RESEARCH PAPER

# Effect of detomidine or romifidine constant rate infusion on plasma lactate concentration and inhalant requirements during isoflurane anaesthesia in horses

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## Abstract

**Objective** Influence of detomidine or romifidine constant rate infusion (CRI) on plasma lactate concentration and isoflurane requirements in horses undergoing elective surgery.

**Study design** Prospective, randomised, blinded, clinical trial.

**Animals** A total of 24 adult healthy horses.

**Methods** All horses were administered intramuscular acepromazine (0.02 mg $kg^{-1}$) and either intravenous detomidine (0.02 mg $kg^{-1}$) (group D), romifidine (0.08 mg $kg^{-1}$) (group R) or xylazine (1.0 mg $kg^{-1}$) (group C) prior to anaesthesia. Group D was administered detomidine CRI (10 μg $kg^{-1}$ $hour^{-1}$) in lactated Ringer's solution (LRS), group R romifidine CRI (40 μg $kg^{-1}$ $hour^{-1}$) in LRS and group C an equivalent amount of LRS intraoperatively. Anaesthesia was induced with ketamine and diazepam and maintained with isoflurane in oxygen. Plasma lactate samples were taken prior to anaesthesia (baseline), intraoperatively (three samples at 30 minute intervals) and in recovery (at 10 minutes, once standing and 3 hours after end of anaesthesia). End-tidal isoflurane percentage (FE′Iso) was analysed by allocating values into three periods: Prep (15 minutes after the start anaesthesia–start surgery); Surgery 1 (start surgery–30 minutes later); and Surgery 2 (end Surgery 1–end anaesthesia). A linear mixed model was used to analyse the data. A value of $p < 0.05$ was considered significant.

**Results** There was a difference in plasma lactate between 'baseline' and 'once standing' in all three groups ($p < 0.01$); values did not differ significantly between groups. In groups D and R, FE′Iso decreased significantly by 18% (to 1.03%) and by 15% (to 1.07%), respectively, during Surgery 2 compared with group C (1.26%); $p < 0.006$, $p < 0.02$, respectively.

**Conclusions and clinical relevance** Intraoperative detomidine or romifidine CRI in horses did not result in a clinically significant increase in plasma lactate compared with control group. Detomidine and romifidine infusions decreased isoflurane requirements during surgery.

***Keywords*** continuous rate infusion, detomidine, horse, lactate, romifidine.

## Introduction

The incidence of death associated with equine anaesthesia is high (up to one in 100) according to the largest known multicentre studies of equine mortality (Johnston et al. 1995; Johnston et al. 2002). Equine mortality rates appear to be higher when anaesthesia is maintained with inhalant anaesthesia (0.99%) than with total intravenous (IV) anaesthesia (0.3%) (Johnston et al. 2002). We believe that the potential decreased risk associated with the use of IV agents was one of the starting points for the use of 'partial IV anaesthesia' where a combination of inhalant and IV drugs is used to provide analgesia and hypnosis with minimal associated side effects (Bettschart-Wolfensberger & Larenza 2007). Many drug

permutations are possible; one such combination includes the IV infusion of an $\alpha_2$-agonist with inhaled isoflurane.

There are numerous published studies reporting a reduction in the requirement for inhalant anaesthetics with $\alpha_2$-agonists. Most authors have found an isoflurane-sparing effect with a bolus of detomidine (Steffey & Pascoe 2002) or a constant rate infusion (CRI) of romifidine (Kuhn et al. 2004). However, Schauvliege et al. (2011) and Devisscher et al. (2010) found no such effect when detomidine and romifidine CRI were administered.

Inhalant anaesthetics and $\alpha_2$-agonists are associated with poor muscle perfusion (Edner et al. 2002; Edner et al. 2005). When poor tissue perfusion (hypoperfusion) results in tissue hypoxia, anaerobic metabolism occurs (Neil 2008). The result is the production of lactate, the ionized form of lactic acid. Lactate can be measured and quantified in plasma by taking an arterial or venous blood sample. In general veterinary practice, lactate is used as a prognostic indicator, as a marker of severe disease, and to measure the response to treatment (Corley et al. 2005; Neil 2008).

The association between the administration of an $\alpha_2$-agonist CRI and the occurrence and magnitude of hyperlactaemia during general anaesthesia is unclear. The main aim of our study was to compare plasma lactate concentration in horses during general anaesthesia with isoflurane combined with a CRI of detomidine, romifidine or lactated Ringer's solution (LRS). The secondary aim was to quantify the intraoperative isoflurane requirements.

We hypothesized that the use of an $\alpha_2$-agonist would be associated with increased plasma lactate concentration during anaesthesia and that intraoperative isoflurane requirements would be reduced by the administration of detomidine or romifidine CRI.

## Materials and methods

### Animals

A total of 24 horses undergoing general anaesthesia for elective surgical procedures with an estimated anaesthetic duration between 1 and 3 hours were recruited for the study. Inclusion criteria included: 1) horses systemically healthy prior to the study as determined by clinical history, physical examination and complete haematological and blood biochemistry profile; 2) horses designated as physical status I or II as described by the American Society of Anesthesiologists (ASA); 3) and horses aged between 1 and 15 years. Exclusion criteria included horses designated ASA status III, IV and V and horses aged $< 1$ or $> 15$ years. The temperament of the horse was scored prior to anaesthesia using a previously published scale (Leece et al. 2008). The scale ranged from 1 (calm, well handled) to 4 (unhandled, requiring sedation).

This study received ethical approval from the Animal Research Ethics Committee (University College Dublin, Ireland). Number: AREC-P-12-73- Hughes. Informed owner consent was not required by our institution or this journal at the time of this study.

### Anaesthetic protocol

Food, but not water, was withheld for 12 hours prior to anaesthesia. One 14 gauge catheter was placed aseptically in the jugular vein prior to anaesthesia. Horses were premedicated with intramuscular (IM) acepromazine (0.02 mg kg$^{-1}$; Calmivet, Vetoquinol, France) 1 hour before the induction of anaesthesia followed by IV detomidine (0.02 mg kg$^{-1}$; Domidine; Dechra Veterinary Products Ltd., UK) (group D) or romifidine (0.08 mg kg$^{-1}$; Sedivet; Boehringer Ingelheim Ltd., UK) (group R) or xylazine (1.0 mg kg$^{-1}$; Chanazine 10%; Chanelle Pharmaceuticals, Ireland) (group C). All intravenous premedication drugs were diluted to a final volume of 7 mL. After 5 minutes, anaesthesia was induced with IV ketamine (2.2 mg kg$^{-1}$; Narketan-10; Vetoquinol, Ireland) and diazepam (0.05 mg kg$^{-1}$; Diazemuls; Actavis Group PTC, Iceland). Orotracheal intubation was performed, and the horse was hoisted to a padded surgery table. If it was not possible to place the endotracheal tube and/or the horse appeared lightly anaesthetised at any stage, a supplemental injection of ketamine (0.2 mg kg$^{-1}$) and/or thiopentone (2 mg kg$^{-1}$; Penthotal Sodium; Intervet Italia, Italy) was administered IV.

Anaesthesia was maintained with isoflurane (Vetflurane; Virbac Animal Health, UK) delivered in oxygen via a circle system (Mallard Medical INC; Model 2800 C, CA, USA). The lungs of all horses were mechanically ventilated to maintain an end-tidal carbon dioxide ($P_E'CO_2$) between 4.5 and 6.0 kPa (35–45 mmHg) using a tidal volume of 10–15 mL kg$^{-1}$ body weight and peak inspiratory pressures between 20 and 30 cm $H_2O$. Ventilator settings were further adjusted based on arterial $CO_2$ values.

### Experimental protocol

Horses were randomly assigned to one of three groups with a random number generator: group D (detomidine CRI 10 μg kg$^{-1}$ hour$^{-1}$); group R (romifidine CRI

 