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Short Communication

Preliminary Results of Behavioral and Cardiopulmonary Effects of a Constant Rate Infusion of Remifentanil–Xylazine for Sedation in Horses

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ABSTRACT

Standing surgical procedures are performed commonly in horses under sedation. The use of a xylazine and remifentanil combination has not been investigated in horses. We proposed to evaluate behavioral and cardiopulmonary effects of an intravenous (IV) infusion of xylazine with remifentanil for sedation in horses. Xylazine (0.8 mg/kg IV) followed in 3 minutes by remifentanil (0.0005 mg/kg IV), and a constant rate infusion of xylazine and remifentanil (0.65 mg/kg/h; 0.0225 mg/kg/h, respectively) was administered in three horses. Heart rate, respiratory rate (RR), arterial blood pressures, quality of sedation, pH, partial pressure of arterial CO_2 ($PaCO_2$), partial pressure of arterial O_2 (PaO_2), ataxia, sedation, and sedation overall outcome were assessed. Heart rate and RR remained within normal values during sedation without significant changes from baseline. Systolic, mean, and diastolic arterial blood pressures were increased during sedation. There were no significant changes in pH, $PaCO_2$, and PaO_2. Sedation developed immediately after injection of xylazine in the three horses but did not increase after remifentanil bolus or IV infusion of both drugs. None of the mares had ataxia. Adverse effects during and after sedation were present: excitement, increase in locomotor activity, and decrease in the gastrointestinal motility. The combination of xylazine and remifentanil sedation protocol produces adverse effects. This protocol cannot be recommended for clinical conditions, at the described doses.

1. Introduction

Equine anesthesia carries a high risk of mortality when compared with general anesthesia in many species; the overall mortality in horses being 0.24% to 1.9%, 10% for emergency procedures, has been reported [1–5].

Sedation of horses for diagnostic or surgical procedures is a routine component of equine veterinary practice [6].

The alpha2-adrenergic agonists comprise the class of drugs most frequently used to facilitate standing medical procedures in horses [7]. The alpha2-adrenergic agonists available for horses include xylazine, detomidine, romifidine, and medetomidine [8,9]. This class of drugs is known to produce sedation, analgesia, and muscle relaxation [10]. The clinical and cardiopulmonary effects and other complications associated with these drugs are well known [9,11–15]. Although their principal actions and side effects (e.g., bradycardia, second degree atrioventricular block, respiratory rate (RR) decrease, and ataxia) are similar, there are some differences in the duration, degree of action, and complications related to these drugs [9,13–15].

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However, monotherapy alpha2-adrenergic agonists may result in insufficient analgesia for some surgical procedures; in such circumstances, the alpha2-adrenergic agonists are administered in combination with opioids or local anesthetics to improve analgesia. Systemic administration of opioids was shown to produce short-term antinociception in horses [16], but its use was associated with decreased gastrointestinal motility [17]. Although administration of opioids has also been shown to cause excitement and increased locomotor activity in horses [16], there is evidence that these effects can be prevented if these drugs are administered in combination with sedatives such as alpha2-adrenergic agonists [18].

Xylazine is the shortest acting alpha2-adrenergic agonist [19]. By adding an opioid drug, dose requirements of alpha2-adrenergic agonists may be reduced and cardiopulmonary function improved. The addition of opioids does not further impair cardiovascular function [20,21].

Xylazine or detomidine combined with butorphanol, morphine, or buprenorphine have been assessed for a variety of standing surgical procedures [22]. The combination of xylazine with remifentanil has not been reported.

Remifentanil, a synthetic opioid, is the methyl ester of 4-methoxycarbonyl-4-[(1-oxopropyl) phenylamino]-l-piperidinepropionic acid and is marketed as a hydrochloride salt [23]. Remifentanil exhibits μ-opioid receptor–mediated effects, analogous to those of structurally related phenylpiperidine derivatives such as fentanyl and sufentanil [24]. Remifentanil produces physiological changes in humans consistent with potent μ-receptor agonist activity, including analgesia and sedation. Remifentanil adverse effects include ventilatory depression, nausea, vomiting, muscular rigidity, bradycardia, and pruritus [25]; most of these adverse effects have not been reported in horses.

Because remifentanil does not cause histamine release on injection, it has fewer adverse hemodynamic effects than morphine [26].

The presence of a methyl ester on the propionic acid side chain of the piperidine ring increases the susceptibility of remifentanil to hydrolytic cleavage by blood and tissue nonspecific esterases, leading to relatively rapid clearance in humans and measured as a plasma half-life of 8 to 10 minutes [23,26], which prevents accumulation of the drug. Remifentanil can, thus, be classified as an ultrashort-acting phenylpiperidine opioid analgesic agent [27].

It is assumed that remifentanil and fentanyl have similar potency in horses [28,29]. The peak analgesic effect in humans is produced 1 to 3 minutes after the administration of the drug, which is faster than that produced by fentanyl. Constant rate infusion (CRI) of remifentanil was reported under general anesthesia [29,30] but is not reported in the use of sedation for standing procedures. Our hypothesis is as follows: The combination of xylazine and remifentanil will induce reliable sedation with minimal cardiopulmonary and behavioral changes.

This preliminary study evaluates behavioral and cardiopulmonary effects of a CRI of xylazine with remifentanil for sedation in horses.

2. Materials and Methods

2.1. Horses

Three mature healthy cross-bred horses (three mares), of 15.33 ± 4.51 years (range: 11 to 20) and a mean weight of 485.33 ± 33.06 kg (range: 460 to 520), were used in this study. All horses were considered healthy, based on complete physical examination and hematology. Food, but not water, was withheld from the horses for 12 hours before beginning each study.

2.2. Preparation and Instrumentation

Horses were held in a standing stock for placement of a 14-gauge, 51-mm-length Teflon catheter (Abbocath-T; Hospira Inc, IL) in the left jugular vein for subsequent drug administration. A 21-gauge, winged needle infusion set (Butterfly; Hospira Inc) was placed in the facial transverse artery for continuous measurement of direct blood pressure and collection of arterial blood samples for measurement (Nova Phox Plus C; Nova Biomedical Corporation, MA) of pH, partial pressure of arterial CO_2 ($PaCO_2$), partial pressure of arterial O_2 (PaO_2), bicarbonate (HCO_3), hemoglobin saturation of oxygen (SO%), electrolytes, total protein (TP), and packed cell volume. An electronic pressure transducer (BD DTX Plus; Becton Dickinson Infusion Therapy Systems, Inc, UT) was positioned and zeroed at the level of the shoulder for systolic (SAP), diastolic (DAP), and mean arterial blood pressure (MAP) continuous display and monitoring (PM 9000 Vet; Mindray Medical International Limited, China). Heart rate (HR), RR, and a lead II electrocardiogram were also monitored (PM 9000 Vet; Mindray Medical International Limited) throughout the experiment. Both HR and RR were verified by manual count.

2.3. Xylazine Bolus and Remifentanil–Xylazine Infusion

Baseline measurements for HR, RR, blood pressure, and arterial blood gases were recorded before drug administration (Fig. 1). A 0.8 mg/kg xylazine (Xylazina 10%; Pro Ser S.A., Buenos Aires, Argentina) [4] loading dose was administered intravenous (IV). Cardiopulmonary measurements (HR, RR, SAP, DAP, and MAP) were recorded every 5 minutes after xylazine administration. Three minutes after xylazine, a remifentanil (Remicit; AstraZeneca S.A., Buenos Aires, Argentina) bolus (IV) of 0.0005 mg/kg and a CRI of remifentanil 0.0225 mg/kg/h [30] and xylazine 0.65 mg/kg/h [4] was administered (VetFlo 7801B; Grady Medical Systems, Inc, CA) for 57 minutes (Fig. 1).

If additional sedation was required (sedation score scale was 0), a bolus of 0.25 mg/kg of xylazine was administered IV and recorded as necessary.

Arterial blood gases were recorded before drug administration, 30 minutes after drug administration, and just before the end of the CRI.