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ORIGINAL RESEARCH

Sedation and Pain Management with Intravenous Romifidine–Butorphanol in Standing Horses

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ABSTRACT

The objective of this study was to determine the sedation, analgesia, and clinical reactions induced by an intravenous combination of romifidine and butorphanol in horses. The study was conducted on six saddle horses weighing 382 to 513 kg (mean ± SD; 449 ± 54 kg) and aged 6 to 14 years. The horses each underwent three treatments: intravenous romifidine 0.1 mg/kg body weight (RM; mean dose, 4.5 mL); intravenous butorphanol 0.05 mg/kg body weight (BT; mean dose, 2.4 mL); and intravenous romifidine 0.1 mg/kg body weight plus butorphanol 0.05 mg/kg body weight (RMBT; mean dose, 7.0 mL). The order of treatments was randomized. Heart rate, arterial pressure, respiratory rate, rectal temperature, sedation, and analgesia were measured at two times before treatments, 15 minutes apart (times –15 and 0) and at 5, 10, 15, 30, 45, 60, 75, 90, 120, 150, and 180 minutes after drug administration. The onset of sedation was approximately 5 minutes after intravenous injection of RM and RMBT, whereas BT did not present this effect. The duration of complete sedation was approximately 60 minutes for RMBT and approximately 35 minutes for RM. The RMBT treatment provided 30 minutes and the RM treatment 20 minutes of complete analgesia. Heart rate decreased significantly ($P < .05$) from basal values in the RM and RMBT treatments. Only RM caused significant decreases ($P < .05$) in the respiratory rate. Arterial pressure did not change significantly ($P > .05$) in any treatment. Intravenous administration of a romifidine–butorphanol combination to horses resulted in longer duration of sedation and analgesia than administration of romifidine or butorphanol alone. These effects probably resulted from a synergistic effect of the two drugs.

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INTRODUCTION

Several minor noxious procedures can be successfully performed in the appropriately restrained and sedated standing horse. Additional analgesia can be provided with appropriate local anesthetic blocks in animals that are at high risk for general anesthesia or when the latter is not an option.[1] The α-2 adrenoreceptor agonists produce excellent sedation in the horse, but their major disadvantage is cardiovascular depression.[2] These effects are dose dependent.[3] Deeper sedation occurs at higher doses, which can cause more cardiovascular depression, with symptoms such as bradycardia, an initial hypertension followed by hypotension, a decrease in cardiac output, an increase in systemic vascular resistance, and variable changes in arterial blood gases.[3,4] Previous studies have investigated the effects of xylazine, detomidine, and medetomidine on cardiovascular function in the horse.[3,5,6] Romifidine induces similar cardiovascular effects with clinical doses similar to those of other α-2 adrenoreceptor agonists.[2] Sedative effects of romifidine in horses have been described[7]; however, studies have reported conflicting results with regard to their analgesic effects.[7,8] One study that included romifidine and the use of an electrical model showed an absence of analgesic effects of the drug in horses.[8] Another study using electrical current and mechanical pressure tests demonstrated that romifidine produces analgesia in horses,[7] with maximal effect at 15 minutes after injection and a gradual decrease to baseline levels at 1 hour, although the effect was less with the mechanical pressure test. The differences noted in the analgesic effects of romifidine may reflect the different analgesic tests used in these studies.

Standing sedation of the horse is mainly achieved using α-2 agonists, alone or in combination with other drugs.[9,10] Morphine has been used experimentally in horses at different doses, alone or in combination with other drugs, to assess its behavioral and cardiovascular effects.[11,12] The use of opioids alone in the horse is limited by the perceived risk of behavioral side effects, such as excitement.[13] Opioid drugs with agonist–antagonist properties are preferred to morphine in clinical equine practice.[14] Butorphanol is

a potent, mixed agonist–antagonist analgesic that belongs to the opioid family.[15] Its predominant action is agonism at κ receptors[16] with competitive agonist and antagonist activity at μ and δ opioid receptors,[17] whereas morphine acts primarily through the μ and δ opioid receptors.[18] Butorphanol, parenterally administered preoperatively and postoperatively, exerts an analgesic effect with a potency approximately five to seven times greater than that of morphine, the prototypical opioid analgesic.[19] Butorphanol is widely used because of its safety and relative lack of side effects, but it is expensive compared with morphine.[20]

The aim of the current study was to determine whether the combination of clinical doses of romifidine and butorphanol administered by the intravenous route in horses produces deep sedation and analgesia of longer duration with fewer side effects than intravenous romifidine or butorphanol administered alone at clinical doses used in veterinary medicine.

MATERIALS AND METHODS

The study and experimental design were approved by the Committee for Animal Experimentation of our institution. The study was conducted on six saddle horses weighing 382 to 513 kg (mean ± SD, 449 ± 54 kg) and aged 6 to 14 years (three males and three females); all were of mixed breed. A routine clinical examination was performed before each experiment to assure that the animals were healthy and sound. During experimentation, horses were provided water and hay ad libitum. All animals were housed in stalls in the Faculty of Veterinary Medicine and Animal Science facilities during the experimental period.

Three treatments were applied to each animal, with a minimum of a 2-week interval between treatments, the order of which was randomized. An hour before each experiment, the horse was examined and weighed. Horses were restrained in stocks and allowed at least 30 to 45 minutes to become accustomed to their surroundings before each experiment. The site of catheterization was clipped, and the skin was surgically scrubbed with povidone iodine. In treatment 1 (RM), animals received 0.1 mg/kg romifidine (Sedivet, Boehringer De Angeli, Química e Farmacêutica Ltda, São Paulo, Brazil); in treatment 2 (BT), animals received 0.05 mg/kg butorphanol (Torbugesic, Fort Dodge Animal Health, Fort Dodge, IA); and in treatment 3 (RMBT), animals received romifidine plus butorphanol (0.1 mg/kg + 0.05 mg/kg, respectively). All drugs were injected via a left jugular catheter. Each dose was injected over a period of 30 seconds with a 14-cm, 14-standard wire gauge catheter.

Arterial pressures (systolic, SAP; diastolic, DAP; mean, MAP), heart rate (HR), respiratory rate (RR), rectal temperature (RT), analgesia, and sedation were measured at two time points before treatments, 15 minutes apart (times –15 and 0) and at 5, 10, 15, 30, 45, 60, 75, 90, 120, 150, and 180 minutes after drug administration. Arterial pressure was measured through a cardiac monitor (EMAI, RX-300[A], Transmai Equipamentos Médicos Hospitalares, São Paulo, Brazil) using a noninvasive device with its cuff over the coccygeal artery. HR was measured as beats/minute, RR was evaluated by the movement of the thoracic wall, and RT was measured with a digital thermometer. Lack of analgesia (a strong positive response to a noxious stimulus) was ensured before drug administration. All animals received a standard noxious stimulus: a skin and deep muscle pinprick of perineum between the ribs and in the lateral neck with a 22-gauge, 2.5-cm-long needle. Degree of analgesia was rated according to the following scale: (1) complete analgesia; (2) moderate analgesia, slight response to a painful stimulus without whole-body reaction; (3) mild analgesia, brisk response to a painful stimulus, with low whole-body reaction; and (4) normal response, vigorous or violent reaction to a painful stimulus. Depth of sedation was rated according to the following scale: (1) marked drowsiness, droopy eyelids, drop of the head with nostril to the carpus, and reluctance to move if encouraged to do so; (2) drowsiness, eyelids slightly droopy, lowering of the head with nostril to the elbow, and spontaneous movements when stimulated to walk; (3) reduced alertness with no other signs; and (4) no sedative effect. Because ataxia is a common manifestation of sedation in horses, motor system involvement was assessed by an observer blinded to the drugs. Ataxia was assessed by the hind limb position, swaying and leaning against the chute, or any knuckling of the fetlocks of the hind limbs. Response to noise and sudden movements of personnel were also recorded during the whole experiment. The horses were housed for observation for 24 hours after each experiment.

Statistical Analysis

All data were analyzed using a general linear model with the SAS software package (SAS Institute Inc., Cary, NC). Data were grouped and summarized as mean ± SD. Data for SAP, DAP, MAP, HR, RR, and RT were grouped and analyzed using two-way repeated measures analysis of variance with treatment and time as independent variables. When a significant difference or interaction was obtained, Dunnett's test or planned comparison was applied as appropriate. For sedation and analgesia variables, the nonparametric Friedman's test was used, followed by multiple comparisons for ranked data using the Dunnett's test, with time 0 as the baseline. In each analysis, differences were considered significant if $P < .05$.

RESULTS

There were no significant differences among the preadministration values of the three treatments. After