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RESEARCH PAPER

# Cardiopulmonary effects of an infusion of remifentanil or morphine in horses anesthetized with isoflurane and dexmedetomidine

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## Abstract

**Objective** To examine the cardiopulmonary effects of infusions of remifentanil or morphine, and their influence on recovery of horses anesthetized with isoflurane and dexmedetomidine.

**Study design** Randomized crossover study with 7-day rest periods.

**Animals** Six adult horses (507 ± 61 kg).

**Methods** After the horses were sedated with xylazine, anaesthesia was induced with ketamine and diazepam, and maintained with isoflurane. After approximately 60 minutes, a dexmedetomidine infusion was started (0.25 μg $kg^{-1}$ then 1.0 $\mu g^{-1}$ $kg^{-1}$ $hour^{-1}$) in combination with either saline (group S), morphine (0.15 mg $kg^{-1}$ then 0.1 mg $kg^{-1}$ $hour^{-1}$; group M), or remifentanil (6.0 μg $kg^{-1}$ $hour^{-1}$; group R) for 60 minutes. Mean arterial pressure, heart rate, end-tidal carbon dioxide tension, and end-tidal isoflurane concentration were recorded every 5 minutes. Core body temperature, cardiac output, right ventricular and arterial blood-gas values were measured every 15 minutes. Cardiac index, systemic vascular resistance (SVR), intrapulmonary shunt fraction, alveolar dead space, oxygen delivery and extraction ratio were calculated. Recoveries were videotaped and scored by two observers blinded to the treatment. Data were analyzed using repeated measures ANOVA followed by Dunnett's or Bonferroni's significant difference test. Recovery scores were analyzed using a Kruskal–Wallis test.

**Results** No significant differences were found among groups. Compared to baseline, heart rate decreased and SVR increased significantly in all groups, and cardiac index significantly decreased in groups S and M. Hemoglobin concentration, oxygen content and oxygen delivery significantly decreased in all groups. The oxygen extraction ratio significantly increased in groups M and R. Lactate concentration significantly increased in group S. Recovery scores were similar among groups.

**Conclusions and clinical relevance** Dexmedetomidine alone or in combination with remifentanil or morphine infusions was infused for 60 minutes without adverse effects in the 6 healthy isoflurane-anesthetized horses in this study.

*Keywords* cardiopulmonary effects, dexmedetomidine, horse, partial intravenous anaesthesia, recovery, remifentanil.

## Introduction

Opioids and alpha$_2$-adrenergic agonists are used as components of partial intravenous anaesthesia (PIVA) techniques in numerous species for their analgesic and anesthetic sparing properties (Ilkiw 1999; Bettschart-Wolfensberger & Larenza 2007; Lamont 2008). However, the potential for adverse effects and species-related singularities have precluded their extensive use for PIVA in horses. Although alpha$_2$-adrenergic agonists reduce the minimum alveolar concentration (MAC) of inhalation anesthetic agents in a dose-dependent manner (Bettschart-Wolfensberger & Larenza 2007; Gozalo-Marcilla et al. 2013), the anesthetic-sparing effect of opioids in horses is unpredictable. Morphine (Steffey et al. 2003) and fentanyl (Thomasy et al. 2006; Knych et al. 2009) administered intravenously (IV) can cause either a reduction or increase in isoflurane MAC in horses, although neither was of clinical significance.

The cardiovascular effects of opioids and alpha$_2$-adrenergic agonists have been evaluated during inhalation anaesthesia in horses. No significant adverse effects were reported in halothane and sevoflurane-anesthetized horses given morphine or fentanyl (Clark et al. 2005; Ohta et al. 2010). Dexmedetomidine, however, has been reported to have a significant impact on hemodynamic variables when administered as an infusion to isoflurane-anesthetized ponies (Marcilla et al. 2010).

The potential post-anesthetic adverse effects of opioids and alpha$_2$-adrenergic agonists remain a limiting factor to their use in horses. The use of morphine during surgery was associated with an increase in the risk of colic (Senior et al. 2004), and alpha$_2$-adrenergic agonists can decrease intestinal motility (Merritt et al. 1998). Increased locomotor activity and excitement during recovery have been observed in isoflurane-anesthetized horses given fentanyl or a high dose of morphine IV (Steffey et al. 2003; Knych et al. 2009). In contrast, the quality of recovery after inhalation anaesthesia can be improved by the use of alpha$_2$-adrenergic agonists (Santos et al. 2003; Marcilla et al. 2012).

Remifentanil is an ultrashort-acting mu-opioid agonist with similar potency to fentanyl in humans (Glass et al. 1999). Its half-life in humans is 3–5 minutes, regardless of the duration of infusion (Glass et al. 1999). This unique pharmacokinetic profile is favorable for its use for PIVA in veterinary anaesthesia. Remifentanil infusions have been successfully used in dogs and cats (Ferreira et al. 2009; Monteiro et al. 2010), but reports of its use in horses are not available. The preliminary unpublished results of the pharmacokinetic study conducted in conjunction with the present study have revealed an elimination half-life of approximately 14 minutes for remifentanil in the horse. Although dexmedetomidine has been suggested to be an ideal agent for infusion in equine anaesthesia (Marcilla et al. 2012), its effects in combination with an opioid and an inhalation anesthetic agent in horses have not been documented.

The primary objective was to evaluate the cardiopulmonary effects of a dexmedetomidine infusion with or without remifentanil or morphine infusion in isoflurane-anesthetized horses, and the secondary objective was to evaluate the effects of these drug protocols on quality of recovery from anaesthesia. It was hypothesized that a combination of remifentanil and dexmedetomidine infusions would be an equally effective option for PIVA in isoflurane-anesthetized horses, when compared to infusions of dexmedetomidine alone or dexmedetomidine in combination with morphine.

## Materials and methods

Approval for the study was obtained from the University Animal Care and Use Committee. Animals were housed and fed according to the Institutional guidelines.

### Animals

Six mixed breed horses (five mares and one gelding) with body weight between 443 kg and 580 kg (507 $\pm$ 61 kg; mean $\pm$ SD), and age between 8 and 20 years (14 $\pm$ 4 years) were used for this study. The horses were deemed healthy based on physical examinations and hematological tests. The horses were kept outdoors, were fed hay, and had free access to water. They were brought indoors the day before the study and fasted for 12–16 hours prior to induction of anaesthesia. The horses were moved outdoors 48 hours after anaesthesia.

### Infusion drug regime

Each horse was anesthetized three times with a washout period of 7 days between study periods. Treatment was assigned according to a randomized crossover design, such that each horse was given all

 