since the skin incision. In this sense, the peak of the nociceptive stimulus is known to occur during the traction of the ovarian pedicles and an

Table 2 - Mean and standard deviation of the propofol rate (mg/kg/min) and time to extubation (minutes), total number of fentanyl administrations (2 µg/kg *bolus*), and median, minimum, and maximum number of respiratory interventions (assisted breathing of three consecutive movements) of female dogs submitted to ovariohysterectomy under general anesthesia with propofol in spontaneous breathing and continuous infusion of ketamine, lidocaine (CON), and dexmedetomidine (DEX) or xylazine (XIL).

Parameter	----------Group----------	----------Value----------
Propofol (mg/kg/min)	CON	0.24 ± 0.09[a]
	DEX	0.16 ± 0.09[a]
	XIL	0.23 ± 0.09
Extubation (minutes)	CON	9 ±4
	DEX	8 ±5
	XIL	7 ±4
Fentanil (*bolus*)	CON	16[b]
	DEX	7[b]
	XIL	6[b]
Respiratory interventions (nº of interventions)	CON	6 (0-15)
	DEX	6 (3-15)
	XIL	3 (0-9)

[a]Difference between CON and DEX groups; [b]Difference between the CON group and DEX and XIL groups, no difference between DEX and XIL groups; P-value less than 5% was considered significant.

increase in the sympathetic tonus would be expected at that moment (BOSCAN et al., 2011). It was also observed in this study, as fentanyl was required in most individuals in the DEX and XIL groups in the traction of the first ovarian pedicle (M5). Moreover, fentanyl had already been required in the skin or abdomen incisionin the CON group (M3 and M4). Another factor that contributed to the maintenance of HR at normal values was the concomitant use of ketamine, which has a sympathomimetic effect, as already reported in other studies, and observed after the initial *bolus* of ketamine in the CON group of the present study (GÜZEL et al., 2018; VLERICK et al., 2020). The maintenance of HR was also influenced by the administration of lidocaine by continuous infusion, which decreases vagal tone and increases peripheral vascular resistance, related to the administration of dexmedetomidine (TISOTTI et al., 2021). Importantly, the effects of fentanyl administration in the trans-operative period were added to the effects of the already administered drugs, which may have contributed to the decrease in HR. However, the fact that fentanyl was administered at similar times in the DEX and XIL groups allows comparison between groups.

The alpha-2 adrenergic agonists decreased the fentanyl requirement relative to the CON group. However, the anesthetic adjuvant effect was higher in the DEX group, which achieved lower propofolrates. This adjuvant effect has already been reported in the literature regarding dexmedetomidine and general anesthetics (GUTIERREZ-BLANCO et al., 2013; SMITH et al., 2017). Importantly, these differences may be related to the used doses. As observed in the XIL group compared to DEX, the dose needed to achieve some analgesic effect is lower than that required to achieve the anesthetic adjuvant effect. Furthermore, the administration of fentanyl was necessary in most dogs (18/21) at the time of traction of the first ovarian pedicle (M5), that is, no protocol was fully effective in nociceptive control.

Although, the time the dogs spent under assisted breathing was not measured, the number of breaths in the XIL group was lower than those observed in the CON and DEX groups, which were similar to each other but with no significant differences. However, the pH in the CON group was lower at the end of the procedure. This observation may be related to the accumulation of carbon dioxide caused by higher $ETCO_2$ values (M5), lower PaO2 values, and higher PaCO2 values in the second arterial blood collection (M9). These changes in the CON group are possibly related to the higher fentanyl consumption compared to the XIL group, as well as fentanyl and propofol compared to DEX, as these drugs promote dose-dependent respiratory depression (WATKINS et al., 1987; NOLAN & REID, 1991; VASILEIOU et al., 2009). Another factor that may have contributed to the lower pH in CON is the increase in metabolism due to the sympathomimetic activity of ketamine,

which was suppressed in the DEX and XIL groups due to the effects of alpha-2 agonists on sympathetic tonus and metabolism, which decreased the cellular activity (AMBRISKO & HIKASA, 2002).

Studies describing the effects of dexmedetomidine on the respiratory system and gas exchange have reported that its use alone at low doses did not interfere with breathing, while its association potentiated the depressant effects of other drugs (LIN et al., 2008; VALVERDE & SKELDING, 2019). Also, dexmedetomidine improved oxygenation in dogs anesthetized with isoflurane and mechanically ventilated due to bronchodilation that decreased pulmonary resistance and vasoconstriction, decreasing intrapulmonary shunt (DI BELLA et al., 2020). Dogs in the present study that received alpha-2 adrenergic agonists showed no significant improvement in respiratory function because they remained in spontaneous breathing.

The difficulty in determining a continuous infusion dose of xylazine in dogs that is equipotent to the used dexmedetomidinedose, especially due to the limited literature on continuous infusion of xylazine in dogs, is among the research limitations. In this sense, we found that the xylazine dose to reduce fentanyl consumption is low, but it was not enough to reduce propofol consumption, and perhaps higher doses could achieve this effect. Another limitation was the absence of mechanical ventilation to standardize respiratory assistance, as respiratory depression is evident, especially in the CON group, despite manual ventilatory assistance. We emphasize that the present study did not subject the dogs to mechanical ventilation and provided a continuous flow of oxygen through a system without rebreathing gases in an attempt to mimic a routine clinical situation. Submitting dogs to protocols that cause some degree of respiratory depression and manual ventilation, when necessary, can be performed in the anesthetic routine for short-term interventions. Finally, further studies with continuous infusion of xylazine in dogs could assess whether higher doses, in addition to an analgesic adjuvant, would also reduce propofol consumption and which the cardiorespiratory effects would be if the dogs were submitted to mechanical ventilation.

CONCLUSION

The addition of xylazine or dexmedetomidine to the total intravenous anesthesia protocol with propofol, lidocaine, and ketamine promotes less fentanyl consumption during surgery, without causing significant cardiorespiratory changes. However, dexmedetomidine also promoted a reduction in propofol consumption and higher blood pressure values under the conditions of the present study.

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DECLARATION OF CONFLICT OF INTEREST

There are no conflicts of interest.

AUTHORS' CONTRIBUTIONS

All authors contributed equally.

BIOETHICS AND BIOSSECURITY COMMITTEE APPROVAL

Approved by the Ethics Committee and Animal Experimentation No. 31312-2019,

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