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Research article

Comparison of two sedation protocols for diagnostic radiography in dogs with hip dysplasia

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ABSTRACT

Hip dysplasia is an alteration with a high incidence in large dogs. The aim of the study was to compare the association of xylazine or dexmedetomidine with fentanyl for radiography with joint distractor for the diagnosis of hip dysplasia. Fifteen healthy dogs, German Shepherd and Belgian Shepherd, were randomly submitted to treatments 0.2 mg/kg xylazine + 2.5 μg/kg fentanyl (XF) or 2 μg/kg dexmedetomidine + 2.5 μg/kg fentanyl (DF), intravenously. HR, *f*, SAP, MAP, DAP and TR were evaluated at intervals of 5 min before and after the administration of treatments; pH, $PaCO_2$, PaO_2, BE, HCO^{3-}, SaO_2, Na^+, K^+ and Hb at 5 and 15 min after treatment administration; and the quality of sedation at intervals of 5 min after administration of treatments. Latency, duration, and recovery times were also compared. The HR values showed a significant reduction in both groups, as well as pH, $PaCO_2$, PaO_2 and SaO_2. Latency, duration and recovery times, and quality of sedation did not differ statistically between groups. Xylazine and fentanyl or dexmedetomidine and fentanyl combinations provide adequate sedation and analgesia for performing diagnostic radiographic procedures for hip dysplasia. However, oxygen supplementation is recommended to increase protocol safety.

Introduction

Hip dysplasia (HD) is a condition characterized by subluxation or displacement of the hip joint, acetabular flattening and flattening of the femoral head, being associated with joint laxity and osteoarthritis (Ginja et al., 2010; Syrcle, 2017; King, 2017). It has a higher incidence in medium to large breeds, such as Golden Retriever, Labrador Retriever, Rottweiler, Border Collie and German Shepherd (Syrcle, 2017; King, 2017; James et al., 2020). For diagnosis, in addition to the clinical examination, the Orthopedic Foundation for Animals (OFA) established a radiographic examination, with a ventrodorsal incidence of the pelvic limbs parallel to the spine and medially rotated, with the patellas overlapping the trochlear grooves (Butler & Gambino, 2017). Another recently developed method involves the use of a device called a joint distractor, in order to predict the occurrence of hip dysplasia in early age dogs (Tôrres et al., 2005; Butler & Gambino, 2017). To perform these techniques, the animals must be under general anesthesia or deep sedation, in order to allow proper positioning of the pelvic limbs (Ginja et al., 2010; Butler & Gambino, 2017).

Several pharmacological agents have been used for sedation of patients during radiographic procedures, being the alpha 2 adrenergic agonists a class of choice due to their sedation and myorelaxation effects (Arunkumar et al., 2017). Dexmedetomidine, the latest selective agonist of alpha 2 adrenergic receptors, when administered intravenously or intramuscularly, provides sedation and moderate analgesia for outpatient procedures, such as dental examinations, radiographs and treatment of otitis (Granholm et al., 2007; Weerink et al., 2017). When used in combination with other drugs, such as opioids and benzodiazepines, it promotes a high level of sedation, myorelaxation and analgesia, allowing even minor surgical procedures to be performed (Ahmad et al., 2011; Trimble et al., 2018). Fentanyl is a synthetic total μ opioid agonist with 100 times greater potency than morphine, used for sedation and analgesia, characterized by short latency and action period (Wegner et al., 2008; Kukanich & Wiese, 2015). When combined with dexmedetomidine, synergism occurs, with potentialization of anesthetic sparing effects and a greater degree of bradycardia (Chabot-Doré et al., 2015). The

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Table 1
Scale system used to assess the quality of sedation in dogs submitted to XF and DF treatments.

Criteria | Scale	Observation
Posture	
0	Standing
1	Seating or in sternal recumbency, with head up
2	Esternal recumbency, with the head down
3	Lateral recumbency
4	Dorsal recumbency, responsive to stimulus
5	Dorsal recumbency, non responsive to stimulus
Resistency to dorsal recumbency	
0	Resistant/Normal atitude
1	Moderate resistant
2	Light resistant
3	No resistant
Mandibular tonus	
0	Normal resistant to opening the mouth
1	No resistant to opening the mouth
Palpebral reflex	
0	Present
1	Reduced
2	Absent
Eyeball positioning	
0	Centralized
1	Rotated

Source: Adapted from Nishimura et al. (2018).

present study aimed to compare the sedative, cardiorespiratory and blood gas effects of fentanyl combined with xylazine or dexmedetomidine. The proposed hypothesis is that the association of xylazine and fentanyl will promote adequate analgesia, sedation and myorelaxation for performing the radiographic procedure, but the association of dexmedetomidine and fentanyl will provide more intense sedative effects.

Materials and methods

Selection and description of subjects

The study was approved by the Ethics Committee on the Use of Animals of the Federal University of Minas Gerais (CEUA-UFMG) under the protocol 146/2017. Fifteen healthy German Shepherd and Belgian Shepherd dogs, 34.4 ± 6.1 kg and 7.2 ± 2.4 years old, from the Military Police Battalion of Belo Horizonte - Minas Gerais, were used. The animals were submitted to a complete and complementary physical examination, complete blood count and biochemistry (kidneys and hepatic function) were performed one week before the anesthetic procedure. Prior to the experimental period, the animals considered fit to participate in the project were submitted to 8 h fasting of food and water *ad libitum*.

Data recording and analysis

On the day of the experiment, the animals were sent to the Veterinary Hospital of the Federal University of Minas Gerais and conducted to the radiology room. After a new physical examination, light physical restraint was performed on the dogs, trichotomy, and antisepsis of the radial and metatarsal regions, followed by an anesthetic button with lidocaine and puncture of the cephalic vein and metatarsal artery, using an 18 G and 20 G catheter, respectively. After fixing the catheters, they were attached to an adaptor PRN and the accesses were heparinized with 1 mL of heparinized saline solution (5UI/mL).

After 30 min of obtaining vascular access, the animals were randomly divided into two groups, by means of a computer drawing, being submitted to different sedation protocols. Thus, the animals in the XF group received the association of 0.2 mg/kg of xylazine and 2.5 μg/kg of fentanyl, and the animals of the DF group received the association of 2 μg/kg of dexmedetomidine and 2.5 μg /kg fentanyl. Both were administered intravenously, followed by a bolus of 1 mL of saline solution, so that no residue was retained in the venous access. The latency period, from the administration of the treatment until the animal remained in lateral recumbency without head movement, was recorded.

Table 2
Scale system used to assess the quality of muscle relaxation in dogs submitted to XF and DF treatments.

Criteria | Scale	Observation
Muscle relaxation	
0	Does not alow extension and positioning of the pelvic limbs at the articular distractor.
1	Moderate rigid pelvic limbs muscles, with moderate dificulty to extension and positioning at the articular distractor.
2	Relaxed pelvic limb muscles, with discret reaction to extention and positioning at the distractor.
3	Relaxed pelvic limbs muscles, no reaction to extention and positioning at the distractor, easily alowing the exam.

Source: Elaborated by the authors.

Before application and at 5-min intervals after application of treatments, heart rate (HR) and heart rhythm were monitored, using DII derivation, by means of electrodes placed on the forelimbs, above the olecranon in its caudal aspect, and on the lower limbs, above the patellar ligaments in its cranial aspect, and invasive blood pressure, by means of a pressure transducer connected to the arterial access and positioned at the level of the scapulohumeral joint of the animals (Digicare™ LifeWindow™ Lite LW8 – Digicare Biomedical, FL, USA). Furthermore, respiratory rate (*f*), obtained by observing the movement of the rib cage, and rectal temperature (RT), measured by a digital thermometer positioned in the anal region, were monitored.

At 5 min and 15 min after the application of treatments, 1 mL of arterial blood was collected, using a specific syringe for blood gas analysis, followed by immediate analysis of hydrogen potential (pH), partial arterial carbon dioxide pressure ($PaCO_2$), partial arterial oxygen pressure (PaO_2), bases excess (BE), bicarbonate concentration (HCO^{3-}), arterial oxygen saturation in hemoglobin (SaO_2), sodium concentration (Na^+), potassium concentration (K^+) and hemoglobin (Hb) (I-Stat®1 – Abbott Point of Care, IL, USA). Every 5-min intervals, the quality of sedation was evaluated by observing posture, resistance to supine position, mandibular tone, eyelid reflex and eyeball positioning (Table 1).

These parameters were scored in an increasing way, so that values close to 0 indicate a lower degree of sedation and values further from 0 indicate a greater degree of sedation. At 10 min, the assessment of the degree of muscle relaxation was carried out following the same classification and, for scores 0 and 1, in which it was not possible to perform the radiographic examination, the animals received additional supplementation, intravenously, of one third of the doses of the initial treatment, with 1 min waiting until a new attempt to perform the test (Table 2). The duration of sedation, from the onset of latency to the onset of spontaneous movement, the time to full recovery, from the onset of latency to spontaneous movement and ambulation, and the total number of supplementary requirements were recorded.

Statistics

All data were submitted to the Shapiro-Wilk normality test. Data referring to physiological and blood gas variables were analyzed using the Tukey test. The comparison between latency, duration and recovery times were performed using Whelch's t-test. For sedation scores, they were submitted to the Mann-Whitney tests, for analysis between groups, and the Kruskal-Wallis followed by Dunn, for intragroup analyses. Parametric data are expressed as mean ± standard deviation and non-parametric data as median and interquartile range. The difference between the data was considered significant when $P < 0.05$.

Table 3
Latency time, duration and recovery of sedation in dogs with 0.2 mg/kg of xylazine and 2.5 μg/kg of fentanyl (XF), and 2 μg/kg of dexmedetomidine and 2.5 μg/kg of fentanyl (DF) in dogs.

		Time (min)
Latency	**XF**	2,1 ± 0,7
	DF	1,7 ± 0,6
Duration	**XF**	23,4 ± 7,8
	DF	32,6 ± 10,7
Recovery	**XF**	26,2 ± 13,6
	DF	36,3 ± 13,3

Consider: Latency - period between the administration of the treatment until the animal remains in lateral recumbency without head movement (minutes); Duration - period between the beginning of latency until the beginning of spontaneous movement (minutes); Recovery - period between onset of latency to spontaneous movement and ambulation (minutes).
Source: Elaborated by the authors.

Table 4
Sedation and muscle relaxation.

		T5	T10	T15
Posture	**XF**	4 [4 – 5]	4 [4 – 5]	5 [3 – 5]
	DF	5 [3 – 5]	5 [5 – 5]	5 [5 – 5]
Resistance to dorsal recumbency	**XF**	3 [3 – 3]	3 [3 – 3]	3 [3 – 3]
	DF	3 [3 – 3]	3 [3 – 3]	3 [3 – 3]
Mandibular tonus	**XF**	0 [0 – 1]	0 [0 – 1]	0 [0 – 1]
	DF	1 [0 – 1]	0 [0 – 1]	0 [0 – 1]
Palpebral reflex	**XF**	1 [0 – 1]	1 [0 – 1]	1 [0 – 1]
	DF	1 [1 – 2]	1 [1 – 2]	1 [1 – 2]
Eyeball positioning	**XF**	1 [1 – 1]	1 [0 – 1]	0 [0 – 1]
	DF	1 [1 – 1]	1 [0 – 1]	1 [0 – 1]

Source: Elaborated by the authors.
Consider: HR values decreased significantly in relation to baseline at all assessment times in both groups. The *f* showed a significant reduction in relation to baseline only at 5 and 10 min after treatment in XF. Blood pressure and rectal temperature did not change significantly during the period evaluated. The physiological parameters are expressed in Table 5 and Fig. 1.

Table 5
Physiological parameters (mean ± standard deviation) in dogs submitted to sedation with 0.2 mg/kg of xylazine and 2.5 μg/kg of fentanyl (XF), and 2 μg/kg of dexmedetomidine and 2.5 μg /kg fentanyl (DF).

		BL	T5	T10	T15	REC
HR	**XF**	106 ± 13[a]	59 ± 23[b]	59 ± 19[b]	57 ± 24[b]	65 ± 15[b]
	DF	119 ± 25[a]	45 ± 8[b]	50 ± 11[b]	54 ± 11[b]	57 ± 5[b]
SBP	**XF**	155 ± 27	165 ± 18	149 ± 17	150 ± 17	135 ± 23
	DF	150 ± 33	153 ± 20	162 ± 15	147 ± 16	135 ± 14
MBP	**XF**	105 ± 20	109 ± 13	100 ± 14	103 ± 17	89 ± 16
	DF	110 ± 22	106 ± 14	106 ± 11	102 ± 11	91 ± 9
DBP	**XF**	83 ± 19	86 ± 11	77 ± 10	79 ± 10	70 ± 12
	DF	84 ± 21	81 ± 20	84 ± 9	81 ± 10	75 ± 9
f	**XF**	114 ± 58[ac]	23 ± 11[b]	22 ± 10[b]	27 ± 9[bc]	60 ± 16[bc]
	DF	80 ± 43[a]	54 ± 60[a]	38 ± 34[a]	35 ± 22[a]	59 ± 39[a]
RT	**XF**	38,5 ± 0,7	38,5 ± 0,7	38,5 ± 0,7	38,4 ± 0,9	38,6 ± 0,5
	DF	38,1 ± 0,7	38,1 ± 0,7	38 ± 0,7	38,1 ± 0,6	37,9 ± 0,6

Consider: BL, moment prior to the administration of the treatment; T5, 5 min after treatment administration; T10, 10 min after treatment administration; T15, 15 min after treatment administration; REC, recovery; HR, heart rate (beats/minute); SBP, systolic blood pressure (mmHg); MBP, mean blood pressure (mmHg); DBP, diastolic blood pressure (mmHg); *f*, respiratory rate (movements/minute); RT, rectal temperature (°C).
[a] statistical difference between moments in the same group. $P < 0.05$.
Source: Elaborated by the authors.

Table 6
Blood gas parameters (mean ± standard deviation) before application and 5 and 15 min after application of sedation with 0.2 mg/kg of xylazine and 2.5 μg/kg of fentanyl (XF), and 2 μg/ kg of dexmedetomidine and 2.5 μg/kg of fentanyl (DF) in dogs.

		BL	T5	T15
pH	**XF**	7,38 ± 0,03[a]	7,31 ± 0,03[b]	7,3 ± 0,04[b]
	DF	7,37 ± 0,05[a]	7,3 ± 0,02[b]	7,3 ± 0,04[b]
$PaCO_2$	**XF**	28,6 ± 4,4[a]	37,1 ± 4,2[b]	38,1 ± 5,6[b]
	DF	29,9 ± 2,1[a]	38,8 ± 3,7[b]	39 ± 2[b]
PaO_2	**XF**	105,2 ± 17,5[a]	72,7 ± 12,1[b]	77,2 ± 15,4[b]
	DF	100,8 ± 4,1[a]	69,8 ± 8,6[b]	78,6 ± 6,5[b]
BE	**XF**	−7,4 ± 2,4	−7 ± 1,7	−6,9 ± 1,4
	DF	−7 ± 2,9	−6,5 ± 2,1	−6,7 ± 2
HCO^{3-}	**XF**	16,5 ± 2,3	17,8 ± 1,7	18 ± 1,4
	DF	17 ± 2,2	18,4 ± 1,8	18,3 ± 1,5
SaO_2	**XF**	96,7 ± 2[a]	84,8 ± 9[b]	86,2 ± 10,2[b]
	DF	96,6 ± 0,8[a]	84,6 ± 7,2[bc]	89,4 ± 2,5[ac]
Na^+	**XF**	149,4 ± 2	150 ± 2,8	149,7 ± 2,5
	DF	150,5 ± 2,3	149,8 ± 3,2	149,5 ± 3
K^+	**XF**	3,5 ± 0,3	3,3 ± 0,3	3,4 ± 0,3
	DF	3,6 ± 0,3	3,4 ± 0,3	3,5 ± 0,3
Cl^-	**XF**	120,2 ± 3,5	119,4 ± 3,5	119,5 ± 3,5
	DF	119,2 ± 2,5	118,3 ± 3,2	118,8 ± 3,8
AG	**XF**	16,1 ± 2[a]	16,1 ± 3,1[a]	15,6 ± 2,6[a]
	DF	18,1 ± 3,8[a]	16,3 ± 3[ac]	15,6 ± 3,2[bc]
Lactate	**XF**	1,84 ± 1,06	1,8 ± 0,63	1,63 ± 0,57
	DF	1,62 ± 0,41	1,85 ± 0,41	1,77 ± 0,47
Hb	**XF**	16,2 ± 3	15,9 ± 2,8	16,1 ± 2
	DF	13,3 ± 2	16,2 ± 3,5	16,7 ± 2,8

Consider: BL, moment prior to treatment administration; T5, 5 min after treatment administration; T15, 15 min after treatment administration; pH, hydrogen potential; $PaCO_2$, partial blood pressure of carbon dioxide (mmHg); PaO_2, partial arterial oxygen pressure (mmHg); BE, base excess (mEq/L); HCO3-, bicarbonate concentration (mEq/L); SaO_2, hemoglobin oxygen saturation (%), Na+, sodium concentration; *K*+, potassium concentration; Cl-, chloride concentration; AG, anion gap; Hb, hemoglobin.
[a] , statistical difference between moments in the same group. $P < 0.05$.
Source: Elaborated by the authors.

Results

After administration of treatments, all dogs were sedated and reached lateral recumbency in less than 3 min. Latency, duration and recovery times are shown in Table 3 and there was no significant difference between the groups. At 50 min, all animals had already assumed the quadrupedal position.

There was no statistical difference regarding the sedative and myorelaxation effect of the two protocols (Table 4). In the DF group, only one animal needed to receive a new dose of treatment. In the XF group, three animals needed two new doses of treatment.

There was a significant reduction in pH, PaO_2 and SaO_2 values at 5 and 15 min after administration of both treatments. $PaCO_2$ was elevated at both evaluated moments when compared to baseline in both groups. The values obtained in the blood gas analysis are described in Table 6. Values related to respiratory changes are expressed inFig. 2.

Discussion

Baseline HR and *f* values were increased due to handling stress and unfamiliar environment for the animals. In addition, as they came from the Military and Civil Police Battalion, they were more aggressive and managed only with the presence of one of the police officers. After the administration of the treatments, there was a significant decrease in HR values due to the activation of alpha 2 adrenergic receptors in the peripheral vasculature, resulting in transient bradycardia due to the action of baroreceptors (Murrell & Hellebrekers, 2005). Nishimura et al. (2018) reports the occurrence of bradycardia, with frequencies lower than 60 bpm, in animals that received alpha 2 adrenergic agonist drugs. The association with fentanyl promotes a decrease in sympathetic tone and

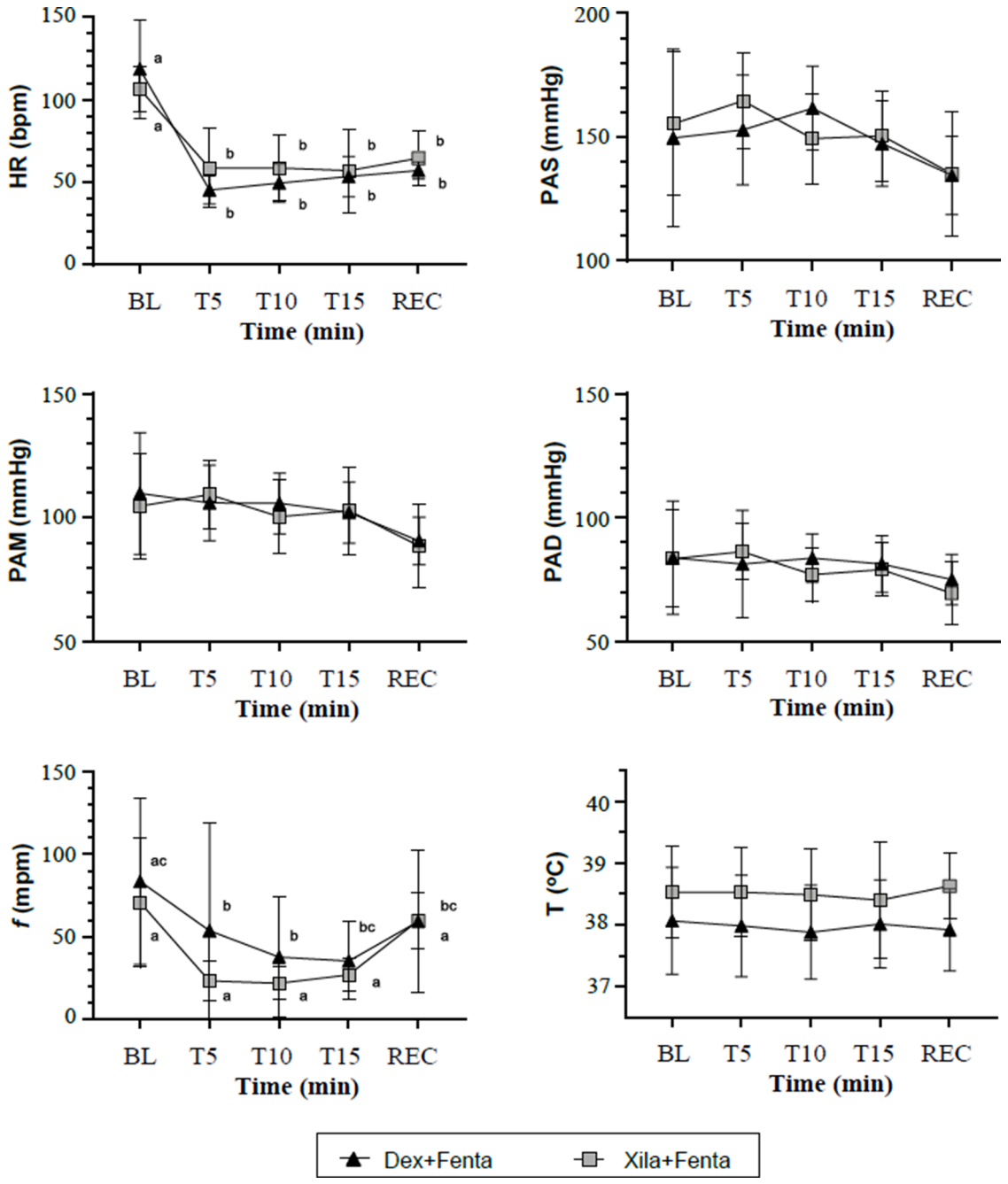

Fig. 1. Physiological parameters (mean ± standard deviation) in dogs submitted to sedation with 0.2 mg/kg of xylazine and 2.5 μg/kg of fentanyl (XF), and 2 μg/kg of dexmedetomidine and 2.5 μg/kg of fentanyl (DF).
Consider BL, moment prior to treatment administration; T5, 5 min after treatment administration; T10, 10 min after treatment administration; T15, 15 min after treatment administration; REC, recovery; HR, heart rate (beats/min); SBP, systolic blood pressure (mmHg); MAP, mean arterial pressure (mmHg); DBP, diastolic blood pressure (mmHg); *f*, respiratory rate (movements/min); TR, rectal temperature (°C).
[a] statistical difference between moments in the same group. $P < 0.05$.
Source Elaborated by the authors.

an increase in vagal tone, making bradycardia more intense, which can also occur with other opioids (Nishimura et al., 2018).

Opioids can cause respiratory depression due to the central depressant effect, reduced level of consciousness and partial obstruction of the upper airways, by promoting relaxation of the muscles in the region (Gupta et al., 2018; Montandon & Horner, 2019; Palkovic et al., 2020). Alpha 2 agonists may participate in this mechanism by promoting a decrease in respiratory rate and hypercapnia response (Lerche & Muir, 2004). Bradypnea is reflected in the reduction of minute ventilation, according to the depression of the activity of the Parabrachial/Kölliker-Fuse and preBötzinger complexes, the nucleus of the solitary tract and the spinal raphe (Palkovic et al., 2020).

This mechanism explains the increase in $PaCO_2$ and the decrease in PaO_2 at 5 and 15 min in both groups, so that 93% and 73% of the animals presented hypoxemia at these moments, respectively. When PaO_2 reaches values below 85 mmHg, there is a drop in tissue oxygen supply and consequent damage to the animal's organism, which can be minimized by the use of oxygen therapy during the anesthetic period (Coutu et al., 2015). A study with medetomidine in dogs showed a reduction in *f* and PaO_2 values close to 70 mmHg (Pettifer an Dyson, 1993). The

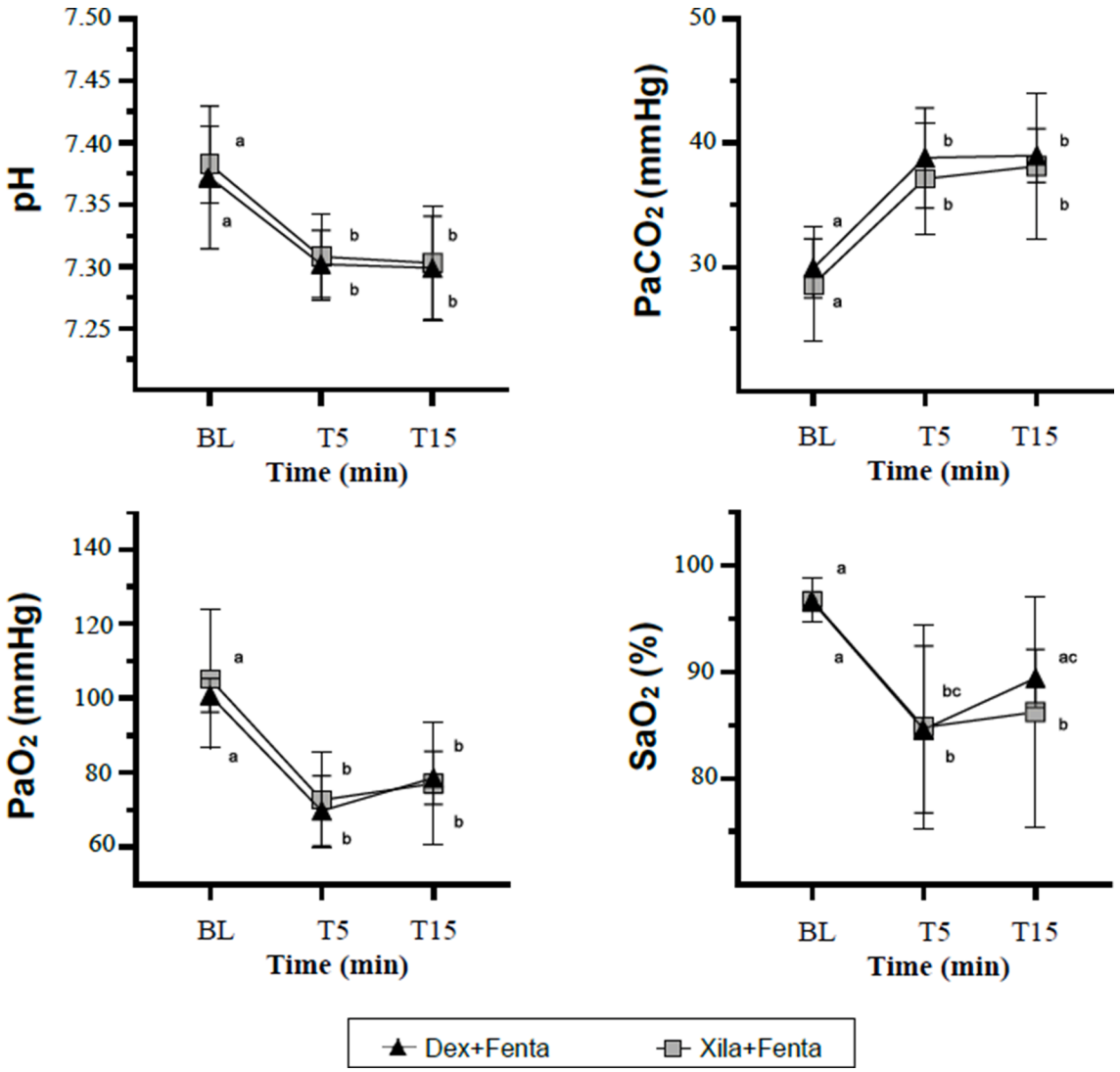

Fig. 2. . Blood gas parameters [pH, $PaCO_2$, PaO_2, SaO2] (mean ± standard deviation) before application and 5 and 15 min after application of sedation with 0.2 mg/kg of xylazine and 2.5 μg/kg of fentanyl (XF), and 2 μg/kg of dexmedetomidine and 2.5 μg/kg of fentanyl (DF).
Consider BL, moment prior to treatment administration; T5, 5 min after treatment administration; T15, 15 min after treatment administration; pH, hydrogen potential; $PaCO_2$, partial blood pressure of carbon dioxide (mmHg); PaO_2, partial arterial oxygen pressure (mmHg); SaO_2, hemoglobin oxygen saturation (%).
[a] statistical difference between moments in the same group. $P < 0.05$.
Source Elaborated by the authors.

association of dexmedetomidine with opioids also showed other blood gas effects, such as a reduction in blood pH and BE, and an increase in $PaCO_2$, evidencing the possibility of worsening respiratory depression when adding an opioid to the protocol (Nishmura et al., 2018).

The sedative effect induced by opioids is mainly related to the mu and kappa receptors and to the depression of impulses from the hypocretin/orexin system in the hypothalamus, which can be verified by characteristic electrocortical changes (Palkovic et al., 2020). Fentanyl promotes an increase in the frequency of delta waves in the electroencephalogram of rats, while reducing the respiratory rate of these animals (Montandon & Horner, 2019).

Dexmedetomidine and xylazine exert their sedative effect through the activation of central alpha 2 adrenergic receptors (Weerink et al., 2017). The locus coeruelus relates the surveillance pathways, being the main norepinephrine release region of the mammalian central nervous system, containing a large amount of alpha 2 adrenergic receptors (Cagnardi et al., 2017). Inhibition of adenylate cyclase is essential for the sedative effect from the activation of these receptors in the locus coeruelus, reducing the sympathetic tone of the central nervous system (Cagnardi et al., 2017). Hyperpolarization by activation of potassium channels and inhibition of voltage-gated calcium channels are also linked to the activity of alpha 2 adrenergic receptors (Yang et al., 2014).

As for the selectivity for binding to alpha 1 adrenergic or alpha 2 adrenergic receptors, dexmedetomidine has a ratio of 1:1620 while xylazine has 1:160 (Rockhill et al., 2011; Weerink et al., 2017). In a study with alpha 2 agonists and propofol, animals that received dexmedetomidine showed greater depression on eyelid and pedal reflexes, in addition to jaw tone, than those that received xylazine, in which the depression of these reflexes were moderate (Jena et al., 2014).

The analgesia provided by alpha 2 adrenergic agonists is mediated by binding to central receptors and the spinal cord (Weerink et al., 2017). There is suppression of pain transmission by the hyperpolarization of interneurons and reduction of the release of pronociceptive transmitters, such as substance P and glutamate, inhibiting the firing of nociceptive neurons (Weerink et al., 2017). Opioids, through binding to mu and kappa receptors, act by activating descending modulatory pathways in the periaqueductal gray (PAG) of the brainstem, inhibiting synapses of neurons in the dorsal horn of the spinal cord, and modulating afferent

synapses of peripheral receptor neurons (Stein & Lang, 1993).

The benefits of the association of several pharmacological classes with an alpha 2 adrenergic agonist have been widely observed and researched, with emphasis on reducing the doses of the respective drugs and a consequent decrease in the occurrence or intensity of adverse effects (Leppänen et al., 2006). The synergism triggered by the combination of an alpha 2 agonist with an opioid allows the performance of a wide variety of procedures in veterinary routine, yet it becomes greater and provides more pronounced sedative effects when performed with mu agonists (Cardoso et al., 2014; Nishimura et al., 2018).

This study presented the important limitation of having a reduced number of participating animals, which reflected in higher standard deviations, interfering with the statistical analysis.

Conclusions

The association of fentanyl with xylazine or dexmedetomidine allows the performance of radiographic exams for the diagnosis of hip dysplasia in dogs using the articular distractor, with adequate analgesia, quality and sedation time. The protocol promotes greater changes in heart rate and arterial oxygen partial pressure. Patient monitoring and oxygen supplementation are recommended after treatment administration, to ensure greater safety to the protocol.

Ethics approval and consent to participate

The study was approved by the Committee on Ethics in Animal Use (CEUA) of the Federal University of Minas Gerais under protocol No. 146/2017. The study was carried out in accordance with institutional guidelines and regulations. The Free and Informed Consent Term was signed by the animal owners.

Consent for publication

Consent for publication was obtained from the Military Police Battalion of Belo Horizonte - Minas Gerais, Brazil, for publication of the results.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author, FGS, upon reasonable request.

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CRediT authorship contribution statement

Suzane Lilian Beier: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Marcos Paulo Antunes de Lima:** Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – review & editing. **Felipe Gaia de Sousa:** Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing. **Renata Andrade Silva:** Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – review & editing. **Natália Fagundes:** Investigation, Methodology, Visualization, Writing – review & editing. **Milena Fascina Bovi:** Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing. **Renato Cesar Sacchetto Tôrres:** Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

Ahmad, R. A., Amarpal, P., Kinjavdekar, H. P., Aithal, H. P., Pawde, A. M., & Kumar, D. (2011). Effects of midazolam or midazolam-fentanyl on sedation and analgesia produced by intramuscular dexmedetomidine in dogs. *Asian Journal of Animal Sciences, 5*, 302–316. https://dx.doi.org/10.3923/ajas.2011.302.316.

Arunkumar, S., Dilipkumar, D., & Shivaprakash, B. (2017). Clinical and physiological evaluation of dexmedetomidine, xylazine and triflupromazine as pre-anaesthetics with propofol-isoflurane anaesthesia for various surgeries in dogs. *The Pharma Innovation Journal, 6*, 100–105.

Butler, J. R., & Gambino, J. (2017). Canine hip dysplasia diagnostic imaging. *Veterinary Clinics Small Animal Practice, 47*, 777–793. https://doi.org/10.1016/j.cvsm.2017.02.002

Cardoso, C. G., Marques, D. R. C., Silva, T. H. M., & Mattos-Junior, E. (2014). Cardiorespiratory, sedative and antinociceptive effects of dexmedetomidine alone or in combination with methadone, morphine or tramadol in dogs. *Veterinary Anaesthesia and Analgesia, 41*, 636–643. https://doi.org/10.1111/vaa.12172

Cagnardi, P., Villa, R., Ravasio, R., Lucatello, L., Di Cesare, F., Capolongo, F., Boccardo, A., & Pravettoni, D. (2017). Pharmacokinetics and sedative effects of dexmedetomidine in dairy calves. *The New Zealand Veterinary Journal, 65*, 14–18. https://doi.org/10.1080/00480169.2016.1237313

Chabot-Doré, A.-. J., Schuster, D. J., Stone, L. S., & Wilcox, G. L. (2015). Analgesic synergy between opioid and α2 -adrenoceptors. *British Journal of Pharmacology, 172*, 388–402. https://doi.org/10.1111/bph.12695

Coutu, P., Caulkett, N., Pang, D., & Boysen, S. (2015). Efficacy of a portable oxygen concentrator with pulsed delivery for treatment of hypoxemia during equine field anesthesia. *Veterinary Anaesthesia and Analgesia, 42*, 518–526. https://doi.org/10.1111/vaa.12246

Ginja, M. M. D., Silvestre, A. M., Gonzalo-Orden, J. M., & Ferreira, A. J. A. (2010). Diagnosis, genetic control and preventive management of canine hip dysplasia: A review. *Veterinary Journal (London, England : 1997), 184*, 269–276. https://doi.org/10.1016/j.tvjl.2009.04.009

Granholm, M., Mckusick, B. C., Westerholm, F. C., & Aspegrén, J. C. (2007). Evaluation of the clinical efficacy and safety of intramuscular and intravenous doses of dexmedetomidine and medetomidine in dogs and their reversal with atipamezole. *Veterinary Record, 160*, 891–897. https://doi.org/10.1136/vr.160.26.891

Gupta, K., Prasad, A., Nagappa, N., Wong, J., Abrahamyan, L., & Chung, F. F. (2018). Risk factors for opioid-induced respiratory depression and failure to rescue: A review. *Current Opinion in Anesthesiology, 31*, 110–119. https://doi.org/10.1097/aco.0000000000000541

James, H. K., McDonnell, F., & Lewis, T. W. (2020). Effectiveness of Canine hip dysplasia and elbow dysplasia improvement programs in Six UK pedigree breeds. *Frontiers in Veterinary Science, 6*, 490. https://doi.org/10.3389/fvets.2019.00490

Jena, B., Das, J., Nath, I., Sardar, K. K., Sahoo, A., Beura, S. S., & Painuli, A. (2014). Clinical evaluation of total intravenous anaesthesia using xylazine or dexmedetomidine with propofol in surgical management of canine patients. *Veterinary World, 7*, 671–680. https://doi.org/10.14202/vetworld.2014.671-680.

King, M. D. (2017). Etiopathogenesis of canine hip dysplasia, prevalence, and genetics. *Veterinary Clinics: Small Animal Practice, 47*, 753–767. https://doi.org/10.1016/j.cvsm.2017.03.001

Kukanich, B., & Wiese, A. J. (2015). Opioids. In K. A. Grimm, L. A. Lamont, W. J. Tranquilli, S. A. Greene, & S. A. Robertson (Eds.), *Veterinary anesthesia and analgesia: The fifth edition of Lumb and Jones* (5th ed., pp. 207–226). New York: John Wiley & Sons.

Lerche, P., & Muir, W. W. (2004). Effect of medetomidine on breathing and inspiratory neuromuscular drive in conscious dogs. *American Journal of Veterinary Research, 65*, 720–724. https://doi.org/10.2460/ajvr.2004.65.720

Leppänen, M. K., McKusick, B. C., Granholm, M. M., Westerholm, F. C., Tulamo, R., & Short, C. E. (2006). Clinical efficacy and safety of dexmedetomidine and buprenorphine, butorphanol or diazepam for canine hip radiography. *Journal of Small Animal Practice, 47*, 663–669. https://doi.org/10.1111/j.1748-5827.2006.00030.x

Montandon, G., & Horner, R. L. (2019). Electrocortical changes associating sedation and respiratory depression by the opioid analgesic fentanyl. *Scientific Reports, 9*, 1–11. https://doi.org/10.1038/s41598-019-50613-2

Murrell, J. C., & Hellebrekers, L. J. (2005). Medetomidine and dexmedetomidine: A review of cardiovascular effects and antinociceptive properties in the dog. *Veterinary Anaesthesia and Analgesia, 32*, 117–127. https://doi.org/10.1111/j.1467-2995.2005.00233.x

Nishimura, L. T., Auckburally, A., Santilli, J., Vieira, B. H. B., Garcia, D. O., Honsho, C. S., & Mattos-Junior, E. (2018). Effects of dexmedetomidine combined with commonly

administered opioids on clinical variables in dogs. *American Journal of Veterinary Research, 79*, 267–275. https://doi.org/10.2460/ajvr.79.3.267

Palkovic, B., Marchenko, V., Zuperku, E. J., Stuth, E. A. E., & Stucke, A. G. (2020). Multi-level regulation of opioid-induced respiratory depression. *Physiology, 35*, 391–404. https://doi.org/10.1152/physiol.00015.2020

Pettifer, G. R., & Dyson, D. H. (1993). Comparison of medetomidine and fentanyl-droperidol in dogs: Sedation, analgesia, arterial blood gases and lactate levels. *Canadian Journal of Veterinary Research = Revue Canadienne de Recherche Veterinaire, 57*, 99–105.

Rockhill, A. P., Chinnadurai, S. K., Powell, R. A., & Deperno, C. S. (2011). A comparison of two field chemical immobilization techniques for bobcats (*Lynx rufus*). *Journal of Zoo and Wildlife Medicine, 42*, 580–585. https://doi.org/10.1638/2010-0152.1

Stein, C., & Lang, L. J. (1993). Peripheral mechanisms of opioid analgesia. *Current Opinion in Pharmacology, 76*, 182–191. https://doi.org/10.1016/j.coph.2008.12.009

Syrcle, J. (2017). Hip dysplasia clinical signs and physical examination findings. *Veterinary Clinics - Small Animal Practice, 47*, 769–775. https://doi.org/10.1016/j.cvsm.2017.02.001

Tôrres, R. C. S., Araújo, R. B., & Rezende, C. M. F. (2005). Articular distractor in the early radiographic diagnosis of canine hip dysplasia. *Arquivo Brasileiro de Medicina Veterinaria e Zootecnia, 57*, 27–34. https://doi.org/10.1590/S0102-09352005000100004

Trimble, T., Bhalla, R. J., & Leece, E. A. (2018). Comparison of sedation in dogs: Methadone or butorphanol in combination with dexmedetomidine intravenously. *Veterinary Anaesthesia and Analgesia, 45*, 597–603. https://doi.org/10.1016/j.vaa.2018.03.008

Weerink, M. A. S., Struys, M. M. R. F., Hannivoort, L. N., Barends, C. R. M., Absalom, A. R., & Colin, P. (2017). Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. *Clinical Pharmacokinetics, 56*, 893–913. https://doi.org/10.1007/s40262-017-0507-7, 2017.

Wegner, K., Horais, K. A., Tozier, N. A., Rathbun, M. L., Shtaerman, Y., & Yaksh, T. L. (2008). Development of a canine nociceptive thermal escape model. *Journal of Neuroscience Methods, 168*, 88–97. https://doi.org/10.1016/j.jneumeth.2007.09.019

Yang, Y.-. C., Meng, Q.-. T., Pan, X., Xia, Z.-. Y., & Che, X.-. D. (2014). Dexmedetomidine produced analgesic effect via inhibition of HCN currents. *European Journal of Pharmacology, 740*, 560–564. https://doi.org/10.1016/j.ejphar.2014.06.031