Sedative and cardiopulmonary effects of buprenorphine and xylazine in horses

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Abstract

This study investigated the sedative, cardiopulmonary, and gastrointestinal effects produced by buprenorphine and xylazine given in combination to horses. Six healthy adult horses underwent 4 randomized treatments, with an interval of 1 wk between treatments. A control group was given a saline solution intravenously (IV) and the experimental groups received buprenorphine [10 μg/kg bodyweight (BW)] in combination with 1 of 3 different doses of xylazine: 0.25 mg/kg BW (BX25), 0.50 mg/kg BW (BX50), or 0.75 mg/kg BW (BX75), all of them by IV. Cardiopulmonary parameters were evaluated for 120 min after the drugs were administered and intestinal motility was observed for 12 h after treatment. Sedation was found to be dose-dependent in all groups receiving buprenorphine and xylazine and it was observed that the heart rate decreased in the first 5 min and increased at the end of the sedation period. Arterial blood gas tension analyses showed minimal alterations during the experiment. Gastrointestinal hypomotility was observed for up to 8 h. The combination of buprenorphine and 0.50 mg/kg BW of xylazine (BX50) provided a 30-minute period of sedation without intense ataxia and maintained cardiopulmonary parameters within acceptable limits for the species.

Résumé

Cette étude avait comme objectif d'examiné les effets sédatifs, cardio-pulmonaires et gastro-intestinaux d'une combinaison de buprénorphine et de la xylazine administrée à des chevaux. Six chevaux adultes en santé ont été soumis aléatoirement à 4 traitements, avec un intervalle de 1 semaine entre les traitements. Un groupe témoin a reçu de la saline par voie intraveineuse (IV) et les groupes témoins recevaient IV de la buprénorphine [10 μg/kg de poids corporel (BW)] combinée avec 1 des 3 différents dosages de xylazine : 0,25 mg/kg BW (BX25), 0,50 mg/kg BW (BX50) ou 0,75 mg/kg BW (BX75). Les paramètres cardio-pulmonaires ont été évalués pour 120 min suite à l'administration des drogues et la motilité intestinale a été observée pour les 12 h qui suivaient le traitement. On observa que la sédation était dose-dépendante dans tous les groupes recevant de la buprénorphine et xylazine, et il a été noté que le rythme cardiaque diminuait au cours des 5 premières minutes et augmentait à la fine de la période de sédation. Les analyses de la tension des gaz sanguins artériels n'ont montré que des altérations minimes au cours de l'expérience. L'hypomotilité gastro-intestinale a été observée pour une période allant jusqu'à 8 h. La combinaison BX50 a induit une période 30 minutes de sédation sans ataxie intense et les paramètres cardio-pulmonaires se sont maintenus à l'intérieur des limites acceptables pour cette espèce.

(Traduit par Docteur Serge Messier)

Introduction

Alpha 2-adrenoceptor agonists are widely used in equine medicine as their sedative and moderate analgesic properties facilitate handling and provide pain relief by activating the central and peripheral nervous system alpha 2-adrenergic receptors (1–3). Despite its wide use, xylazine has the drawback of conferring only a short period of action of approximately 20 to 30 min, which impedes its use when prolonged analgesia is necessary (4). In addition, it can produce an intense hemodynamic depression, which may involve bradycardia with second degree atrioventricular block, transient hypertension, hypotension, reduction of stroke volume and cardiac output, as well as respiratory depression, which could worsen the state of shock or the effects of other depressants (5–7).

Although used in equine analgesic therapy, opioids are still relatively restricted, mainly due to the excitation that they produce (8,9). However, this excitation is generally observed when opioids are administered alone and in animals without pain (10) or when higher than recommended doses are used. In order to avoid this effect, opioids are given in combination with sedative drugs, which enhances sedative and analgesic effects and prolongs the period of action. It is therefore possible to reduce the doses necessary to produce sedation and analgesia, due to the synergic effect observed, which also reduces collateral effects (10,11).

Buprenorphine is a semi-synthetic opioid derived from the highly lipophilic thebaine, which has a partial agonist action on the OP3 receptors and is widely used as an analgesic agent in cats and dogs (12–14). In horses, however, buprenorphine presents restrictions

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due to its side effects, mainly of an excitatory nature, despite providing prolonged analgesia at a dose of 10 μg/kg (15) observed by other authors (15,16) who evaluated physiological, algesimetric, and behavioral parameters. Nevertheless, the animals presented moderate excitation and an elevation of hemodynamic parameters.

The action of buprenorphine on the cardiopulmonary system has shown ambiguous results. In humans and small animals, it produces minimal alterations (17,18). Contradictory results have been reported in horses, with some authors observing discreet alterations (19) and others observing a stimulation of the hemodynamic system (15,16,20) in healthy animals and in those with chronic obstructive pulmonary disease, but minimal respiratory effects and no acid-base alterations.

The objective of this study was to investigate the sedative, cardiopulmonary, and gastrointestinal effects produced in horses by the neuroleptanalgesic combination of buprenorphine and 3 different doses of xylazine.

Materials and methods

Animals

Six healthy adult Standardbred horses were used [3 males and 3 females; mean ± standard deviation *(s)* body weight (BW): 384 ± 89 kg]. Health status was assessed on the basis of results of clinical examination and complete blood (cell) count (CBC). The study was approved by an institutional Animal Care Committee (Protocol no. 50/2006).

Experimental design

After a pilot study using the higher dose of xylazine (Sedazine; Schering-Plough, Rio de Janeiro, Brazil), 1 mg/kg BW, each horse received 4 treatments: 10 mL of saline (0.9% NaCl) solution IV (control) and 3 groups received buprenorphine (Temgesic; Schering-Plough), 10 μg/kg, BW, IV in combination with xylazine at doses of 0.25 mg/kg BW (BX25), 0.50 mg/kg BW (BX50), and 0.75 mg/kg BW (BX75), with both drugs mixed in the same syringe and given intravenously. The animals were randomized into the groups to avoid possible conditioning to experimental conditions and installations, with 1-week intervals between treatments.

Each horse was previously acclimatized to the experimentation room and conditioned to remain undisturbed for about 3 h while restrained in a stock to allow instrumentation and cardiopulmonary data to be collected during the experiment. On the day before the study, the horses were placed in individual stalls with food and water provided ad libitum. Hay and commercial food was given at 7 o'clock in the morning. One hour later, each horse was restrained in a stock for instrumentation. During that period, data sample collection and the movement and conversation of all personnel involved in the study were reduced to the minimum required to avoid stimulating the horses. A 16-gauge catheter was placed in the right jugular vein to facilitate injection of the drugs, which were administrated for a period of 5 s.

Evaluation of sedative activity

Sedation was indirectly assessed by measuring the distance from the lower lip to the ground in centimeters using a ruler fixed to the wall near the animal's head. The intensity of head ptosis was recorded every 15 min up to 120 min. This was considered to be the difference between the value obtained at 0 min and the value obtained at a given time for the same animal, thus eliminating individual variation. In addition, a dose-response curve was established to verify the relation between the increase in the dose of xylazine and the sedative response. For this purpose, the area under the curve of the corresponding group was obtained by the GraphPad InStat program (GraphPad Prism; GraphPad Software, San Diego, California, USA).

Evaluation of physiological parameters

Hemodynamic parameters were obtained with a multiparameter monitor (Monitor Modular Máximo; Ecafix Industria Comercial, São Paulo, Brazil). Adhesive electrodes were placed according to a base-apex lead attachment to display the electrocardiogram (ECG). Heart rate (HR) and rhythm were obtained from the ECG tracing. After local anesthesia with 1 mL of 2% lidocaine, a 20-gauge catheter was inserted into the transverse facial artery to measure systolic, mean, and diastolic arterial pressure (SAP, MAP, and DAP). The catheter was connected to a fluid-filled pressure transducer that had previously been calibrated with the zero reference point at the level of the olecranon. Respiratory rate (f_R) was determined by counting the number of movements of the chest wall over 1 min. Those variables were done at 0, 5, and 15 min and then every 15 min up to 120 min. For analysis of blood gas tension, arterial blood samples were collected from the transverse facial artery at 0, 30, and 60 min in a 1-mL syringe previously heparinized (Omni C Blood Gas Analyzer; Roche Diagnostica Brazil, São Paulo, Brazil). This included pH, $PaCO_2$, PaO_2, SaO_2, HCO_3^-, Na^+, and K^+. All values were adjusted according to the animal's body temperature.

A normal abdominal auscultation score (16,21) was assessed at −30, 0, 5, and 15 min, every 15 min up to 120 min, and every 2 h up to 12 h. The 4 abdominal quadrants were auscultated (superior and inferior on the left and right sides). There was a small delay (1 min) between quadrant evaluations. A subjective score was designated for each quadrant in accordance with the following scale: 0 = no intestinal sounds; 1 = mild, low-pitched, audible, crepitation-like sounds at a frequency of 1 per min on both sites within a quadrant; 2 = low-pitched, crepitation-like sounds at a frequency of more than 1 per min on both sites within a quadrant; 3 = long, loud gurgling sounds audible once per min at both sites within a quadrant; 4 = long, loud gurgling sounds audible more than once per min on both sites within a quadrant. The score of the 4 quadrants was totaled, giving a range of 0 (absence of intestinal movement) to 16.

Body temperature was measured in degrees Celsius (°C) using a digital thermometer (Monitor Modular Máximo; Ecafix Industria Comercial) inserted in the rectum.

Statistical analysis

Statistical analysis was carried out using the GraphPad InStat program GraphPad Software. For each group, all parametric variables were analyzed by a repeated measure analysis of variance (ANOVA), followed by a Dunnett test to compare all sample collection times

with baseline data (0 min). For comparisons among groups, a repeated measure ANOVA was performed for each time, followed by a Tukey test. A Wilcoxon matched pairs test was used to compare abdominal auscultation scores obtained throughout the study with the baseline data (0 min). Differences were considered significant at $P < 0.05$. All parametric results were expressed as mean ± standard deviation *(s)* and intestinal motility scores were expressed as median ± interquartile interval.

Results

While sedation was observed in all groups that received the neuroleptanalgesia, the xylazine brought about the most intense and long-lasting sedative response, which varied in relation to the increased doses (Figures 1 and 2), of 15 min to BX25, 30 min to BX50, and 45 min to BX75. In addition, 2 animals of BX75 showed intense sedation up to 15 min and were leaning against the stock to prevent falling. In all groups, a slight excitation was observed after sedation time, which was characterized by head nodding, head shaking and neighing, and pawing and shifting of all 4 limbs for ground support. All buprenorphine-xylazine groups differed from the control in this respect.

Those groups receiving buprenorphine-xylazine presented an initial intense bradycardia, with the appearance of a second-degree atrioventricular block within the first 2 min after administration. Heart rate (HR) was 23 ± 2 beats/min in BX25, 21 ± 2 beats/min in BX50, and 16 ± 2 beats/min in BX75. Atrioventricular block was most evident in BX75, with all animals presenting this alteration. Compared to the control group, bradycardia persisted for only up to 5 min in BX50 and BX75. During the period of sedation for each group, no significant differences were observed in arterial pressure, when compared to both 0 and the control (Table I).

At the end of the sedation period, HR was elevated compared to the baseline (after 45 min in BX25 and after 75 min in BX50 and BX75). This persisted until the end of the evaluation period. A similar pattern was observed for the arterial pressures, particularly the mean arterial pressure (MAP), which showed an elevation compared to the baseline after 30 min in BX25, after 45 min in BX50, and after 60 min in BX75. This persisted until the end of the evaluation period in all groups (Table I).

A decrease in respiratory rate (f_R) compared to the control was observed from 5 to 30 min in BX25, from 15 to 30 min in BX50, and from 5 to 45 min in BX75 (Table I). No alterations were observed in arterial blood gas tensions and electrolytes either when compared to the baseline or among groups. There was an increase in HCO_3^- at 30 and 60 min only in BX75 compared to the baseline, but there was no difference when compared to the other groups (Table II).

Hypomotility was observed in all groups receiving the combination of buprenorphine and xylazine. Hypomotility was observed in BX25 for up to 480 min, while in groups BX50 and BX75, it was observed for up to 360 and 480 min, respectively (Figure 3). There was no significant difference in body temperature, which remained stable and within a normal physiological range for the species throughout the evaluation period.

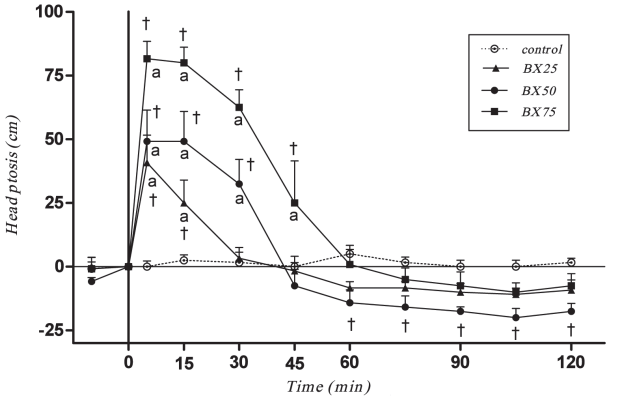

Figure 1. Sedation effects of IV administration of 0.9% NaCl saline solution (control) or buprenorphine (10 µg/kg BW) combined with 0.25 mg/kg BW (BX25), 0.50 mg/kg BW (BX50), or 0.75 mg/kg BW (BX75) of xylazine, evaluated by head ptosis.
a — Statistical difference ($P < 0.05$) with measurement at 0 time (baseline).
† — Statistical difference ($P < 0.05$) from control at the same time.

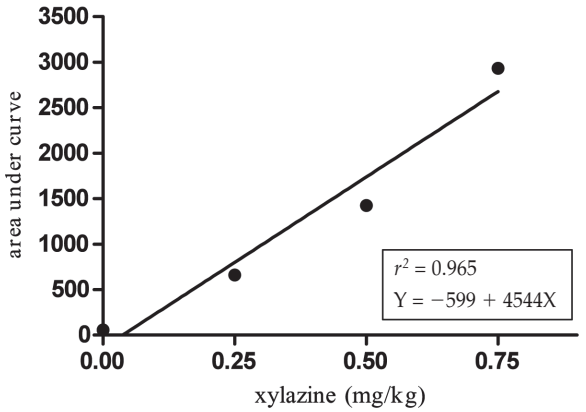

Figure 2. Dose-response curve (area under curve) for the sedative effect of 0.9% NaCl saline solution (control) or buprenorphine (10 µg/kg BW) combined with 0.25 mg/kg BW, 0.50 mg/kg BW, or 0.75 mg/kg BW of xylazine.

Discussion

Sedation caused by alpha 2-adrenoceptor agonists in horses is characterized by head ptosis, eyelid and lip ptosis, and ataxia (22). Different techniques have been used to evaluate sedation in horses, such as the measurement of head ptosis (4). In the present study, the method used was shown to be efficient. Differences in the degree of sedation were observed between the groups given different doses of xylazine, which demonstrates an excellent dose-dependent response and was confirmed by the dose-response curve.

The combination of 10 µg/kg BW of buprenorphine and 0.25 mg/kg BW of xylazine (BX25) produced sedation for about 15 min, while 0.75 mg/kg BW of xylazine (BX75) produced approximately 45 min of sedation. In addition, animals receiving the higher dose occasionally leaned against the stock to avoid falling, which characterizes intense sedation and has been reported as one of the greatest problems in using neuroleptanalgesia in horses (23). In the pilot study with 2 animals, 1 mg/kg BW of xylazine combined with

Table I. Effects of IV administration of 0.9% NaCl saline solution (control) or buprenorphine (10 µg/kg BW) combined with 0.25 mg/kg BW (BX25), 0.50 mg/kg BW (BX50), or 0.75 mg/kg BW (BX75) of xylazine on physiological parameters in 6 horses. Results are expressed as mean ± standard deviation (*s*)

Time points (min)	0	5	15	30	45	60	75	90	105	120
HR (beats/min)										
control	38 ± 5	38 ± 5[a]	39 ± 6	38 ± 5	36 ± 6[a]	37 ± 4[a]	38 ± 14	37 ± 14[a]	37 ± 15[a]	35 ± 14[a]
BX25	36 ± 6	35 ± 4[a,b]	36 ± 4	39 ± 5	42 ± 6[*,a,b]	44 ± 4[*,a,b]	44 ± 16[*]	43 ± 19[*,a,b]	46 ± 17[*,a]	44 ± 18[*,a,b]
BX50	37 ± 7	31 ± 6[b]	34 ± 7	35 ± 7	41 ± 7[a]	42 ± 9[a]	45 ± 18[*]	44 ± 18[*,a,b]	45 ± 18[*,b]	46 ± 19[*,b]
BX75	38 ± 6	32 ± 3[a]	35 ± 8	38 ± 3	37 ± 5[a]	40 ± 5[a]	46 ± 110[*]	46 ± 17[*,b]	46 ± 16[*,b]	47 ± 18[*,b]
SAP (mmHg)										
control	133 ± 11	140 ± 32	127 ± 20	140 ± 33	137 ± 21[a]	140 ± 18[a]	135 ± 128	140 ± 113	141 ± 113[a]	136 ± 119[a]
BX25	138 ± 7	122 ± 10	123 ± 15	155 ± 21	161 ± 20[a,b]	167 ± 35[*,a,b]	167 ± 134[*]	169 ± 135[*]	167 ± 132[*,a,b]	171 ± 136[*,a,b]
BX50	129 ± 12	131 ± 8	126 ± 13	140 ± 26	173 ± 32[*,b]	174 ± 31[*,a]	173 ± 127[*]	175 ± 126[*]	178 ± 123[*,a,b]	177 ± 115[*,a,b]
BX75	136 ± 9	135 ± 16	126 ± 13	124 ± 16	134 ± 24[a]	161 ± 21[a]	177 ± 133[*]	181 ± 130[*]	183 ± 129[*,b]	187 ± 130[*,b]
MAP (mmHg)										
control	114 ± 10	114 ± 15	103 ± 15[*]	113 ± 9[a]	109 ± 11[a]	113 ± 10[a]	107 ± 111[a]	110 ± 19[a]	113 ± 110[a]	107 ± 113[a]
BX25	111 ± 13	104 ± 14	105 ± 6	130 ± 14[*,a]	139 ± 19[*,b]	141 ± 26[*,b]	136 ± 118[*,a,b]	138 ± 125[*,a,b]	138 ± 116[*,a,b]	138 ± 119[*,b]
BX50	105 ± 14	110 ± 10	106 ± 13	117 ± 25[a,b]	139 ± 20[*,b]	142 ± 18[*,a,b]	146 ± 125[*,a,b]	152 ± 126[*,b]	151 ± 123[*,b]	148 ± 118[*,b]
BX75	106 ± 13	116 ± 12	103 ± 10	98 ± 13[a,b]	111 ± 24[a]	132 ± 14[*,a,b]	140 ± 118[*,a,b]	142 ± 116[*,a,b]	144 ± 115[*,b]	141 ± 120[*,b]
DAP (mmHg)										
control	96 ± 14	97 ± 10	89 ± 13	94 ± 5	93 ± 9[a]	93 ± 8	95 ± 17[a]	93 ± 111[a]	93 ± 19	93 ± 113
BX25	92 ± 14	93 ± 17	90 ± 4	105 ± 20	119 ± 20[*,a]	103 ± 50	112 ± 114[a,b]	114 ± 123[a]	114 ± 111	112 ± 112
BX50	89 ± 16	100 ± 17	93 ± 21	99 ± 23	116 ± 20[*,a,b]	118 ± 24[*]	125 ± 124[*,b]	128 ± 120[*,b]	125 ± 124[*]	122 ± 124[*]
BX75	89 ± 15	99 ± 11	88 ± 12	85 ± 14	91 ± 20[a,b]	106 ± 15[*]	103 ± 19[a,b]	111 ± 116[*,a,b]	113 ± 113[*]	112 ± 116[*]
f_R (mov/min)										
control	21 ± 12	20 ± 9[a]	20 ± 11[a]	22 ± 10[a]	23 ± 11[a]	22 ± 11	19 ± 18	19 ± 18	20 ± 18	20 ± 19
BX25	11 ± 2	10 ± 4[b]	10 ± 2[b]	11 ± 3[b]	12 ± 2[a,b]	13 ± 5	15 ± 18	18 ± 18[*]	16 ± 16	16 ± 13
BX50	14 ± 6	11 ± 7[a]	10 ± 7[b]	11 ± 6[b]	16 ± 10[a,b]	19 ± 12	22 ± 115	20 ± 113	20 ± 14	20 ± 110
BX75	12 ± 3	9 ± 3[b]	9 ± 2[b]	9 ± 3[b]	8 ± 2[b]	12 ± 13	12 ± 13	15 ± 16	14 ± 14	14 ± 15

[*] Statistical difference with value at 0 time (baseline) ($P < 0.05$).

[a,b] The same letter showed no difference between group comparisons ($P < 0.05$).

HR — heart rate; SAP — systolic arterial pressure; MAP — mean arterial pressure; DAP — diastolic arterial pressure; f_R — respiratory rate.

Table II. Effects of IV administration of 0.9% NaCl (control) or buprenorphine (10 µg/kg BW) combined with 0.25 mg/kg BW (BX25), 0.50 mg/kg BW (BX50), or 0.75 mg/kg BW (BX75) of xylazine on arterial blood gas tension analysis in 6 horses

	Time (min)		
	0	30	60
pH			
control	7.411 ± 0.02	7.419 ± 0.02	7.418 ± 0.01
BX25	7.419 ± 0.02	7.429 ± 0.04	7.424 ± 0.03
BX50	7.366 ± 0.06	7.375 ± 0.06	7.424 ± 0.03
BX75	7.379 ± 0.02	7.407 ± 0.02	7.418 ± 0.03
HCO_3^- (mmol/L)			
Control	27.8 ± 1.6	28.1 ± 1.4	28.4 ± 1.9
BX25	29.4 ± 2.9	29.5 ± 2.9	28.4 ± 1.9
BX50	26.4 ± 2.7	27.3 ± 2.2	27.6 ± 2.2
BX75	28.1 ± 1.3	30.0 ± 0.9[a]	30.5 ± 1.1[a]
$PaCO_2$ (mmHg)			
control	45.1 ± 3.1	48.4 ± 3.0	43.2 ± 4.4
BX25	45.8 ± 2.5	44.5 ± 3.2	45.5 ± 3.0
BX50	48.0 ± 5.3	48.7 ± 1.8	46.6 ± 0.5
BX75	47.1 ± 7.0	44.8 ± 1.1	44.7 ± 2.5
PaO_2 (mmHg)			
control	109.8 ± 7.1	107.7 ± 8.7	103.8 ± 8.4
BX25	100 ± 9.2	103.7 ± 11.3	103.1 ± 7.4
BX50	106 ± 6.2	109.7 ± 13	109 ± 40.1
BX75	103 ± 8.8	107.9 ± 13.4	107.2 ± 15.2
SaO_2 (%)			
control	98.1 ± 0.4	97.9 ± 0.6	97.9 ± 0.5
BX25	97.6 ± 0.4	98.0 ± 0.6	97.8 ± 0.4
BX50	97.7 ± 0.6	98.0 ± 0.5	98.3 ± 1.0
BX75	98.0 ± 0.5	98.1 ± 0.6	98.0 ± 0.7
K^+ (mmol/L)			
control	3.51 ± 0.29	3.42 ± 0.32	3.39 ± 0.20
BX25	3.79 ± 0.26	3.65 ± 0.25	3.57 ± 0.36
BX50	3.92 ± 0.51	3.75 ± 0.53	3.65 ± 0.57
BX75	3.93 ± 0.72	3.54 ± 0.43	3.43 ± 0.37
Na^+ (mmol/L)			
control	141 ± 3.7	141 ± 2.3	141 ± 1.4
BX25	136 ± 1.6	133 ± 12.9	138 ± 3.8
BX50	134 ± 11.4	127 ± 2.2	127 ± 2.2
BX75	138 ± 2.9	139 ± 2.7	139 ± 1.8

[a] Statistical difference with value at 0 time (baseline) ($P < 0.05$).

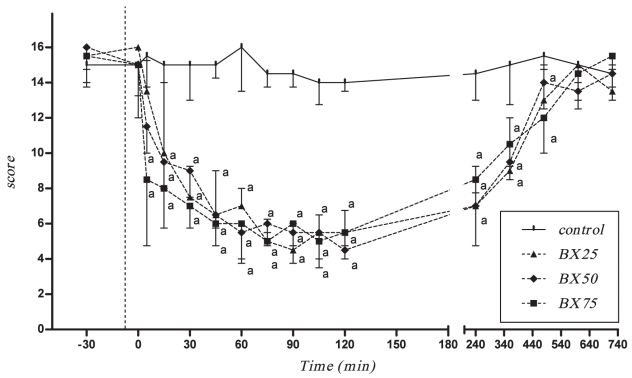

Figure 3. Intestinal motility score by IV administration of 0.9% NaCl saline solution (control) or buprenorphine (10 µg/kg BW) combined with 0.25 mg/kg BW (BX25), 0.50 mg/kg BW, or 0.75 mg/kg BW (BX75) of xylazine. Values are expressed as median and interquartile interval.
a — Significant difference ($P < 0.05$) from the baseline value (0 min).

buprenorphine produced such severe sedation that the animals almost fell in the stall, which led to the elimination of that dose. In the groups studied, the period of sedation was probably not longer because of the excitatory effect provoked by the opioid. According to the previous study (15), excitation in horses receiving 10 µg/kg BW of buprenorphine IV occurred after approximately 5 to 10 min and persisted for up to 14 h.

Bradycardia observed at the beginning of the evaluation period in the buprenorphine-xylazine groups is mainly due to the direct stimulation of vascular receptors caused by alpha 2-adrenoceptor agonists (24,25), which promote vasoconstriction, especially when given intravenously, and by a direct vagomimetic action (24). In a review (3), hypertension occurs for a transitory period of 2 to 5 min. Nevertheless, in this study, initial hypertension cannot be confirmed because the parameters were evaluated after 5 min at which point the hypertensive effect had probably already ceased.

Hypotension was not observed in this study, which was contrary to our expectations, as a prolonged period of hypotension is generally observed after a short hypertensive phase due to the decrease in sympathetic tonus and the increase in vagal activity (24). This finding might have been a result of the possible central stimulation observed with the use of buprenorphine in horses (16), which suppressed the hypotensive effect of the xylazine.

The elevation of hemodynamic variables is attributed to central stimulation by the opioid, as observed in other studies (16,20). The alpha 2-adrenoceptor agonists produce a dose-dependent sedative effect (25,26), which lasts from 15 to 60 min. This corroborates the findings in the present study, in which sedation evaluated by head ptosis lasted for approximately 30 min in BX25 and increased gradually with the increasing doses.

The initial occurrence of bradypnea in the buprenorphine-xylazine groups, which was most intense in BX75, was due to the combination of the drugs and the dose-dependent effect of xylazine, since the f_R increased after 30 min, but not enough to be considered tachypnea. A review (22) shows that xylazine promotes respiratory depression, but without altering blood pH, PaO_2, or $PaCO_2$. Results for f_R in horses receiving opioids are contradictory. It was reported in a previous study (16) that buprenorphine caused tachypnea and increased pH, although it remained within physiological parameters, but did not alter blood gases. On the other hand, other authors reported that buprenorphine alone (20) or in combination with detomidine (19) did not cause significant alterations in f_R. In the present study, there was a significant difference in RR only between the baseline and 90 min in BX25, which may have been due to the excitation caused by the buprenorphine.

No differences were observed for pH and arterial blood gas tension during the period of evaluation. This may be due to the neuroleptanalgesic combination, by which alpha 2-adrenoceptor agonists caused an initial respiratory depression and the opioid-mediated excitation caused an increased respiratory rate, maintaining values

close to normal. Although HCO_3^- was slightly above what is considered to be normal, there was no difference from the control. The HCO_3^- values may have been a result of the feed given before the study.

Although it is claimed that evaluating intestinal motility by auscultation is limited in sensitivity and specificity, this method proved to be efficient in the present study and in agreement with other studies (6,16,21). The hypomotility observed at the beginning of the evaluation period may have been a result of the combined effects of xylazine and buprenorphine. The depressive effect of alpha 2-adrenoceptor agonists seems to be mediated by activation of receptors in the myoenteric plexus, which alters contractions of the gastrointestinal muscles by inhibiting acetylcholine (22,27). On the other hand, opioids also have a depressive effect on the gastrointestinal tract. A previous study (16) reported that 10 μg/kg BW of buprenorphine IV caused hypomotility for a period of 4 h. Although opioid agonists may increase tonus of the smooth muscle in the intestines, a depression of mechanisms is involved in intestinal propulsion (28). Another study (29) found that opioids induced hyperpolarization and reduction of acetylcholine and other neurotransmitters by activating K^+ channels or inhibiting N-type Ca^+ channels, mediated by pre-synaptic receptors in intrinsic neurons of the myoenteric plexus. Although there was prolonged hypomotility, no discomfort was observed in the animals during the period of evaluation.

Conclusions

The combination of buprenorphine and 0.50 mg/kg BW of xylazine (BX50) provided a satisfactory period of sedation (30 min) without intense ataxia and maintained cardiopulmonary parameters within acceptable limits for the species.

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