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Comparative study between ketamine-S-dexmedetomidine and ketamine-S-midazolam-methadone in the anesthesia of capuchin monkeys (*Sapajus apella*)

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ABSTRACT: *Anesthetic protocols have been developed to obtain the most effective and safe association in wildlife. This study compared the anesthetic effects and cardiorespiratory parameters of ketamine-S (+) (10 mg/kg)/dexmedetomidine (0.020 mg/kg) (KD) and ketamine-S (+) (10 mg/kg)/midazolam (0.5 mg/kg)/methadone (1.0 mg/kg) (KMM) in capuchin monkeys (Sapajus apella). Eight capuchin monkeys were randomly assigned to KD (n = 4) or KMM (n = 4) to evaluate induction, immobilization, and recovery scores, heart and respiratory rate parameters, besides systolic, mean, diastolic arterial pressure and arterial blood gas. There was no difference (P = 0.56) in the quality of induction, immobilization, and anesthetic recovery between the protocols. The time for anesthetic induction was 4 ± 1 min in the KD group and 5 ± 1 min in the KMM group, and these values were statistically equal (P = 0.28). The mean immobilization time in the KD and KMM groups were 35 ± 13 and 33 ± 15 min, respectively. Heart rate was lower in animals in the KD group (P < 0.001), while respiratory rate (P = 0.03), and mean blood pressure (P = 0.046) were higher than that of the animals in the KMM group. Respiratory acidosis occurred in the KMM group, with lower pH (7.25±0.047; P = 0.0055) and higher pCO_2 (51 ± 6;mmHg; P = 0.008). Both protocols exhibited good induction quality, immobilization, and anesthetic recovery, despite cardiorespiratory and blood gas alterations observed, which warrants monitoring of cardiorespiratory variables during KD or KMM chemical restraint.*
Key words: *alpha-2 adrenergic agonist, benzodiazepine, immobilization, opioid, primates.*

Estudo comparativo entre quetamina-S-dexmedetomidina e quetamina-S-midazolam- metadona na anestesia de macacos-prego (*Sapajus apella*)

RESUMO: *Protocolos anestésicos foram desenvolvidos para obter a associação mais eficaz e segura em animais selvagens. O objetivo deste estudo foi comparar os efeitos anestésicos e os parâmetros cardiorrespiratórios de cetamina-S (+) (10 mg / kg) / dexmedetomidina (0,020 mg / kg) (KD) e cetamina-S (+) (10 mg / kg) / midazolam (0,5 mg / kg) / metadona (1,0 mg / kg) (KMM) em macacos-prego (Sapajus apella). Oito macacos-prego foram distribuídos aleatoriamente em KD (n = 4) ou KMM (n = 4) para avaliar os escores de indução, imobilização e recuperação, parâmetros de frequência cardíaca e respiratória, além da pressão arterial sistólica, média, diastólica e gasometria arterial. Não houve diferença (P = 0,56) na qualidade da indução, imobilização e recuperação anestésica entre os protocolos. O tempo de indução anestésica foi de 4 ± 1 min no grupo KD e 5 ± 1 min no grupo KMM, sendo esses valores estatisticamente iguais (P = 0,28). O tempo médio de imobilização nos grupos KD e KMM foram 35 ± 13min e 33 ± 15 min, respectivamente. A frequência cardíaca foi menor nos animais do grupo KD (P < 0,001), enquanto a frequência respiratória (P = 0,03) e a pressão arterial média (P = 0,046) foram maiores do que nos animais do grupo KMM. Acidose respiratória ocorreu no grupo KMM, com menor pH (7,25 ± 0,047; P = 0,0055) e maior pCO_2 (51 ± 6; mmHg; P = 0,008). Ambos os protocolos apresentaram boa qualidade de indução, imobilização e recuperação anestésica, apesar das alterações cardiorrespiratórias e gasométricas observadas, o que justifica o monitoramento das variáveis cardiorrespiratórias durante a contenção química com KD ou KMM.*
Palavras-chave: *agonista alfa-2 adrenérgico, benzodiazepínico, imobilização, opioide, primatas.*

INTRODUCTION

Knowledge regarding anesthesia methods and cardiovascular parameters are essential to ensure the safe manipulation of capuchin monkeys. Ketamine (SHIIGI & CASEY, 1999), is widely employed in wild animals anesthesia in view of its satisfactory intramuscular absorption. However, its use may cause muscle rigidity, excessive salivation, and occasionally convulsions (BRANSON, 2013). Alpha-2-adrenergic agonists are commonly co-administrated with ketamine, due to their ability to promote muscle relaxation, sedation, and some degree of visceral analgesia (THERIAULT et al.

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2008). In addition, alternative techniques also combine opioids and benzodiazepines to anesthesic dissociative agents (CARPENTER & BRUNSON 2013). Benzodiazepines bind mainly to GABA receptors and hold the main advantageous because of their anxiolytic action, sedation promotion, and muscle relaxation, with minimal impact on the cardiovascular system (ROWLETT et al., 2015). Opioids are widely used for primate anesthesia because of their minimal cardiovascular effects when used for pre -, intra -, and postoperative pain control, and because they allow the dose reduction of other associated anesthetic agents (HORNE et al., 2001). The main advantage of methadone over other opioids is its effect on N-methyl-D-aspartate receptors, which are used to treat hyperalgesia and refractory pain (AXELROD et al., 2007). To the best of the author's knowledge, there is no published research in which this drug has been associated with further anesthesic agents for chemical restraint of *Sapajus apella.*

This study evaluated the cardiorespiratory effects and blood gas variables of capuchin monkeys (*S.apella*) immobilized with ketamine-S (+) and dexmedetomidine or ketamine-S (+), midazolam, and methadone, as well as assessed the quality and safety of both protocols.

MATERIALS AND METHODS

Eight capuchin monkeys (*Sapajus apella*), five males and three females, residing in a rehabilitation center of wild animals kept in a collective enclosure, were anesthetized for this study. The animals were considered healthy, as they were active, with normal body scores, and behaviors characteristic of the species on daily observation. In addition, they exhibited no signs indicative of diseased states. The dose was calculated based on the weight estimation made by the keepers. Following a fasting period of 12-hours for food and 2-hours for water, the animals were captured with the aid of a net, and randomly divided into two groups (n = 4), followed by intramuscular administration in the vastus lateralis muscle of the thigh, ketamine-S (+) (10 mg/kg) (Ketamin - Cristália Prod. Here. Farm. Ltda, Itapira /SP, Brazil) associated with dexmedetomidine (Dexdomitor; Zoetis Indústria de Produtos Veterinários Ltda, SP, Brazil) (0.020 mg/kg) (KD group) or ketamine-S(+) (10 mg/kg) associated with midazolam (Dormire, Cristália Produtos Químicos e Farmacêuticos Ltda, São Paulo, SP, Brazil) (0.5 mg/kg) and methadone (Mytedom; Cristália Produtos Químicos e Farmacêuticos Ltda, SP, Brazil) (1.0 mg/kg) (KMM group). For the administration, the drugs were combined in the same 3 ml syringes coupled with 25 × 7 mm needles. The groups were divided randomly, with the two protocols interspersed between them. The capture was carried out for convenience, with the captured animal being the one closest to the keeper, since they had no individual identification and were all kept together in the same room The evaluators who performed the data collection received a syringe containing the drugs without identification of the protocol, characterizing a blinded study.

Once immobile, the animals were weighed, positioned in the supine position, and then evaluated for heart rate (HR), respiratory rate (RR), systolic (SAP), diastolic (DAP), and mean arterial pressure (MAP) (oscillometry), rectal temperature (°C) (digital thermometer) , and oxyhemoglobin saturation ($SatO_2$) (Multiparametric Monitor; Dixtal, Manaus-AM, Brazil). All these measurements were made once in each moment. The oximeter was positioned in the interdigital region of the left pelvic paw. From the termination of movements until their return, the parameters were evaluated every 10 min. The animals were kept in room air on a stainless steel plate without oxygen supplementation or an external heating source. The cuff for blood pressure measurement was positioned around radioulnar region, so that the cuff width corresponded to 40% of the forearm circumference. Arterial blood samples were collected immediately after immobilization and at the time of recovery, by femoral artery puncture using a using a 1 mL seringe with 13 × 4 mm heparinized needle (Hemofol, Cristália, Prod. Here. Farm. Ltda. Itaquira/SP, Brazil), after trichotomy and asepsis of the region. After collection, they were maintained in a thermal box cooled with reusable ice and transported within 2 h for gasometric analysis. Partial pressure of CO_2 [pCO_2], partial pressure of O_2 [pO_2], serum electrolyte levels (sodium, potassium, ionic calcium, chlorine, and bicarbonate), and pH (Cobas221 apparatus) were analyzed.

For the study, the quality of induction (period between anesthetic administration to movement interruption), immobilization (period for which the animal is immobile on manipulation), and anesthetic recovery (period to first voluntary movement) were recorded and analyzed evaluated jointly after recovery while quality of muscle tension, interdigital reflex, and eyelid reflex were evaluated once during immobilization (at 10min moment). Quality was scored according to BAKKER et al. (2013) (Table 1).

Table 1 - Scores for evaluation of quality of sedation, immobilization and anesthetic recovery, muscle tension, interdigital reflex and eyelid reflex according to BAKKER et al. (2013).

Evaluation	Score	Quality	Features
Quality of sedation, immobilization and recovery	1	Good	No vocalization, salivation, compulsive licking or sneezing. No greater attention to injection site, no involuntary/uncoordinated muscle activity.
	2	Satisfactory	Little vocalization and/or involuntary/uncoordinated muscle activity, salivation, compulsive licking, sneezing, some injection discomfort (< 5 min).
	3	Unsatisfactory	Too much vocalization / without immobilization, severe discomfort at the injection site (increased attention to injection site > 5 min), excessive salivation, vomiting, compulsive licking, sneezing, involuntary muscle activity.
Interdigital reflex	0	No reflex	No increase in muscle tension and/or knee flexion for at least one second after removing the hemostatic force clamps
	1	Normal reflex	There was muscle tension and/or knee flexion
	2	Increased reflex	There was increased muscle tension, knee flexion, and muscle contractions/involuntary movements of other limbs
Muscle tension	0	No muscular tension	Complete relaxation, adequate muscle relaxation for performing minor invasive procedures
	1	Normal	Partial relaxation
	2	Increase	Rigidity in muscles
Eyelid reflex	0	No muscular tension	No narrowing of the eyelids or muscle movement
	1	Moderate	Delay in closing and / or incomplete eyelids
	2	Normal	Eyelids close immediately fully

The animals' scores were classified only after recovery, since the quality of induction, immobilization and recovery were assessed together. Muscle tension, interdigital reflex, and eyelid reflex were evaluated to assess the quality of immobilization; these scores were evaluated only during the immobilization period. Until complete anesthetic recovery (quadrupedal position and normal ambulation), the animals were kept in individual cages and were later relocated to their enclosures.

The data were analyzed with the help of the BioStat 5.3 program, and the Shapiro-Wilk test and analysis of variance (ANOVA) were used to evaluate the significance of the differences between values. For nonparametric variables, the Kruskal-Wallis test was performed for comparison between the two groups. The Mann–Whitney test was used to the analyze of the scores. Differences were considered statistically significant at $P < 0.05$.

RESULTS AND DISCUSSION

The average weight of the animals was 2.6 ± 0.6 kg, all of them presenting good body scores. Based on the actual weight of the animals, 12.16 ± 3.21 mg / kg of ketamine, 0.024 ± 0.006 mg / kg of dexmedetomidine, 0.608 ± 0.16 mg / kg of midazolam and 1.216 ± 0.321 mg / kg of methadone were used. In the KD group, three males and one female were anesthetized while two males and two females were anesthetized in the KMM group. The time for anesthetic induction was 4 ± 1 min in the KD group and 5 ± 1 min in the KMM group, and these values were statistically equal ($P = 0.28$). The mean immobilization time in the KD group was 35 ± 13 min and 33 ± 15 min in the KMM group, with no difference between the groups ($P = 0.87$). Half of the individuals (n = 2) the longest immobilization time had an average of 45 ± 7 min, and 40 ± 14 min in the KD and KMM groups, respectively. One capuchin monkeys from each group exhibited longer periods of anesthesia, lasting 50 min. There was no statistical difference in the induction, immobilization and anesthetic recovery scores ($P = 0.56$) between the protocols (Figure 1). The degree of muscle tension was also similar between the groups ($P = 0.31$). There were no complications during the evaluation period.

Five of eight anesthetized animals maintained the normal eyelid reflex (three in the KMM group and two in the KD group), as expected, since the use of dissociative anesthesia allows for the maintenance of protective reflexes in most animals. Two animals exhibited a retardation and absence of eyelid reflex. The absence of interdigital reflex in

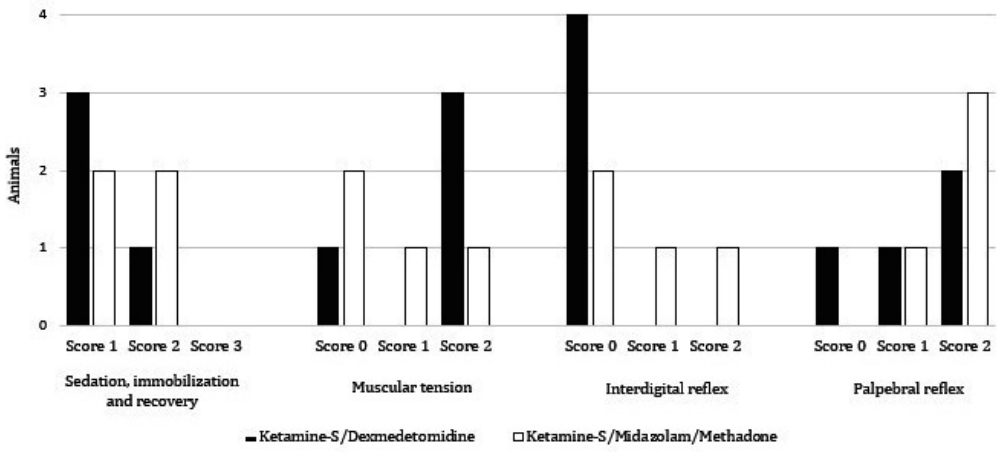

Figure 1 - Quality of induction, immobilization, anesthetic recovery, muscle tension, interdigital reflex, and eyelid reflex evaluated by scores according to Bakker et al. (2013).

most animals was due to the satisfactory degree of muscle relaxation obtained by anesthetic associations.

The results of the mean and standard deviation of cardiorespiratory parameters, temperature, and hemogasometry are presented in tables 2 and 3.

The animals in the KD group, when compared with those in KMM group (mean of all moments on each group) presented a lower mean heart rate (129 ± 15 vs 196 ± 24 beats/min;P > 0.001) and higher a respiratory rate (57 ± 13 vs 42 ± 16 mpm; P = 0.03) and mean arterial pressure (95 ± 17 vs 86 ± 15 mmHg; P = 0.046). The mean temperature was similar between the two groups (P = 0.6521), with a statistical difference (P = 0.043) at 20 min (KD = 38.9 ± 0.5 °C versus KMM = 37.5 ± 1.2 °C).

Potassium, sodium and chlorine remained within the specie's reference ranges (LARSSON et al. 1997). There was a statistical difference in the pH values (P = 0.0055), pCO_2 (p = 0.008), and potassium (P = 0.04) between the groups (Table 3). The others hemogasometric variables (bicarbonate, sodium, ionic calcium, chlorine, and lactate) showed no statistical difference between the groups and time points. Since they are wild animals, samples for hemogasometric analyses are collected under anesthesia, causing the lactate levels to range from 0.6 ± 0.01 mmol/L to 11.23 ± 3.99 mmol/L between different studies and anesthetic protocols employed (SOUZA et al., 2018; GALANTE et al., 2019). In this study, lactate remained stable throughout anesthesia, when compared to the baseline moment. The blood lactate level is directly related to tissue perfusion, with high levels attributed to several factors, such as shock, anaerobic muscle activity and liver failure (ANDERSEN et al., 2013; WARDI et al., 2020). In this study, the excess muscle activity after physical restraint at the time of capture may have led to increased consumption of tissue oxygen (FAHLMAN, 2008; ANDERSEN et al., 2013), causing the cellular energy obtained from glycolysis, with consequent formation of pyruvate, to be converted to lactate by lactate dehydrogenase (WARDI et al., 2020). The wild nature of the species made parametric measurements and blood sample collection impossible, thereby compromising data analyses by the containment. However, the statistically equal basal lactate values compared to those at the recovery moment led to the conclusion that the anesthetic protocols did not impair tissue perfusion during the analysis period.

The direct effect of dexmedetomidine on heart rate was evident in the KD group, starting with a mean of 151 beats/min in the first evaluation up to an average value of 119 beats/min at 30 min. This parameter remained under 140 beats/min, which is the normal mean for the species (SOUZA et al. 2018). Two mechanisms may explain this effect: the direct action of dexmedetomidine on the autonomic nervous system from pre-synaptic activation of α2-adrenoceptors, resulting in lower peripheral release of norepinephrine (TALKE at al. 2000; FANTONI & CORTOPASSI 2002), with consequent sympathetic

Table 2 - Mean and standard deviation of heart rate (HR) and respiratory rate (RR),systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and mean arterial pressure (MAP), rectal temperature (T °C), oxyhemoglobin saturation (SpO_2) in capuchin monkeys (*Sapajus apella)* anesthetized with ketamine-S/dexmedetomidine (KD) and ketamine-S/midazolam/methadone (KMM) over the moments evaluated.

Variables	Groups	Moments				
		Medium	0	10 min	20 min	30min
HR (beats/min)	KD	129±15	151±20Aa	130±7a	126±7a	119±6Ba
	KMM	196±24	213±23b*	192±35b*	190±32b*	192.3±22b*
RR (breaths/min)	KD	57±13	63±18	64±17a	54±7	52±10
	KMM	42±16	66±20	38.5±5b	39±10	37±10
SAP (mmHg)	KD	117±18	105±31	121±15	120±5a	129±4a
	KMM	109±11	116±16	109±14	104±9b	103±5b
DAP (mmHg)	KD	81±14	76±22	85,5±9,6	76±2,9	91±19,2
	KMM	69±16	73±19	65±18	63±25	66±2
MAP (mmHg)	KD	95±17	88±29	95±19	95,7±6,3	108±9a
	KMM	86±15	91±19	83±24	79±16	83±3b
T °C	KD	38.9±1,2A	40±0,17	39.5±0,55	38.9±0,5a	38.1±0,96B
	KMM	37.5±0,9	39.1±1	38.3±1	37.5±1,2b	38±0,6
SpO_2 (%)	KD	94±3	92±6	94±3	94±2	94±3
	KMM	93±2	93±3	92±3	95±4	97±1

Moments of measurement of parameters at 10-minute intervals. 0: basal moment (moment when immobilization occurs); 10 min: moment 10 min; 20 min: moment 20 min; 30 min: moment 30 min;
Values followed by different capital letters differ significantly between times. $P < 0.05$.
Values followed by different lowercase letters differ significantly between groups. $P < 0.05$.

blocking and bradycardia, and reflex bradycardia to increased blood pressure (CONGDON et al. 2011). A similar result was reported by RAPOSO et al. (2015) with *Sapajus* sp., in which, when using the combination of ketamine with dexmedetomidine, obtained a significant reduction in heart rate at the time of the final evaluation, when compared to the groups anesthetized with tiletamine-zolazepam, ketamine-xylazine, and ketamine-midazolam. The significant reduction in heart rate caused by dexmedetomidine can endanger the patient's life due to coronary vasoconstriction, resulting in ischemia and consequent myocardial dysfunction (GERLACH et al. 2009).

Both protocols demonstrated mean oxygen saturation levels of over 93%. However, some animals intermittently presented lower saturation, with values reaching 88% (two animals, in two isolated moments, one in each group). This finding justifies the use of supplemental oxygen during anesthesia in both protocols, which can be provided via facial mask or nasal cannula. The markedly low values of arterial oxygen obtained in the hemogasometric samples may be due to the prolonged period (within two hours) between the collection and processing of the samples, which were performed in a laboratory outside the experiment site. The oxygen reduction in these samples occurred due to the continued cellular metabolism after collection (GARCIA-ROA, 2017). The evidence of a pre-analytical error is due to the fact that the animals maintained an average oxygen saturation over 93%, observed on pulse oximetry throughout the procedure.

The saturation level in both protocols obtained by pulse oximetry can be attributed to the direct effect of dexmedetomidine and methadone-midazolam on the respiratory center and skeletal musculature. The low interference of benzodiazepines on ventilation is related to low binding brainstem receptors. However, when associated with opioids, respiratory depression induced by this group may become evident (NORDT & CLARK, 1997; CORKERY et al., 2004). Methadone is responsible for respiratory depression due to direct action on μ2 receptors located in the brainstem, reducing sensitivity to carbon dioxide. At lower concentrations, however, it can cause a reduction in the tidal volume without changing the respiratory rate (CORKERY et al., 2004). Dexmedetomidine also induces respiratory depression by acting directly on respiratory centers.

Table 3 - Means and standard deviation of hemogasometric parameters analyzed at baseline (moment when immobilization occurs) (MB) and recovery moment (period of first voluntary movement) (RM) of capuchin monkeys *(Sapajus apella) anesthetized* with ketamine/dexmedetomidine (KD) and ketamine/midazolam/methadone (KMM).

Variables	Groups	----------Moments----------	
		MB	RM
pH	KD	7.36±0.017Aa	7.37±0.053Ba
	KMM	7.24±0.052Ab	7.25±0.047Bb
pCO_2 (mmHg)	KD	35±4a	37±4a
	KMM	42±8a	51±6b
K (mmol/L)	KD	3.53±0.35Aa	3.92±0.87B
	KMM	2.91±0.32Ab	3.15±0.64B
pO_2 (mmHg)	KD	62±15	63±16
	KMM	73±9	79±6
HCO_3 (mEq/L)	KD	19±1	21±1
	KMM	18±3	22±1
$SatO_2$ (%)	KD	85±10	86±7
	KMM	86±5	90±8
Na (mmol/L)	KD	153±2	152±5
	KMM	153±3	152±5
Lactate	KD	2.67±0.8	1.86±1.28
	KMM	4±1.8	3±3.2
Cl (mmol/L)	KD	112.8±1.7	113.1±3.6
	KMM	112.6±1.7	112.6±1.7
iCa (mmol/L)	KD	0.68±0,11	0.72±0.26
	KMM	0.67±0,21	0.77±0.28

pH, hydrogenic potential; pCO_2, partial pressure of carbon dioxide; K, potassium; pO_2, partial oxygen pressure; HCO^3, bicarbonate; $SatO_2$, oxygen saturation; Na, sodium; Cl, chlorine; iCa, ionized calcium.
Averages followed by different capital letters differ significantly between moments. $P < 0.05$.
Averages followed by different lowercase letters differ significantly between groups. $P < 0.05$.

In addition, this effect inhibits the release of excitatory neurotransmitters, which promotes deep muscle relaxation capable of affecting respiratory movements (ALVES, 2000).

However, the KD group exhibited RR values (57 ± 13 breaths/min) above the normal values for the species (30-50 breaths/min) (CARPENTER & BRUNSON., 2013), with higher values at 10 min (64 ± 17.3 breaths/min). The RR increase in the the dexmedetomidine group may have been a compensatory mechanism to counteract the lower ventilatory quality caused by muscle relaxation. This compensation shows the low interference of this drug directly on the respiratory system, since it was efficient in maintaining blood gas parameters within the reference range for the species (BAGATINI et al. 2002; KAUR & SINGH 2011).

Although, the respiratory rate in the KMM group was within the reference range, hemogasometric alterations demonstrated the occurrence of respiratory acidosis. The opioid in the KMM group may have acted on the respiratory center in the brainstem, resulting in a decrease in volume/minute caused by reduced respiratory depth (DAHAN et al. 2010), thereby to an increase in $pCO_{2,}$ despite the normal RR. However, this increase was not enough to induce an increase in bicarbonate by renal compensation, as this change was acute and transient (NATALINI et al. 2001).

The KMM group had a lower mean arterial pressure (86 ± 15 mmHg) than the KD group (95 ± 17 mmHg). This can be attributed to decreased systemic vascular resistance caused by reduced opioid-induced sympathetic tone (LAYSON-WOLF et al., 2002; CHEN & ASHBURN 2015). The hemodynamic effects of methadone vary according to the species and route of administration. In dogs, increased peripheral vascular resistance has been reported after intravenous methadone application (MAIANTE et al., 2009; GAROFALO et al. 2012). It has been

shown that this effect independent of vasopressin, but is attributed to the release of catecholamines caused by drug-induced dysphoria (GAROFALO et al., 2012). However, in humans, hemodynamic stability has been verified after drug administration via in the same route (ANDERSON & ALVARADO 2003; BOWDLE et al., 2004), and this difference can be attributed to the intrinsic characteristics of each species. In addition, the route of administration of methadone in the present study may also have resulted in different hemodynamic responses. Also in humans, the intramuscular administration of methadone reduces the rate of absorption and bioavailability of the drug when compared with the intravenous route, resulting in a concentration ≤ 40% (RASSOULI et al. 2020), lacking studies in *Sapajus apella* specie. The highest mean arterial pressure in the KD group (95 ± 17 mmHg) occurred due to the predominance of α2-adrenergic receptors present in the endothelium of the vascular wall, resulting in vasoconstriction (ALVES et al. 2000).

The limitations of this study were the use of scale proposed by Bakker (2013) in only one moment, since a single evaluation does not reflect the total immobilization period and that it is not possible to compare the times; and delay in the processing of blood gas samples. Both protocols were effective in promoting the anesthesia of capuchin monkeys. Although, the dose of ketamine used by RAPOSO et al. (2015) was slightly larger than that used in the present study (14.3 ± 3.0 mg / kg to 16.5 ± 2.7 mg / kg), both protocols resulted in a satisfactory degree of muscle relaxation.

CONCLUSION

This study demonstrated that the combination of ketamine-S/dexmedetomidine or ketamine-S/midazolam/methadone promoted efficient anesthesia of capuchin monkeys. Bradycardia observed in the dexmedetomidine group and respiratory acidosis developed in the methadone group reveal the need for caution in the use of both anesthetic protocols in capuchin monkeys, and the importance of monitoring possible complications such as hypoxemia.

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DECLARATION OF CONFLICT OF INTEREST

We have no conflict of interest to declare. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

ETHICS AND BIOSAFETY COMMITTEE

The procedures were approved by the Comissão de Ética no Uso de Animais (CEUA) of the Universidade Federal do Mato Grosso do Sul (UFMS) (protocol no. 837/2017), licensing of the Instituto Chico Mendes de Conservação da Biodiversidade (ICMBio) (registration 62176-1) and followed good practices and guidelines for wild animals.

AUTHORS' CONTRIBUTION

The authors contributed equally to the article.

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