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Selection of the Optimal Dose of Dexmedetomidine and its Cardiovascular Effects when used as Part of Combined Anesthesia for Surgical Correction of Kyphosis in Dogs

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ABSTRACT

The development, clinical and instrumental characterization, and evaluation of the effectiveness of various schemes of combined general anesthesia in dogs are important problems in veterinary surgery. The effects of varying doses of dexmedetomidine in combination with tiletamine–zolazepam and isoflurane have not been studied in the surgical treatment of dogs with kyphosis. We aimed to evaluate the changes in the functional characteristics of the cardiovascular system and the clinical effectiveness of intramuscular administration of dexmedetomidine (Dex) at doses of 5, 7.5, and 10µg/kg followed by intravenous administration of tiletamine–zolazepam and isoflurane inhalation for anesthesia in dogs with kyphosis. The study involved 60 dogs with kyphosis, with an anesthetic risk group of categories I or II according to the ASA (American Society of Anesthesiologists) classification and without anomalies of the cardiovascular system. All dogs were randomly divided into equal 3 groups: Dex 5, Dex 7.5, and Dex 10. Intravenous administration of tiletamine–zolazepam (induction) in dogs with kyphosis and inhalation of isoflurane (maintenance of anesthesia) did not cause changes in the heart rate, or systolic, diastolic or mean arterial blood pressure compared with baseline values. Combined dexmedetomidine–tiletamine–zolazepam–isoflurane anesthesia is highly effective and safe in the surgical correction of kyphosis in sick dogs. Dexmedetomidine intramuscularly administered at a dose of 5.0-7.5µg/kg is the optimal premedication for examining or performing the surgical correction of spinal pathologies in dogs.

Key words: Anesthesia, Dexmedetomidine, Tiletamine, Zolazepam, Isoflurane, Kyphosis

INTRODUCTION

Kyphosis in dogs is quite rare; it is a genetically determined degenerative disease that affects certain breeds of dogs, leads to significant deterioration in the quality of life of pets and also causes anxiety among their owners (Wyatt et al. 2019; De Decker et al. 2019; Lackmann et al. 2022). Questions on the surgical treatment of dogs with kyphotic deformities of the thoracic and lumbar spine require further study (Guevar et al. 2014; Mathiesen et al. 2018). Currently, there is no uniformly accepted treatment strategy for such dogs. This is due to the wide variability of the etiological factors that contribute to the formation of spinal kyphosis (Mathiesen et al. 2018). Moreover, it is known that conservative treatment not only does not correct the deformity but also does not stop its progression (Aikawa et al. 2014; Rudenko et al. 2022; Li et al. 2023).

The most important aspect that influences the success of surgical intervention for spinal pathologies in dogs is the adequacy of anesthesiology (Gross et al. 2019; Noonan et al. 2023). Of the large number of factors that contribute to the cascade of secondary damage initiated by general anesthesia, soft-tissue perfusion and visceral perfusion are known to be among the most important variables (Hofmeister et al. 2009; Raszplewicz et al. 2013). Indeed, the outcome of corrective spinal surgery is positively correlated with perfusion of the injured spinal cord. Since perfusion of body tissues during general anesthesia is

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highly dependent on systemic blood pressure, cardiovascular parameters are the most important parameters to be monitored in both veterinary and human medicine, as well as under experimental conditions (Moran-Muñoz et al. 2017; Nejamkin et al. 2020; Limprasutr et al. 2021).

In veterinary medicine, dexmedetomidine is widely used to provide sedation and analgesia for minor surgical and diagnostic procedures, representing a highly effective premedication prior to anesthesia (Hellyer et al. 1989; Jang et al. 2015; Kusolphat et al. 2022). In physiologically healthy dogs administered sedating doses of dexmedetomidine, the heart rate is significantly reduced, and systolic blood pressure (Karna et al. 2022) and left-ventricular systolic function are modestly reduced; a significant increase in systemic vascular resistance, which is caused by vasoconstriction, is also observed (Huuskonen et al. 2022; Hiebert et al. 2022).

A literature search of scientific databases revealed a lack of studies that examine the effect of different doses of dexmedetomidine on the efficacy and cardiovascular effects of combined tiletamine–zolazepam–isoflurane anesthesia in dogs undergoing surgical correction of kyphosis.

The aim of this work was to empirically select the optimal dose of dexmedetomidine and study its cardiovascular effects when used as part of combined anesthesia for the surgical treatment of dogs with kyphosis.

MATERIALS AND METHODS

Ethical approval

The animal study protocol was approved by the Ethics Committee of Peoples' Friendship University of Russia (# EA1/1811: 10-May-2020).

Determination of sample size

When analyzing literature data from research assessing parameters in dogs with intervertebral disc disease in the thoracolumbar region, it was found that the ratio of clinically significant difference in group average values to standard deviation should be at least 0.9 (Ferré et al. 2022). Then, considering a level of statistical significance of 0.05 and study power of 0.80, the minimum sample size in the experimental groups had to be at least 20 dogs.

Study design

The study was conducted on 60 small-breed dogs admitted for an initial appointment at the Center for Veterinary Innovative Medicine of Peoples' Friendship University of Russia (Moscow, Russian Federation). Equal three groups of dogs were formed according to the principles of analogs: Group 1 — group Dex 5 — included 20 dogs requiring surgery for kyphosis that were treated with dexmedetomidine intramuscularly at a dose of 5μg/kg BW as premedication. Group 2 — Dex 7.5 — included 20 dogs requiring surgery to correct kyphosis that was premedicated with dexmedetomidine intramuscularly at a dose of 7.5μg/kg BW. Group 3 — Dex 10 — included 20 dogs with kyphosis that were treated with dexmedetomidine intramuscularly at a dose of 10μg/kg BW before surgical correction.

Inclusion criterion: The study included dogs with kyphosis.

Exclusion criterion: Presence of comorbid diseases.

The randomization procedure was carried out as follows: An employee of the statistics department of RUDN University numbered 60 envelopes (in accordance with the number of dogs with kyphosis included in the study), placed notes with group codes in each of them (Dex 5 — 20 pieces; Dex 7.5 — 20 pieces; Dex 10 — 20 pieces) and sealed the envelopes.

A total of 60 dogs (20 in each group), 33 males and 27 females, were included in this study. The average weight of the dogs was 6.8±0.95kg (range of 3.9-9.5). The study included dogs of mixed breeds (n=29), French Bulldogs (n=9), Dachshunds (n=8), Pekingese dogs (n=6), Chihuahuas (n=4), Poodles (n=2), Yorkshire Terriers (n=2).

Methodology for preparing animals for surgery

A computed tomography scan was performed to make an accurate diagnosis. Before the start of the surgical intervention, graphical radiography with a marker was performed, which made it possible to reduce the time of surgical intervention and to reduce injury to the animal. The assessment of the degree of anesthetic risk in dogs was carried out according to the generally accepted method (Huuskonen et al. 2022; Le Chevallier et al. 2023), the doses of drugs for premedication, and induction, and maintenance of anesthesia were recorded and were based on the weight of the animal and intraoperative monitoring indicators (Aarnes et al. 2023; Saha et al. 2024).

Method for general anesthesia

Before transporting the animals to the clinic on the day of surgery, gabapentin (PIK-PHARMA LEK, Russia; 300mg capsules) at a dose of 50mg/kg was given to the dogs once orally by the owners of the animals. Before surgery, 15-20min before general anesthesia, depending on the size of the dog, all dogs had a 22G intravenous catheter inserted into the anterior saphenous vein of the forearm. Premedication was performed using dexmedetomidine (Dexdomitor; Orion Pharma, Finland; 0.5mg/ml). Dogs in the Dex 5 group were administered dexmedetomidine intramuscularly at a dose of 5μg/kg; in the Dex 7.5 group, the dose was 7.5μg/kg, and in the Dex 10 group, the dose was 10μg/kg. Preoxygenation was performed with an AtmungLFY-I-5A oxygen concentrator (Atmung 5L-I, Germany) for 3-5min before induction of anesthesia (Jang et al. 2015; Sachivkina et al. 2022). At the start of sedation, anesthesia was induced with tiletamine–zolazepam (Zoletil®, Virbac, France). Zoletil (Zol) powder was diluted in 5mL of sterile water for injection. The resulting zoletil solution contained 50mg/mL tiletamine and 50mg/ml zolazepam. Zoletil was administered intravenously as a bolus at a dose of 3mg/kg for loss of tone of the lower jaw. The monitoring of the frequency and characteristics of the heart rhythm was carried out on an EcoMed-50 veterinary monitor in the second standard lead (Vatnikov et al. 2019a, 2019b). Electrodes (EuroECG electrodes, model F9079) were attached to the surface of the paw pads (to the two thoracic limbs and the left pelvic limb). Temperature was measured rectally with an AdtempTM422 veterinary electronic thermometer (USA) five times; the average value was reflected in the protocol.

Next, the required area of hair was shaved, depending on the location of the operation, using a CodosCP-6800 veterinary animal clipper (China). The remaining shaved hair was removed using a MysteryMVC-1127 vacuum cleaner (China). During surgery, arterial blood hemoglobin

oxygen saturation was monitored using a pulse oximeter on an EcoMedEPM-50 veterinary monitor (China) using a non-invasive method (El-Hawari et al. 2022). During the entire operation, the animal's body temperature was monitored using the touch temperature sensor of the EcoMedEPM-50 monitor. To prevent hypothermia during surgery, animals were placed on a Crocus RT 300 SI heating device (Russia), a heating system for newborns designed to prevent hypothermia and associated complications. During surgical treatment, as a means of supporting hemodynamics and preventing hypovolemia in dogs weighing up to 10kg, the animals received infusion therapy with Ringer's solution at 5 ml/kg/hour (Vilkovyskiy et al. 2020), for which we used a veterinary single-channel syringe pump (BYZ-810 DVet; China). After completion of the surgical procedure, all dogs were intravenously administered 0.1mg/kg atipamezole hydrochloride (Antisedan; Orion Pharma, Finland; 5mg/ml). The severity of postoperative pain syndrome was assessed using the short form of the Glasgow Combined Pain Scale, adapted for dogs (Testa et al. 2021). Pain syndrome was treated with non-narcotic, centrally acting analgesic (nefopan hydrochloride at 0.3mg/kg) (Chernigova et al. 2019). The criteria for determining the awakening of an animal after anesthesia included the animal's reaction to the endotracheal tube (cough), independent immersion of the tongue into the oral cavity, the presence of positive palpebral and corneal reflexes, and the ability to move independently (Kramer et al. 2022; Saha et al. 2024).

Method for performing surgical intervention

Surgical access to correct kyphosis using the transthoracic stabilization method was carried out by employing a linear, right-sided approach to the chest at the level of the deformity confirmed with radiography. Next, a right thoracotomy was performed through the dissection of the latissimus scalene and intercostal muscles. Intercostal spaces were formed using rib expanders. The area of deformity was examined; the vertebral bodies were skeletonized; and the intervertebral discs were fenestrated with a surgical cutter at the level of the deformity. The next step was to insert one transpedicular screw into the body of the thoracic vertebra cranial and caudal to the deformity. In this case, the screws were inserted bicortically. Then, a fixation beam was inserted into the transpedicular screw system (Noonan et al. 2023). Next, the vertebrae were distracted until the spinal column was visually straightened; afterwards, the beam was fixed in the pedicle screws (Gross et al. 2019). Once the beam was secured, an additional beam was installed in a similar manner to create two levels of stability. At the end of this procedure, the surgical wound was lavaged with an isotonic solution, and it was sutured in layers with monofilament threads.

Clinical methods

Thermometry, palpation, percussion, examination, tonometry, electrocardiography, echocardiography, and biochemical analysis of blood serum were performed. We assessed for the presence of back pain using finger pressure on the spinous processes; neurological deficit of the pelvic limbs; abdominal wall tension; the presence of proprioception deficit, paresis, or paralysis of the pelvic limbs and tail; and the presence of lameness in the pelvic limbs. Anesthetic risk was assessed using the ASA four-point scoring system (Rudenko et al. 2021; Olabode et al. 2023). During the clinical examination of the state of the cardiovascular system, cardiac apical impulse, capillary refill rate (CRF) and the degree of pulse filling were assessed. During the physical examination of the animal, attention was paid to its constitution, posture and fatness. The condition of the respiratory system organs was assessed as follows: assessment of breathing patterns and respiratory rate, auscultation of the lungs and palpation of the trachea (tracheal reflex) were performed (Hampton et al. 2019).

Statistical analysis

Statistical analysis of the study results was carried out after studying the shape of the distribution of the central characteristics of the data under study. The normal distribution of digital data was assessed using the Shapiro–Wilk method. The mean value and its 95% confidence limits were assessed; the data are presented as the arithmetic mean±SD. The comparison of the observed changes in the indicators in the studied groups was analyzed with parametric variance pairwise comparisons (paired Student's t-test). When comparing the three groups, the parametric method of one-way analysis of variance (one-way ANOVA) was used. The exact p-value was calculated (differences were considered significant at $P<0.05$). The biometric processing of the results was carried out using Statistica for Windows, V.5.5A (StatSoft, Inc.) (Olabode et al. 2023).

RESULTS

The normal distribution of digital experimental data was established using the Shapiro–Wilk method.

Table 1 shows the effect of various doses of intramuscularly administered dexmedetomidine as part of combined general anesthesia on dogs' heart rates.

From the data in Table 1, it follows that in dogs with kyphosis in the Dex 5 group, there were significant ($P\leq0.001$) decreases in the heart rate compared with the initial data: by 1.54 times 5min after premedication with dexmedetomidine, by 1.86 times after 10 min, by 2.07 times after 15min and by 2.27 times after 20min. It should be noted that after induction of anesthesia with zoletil and while maintaining the level of anesthesia with isoflurane (Iso), there was a tendency towards the normalization of the heart rate. In this group of dogs, there was no need to use atropine sulfate to correct bradycardia.

In dogs with kyphosis that were premedicated with dexmedetomidine intramuscularly at a dose of 7.5μg/kg (Dex 7.5 group), significant ($P\leq0.001$) decreases in the heart rate compared with the initial data were observed: by 1.61 times 5min after premedication with dexmedetomidine, by 2.0 times after 10min, by 2.19 times after 15min and by 2.2 times after 20min. After induction of anesthesia, there was a trend toward the normalization of the heart rate.

During the anesthesiologic monitoring of dogs in the Dex 10 group, significant ($P\leq0.001$) decreases in the heart rate compared with the initial data were noted: by 1.69 times 5min after premedication with dexmedetomidine, by 2.11 times after 10min, by 2.33 times after 15min and by 2.40 times after 20min. During the implementation of tiletamine–zolazepam–isoflurane anesthesia, there was a tendency towards normalizing the heart rate. In three dogs

Table 1: Effect of different doses of dexmedetomidine on the heart rate of dogs

Group		Heart Rate (bpm) in Dogs in Different Groups			P Value
		Dex 5 (n=20)	Dex 7.5 (n=20)	Dex 10 (n=20)	
Original data (0 min)		132.2±11.51	128.7±9.23	126.7±7.81	P≤0.5
After the introduction of dexmedetomidine, min	5	85.6±1.05a	79.9±1.15b	75.1± 6.72c	P≤0.1
	10	71.2±8.53a	64.3±6.73b	60.1±5.91c	P≤0.5
	15	63.7±5.31a	58.7±6.29b	54.3±5.27c	P≤0.5
	20	58.1±5.95a	56.3±4.91b	52.7±5.59c	P≤0.1
Zol		126.7±8.53	111.7±5.9	102.7±7.37	P≤0.5
Iso		124.3±6.76	115.7±3.47	108.9±4.91	P≤0.5
72 hours after anesthesia		129.7±9.79	120.9±7.24	124.3±10.21	P≤1

Mean±SD bearing alphabets in a row are P≤0.001.

Table 2: Effect of different doses of dexmedetomidine on systolic blood pressure in dogs

Group		SBP (mmHg) in Dogs in Different Groups			P Value
		Dex 5 (n=20)	Dex 7.5 (n=20)	Dex 10 (n=20)	
Original data (0 min)		139.2±7.69	145.3±6.97	142.7±5.93	P≤1
After the introduction of dexmedetomidine, min	5	134.9±10.72	127.6±11.31	121.9±8.23a	P≤0.1
	10	132.9±8.91	129.9±7.03	126.1±5.97a	P≤0.5
	15	121.8±6.17	123.7±8.93	120.7±5.47b	P≤1
	20	124.7±9.51	122.7±6.52	118.3±5.21b	P≤0.5
Zol		153.5±7.91	154.2±8.05	152.1± 6.31	P≤0.5
Iso		155.7±5.27	151.3±6.21	146.9±4.20	P≤1
72 hours after anesthesia		144.3±9.71	140.4±5.91	141.5±7.32	P≤0.5

Mean±SD bearing different alphabets in a row differ significantly (P<0.05).

in this group (15%), bradycardia was corrected with atropine sulfate, as shown in Table 2.

From the data presented in Table 2, it can be seen that in dogs in the Dex 5 and Dex 7.5 groups, an unreliable trend towards a decrease in systolic blood pressure was established. Furthermore, the use of dexmedetomidine at an intramuscular dose of 10μg/kg led to significant decreases (by 1.17 times after 5min (P≤0.05), by 1.13 times after 10min (P≤0.05), by 1.18 times after 15min (P≤0.01) and by 1.21 times after 20min (P≤0.01) in systolic blood pressure compared with the initial data in dogs in the Dex 10 group. During anesthesia with zoletil and isoflurane, systolic blood pressure increased slightly in dogs in all groups. Inter-group changes in systolic blood pressure levels were not statistically significant.

The indirect tonometry method did not establish statistically significant deviations in the dynamics of combined anesthesia in dogs with kyphosis or in animals in different experimental groups (Table 3).

Table 4 shows the results of studying the effect of various doses of intramuscularly administered dexmedetomidine on the level of mean arterial blood pressure in dogs.

In dogs with kyphosis (Dex 10 group), a significant (P≤0.05) decrease in mean arterial blood pressure compared with baseline data was observed by 1.32 times 20min after intramuscular administration of dexmedetomidine. After induction of anesthesia, this physiological parameter was normalized.

The assessment of the level of oxygen saturation in dogs' blood using pulse oximetry showed the absence of significant changes both in inter-group comparisons and in the dynamics of combined anesthesia (Table 5).

It should also be added that when combined anesthesia was administered to dogs in the Dex 5 group for surgical treatment of kyphosis, a lack of weight-bearing ability and muscle relaxation (myorelaxation) was revealed in a time interval from 40 to 72 seconds (on average, for 49.9±5.1 seconds). No vomiting or regurgitation was detected in dogs in this group during induction. A decrease in the corneal reflex was observed in dogs in a time interval from 125 to 198 seconds (on average, for 163.9±10.8 seconds after induction). We recorded agitation and manifestations of myoclonus and opisthotonus in two (10.0%) dogs during induction of anesthesia.

When conducting combined anesthesia in dogs in the Dex 7.5 group for surgical treatment of kyphosis, we recorded the absence of weight-bearing ability and muscle relaxation in a time interval from 41 to 66 seconds (on average, for 43.7±6.2seconds). No vomiting or regurgitation was detected in dogs in this group during initial induction. A decrease in the corneal reflex was observed in dogs in a time interval from 108 to 169 seconds (on average, for 143.4±8.9 seconds after initial induction). We did not record any excitement or manifestations of myoclonus and opisthotonus in any dog during induction of anesthesia.

When performing combined anesthesia in dogs in the Dex 10 group for surgical treatment of kyphosis, we observed a lack of support ability and muscle relaxation (myorelaxation) in a time interval from 38 to 65 seconds (on average, for 40.2±5.1 seconds). No vomiting or regurgitation was detected in dogs in this group during initial induction. A decrease in the corneal reflex was observed in dogs in a time interval from 111 to 173 seconds (on average, for 147.2±9.7 seconds after induction).

The body temperature results showed that when combined anesthesia was used in the Dex 5 group of dogs for surgical treatment of kyphosis, the body temperature was 38.2±0.09°C during induction; after 5 minutes, it decreased to 37.8±0.15°C; after 30 minutes, it decreased to 37.6±0.23°C; finally, 60 minutes after initial induction, the body temperature decreased to 37.1±0.12°C.

At the same time, when combined anesthesia was used in the Dex 7.5 group of dogs for surgical treatment of kyphosis, during induction, the body temperature was 38.1±0.19°°C; after 5min, it decreased to 37.9±0.21°C; after 30 min, it decreased to 37.7±0.17°C; finally, 60mins after initial induction, the body temperature decreased to 37.5±0.18°C.

Table 3: Effect of different doses of dexmedetomidine on diastolic blood pressure in dogs

Group		DBP (mmHg) in Dogs in Different Groups			P Value
		Dex 5 (n=20)	Dex 7.5 (n=20)	Dex 10 (n=20)	
Original data (0 min)		72.3±6.17	69.7±5.95	71.2±7.21	P≤0.5
After the introduction of dexmedetomidine, min	5	68.5±5.37	66.7±4.29	63.7±8.71	P≤0.5
	10	66.4±7.21	63.5±8.01	61.0±5.29	P≤0.5
	15	62.1±5.95	61.5±4.21	59.3±4.81	P≤1
	20	59.2±6.21	58.1±4.75	56.9±6.31	P≤0.1
Zol		69.8±7.87	67.9±8.01	66.7±10.07	P≤0.5
Iso		71.2±6.33	72.7±5.91	69.9±9.05	P≤0.5
72 hours after anesthesia		70.5±5.91	72.1±4.85	73.7±4.63	P≤1

Table 4: Effect of different doses of dexmedetomidine on mean arterial pressure in dogs

Group		MAP (mmHg) in Dogs in Different Groups			P Value
		Dex 5 (n=20)	Dex 7.5 (n=20)	Dex 10 (n=20)	
Original data (0 min)		94.2±6.21	94.1±5.95	95.2±4.75	P≤0.5
After the introduction of dexmedetomidine, min	5	91.3±5.92	87.1±6.23	83.2±4.85	P≤0.1
	10	87.2±5.87	86.5±6.21	83.7±7.21	P≤0.5
	15	82.4±5.83	83.1±4.79	80.7±6.11	P≤0.5
	20	81.7±5.73	80.5±4.21	72.3±7.51a	P≤0.5
Zol		98.3±6.21	97.2±6.03	95.8±7.95	P≤0.5
Iso		99.2±3.25	99.4±9.51	95.1±8.53	P≤0.5
72 hours after anesthesia		95.7±7.06	95.3±5.97	97.5±6.34	P≤1

Mean+SD bearing different alphabets in a row (a) differ significantly (P<0.05)

Table 5: Effect of different doses of dexmedetomidine on blood oxygen saturation in dogs.

Group		SpO_2 (mmHg) in Dogs in Different Groups			P Value
		Dex 5 (n=20)	Dex 7.5 (n=20)	Dex 10 (n=20)	
Original data (0 min)		96.2±1.81	96.4±0.92	95.7±1.31	P≤1
After the introduction of dexmedetomidine, min	5	96.1±1.21	96.7±1.03	95.5±1.11	P≤1
	10	96.3±1.91	95.4±1.63	95.9±1.75	P≤1
	15	95.0±0.86	95.1±1.23	95.0±1.15	P≤1
	20	95.1±0.93	95.7±1.54	95.9±1.35	P≤1
Zol		96.8±1.25	95.3±1.37	95.1±1.27	P≤1
Iso		96.2±0.98	96.1±0.75	96.0±1.23	P≤1
72 hours after anesthesia		96.0±0.95	96.3±1.11	96.8±1.29	P≤1

According to the results of the body temperature, when combined anesthesia was used in the Dex 10 group, during induction, this parameter was 37.7±0.09°C; after 5min, a decrease in values to 37.7±0.15°C was observed; after 30min, the body temperature decreased to 37.3±0.19°C; after 60min, the temperature dropped to 36.8±0.19°C. At the same time, the detected fluctuations did not go beyond the boundaries of the reference values for each dog and were not statistically significant.

The effect of different doses of dexmedetomidine on the rate of sedation in dogs during surgical correction of kyphosis is shown in Fig. 1.

It was found that in dogs with kyphosis in the Dex 5 group (Fig. 1), there were significant (P≤0.01) increases in the sedation index compared with the initial data (1.3±0.31 points): to 4.2±0.53 (3.23 times) 5min after intramuscular administration of dexmedetomidine, to 7.3±0.72 (5.62 times) after 10min, to 8.7±0.69 (6.69 times) after 15min and to 9.5±0.89 points (7.31 times) after 20min. It should be noted that after induction of anesthesia with zoletil and while maintaining the level of anesthesia with isoflurane, sufficient levels of sedation were noted, namely, 11.5±0.75 and 11.5±0.65 points, respectively. In the early postoperative period (72 hours), the rate of sedation in animals in this group did not differ from the initial level.

In dogs with kyphosis that were administered dexmedetomidine intramuscularly at a dose of 7.5μg/kg (Dex 7.5 group), significant (P≤0.01) increases in the sedation rate compared with the initial data (1.5±0 .22 points) were diagnosed: up to 4.1±0.43 (2.73 times) 5min after intramuscular administration of dexmedetomidine, 7.8±0.67 (5.2 times) after 10min, 9.3±0.75 (6.2 times) after 15min and 10.2±0.81 points (6.8 times after 20min). The period of induction of anesthesia with tiletamine–zolazepam was characterized by a sedation index of 11.8±0.89, and the period of maintenance with isoflurane, by a sedation index of 11.9±0.73 points.

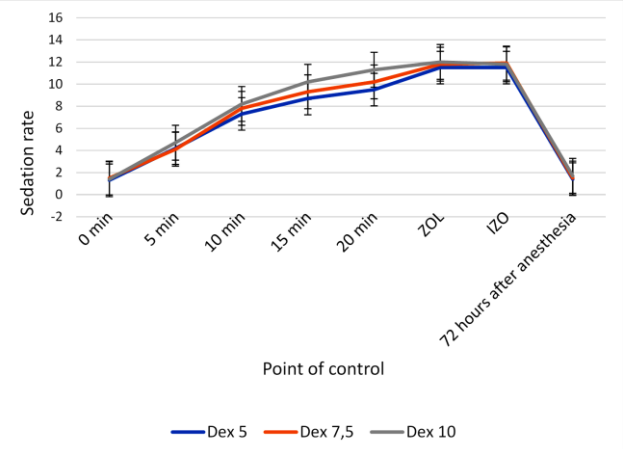

Fig. 1: Effect of different doses of dexmedetomidine on the rate of sedation in dogs with kyphosis (data format: Arithmetic mean±SD).

During the anaesthesiologic monitoring of dogs in the Dex 10 group (Fig. 1), significant ($P \leq 0.01$) increases in the sedation rate compared with the initial data (1.4±0.27 points) were noted: to 4.7±0.67 (3.36 times) 5min after premedication with dexmedetomidine, 8.2±0.53 (5.85 times) after 10min, 10.2±0.81 (7.29 times) after 15min and 11, 3±0.65 (8.07 times) after 20min. While implementing tiletamine–zolazepam–isoflurane Anesthesia, the sedation index remained at sufficient levels: 12.0±1.21 (induction) and 11.8±0.59 points (maintenance). After 72min, the sedation rate in animals in this group averaged 1.7±0.19 points and was not statistically different from the initial level. In an inter-group comparison, we did not note statistically significant deviations; however, a higher dose of dexmedetomidine as a premedication caused a stronger increase in the sedation rate.

DISCUSSION

Successful surgical correction of kyphotic lesions of the thoracolumbar spine in dogs largely depends on the use of highly effective anesthetic regimens (Aikawa et al. 2014; Guevar et al. 2014; Mathiesen et al. 2018; Wyatt et al. 2019; De Decker et al. 2019; Lackmann et al. 2022; Li et al. 2023; Noonan et al. 2023). The clinical rationale for the development of postoperative complications in dogs with kyphotic deformities of the spinal column is a set of factors that influence the decrease in the function or reserve of the organ. Under normal, non-stressful conditions, physiological changes that occur in organs and the brain cause only minimal functional changes. However, during acute illness, injury or surgery, and thus under stress, the reduced reserve capacity of pets impairs their response to increased energy demands (Huang et al. 2017; Vatnikov et al. 2020; Ramasubbu et al. 2023).

Stress is a nonspecific protective reaction to the influence of any pathological damaging factor (Rudenko et al. 2022). Functional disorders of the neuroendocrine system can reduce the resistance of cells, tissues and physiological functions of the body. Pathological conditions are the main causes of intraoperative and postoperative complications and mortality (Moran-Muñoz et al. 2017; Lovell et al. 2022). A well-conducted preoperative examination largely determines the degree of anesthetic risk and prognosis. Importance should be given to indicators of hemodynamics, perfusion and microcirculation (Hampton et al. 2019). Meanwhile, dexmedetomidine has a sedative effect with a maximum effect 15-20min after intramuscular administration, and this effect has a pronounced dose-dependent nature.

Intramuscular doses of 5–10mg/kg dexmedetomidine in dogs with kyphosis resulted in a significant decrease in the heart rate during the first 20min after administration of the drug but no significant decreases in the levels of systolic, diastolic and mean arterial pressure. The findings are consistent with other studies that assessed the hemodynamic effect following intramuscular administration of dexmedetomidine as premedication in dogs (Hellyer et al. 1989).

In other studies, the combination of α-2-adrenergic agonists with dissociative narcotics (ketamine or tiletamine–zolazepam) significantly increased the effectiveness and severity of general anesthesia and significantly reduced the incidence of various side effects (Nejamkin et al. 2020). Our study found that complex anesthesia consisting of intramuscular administration of dexmedetomidine in doses of 5.0-10μg/kg, induction with tiletamine–zolazepam intravenous bolus at a dose of 3mg/kg and maintenance of anesthesia with isoflurane did not lead to significant side effects in dogs with kyphosis. Tiletamine and other dissociative drugs cause pronounced sympathetic stimulation, which leads to significant increases in heart rate, systolic blood pressure, stroke volume and cardiac output (Hiebert et al. 2022; Ferré et al. 2022; El-Hawari et al. 2022; Bustamante et al. 2022). Our study showed that in dogs with kyphosis, the combination of dextiletamine–zolazepam–isoflurane did not significantly change the cardiovascular parameters of heart rate, or systolic, diastolic and mean arterial pressure compared with baseline values in all experimental groups of dogs.

Pronounced sedation was previously described in all dogs intravenously treated with 10μg/kg dexmedetomidine (Chernigova et al. 2019; Stabile et al. 2023). It was also found that the combination of dexmedetomidine and other drugs led to a greater sedative effect than dexmedetomidine alone. In our study, intramuscular dexmedetomidine resulted in a significant increase in sedation levels compared with baseline values (indicating a moderate sedation score, 5–10).

We consider the prospects for further work to be applying toxicological research methods, in particular determining the parameters of oxidative stress by assessing the serum concentration of malondialdehyde.

Conclusion

Intramuscular administration of dexmedetomidine in dogs with kyphosis at doses of 5.0, 7.5 and 10.0μg/kg caused a pronounced dose-dependent sedation effect. Moreover, a more pronounced sedative effect was observed when we used dexmedetomidine in combination with tiletamine–zolazepam and isoflurane. In addition, intramuscular administration of dexmedetomidine alone (10μg/kg) caused a significant decrease in the heart rate and mean arterial blood pressure. Intravenous administration of tiletamine–zolazepam (induction) and isoflurane inhalation (maintenance of anesthesia) did not cause changes in heart rate, or systolic, diastolic and mean arterial blood pressure compared with baseline values in dogs with kyphosis. Thus, dexmedetomidine intramuscularly administered at a dose of 5.0-7.5μg/kg is the optimal premedication for examination or surgical correction of spinal pathologies in dogs to avoid the development of unwanted side effects. In addition, these results confirm that dexmedetomidine in combination with tiletamine–zolazepam and isoflurane is another option for multimodal, opioid-free general anesthesia in dogs, since this method does not have a clinically significant effect on cardiovascular parameters.

Authors' contribution

Andrei Rudenko, Yuri Vatnikov, Oleg Novikov, and Arfenya Karamyan had the original idea for the study and carried out the design; Mariana Samoilova and Olesya Petrukhina collected the samples; Andrei Rudenko and Nadezhda Sachivkina were responsible for data analysis and data cleaning. Valeriy Murylev and Vladimir Lutsay drafted the manuscript. Pavel Elizarov, Aleksei

Muzychenkov - project administration; funding acquisition and data curation. The final draft manuscript was revised by all authors. All authors edited, read, and approved the final manuscript.

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