Epidural anesthesia and postoperatory analgesia with alpha-2 adrenergic agonists and lidocaine for ovariohysterectomy in bitches

Virgínia H. Pohl, Adriano B. Carregaro, Carlize Lopes, Martielo I. Gehrcke, Daniel C.M. Muller, Clarissa D. Garlet

Abstract

The aim of this study was to determine the viability and cardiorespiratory effects of the association of epidural alpha-2 adrenergic agonists and lidocaine for ovariohysterectomy (OH) in bitches. Forty-two bitches were spayed under epidural anesthesia with 2.5 mg/kg body weight (BW) of 1% lidocaine with adrenaline (CON) or in association with 0.25 mg/kg BW of xylazine (XYL), 10 μg/kg BW of romifidine (ROM), 30 μg/kg BW of detomidine (DET), 2 μg/kg BW of dexmedetomidine (DEX), or 5 μg/kg BW of clonidine (CLO). Heart rate (HR), respiratory rate (f_R) and arterial pressures were monitored immediately before and every 10 min after the epidural procedure. Blood gas and pH analysis were done before, and at 30 and 60 min after the epidural procedure. Animals were submitted to isoflurane anesthesia if they presented a slightest sign of discomfort during the procedure. Time of sensory epidural block and postoperative analgesia were evaluated. All animals in CON and DEX, 5 animals in ROM and CLO, 4 animals in XYL, and 3 in DET required supplementary isoflurane. All groups, except CLO, showed a decrease in HR. There was an increase in arterial pressures in all groups. Postoperative analgesia lasted the longest in XYL. None of the protocols were totally efficient to perform the complete procedure of OH; however, xylazine provided longer postoperative analgesia than the others.

Résumé

L'objectif de la présente étude était de déterminer l'efficacité et les effets cardio-respiratoires d'une anesthésie épidurale par combinaison d'agonistes adrénergiques alpha-2 et de lidocaïne pour effectuer une hystéro-ovariectomie (OH) chez des chiennes. Quarante-deux chiennes ont été châtrées sous anesthésie épidurale réalisée avec de la lidocaïne 1 % à un dosage de 2,5 mg/kg de poids vif (BW) avec de l'adrénaline (CON) ou en association avec 0,25 mg/kg BW de xylazine (XYL), 10 μg/kg BW de romifidine (ROM), 30 μg/kg BW de detomidine (DET), 2 μg/kg de dexmedetomidine (DEX), ou 5 μg/kg BW de clonidine (CLO). La fréquence cardiaque (HR), le rythme respiratoire (f_R) et la pression artérielle ont été mesurés immédiatement avant et à des intervalles de 10 minutes après la procédure épidurale. Des analyses des gaz sanguins et du pH ont été effectuées avant et 30 et 60 minutes après la procédure épidurale. Les animaux ont été mis sous anesthésie à l'isoflurane s'ils présentaient le moindre signe d'inconfort durant la procédure. La durée du temps de blocage sensitif et d'analgésie post-opératoire a été évaluée. Tous les animaux CON et DEX, 5 animaux ROM et CLO, 4 animaux XYL et 3 animaux DET ont nécessité de l'isoflurane. Tous les groupes, sauf le groupe CLO, ont présenté une réduction de HR. Il y a eu une augmentation de la pression artérielle dans tous les groupes. L'analgésie post-opératoire a été la plus longue dans le groupe XYL. Aucun des protocoles n'était complètement efficace pour permettre la procédure complète d'OH; toutefois, la xylazine a fourni une analgésie post-opératoire plus longue que les autres médicaments.

(Traduit par Docteur Serge Messier)

Introduction

Ovariohysterectomy (OH) is a common surgical procedure performed in bitches, and is usually done under general anesthesia. However, alternatives are investigated for providing a safe and accessible anesthetic protocol, especially for conditions in which equipment is not available, as in animal population control programs.

Epidural anesthesia is a procedure used in many post-umbilical surgeries (1). However, the lidocaine, especially using the routine volume of 0.25 mL/kg body weight (BW), is not effective when performing OH. This is because of the origin of the ovarian innervation, which derives from the third and fourth lumbar nerves (2), is cranial to the area of the lidocaine blockade, which usually does not extend beyond the fourth or fifth lumbar vertebrae (3). Nevertheless, it has been suggested that using other drugs such as xylazine in association with lidocaine, provides cranial extension of the block, reaching the region between the last thoracic and the first lumbar vertebra (3). Aminkov and Zlateva (4) demonstrated that use of xylazine in association with lidocaine was sufficient to carry out OH in bitches. However, the cardiovascular effects, epidural block time, and postoperative analgesia were not evaluated. New studies are, therefore, necessary to evaluate the effects produced by xylazine and if they also occur with other alpha-2 adrenergic agonist drugs.

Rural Science Center, Federal University of Santa Maria, Santa Maria, RS, Brazil, 97105-900 (Pohl, Lopes, Gehrcke, Muller, Garlet); Department of Zootechnical Science, University of São Paulo, Pirassununga, SP, Brazil, 13635-900 (Carregaro).

Address all correspondence to Dr. Adriano B. Carregaro; telephone: (55) 19-35654092; fax: (55) 19-3565-4114; e-mail: carregaro@usp.br

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The epidural administration of alpha-2 adrenergic agonists is an analgesic alternative to opioids, presenting the advantages of absence of pruritus and development of tolerance and dependence (5). The antinociceptive effects derived from its administration are primarily due to stimulation of alpha-2 adrenoceptors in the spinal cord. The interaction with these receptors results in noradrenaline release, hyperpolarizing the dorsal horn neurons and inhibiting substance P (6). Besides that, C fibers are preferentially blocked as are A-delta fibers, but to a lesser extent; xylazine seems to provide a more specific block (7).

The analgesia provided by the administration of alpha-2 adrenergic agonists has been confirmed in various species, such as humans, dogs, horses, and cattle. In dogs, the administration of epidural xylazine provides analgesia for up to 4 h with minimal cardiorespiratory effects (8). The administration of epidural clonidine results in reduction of postoperative pain and analgesics required in human patients after abdominal surgery (9). Detomidine has not been evaluated in small animals; however, it provides moderate analgesia in cattle and horses (10,11). The administration of epidural romifidine in dogs submitted to coxofemoral surgery provides intense transoperative analgesia and satisfactory analgesia for up to 2 h after surgery (5). Epidural dexmedetomidine presents accentuated analgesic action in humans, with a dose-dependent effect and superior effects to that obtained by intravenous administration (12).

The aim of this study was to evaluate the viability of performing OH under epidural anesthesia using associations of different alpha-2 adrenergic agonists and lidocaine, as well as the cardiorespiratory effects, epidural block time, and postoperative analgesia in bitches.

Materials and methods

Forty-two adult mongrel bitches weighing 14.9 ± 4.0 kg were admitted for OH. The animals were acquired from an animal protection society and placed for adoption after completing the experiment. They were included in the study if found to be clinically healthy through physical examination and laboratory testing [complete blood (cell) count (CBC) and liver and kidney screening]. The dogs were adapted to the experimental environment and the observers for at least 1 wk before the surgical procedure. This study was approved by the Institutional Animal Care Committee (number 01/2009).

The animals were randomly allocated into 6 groups (n = 7), in a blind study, maintained under lumbosacral epidural anesthesia with 1% lidocaine with adrenaline (1:200.000) (Xilestesin 1%; Cristália, Itapira, SP, Brazil) (CON) 2.5 mg/kg BW, or in addition to xylazine (Anasedan; Agribrands Purina do Brasil, Paulínia, SP, Brazil) (XYL) 0.25 mg/kg BW, romifidine (Sedivet; Boehringer, São Paulo, SP, Brazil) (ROM) 10 μg/kg BW, detomidine (Dormium V; Agener União — Saúde Animal, São Paulo, SP, Brazil) (DET) 30 μg/kg BW, dexmedetomidine (Precedex; Abbott, São Paulo, SP, Brazil) (DEX) 2 μg/kg BW, or clonidine (Clonidin; Cristália, Itapira, SP, Brazil) (CLO) 5 μg/kg BW, obtaining a final volume of 1 mL/4 kg BW. The doses of alpha-2 agonists were determined from previous studies in bitches (4,5,13), even in other species (11,14,15) and the doses commonly used by the authors in some post umbilical surgeries.

Two hours before the surgical procedure, the animals were anesthetized with propofol (Propovan; Cristália, Itapira, SP, Brazil), 5 mg/kg BW. A 22G catheter was placed in the dorsal pedal artery to collect blood samples for blood gas analysis and to measure systolic (SAP), mean (MAP), and diastolic (DAP) arterial pressures in mmHg, by means of a multiparameter monitor (PM-9000 Express — Mindray Medical International, Shenzhen, China) via a pressure transducer connected to the catheter during the transoperative period and calibrated prior to initiating the readings, setting the zero-reference point at the level of the manubrium. Subsequently, the animals were allowed to completely recover.

Animals were premedicated with acepromazine (Acepran, Univet, São Paulo, SP, Brazil), 0.1 mg/kg BW, IM 20 min before epidural administration. The cephalic vein was catheterized and fluid therapy was used with isotonic saline solution 10 mL/kg per hour. Afterward, animals were submitted to deep sedation with 2 mg/kg of propofol to perform lumbosacral epidural anesthesia according to the designated treatment. The epidural block was confirmed (up to 5 min) by anal sphincter relaxation and loss of pedal withdrawal reflex. Then, animals were laid down on the surgical table and lightly restrained with a 3-inch gauze roll bandage. The surgical procedures were initiated 15 min after epidural anesthesia, by median laparotomy. All surgeries were performed by the same experienced surgeon.

Heart rate (HR), systolic (SAP), mean (MAP), and diastolic (DAP) arterial pressures and respiratory rate (f_R) were evaluated before premedication (baseline), before epidural anesthesia (0 min), and at 5, 10, 20, 30, 40, 50, and 60 min after epidural anesthesia, by an observer blinded to the treatments. Arterial blood samples were collected before epidural (0 min) and 30 and 60 min afterwards in order to obtain values of pH, bicarbonate ion (HCO_3^-), arterial partial pressures of oxygen (PaO_2) and carbon dioxide ($PaCO_2$), arterial saturation of oxygen (SaO_2), Na^+ and K^+. Body temperature was maintained between 36.5°C and 39.0°C with the use of a heating mattress.

Animals were maintained under epidural anesthesia; however, at the slightest sign of discomfort when clamping the ovarian stumps shown by changes in cardiorespiratory parameters, head and/or front limb movement, general inhalation anesthesia was instituted via facial mask with isoflurane (Forane; Abbott, São Paulo, SP, Brazil) at maximum concentration necessary (1–2 min), followed by intubation and maintenance of the anesthesia with 1.5% of end-tidal isoflurane concentration (Poet IQ2; Criticare Systems, Waukesha, Wisconsin, USA), in 100% oxygen at 50 mL/kg per minute flow rate.

Postoperative analgesia was assessed every hour through the visual analogue scale (VAS) by 2 observers blinded to the treatments, until the moment of rescue analgesia. Animals presenting VAS values > 50 (0 to 100) were promptly treated with morphine (Dimorf; Cristália, Itapira, SP, Brazil), 0.5 mg/kg BW, IM and meloxicam (Maxicam; Ouro Fino, Cravinhos, SP, Brazil), 0.2 mg/kg BW, IM. This was only considered the first administration of rescue analgesia to determine the time of postoperative analgesia of each group. In addition, the duration of the time of sensory epidural block was evaluated through the pedal withdrawal reflex in both pelvic limbs by pinching using a Kelly hemostatic forceps.

Normality of all quantitative data were analyzed (Prism 5.0; GraphPad Software, La Jolla, California, USA) by the Kolmogorov-Smirnov test. The physiologic parameters were analyzed by repeated-measures analysis of variance (ANOVA) and Dunnett's

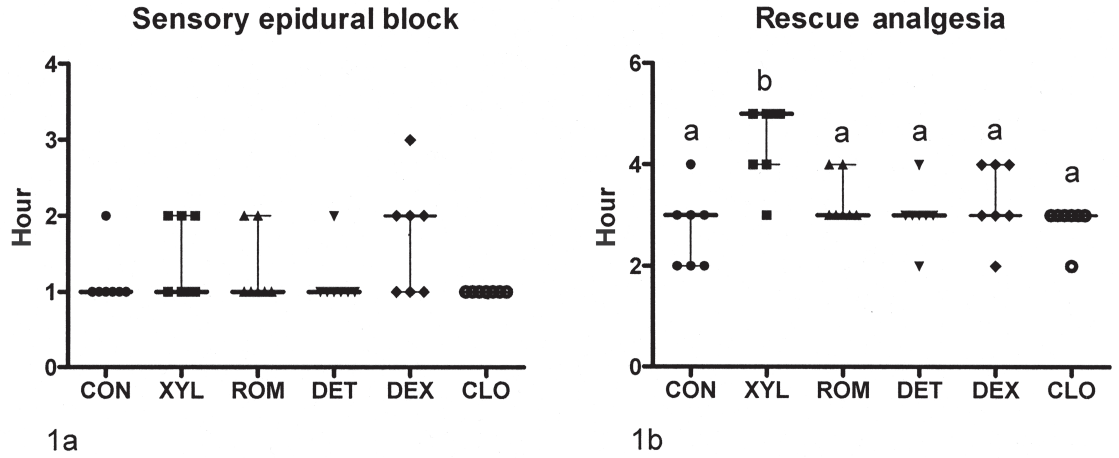

Figure 1. Time of sensory epidural block (a) and time of rescue analgesia (b) in bitches submitted to ovariohysterectomy with lidocaine (CON) and with the use of xylazine (XYL), romifidine (ROM), detomidine (DET), dexmedetomidine (DEX), and clonidine (CLO). Scatter dot plot with median (major trace) and interquartile range. Different letters indicate difference between groups.

test was used for comparison between times with 0 min. Welch correction test was used when the standard deviation values differed between groups. A two-way ANOVA and Tukey's test was used for comparisons between groups. A Kruskal-Wallis test was used to compare the duration of surgery, time of sensory epidural block, postoperative analgesia, and number of animals submitted to inhalation anesthesia. The differences were considered significant when $P < 0.05$.

Results

The duration of surgery did not differ between groups, and the average of all procedures was 27 ± 11.8 min. Regarding need of general inhalation anesthesia with isoflurane, only DET differed from CON, where only 3 animals from DET required isoflurane anesthesia, which was initiated between 20 and 30 min after epidural procedure. Four animals in XYL (between 15 and 25 min), 5 in CLO (between 20 and 30 min) and ROM (between 20 and 25 min) and all of them in CON (between 15 and 25 min) and in DEX (between 15 and 35 min) required isoflurane anesthesia. The time of sensory epidural block time did not differ in relation to CON in any of the treated groups (Figure 1a). However, the duration of the postoperative analgesia differed in relation to the CON in XYL, lasting for up to 4 h (Figure 1b).

All alpha-2 groups, except CLO, showed reduction in HR 10 min after epidural; however, this effect was longer in DET (5 to 20 min after epidural). In comparison to the 0 min, a decrease in HR after the epidural procedure in DET and DEX was observed and values were lower than baseline for up to 60 min. Clonidine showed an increase in HR compared with 0 min, remaining elevated until inhalation anesthesia was given (Table I). An occurrence of second degree atrioventricular block (AVB) was observed in 2 animals in DET, 1 in XYL and 1 in ROM.

DET showed the most elevated values of arterial pressures, observing a marked increase at 5 to 20 min after epidural procedure. Hypotension (MAP below 60 mmHg) was not observed in any of the groups at any evaluated moment. The MAP increased at 30 min in XYL, and in up to 20 min for the other alpha-2 groups comparing to 0 min. The SAP increased in DET and in DEX in up to 20 min and the DAP followed the values of MAP in all groups, except in CLO, which keeping elevated at 5 to 40 min (Table I).

The f_R values did not differ when the alpha-2 groups are compared from CON. In CON and DEX, a decrease in f_R was observed in relation to 0 min and in CLO at 50 min after the epidural (Table I). The blood gas analysis did not differ among the groups at any moment (Table II). A slight decrease in pH in almost all groups at 30 min and even at 60 min in ROM and DEX was observed. PaO_2 was higher at 30 min in CON, ROM, DEX, and CLO and at 60 min in all groups (Table II). Some statistical differences in $PaCO_2$, HCO_3^- and Na^+ were observed but all data were within the reference values for the species (Table II).

Discussion

None of the tested alpha-2 adrenergic agonists allowed completion of OH surgery without administration of isoflurane anesthesia in some of the animals, although DET showed better results. To the authors' knowledge, there are no studies in which the effects of epidural detomidine were evaluated in dogs. However, we believe this effect was probably due to the higher dose of detomidine compared with the other agonists, even in other species (7), which can be 3× greater than an equipotent xylazine dose. Moreover, DET could present a greater cranial extension of the epidural block in horses, compared with xylazine (16). In relation to the time of sensory epidural block, the present study did not show any improvement, even though the literature reports that the association of alpha-2 agonists and local anesthetics produces prolonged effect over the local anesthetic alone (17).

The postoperative analgesia provided by the epidural administration of xylazine lasted up to 4 h and was the only group to differ significantly from CON. The epidural administration of xylazine in dogs at a dose of 0.25 mg/kg BW provided analgesia for up to 4 h (13,18), similar to the result obtained in the present study, but without a surgical procedure. Epidural xylazine produces more potent and longer lasting analgesia than lidocaine (19). This effect occurs

Table I. Cardiorespiratory parameters of bitches submitted for ovariohysterectomy with lidocaine (CON) and with use of xylazine (XYL), romifidine (ROM), detomidine (DET), dexmedetomidine (DEX), and clonidine (CLO)

		Time (min)								
Parameter	Group	Baseline	0	5	10	20	30	40	50	60
HR	CON	99 ± 20	99 ± 37[a]	111 ± 37[a,d]	129 ± 51[a]	120 ± 28[a]	108 ± 26	102 ± 16	102 ± 16	100 ± 16
	XYL	103 ± 32	85 ± 19[a]	73 ± 19[a]	70 ± 19[b]	82 ± 31[a]	70 ± 9	67 ± 12	66 ± 18	76 ± 29
	ROM	91 ± 29	76 ± 17[a]	88 ± 32[a,b,d]	62 ± 12[b]	84 ± 38[a]	85 ± 29	78 ± 27	80 ± 27	81 ± 23
	DET	124 ± 30	114 ± 36[a,b]	57 ± 13[b,c]*	52 ± 11[b]*	69 ± 27[b]*	81 ± 31*	77 ± 25*	73 ± 27*	73 ± 26*
	DEX	120 ± 20	149 ± 38[b]	85 ± 21[a,c]*	79 ± 21[b]*	81 ± 21[a,b]*	90 ± 27*	89 ± 18*	85 ± 15*	82 ± 14*
	CLO	98 ± 35	93 ± 29[a]	126 ± 40[d]*	127 ± 45[a]*	120 ± 30[a]	105 ± 27	97 ± 24	97 ± 25	94 ± 25
f_R	CON	24 ± 6	23 ± 4	20 ± 2	20 ± 4	16 ± 6*	14 ± 8*	12 ± 5*	13 ± 4*	13 ± 3*
	XYL	23 ± 9	20 ± 2	19 ± 1	18 ± 9	19 ± 9	16 ± 5	13 ± 3	13 ± 4	16 ± 5
	ROM	25 ± 5	23 ± 7	19 ± 3	17 ± 3*	16 ± 8*	14 ± 7*	11 ± 5*	11 ± 5*	11 ± 5*
	DET	26 ± 8	23 ± 9	21 ± 4	21 ± 3	20 ± 8	15 ± 5	15 ± 8	16 ± 8	15 ± 8
	DEX	29 ± 5	26 ± 5	19 ± 1	20 ± 6	18 ± 7*	13 ± 7*	11 ± 5*	10 ± 5*	11 ± 4*
	CLO	29 ± 9	21 ± 5	22 ± 7	27 ± 11	25 ± 11	15 ± 7	13 ± 7	11 ± 5*	12 ± 6*
SAP	CON	131 ± 19	118 ± 16	109 ± 30[a]	109 ± 24[a]	129 ± 18[a]	129 ± 33	119 ± 28	113 ± 27	111 ± 26
	XYL	125 ± 27	114 ± 27	134 ± 33[a]	137 ± 31[a,c]	132 ± 23[a]	142 ± 24	135 ± 19	137 ± 24	129 ± 34
	ROM	132 ± 26	124 ± 19	128 ± 21[a]	145 ± 18[a,b]	147 ± 31[a,b]	135 ± 30	136 ± 18	129 ± 23	129 ± 24
	DET	142 ± 35	139 ± 14	184 ± 18[b]*	183 ± 15[b,c]*	178 ± 27[b]*	145 ± 41	142 ± 41	146 ± 41	152 ± 44
	DEX	126 ± 18	116 ± 20	131 ± 23[a]	141 ± 24[a]*	154 ± 37[a,b]*	135 ± 30	121 ± 20	117 ± 19	111 ± 20
	CLO	136 ± 22	135 ± 15	141 ± 17[a]	153 ± 17[b,c]	154 ± 17[a,b]	148 ± 7	147 ± 11	135 ± 8	136 ± 9
MAP	CON	100 ± 16	89 ± 10	86 ± 24[a]	84 ± 15[a]	105 ± 13[a]	104 ± 26	93 ± 23	87 ± 20	86 ± 22
	XYL	92 ± 15	86 ± 16	98 ± 24[a]	102 ± 23[a,c]	100 ± 16[a]	112 ± 19*	107 ± 13	107 ± 15	100 ± 18
	ROM	103 ± 26	92 ± 10	97 ± 11[a]	110 ± 14[a,c]	119 ± 25[a,b]*	110 ± 22	108 ± 12	99 ± 16	98 ± 17
	DET	112 ± 31	104 ± 17	140 ± 18[b]*	141 ± 12[b]*	138 ± 23[b]*	114 ± 32	110 ± 32	114 ± 36	119 ± 39
	DEX	108 ± 19	98 ± 18	112 ± 21[a]	119 ± 21[b,c]	131 ± 37[a]*	116 ± 27	105 ± 20	100 ± 18	91 ± 18
	CLO	100 ± 17	95 ± 10	107 ± 13[a]	115 ± 12[a,b]*	121 ± 13[a,b]*	119 ± 6	115 ± 10	110 ± 6	109 ± 8
DAP	CON	85 ± 19	74 ± 12	75 ± 23[a]	71 ± 12[a]	93 ± 13,9[a,b]	91 ± 24	81 ± 22	74 ± 18	73 ± 19
	XYL	75 ± 12	72 ± 13	81 ± 20[a]	85 ± 21[a]	85 ± 13[b]	96 ± 17*	92 ± 12	91 ± 11	85 ± 15
	ROM	83 ± 12	76 ± 11	82 ± 8[a]	93 ± 14[a,b]	106 ± 23[a]*	98 ± 19	94 ± 10	85 ± 14	84 ± 15
	DET	97 ± 31	85 ± 19	118 ± 18[b]*	122 ± 12[b]*	118 ± 22[a]*	98 ± 28	81 ± 42	97 ± 36	102 ± 36
	DEX	100 ± 19	89 ± 16	103 ± 21[ab]	109 ± 20[b]	121 ± 38[a]*	106 ± 28	96 ± 21	91 ± 17	82 ± 18
	CLO	81 ± 17	75 ± 11	91 ± 12[ab]*	96 ± 13[a,b]*	104 ± 13[a]*	104 ± 7*	98 ± 11*	95 ± 7	93 ± 10

HR — Heart rate; f_R — Respiratory rate; SAP — Systolic arterial pressure; MAP — Mean arterial pressure; DAP — Diastolic arterial pressure. * — Different from 0 min. Different letters indicate difference between groups.

Table II. Arterial blood gas tension analysis in bitches submitted for ovariohysterectomy with lidocaine (CON) with use of xylazine (XYL), romifidine (ROM), detomidine (DET), dexmedetomidine (DEX), and clonidine (CLO)

	Time (min)		
	0	30	60
pH			
CON	7.36 ± 0.06	7.26 ± 0.08*	7.30 ± 0.05
XYL	7.34 ± 0.02	7.30 ± 0.06	7.31 ± 0.09
ROM	7.32 ± 0.04	7.26 ± 0.05*	7.26 ± 0.07*
DET	7.35 ± 0.04	7.24 ± 0.12*	7.30 ± 0.05
DEX	7.37 ± 0.01	7.27 ± 0.06*	7.27 ± 0.08*
CLO	7.34 ± 0.02	7.30 ± 0.05	7.29 ± 0.05
PaO_2 (mmHg)			
CON	105 ± 6	352 ± 125*	364 ± 147*
XYL	114 ± 10	231 ± 129	241 ± 152*
ROM	110 ± 10	270 ± 115*	325 ± 154*
DET	119 ± 10	191 ± 105	226 ± 131*
DEX	116 ± 9	309 ± 99*	357 ± 12*
CLO	108 ± 11	260 ± 111*	288 ± 118*
$PaCO_2$ (mmHg)			
CON	37 ± 6	48 ± 13	43 ± 7
XYL	37 ± 2	43 ± 5	42 ± 10
ROM	37 ± 3	45 ± 8*	46 ± 11*
DET	35 ± 2	43 ± 9*	43 ± 6*
DEX	33 ± 2	45 ± 8*	48 ± 12*
CLO	36 ± 1	41 ± 7	40 ± 5
HCO_3^- (mEq/L)			
CON	20.5 ± 2.2	21.0 ± 2.0	20.3 ± 1.6
XYL	19.8 ± 2.1	21.2 ± 1.7	20.3 ± 1.6
ROM	19.2 ± 0.4	20.0 ± 1.4	20.0 ± 1.6
DET	18.7 ± 1.8	20.5 ± 2.0	20.9 ± 1.7*
DEX	19.2 ± 1.1	20.4 ± 1.8	21.3 ± 1.7*
CLO	19.0 ± 1.2	19.5 ± 1.4	19.4 ± 0.9
Na^+ (mEq/L)			
CON	150 ± 1.6	150 ± 1.8	150 ± 1.7
XYL	150 ± 3.1	148 ± 3.3*	149 ± 2.5
ROM	151 ± 2.3	150 ± 1.7	150 ± 1.2*
DET	151 ± 2.3	150 ± 0.9	149 ± 1.6
DEX	150 ± 3.1	150 ± 2.6	148 ± 2.6
CLO	150 ± 2.3	148 ± 1.9	149 ± 1.4
K^+ (mEq/L)			
CON	3.9 ± 0.2	3.7 ± 0.2	3.7 ± 0.2
XYL	4.1 ± 0.2	4.1 ± 0.6	4.2 ± 0.3
ROM	3.9 ± 0.3	4.0 ± 0.4	4.0 ± 0.4
DET	4.1 ± 0.3	4.2 ± 0.3	4.1 ± 0.1
DEX	4.0 ± 0.2	3.8 ± 0.3	3.9 ± 0.3
CLO	3.8 ± 0.1	4.0 ± 0.2	3.8 ± 0.2

* — Different from 0 min.

because xylazine, in addition to provoking activation of alpha-2 adrenoceptors in the spinal cord, possesses a local anesthetic effect, characterized by a blockade of the action potential and conduction velocity, providing a prolonged analgesic activity (20). Besides, xylazine has low lipophilicity (octanol/buffer coefficient of 0.15) compared with other alpha-2 agonists and to lidocaine, and its low molecular weight (220) promotes more rostral spread with the CSF along the spinal cord (1,21).

In the present study, all alpha-2 groups except CLO promoted a decrease in HR at any moment, especially up to 20 min after the epidural procedure. Alpha-2 adrenergic agonists are capable of producing multiple, at times intense, cardiovascular effects. The main effect is a decrease in heart rate (22) which corroborates the effect observed in the present study. This activity is due to the increase in systemic vascular resistance, which produces a compensatory bradycardia reflex mediated by baroreceptors. As a result of increased vagal tonus, heart rate can be reduced by up to 50% (22). Xylazine causes a decrease in heart rate after epidural administration in dogs (4,18). The effects of epidural detomidine in small animals were not evaluated; however, DET causes bradycardia in dogs when administered intramuscularly (23). Moreover, its epidural administration causes bradycardia in equines and bovines (10,11). Bradycardia was also reported as one of the complications after epidural administration of romifidine in dogs (5). Dexmedetomidine also causes a decrease in heart rate in canines (24). Clonidine did not promote decrease in heart rate, which was similar that observed in horses (20). In dogs, epidural administration of clonidine caused a decrease in HR, although within physiological parameters and less intense compared with romifidine (5). The occurrence of 2nd degree AVB observed in some animals of DET, XYL, and ROM is a frequent complication observed immediately after administration of alpha-2 adrenergic agonists, as is sinus arrhythmia and sinoatrial block (6).

As well as causing changes in heart rate, alpha-2 adrenergic agonists cause important changes in arterial pressure, usually observing a temporary increase followed by a decrease below basal values (22). In the present study, a slight increase in arterial pressures was observed in almost all alpha-2 groups after epidural procedure. This initial period of vasoconstriction and hypertension is caused by the stimulation of alpha-2 and alpha-1 vascular receptors and is partially responsible for developing bradyarrhythmias due to increases in baroreflex activity and vagal tonus (6). The epidural administration of xylazine in dogs did not induce significant changes in arterial pressure (8,15) and a similar result was observed in the present study, which was equal to the CON at all evaluated moments. The most intense hypertension observed in DET was probably due to the detomidine doses used, as previously discussed (7). A small decrease in arterial pressures in all groups could be observed 30 min after the epidural administration, coincidently with the moment at which inhalation anesthesia was initiated, returning to values similar to time zero of each group. This was probably due to the vasodilator effect of isoflurane, which causes a decrease in arterial pressure (25).

There was no difference in f_R between the alpha-2 groups in relation to the CON. The literature mentions that alpha-2 adrenergic agonists cause a decrease in respiratory rate; however, alveolar ventilation is maintained due to an increase in tidal volume (6). In

the present study, only romifidine caused a decrease in f_R at 10 min after epidural. In the other groups, including CON, the decrease in f_R was observed after initiating inhalation anesthesia. Therefore, this was probably due to the action of isoflurane, which induces respiratory depression (26).

Values regarding blood gas did not differ in relation to CON when it was compared to any of the other groups, indicating absence of respiratory depression induced by alpha-2 adrenergic agonists. When appropriate doses of these drugs are used in healthy patients, the acid-base balance is maintained, as is the pressure of blood gases within the normal parameters (6). However, it was shown that PaO_2 was higher in all groups compared to 0 min, and the standard deviations were high in all groups. Obviously, the results were disguised because some animals in all groups were submitted to general inhalation anesthesia, kept in 100% oxygen. In addition, it was shown that the pH decreased in almost all groups, which also occurred due to the respiratory depression by isoflurane (26).

In conclusion, although the association of lidocaine and 30 μg/kg of detomidine enabled performing OH in most of the animals, none of the protocols were effective enough for the procedure. Nevertheless, the analgesic efficacy of 0.25 mg/kg of epidural xylazine is emphasized, which provided postoperative analgesia for up to 4 h.

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