

Physiological and Behavioral Effects of Continuous Remifentanil-Xylazine Administration in Donkeys

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ABSTRACT

Background: Remifentanil and xylazine are drugs that can allow standing equine surgery when in continuous infusion. The literature presents no reports of this association in donkeys. **Objectives:** To evaluate the behavioral, sedative, and cardiorespiratory effects of continuous intravenous infusion of remifentanil and xylazine in donkeys. **Study design:** Experimental, prospective, non-blinded study. **Methods:** 10 donkeys were sedated with an intravenous bolus of xylazine (0.8 mg/kg). After 3 minutes, continuous infusions of xylazine (0.65 mg/kg/h) and remifentanil (6 µg/kg/h) were administered for 60 minutes. Cardiorespiratory physiological parameters, rectal temperature, gastrointestinal motility, and sedation and ataxia scores were evaluated by a simple descriptive scale at M0 (baseline) and every 5 minutes, up to M60 (60 min), with scores 0-3. Head height concerning the ground was also evaluated. Dunnett and Friedman statistical tests ($p < 0.05$) were used. **Results:** Heart rate ($p = 0.049$) and respiratory rate ($p = 0.001$) decreased significantly at M10 and M5, respectively, compared to M0. There was a significant decrease in systolic ($p = 0.04$), mean ($p = 0.02$), and diastolic ($p = 0.03$) blood pressure at M15 compared to M0. The capillary refill time at M20 was statistically different ($p = 0.001$) from M0. The head height in relation to the ground reduced significantly from M5 (p

26 = 0.001) to M60. Satisfactory sedation was obtained from M15 to M60. After stopping the
27 infusion, all donkeys recovered successfully (7.1 ± 2.4 minutes). No adverse effects were
28 observed during and after the infusion. **Primary limitations:** No painful stimulus or surgical
29 procedure was performed. **Conclusions:** Combining remifentanyl and xylazine at the doses used
30 caused adequate sedation and short recovery time. Remifentanyl did not cause excitation in the
31 donkeys. Future studies are necessary to test the protocol with painful stimuli.

32 **Keywords:** Asinine; Equine; Remifentanyl; Sedation.

1 Introduction

Donkeys (*Equus asinus*) are rustic animals whose importance is often neglected due to their specific characteristics, both in morphophysiological and pharmacological perspectives, as well as their temperament.¹ Thus, some studies have evaluated the effects of drugs on donkeys^{2,3}. However, protocols for this species are still scarce.

It is common to associate drugs to chemically contain equines, avoiding the complications and costs of general anesthesia. The adrenergic alpha₂-agonist drugs produce sedation, analgesia, and muscle relaxation despite their adverse effects.⁴⁻⁶ Among adrenergic alpha₂-agonists, xylazine is the shortest acting and may result in insufficient analgesia for some surgical or outpatient procedures in monotherapy. In these circumstances, they are administered in association with opioids or with local blocking techniques to improve analgesia.⁷

Opioids are useful in anesthesiology because of their ability to decrease sympathetic and somatic responses to harmful stimulation.⁸ Combinations of an alpha₂-agonist with an opioid in single or repeated administrations, or even as part of a peri anesthetic protocol, can provide synergistic analgesic effects and good sedation. This association reduces the potential for excitation at the level of the central nervous system.⁹

Remifentanil is an opioid derivative of phenylpiperidine, supplied as remifentanil hydrochloride, a lyophilized powder. Animal studies indicate that the pharmacological properties of remifentanil are similar to those of other potent μ -opioid receptor agonists, such as alfentanil.¹⁰ Characterized as a potent opioid of ultra-short duration, its use has been described in studies conducted in different species, where it was shown to be a safe drug, producing minimal hemodynamic changes, in addition to its onset of action and rapid recovery after cessation of use, regardless of the duration of its administration. Therefore, remifentanil

appears to be a highly titratable opioid, providing profound analgesia for very brief periods in which analgesia is necessary or for prolonged periods without the concern of prolonged recovery.^{8,12} Some studies describe its use in horses^{5,6,12}. However, the literature has no information on the systemic effects of remifentanyl in donkeys.

In this context, this study aimed to evaluate the physiological and sedative effects of continuous intravenous infusion of remifentanyl and xylazine in donkeys from the northeastern region of Brazil. We hypothesized that adverse effects would be insignificant when associating the drugs in low doses and continuous infusion, and the sedation protocol can be considered for seasonal surgical procedures.

2 Material and Methods

2.1 Animals

The study conditions were submitted to and approved by the Animal Use Ethics Committee (CEUA/UFERSA) under protocol number No. 42/22. Ten adult donkeys from the northeastern region of Brazil, seven males and three females, aged 5.3 ± 2.2 years and weighing 120.4 ± 21.4 kg, were used. The animals were classified as healthy after clinical and laboratory examination (blood count, urea, creatinine, aspartate aminotransferase, alanine aminotransferase, and total proteins) for the inclusion criteria. A sample calculation was performed based on a pilot study with three animals using the dose presented in the study with horses⁶. The calculation was done using GPower 3.1.9.7. This calculation and the mean and standard deviation of sedation of M5, alpha 0.05, and Power 0.8 were compared with the constant 0 of M0. The animals were dewormed with ivermectin (Ivomec®, Boehringer

Ingelheim), associated with trichlorfon and mebendazole (Trichlorsil paste®, Vansil), and vaccinated against rabies four weeks prior to the start of the study. The animals were housed in groups of five, in pickets of 10 x 7 m in the open air, with shade, and fed with voluminous grass (*Pennisetum purpureum*) and concentrate (ground corn, soybean meal, wheat bran, common salt, and calcitic limestone) twice a day, with water *ad libitum*. The acclimatization to the new environment took four weeks.

2.2 Experimental study

One day before the procedure, the animals were transferred to individual stalls. Prior to the experiment, they were subjected to a 12-hour fast from solid food and had access to water *ad libitum*.

Initially, the physiological parameters of respiratory rate (RR) by inspection of the costal grid, capillary refill time (CRT), heart rate (HR) by cardiac auscultation, rectal temperature (RT), mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP) through a multiparametric monitor (multiparametric monitor, touch screen, Delta Life, model DL1000), and gastrointestinal motility by auscultation, assessing intestinal borborygmus in the dorsal and ventral quadrants of the right and left side, were evaluated at baseline (M0). After M0, trichotomy and antisepsis of the jugular vein were performed for catheterization, using a 16-gauge catheter coupled to a 3-way stopcock.

Subsequently, the animals received a 0.8 mg·kg⁻¹ bolus of xylazine (xylazine hydrochloride 2%, Syntec®) administered within 60 seconds by infusion pump (RS700 VET, RZVET®) and, after 3 minutes, continuous infusions of xylazine and remifentanyl (remifentanyl hydrochloride, Eurofarma®) were initiated at the rates 0.65 mg/kg/h and 6 µg/kg/h,

respectively, and discontinued over 60 minutes after three minutes of the initial xylazine bolus (Figure 1).

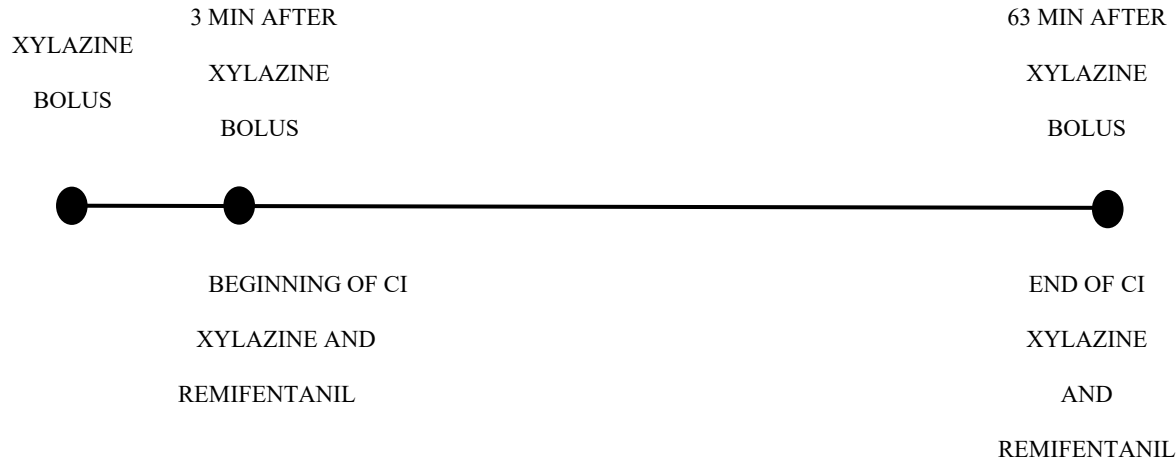


Figure 1. Linear representation of the beginning and end of xylazine and remifentanyl infusions in donkeys.

Adapted from Palarrols *et al.*, 2020.

The same physiological parameters evaluated at M0 (HR, RR, CRT, RT, MAP, SBP, and DBP) were monitored every 5 minutes until 60 minutes after drug administration (M60). Gastrointestinal motility was evaluated 15 min, 1h, 4h, 8h, and 24h after the infusions (M60).

The head height above the ground was measured using a tape measure graduated in centimeters from 0 to 160 cm, which was fixed to the lateral bar of the physical containment trunk to evaluate sedation. The distance between the ground and the mandibular symphysis was measured before beginning the instrumentation, in an environment free of external stimuli, considering the head height of the animal at M0. Sedation was also evaluated using a simple descriptive scale, assessing the level of sedation and ataxia,^{5,13} with scores from 0 to 3 for both items (Table 1).

Table 1: Simple descriptive scale (SDS) scoring system for sedation and ataxia (FUNCIA *et al.*, 2016)⁵.

SEDATION SCORE	SIGNS
0	No sedation. The animal is alert, with normal posture and response to contact with the evaluator. Normal objection to intervention.
1	Light sedation. Head lowered, facial muscles relaxed, and lower lip hanging. Some response to intervention.
2	Moderate sedation. Head lowered towards the floor and swinging the hind legs. Slight response to intervention.
3	Marked sedation. Tries or becomes recumbent. No response to intervention.
ATAXIA SCORE	SIGNS
0	No ataxia. The animal stands and walks normally; can rotate with force.
1	Mild Ataxia. The animal can walk, but with some lack of limb control.
2	Moderate ataxia. The animal can only walk with support, staggers, but avoids falling.
3	Marked ataxia. The animal cannot walk without danger of falling, staggers, falls, turns over.

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118 The patient's quality and total recovery time were evaluated from the end of the
119 infusions to the time the patient presented with a score of zero for sedation and minimal ataxia.
120 The sedation score was assessed every two minutes after stopping the continuous infusion of
121 xylazine and remifentanyl.

122 Any need for more drugs for sedation, decreased administration, or any unexpected
123 effect would be reported from the first xylazine *bolus* until recovery.

2.3 Statistical Analysis

Data were expressed as mean \pm standard deviation, median, minimum, and maximum values using the SAS V8 statistical program (System for Windows - SAS Institute Cary, North California; USA). After verifying the parametric assumptions, statistical differences between the times studied (M0 – M60) were verified through analysis of a mixed-effects model for repeated measures (Proc Mixed of the SAS program) for each variable studied, followed by the Dunnett test. The baseline moment (T0) was used as the base comparison variable. Nonparametric data were analyzed using the method described by Friedman. The significance level considered was 5%.

3 Results

The sedation and ataxia obtained were satisfactory in all animals throughout the procedure, soon after xylazine administration. After 20 minutes, moderate ataxia and sedation were observed, with a median sedation and ataxia score of 2 for both parameters remaining throughout the procedure. The height of the head in relation to the ground was significantly lower ($p = 0.001$) at baseline during the entire infusion time (Table 2).

Table 2 - Mean \pm standard deviation (SD) for sedation score, ataxia score, and head height of donkeys submitted to continuous infusion of remifentanyl and xylazine for 60 minutes.

Variables	Measures	M0	M5	M10	M15	M20	M30	M45	M60
Sedation score (0-3)	Mean	0	0.9	1.0	1.2	1.6	1.7	1.9	1.9
	\pm SD	± 0	$\pm 0.6^{**}$	$\pm 0.5^{**}$	$\pm 0.4^{**}$	$\pm 0.2^*$	$\pm 0.5^*$	$\pm 0.3^*$	$\pm 0.3^*$
	Median	0	1	1	1	2	2	2	2
	Min - max	0 - 0	0 - 2	0 - 2	1 - 2	1 - 2	1 - 2	1 - 2	1 - 2

Ataxia score (0-3)	Mean	0	0.8	1.0	1.1	1.6	1.7	1.8	1.9
	± SD	± 0	± 0.6**	± 0.5**	± 0.6**	± 0.5*	± 0.5*	± 0.4*	± 0.3*
	Median	0	1	1	1	2	2	2	2
	Min - max	0 - 0	0 - 2	0 - 2	0 - 2	1 - 2	1 - 2	1 - 2	1 - 2
Head height (cm)	Mean	83.0	28.7	28.78	18.11	16	17	16.56	14.44
	± SD	± 9.5*	± 28.3**	± 33.1**	± 25.3**	± 22.2**	± 21.3**	± 21.4**	± 17.3**
	Median	82.5	15	15	5	5	10	5	10
	Min - max	65 - 100	0 - 85	0 - 84	0 - 78	0 - 69	0 - 63	0 - 63	0 - 56

*, ** Different asterisks on the same line indicate statistically significant difference ($p < 0.05$ - Dunnett).

142 HR decreased significantly ($p = 0.049$) ten minutes after xylazine administration and its
143 continuous infusion with remifentanyl (M10), while RR decreased significantly ($p = 0.001$) after
144 5 minutes of the xylazine bolus (M5). MAP ($p = 0.02$), SBP ($p = 0.04$), and DBP ($p = 0.03$)
145 decreased significantly from M15, while RT remained stable throughout the procedure (Table
146 3).
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Table 3 - Mean values ± standard deviation (SD) for heart rate (HR), respiratory rate (RR), systolic blood pressure (SBP), mean arterial pressure (MAP), diastolic pressure (DBP), capillary refill time (CRT), and rectal temperature (RT) of donkeys submitted to continuous infusion of remifentanyl and xylazine in 60 minutes.

Variables	Measures	M0 [‡]	M5	M10	M15	M20	M30	M45	M60
HR (bpm)	Mean	44.4	40.9	39.8	39.3	39.5	37.1 ± 8.4	38	41.5
	± SD	± 6.2*	± 6.1*	± 7.9**	± 7.1**	± 9**	**	± 7.8**	± 13.6**
RR (bpm)	Mean	34.3	18.0	15.3	14.1	13.8	11	9.8	10.5 ± 6.3**
	± SD	± 7.6*	± 9.0**	± 7.8**	± 7.9**	± 6.5**	± 5.1**	± 5.7**	
†SBP (mmHg)	Mean	166.8	160.7	153.7	137.6	136.3	144.8	147.3	131.7
	± SD	± 23.5*	± 34.2*	± 28.5*	± 34.4**	± 28.3**	± 32.8**	± 39.9**	± 30.3**

†MAP	Mean	137.9	141.4	133.6	113.9	109.9	128.2	123.3	108.9
(mmHg)	± SD	±32.0*	±41.76 *	±31.3 *	±38.1 **	±32.4 **	±37.3 *	±35.9**	±33.8**
DBP	Mean	118.8	106.5	110.4	99.1	95.7	101	93.6	
(mmHg)	± SD	±41 *	±40.1 *	±30 *	±37.2 **	±30.5 **	±39.4 **	±27**	86.8 ±27**
†CRT	Mean	2.6		2.0		2.0	1.8 ± 0.6	1.7 ±0.4	
(sec)	± SD	±0.7*	2.1 ±0.4*	±0.2**	2.1 ±0.4*	±0.2**	**	**	1.8 ±0.3 **
RT	Mean	37	37.0	36.9	37	36.9	36.6	36.6	36.2 ± 0.8
	± SD	±0.4*	±0.6 *	±0.5 *	±0.5 *	±0.6*	±0.7*	±0.5*	*

† Friedman; ‡ Base moment used for comparison through Dunnett's test.

*, ** Different asterisks on the same line indicate statistically significant difference (p < 0.05 - Dunnett).

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149 All animals recovered from sedation with 7.1 ± 2.4 minutes after discontinuing the drugs
150 and could move with minimal signs of ataxia.

151 No adverse effects were observed during and after the infusion. Behavior, physiological
152 parameters (HR, RR, SBP, DBP, MAP, and RT), appetite, and gastrointestinal movements
153 remained stable compared to M0 after recovery from xylazine and remifentanil infusion.

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155 4 Discussion

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157 This study demonstrated that continuous infusion of xylazine and remifentanil can be
158 an option for sedating donkeys during standing procedures. Objective assessment and
159 quantification of sedation are difficult. There are currently no validated sedation scoring
160 systems for donkeys. The doses of xylazine and remifentanil were based on a previous study⁶
161 on horses. Although the association between alpha2-agonists and opioids has already been
162 studied in donkeys,^{14,15} this is the first study to use remifentanil; therefore, we chose to use the
163 same doses used in horses. A moderate degree of sedation was observed in a preliminary study

conducted with two horses, suggesting that higher doses of this association are unnecessary in donkeys.⁶ The results obtained were satisfactory regarding sedation and ataxia, thus corroborating what was described by Lizagarra and Castillo-Alcala¹⁴. These authors also used an association of an α_2 -agonist, xylazine, with an opioid, butorphanol, in donkeys and considered the association appropriate for sedating these animals for clinical procedures.

In a study using the association of butorphanol with dexmedetomidine or xylazine for seasonal unilateral ovariectomy, the authors reported that the donkeys obtained moderate to severe sedation (score 2-3). Both protocols were indicated for performing standing procedures for donkeys¹⁵. Although the opioid used is different from that of our study, the xylazine dose chosen was lower (0.5 mg/kg bolus and 0.5 mg/kg/h). It was reduced to 0.32 mg/kg/h during the continuous infusion, which leads us to believe that the combination of drugs caused an effective sedation. Similar results have been found by other authors¹⁴ who associated xylazine with different doses of butorphanol in a bolus. The donkeys' sedation was deeper and longer-lasting when employing a dose of 0.04 mg/kg.

The depth of sedation was also objectively assessed using head height relative to the ground, as reported in previous studies on horses.¹⁶ Although the difference in height between the mentioned species is debatable, a significant lowering of the head was observed between the basal time and the other evaluated moments in donkeys and horses. This also corroborates the study of Dzikiti *et al.*¹⁶ Although sedation was effective and complementary doses of drugs were not necessary, no painful stimulus or surgical procedure was performed, which can be considered a study limitation. Pollarols *et al.*⁶ used the same protocol in two horses submitted to seasonal laparoscopy; one of the animals required 0.25 mg/kg of xylazine to improve sedation, which can probably suggest that complementary doses of xylazine are necessary to improve the degree of sedation of animals in clinical and surgical situations.

There was little evidence of any serious cardiovascular or respiratory effects. Slowing the heart rate is a well-known effect of adrenergic alpha-2 agonists.¹⁷ However, this decrease was no longer significantly pronounced throughout the infusion. This may be related to the doses selected and the slow administration of the initial bolus. Moreover, such a reduction was insufficient to promote clinical repercussions and remained within the appropriate range for the species.

Opioid-related adverse effects such as excitation, increased motor activity, or muzzle tremors were not observed in donkeys, differing from previous studies¹⁵ with horses, which showed such signs. Narcotic analgesics have been associated with excitation or, as often stated, unpredictable reactions in horses. Stimulation of the central nervous system and increased locomotor capacity are highly predictable and dose-related responses after administration of most narcotic analgesics to horses.¹⁸ Even today, there is a reluctance to use opioids in horses due to possible adverse effects, one of which is decreased gastrointestinal motility.¹⁹ During the study, all animals were evaluated for gastrointestinal motility before and after the infusions. After the infusions (M60), gastrointestinal motility was evaluated within 24 h after drug administration, presenting no changes in all animals.

All animals recovered from sedation 7.1 ± 2.4 minutes after stopping the continuous infusion of xylazine and remifentanyl, being able to move with minimal ataxia. These data corroborate a previous study⁷ in which the authors evaluated the blood concentrations of remifentanyl during and after infusion in horses anesthetized with isoflurane and dexmedetomidine, observing that the blood concentration of remifentanyl decreased rapidly after the infusion, which is consistent with its short half-life (12.8 ± 2.1 min). The data suggest that the likelihood of remifentanyl causing excitation in horses during the recovery period after an intravenous infusion is low. This information can also be considered for donkeys, although pharmacokinetic studies are necessary for the species.

5 Conclusion

The association of xylazine and remifentanil at the doses used caused adequate sedation in donkeys from the northeastern region of Brazil during standing procedures. Remifentanil did not cause excitation in the donkeys. Further studies are needed to confront the protocol with painful stimuli.

Funding information

The Article Processing Fee for the publication of this research was paid by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES (ROR identifier: 00x0ma614).

Conflict of interest

The authors declare no conflicts of interest.

Authors' contribution

Valéria V. de Paula conceptualized, drafted, supervised the writing of the final version of the manuscript, and developed the methodology. Kássia F. A. Damasceno contributed to the original draft, data curation, investigation, and writing of the manuscript. Andressa N. Mouta and Káthryn Nóbrega contributed to data curation, investigation, and writing of the manuscript. Larissa S. Alves, Herbert Reis Aragão, and Jerson Marques Cavalcante contributed to data curation and investigation.

References

1. Lizarraga I, Sumano H, Brumbaugh G W. Pharmacological and pharmacokinetic differences between donkeys and horses. *Equine Vet Educ.* 2004; 16: (2)102-112. Doi: 10.1111/j.2042-3292.2004.tb00275.x
2. Naddaf H, Baniadam A, Rasekh A, Arasteh A, Sabiza S. Cardiopulmonary effects during anaesthesia induced and maintained with propofol in acepromazine pre-medicated donkeys. *Vet Anaesth Analg.* 2015;42(1):83-7. Doi: 10.1111/vaa.12138
3. Lizarraga I, Castillo-Alcala F, Robinson LS. Comparison of sedation and mechanical antinociception induced by intravenous administration of acepromazine and four dose rates of dexmedetomidine in donkeys. *Vet Anaesth Analg.* 2017;44(3):509-517. Doi: 10.1016/j.vaa.2016.08.003
4. Valverde A. Alpha-2 agonists as pain therapy in horses. *Vet Clin North Am Equine Pract.* 2010;26(3):515-32. Doi: 10.1016/j.cveq.2010.07.003
5. Funcia J P, Lamuraglia, R, Guglielminetti A, Soriano M, Melo L M. Preliminary Results of Behavioral and Cardiopulmonary Effects of a Constant Rate Infusion of Remifentanil–Xylazine for Sedation in Horses. *J. Vet. Sci.* 2016; 37:49-53 Doi: 10.1016/j.jevs.2015.12.005
6. Pallarols NB, Lamuraglia R, Guglielminetti A, Ortiz de Elguea MF, Carossino M, Funcia JP. Behavioral and Cardiopulmonary Effects of a Constant Rate Infusion of Remifentanil-Xylazine for Sedation in Horses. *J Equine Vet Sci.* 2020; 91:103111. Doi: 10.1016/j.jevs.2020.103111
7. Benmansour P, Billinsky J, Duke-Novakovski T, Alcorn J. Blood concentrations of remifentanil during and after infusion in horses anesthetized with isoflurane and dexmedetomidine. *Res Vet Sci.* 2016; 107:202-206. Doi: 10.1016/j.rvsc.2016.06.008
8. Michelsen LG, Hug CC Jr. The pharmacokinetics of remifentanil. *J Clin Anesth.* 1996 Dec;8(8):679-82. Doi: 10.1016/s0952-8180(96)00179-1

9. Sanchez LC, Robertson SA. Pain control in horses: what do we really know? *Equine Vet J.* 2014;46(4):517-23. Doi: 10.1111/evj.12265
10. Glass PSA, Gan TJ, Howell S. A review of the pharmacokinetics and pharmacodynamics of remifentanyl. *Anesth Analg.* 1999;89(4):7. Doi: 10.1097/00000539-199910001-00003
11. Lehner AF, Almeida P, Jacobs J, Harkins JD, Karpiesiuk W, Woods WE, Dirikolu L, Bosken JM, Carter WG, Boyles J, Holtz C, Heller T, Nattrass C, Fisher M, Tobin T. Remifentanyl in the horse: identification and detection of its major urinary metabolite. *J Anal Toxicol.* 2000;24(5):309-15. Doi: 10.1093/jat/24.5.309
12. Lamuraglia R, Kirkby P, Funcia J P. Cardiopulmonary Effects and Recovery Quality of Remifentanyl–Isoflurane Anesthesia in Horses. *J Vet. Sci.* 2015;35(4): 271-276. Doi: 10.1016/j.jevs.2015.01.011
13. Samimi AS, Molaei MM, Azari O, Rezaei MA, Hashemian A. Comparative Evaluation of the Sedative and Analgesic Effects of Caudal Epidural Administration of Lidocaine Alone or in Combination With Xylazine, Detomidine, Medetomidine, and Dexmedetomidine in Mediterranean Miniature Donkeys. *J Equine Vet Sci.* 2022;113:103915. doi: 10.1016/j.jevs.2022.103915.
14. Lizarraga I, Castillo-Alcala F. Sedative and mechanical hypoalgesic effects of butorphanol in xylazine-premedicated donkeys. *Equine Vet J.* 2015;47(3):308-12. doi: 10.1111/evj.12274.
15. Dzikiti TB, Maney JK, Thorogood J, Segabinazzi L, Peterson E, Dzikiti LN, Escobar A. Sedation with dexmedetomidine-butorphanol or xylazine-butorphanol continuous intravenous infusions during unilateral ovariectomy in standing donkeys. *Equine Vet J.* 2024;56(6):1243-1250. Doi: 10.1111/evj.14052

- 285 16. Lawless SP, Cohen ND, Lawhon SD, Chamoun-Emanuelli AM, Wu J, Rivera-Vélez A,
286 Weeks BR, Whitfield-Cargile CM. Effect of gallium maltolate on a model of chronic,
287 infected equine distal limb wounds. PLoS One. 2020;15(6):e0235006. Doi:
288 10.1371/journal.pone.0235006
- 289 17. Taylor P. Veterinary anaesthesia and analgesia: from chloroform to designer drugs. Vet
290 Rec. 2014;174(13):318-21. Doi: 10.1136/vr.g2249
- 291 18. Kamerling S, Wood T, DeQuick D, Weckman TJ, Tai C, Blake JW, Tobin T. Narcotic
292 analgesics, their detection and pain measurement in the horse: a review. Equine Vet J.
293 1989;21(1):4-12. Doi: 10.1111/j.2042-3306.1989.tb02081.x
- 294 19. Boscan P, Van Hoogmoed LM, Farver TB, Snyder JR. Evaluation of the effects of the
295 opioid agonist morphine on gastrointestinal tract function in horses. Am J Vet Res.
296 2006;67(6):992-7. Doi: 10.2460/ajvr.67.6.992