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RESEARCH PAPER

Clinical comparison of dexmedetomidine and medetomidine for isoflurane balanced anaesthesia in horses

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Abstract

Objective To compare the effects of two balanced anesthetic protocols (isoflurane–dexmedetomidine *versus* medetomidine) on sedation, cardiopulmonary function and recovery in horses.

Study design Prospective, blinded, randomised clinical study.

Animals Sixty healthy adult warm blood horses undergoing elective surgery.

Methods Thirty horses each were sedated with dexmedetomidine 3.5 μg kg^{-1} (group DEX) or medetomidine 7 μg kg^{-1} (group MED) intravenously. After assessing and supplementing sedation if necessary, anaesthesia was induced with ketamine/diazepam and maintained with isoflurane in oxygen/air and dexmedetomidine 1.75 μg kg^{-1} $hour^{-1}$ or medetomidine 3.5 μg kg^{-1} $hour^{-1}$. Ringer's lactate (7–10 mL kg^{-1} $hour^{-1}$) and dobutamine were administered to maintain normotension. Controlled mechanical ventilation maintained end-tidal expired carbon dioxide pressures at 40–50 mmHg (5.3–6.7 kPa). Heart rate, invasive arterial blood pressure, inspired and expired gas composition and arterial blood gases were measured. Dexmedetomidine 1 μg kg^{-1} or medetomidine 2 μg kg^{-1} was administered for timed and scored recovery phase. Data were analysed using two-way repeated-measures analysis of variance and chi-square test. Significance was considered when $p \leq 0.05$.

Results In group DEX, significantly more horses ($n = 18$) did not fulfil the sedation criteria prior to induction and received one or more supplemental doses, whereas in group MED only two horses needed one additional bolus. Median (range) total sedation doses were dexmedetomidine 4 (4–9) μg kg^{-1} or medetomidine 7 (7–9) μg kg^{-1}. During general anaesthesia, cardiopulmonary parameters did not differ significantly between groups. Recovery scores in group DEX were significantly better than in group MED.

Conclusions and clinical relevance Horses administered dexmedetomidine required more than 50% of the medetomidine dose to reach equivalent sedation. During isoflurane anaesthesia, cardiopulmonary function was comparable between the two groups. Recovery scores following dexmedetomidine were better compared to medetomidine.

Introduction

A balanced anaesthetic protocol with partial intravenous anaesthesia (PIVA) using two or more ancillary agents is a common concept in modern equine general anaesthesia (Gozalo-Marcilla et al. 2014, 2015). It allows reducing the amount of volatile agents and therefore keeps undesirable effects to a minimum. Constant rate infusions (CRIs) of different alpha$_2$-adrenergic agonists in combination with isoflurane have been used in anaesthetized horses for this purpose (Ringer et al. 2007; Devisscher et al. 2010; Schauvliege et al. 2011;

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Marcilla et al. 2012; Pöppel et al. 2015). Furthermore, the analgesic effects of these drugs can improve recovery qualities (Bettschart-Wolfensberger & Larenza 2007; Gozalo-Marcilla et al. 2015).

Medetomidine, a highly selective, short acting alpha$_2$-adrenergic agonist [selectivity ratio (α_2:α_1) 1620:1] (Virtanen et al. 1988), has been shown to reduce the minimum alveolar concentration of isoflurane and to provide rapid recoveries of good quality in ponies and horses (Bettschart-Wolfensberger et al. 2001; Ringer et al. 2007). Classic side effects of alpha$_2$-adrenergic agonists including bradycardia, arrhythmias, decreases in cardiac output and increases in systemic vascular resistance have been documented for medetomidine (Bettschart-Wolfensberger et al. 1999a; Yamashita et al. 2000; Grimsrud et al. 2012). Compared to a CRI, more prominent side effects were described following an intravenous (IV) bolus (Bettschart-Wolfensberger et al. 1999a). However, within 30 minutes, when steady-state conditions of medetomidine plasma levels were achieved (Bettschart-Wolfensberger et al. 1999b), an improvement of cardiopulmonary variables was demonstrated. Therefore, it was concluded that the infusion of 3.5 μg kg^{-1} hour^{-1} causes minimum cardiopulmonary depression, once the effects of a 5 μg kg^{-1} bolus have waned (Bettschart-Wolfensberger et al. 1999a).

A bolus of dexmedetomidine, the dextro-rotary and active enantiomer of medetomidine, showed a large volume of distribution at steady state with a rapid clearance, resulting in a shorter plasma elimination half-life than medetomidine in horses (8 minutes for dexmedetomidine 10 μg kg^{-1} *versus* 29 minutes for medetomidine 5 μg kg^{-1}; Grimsrud et al. 2012; Rezende et al. 2015). A dexmedetomidine bolus also had shorter lasting cardiopulmonary effects without a decrease in heart rate (HR) compared with medetomidine (Bettschart-Wolfensberger et al. 1999b, 2005). The use of a dexmedetomidine CRI at a rate of 1.75 μg kg^{-1} hour^{-1} in isoflurane-anaesthetized horses under clinical circumstances produced limited cardiopulmonary effects, significantly improving recovery qualities compared to isoflurane alone (Marcilla et al. 2012).

Preliminary studies in horses by Bettschart-Wolfensberger et al. (2005) showed that medetomidine 7 μg kg^{-1} had equivalent sedative effects to dexmedetomidine 3.5 μg kg^{-1}. Direct comparative clinical studies with dexmedetomidine at a 50% dose of medetomidine have been conducted in dogs (Granholm et al. 2007; Raszplewicz et al. 2013) and sheep (Kästner et al. 2001).

The main purpose of the study was to compare two different PIVA protocols (isoflurane with either dexmedetomidine or medetomidine) in horses undergoing elective surgeries to assess the effects on sedation, cardiopulmonary parameters and recovery phase. The hypothesis of our study was that the sedation doses were expected to be similarly potent, with no unexpected side effects after either dexmedetomidine or medetomidine bolus. Moreover, based on the available pharmacokinetic data and previous clinical reports, fewer and shorter lasting cardiopulmonary effects with a lower incidence of partial pressure of oxygen (PaO_2) < 80 mmHg (10.7 kPa) were hypothesized during dexmedetomidine CRI compared with medetomidine in isoflurane-anaesthetized horses. Quiet recoveries were expected with both drugs.

Material and methods

Study design and animals

This prospective randomised blinded clinical study was performed with the ethical approval of the local committee for animal experimentation (Canton of Zurich, Switzerland; number of approval 5455, 203/2014). Written owners' consent was obtained.

Sixty client-owned, non-food-producing horses of various breeds presented for elective surgeries were included in the study. Inclusion criteria were body weight (≥200 kg), age (2−20 years), physical status American Society of Anaesthesiologists 1 or 2 based on a physical examination, and procedure type (no surgery of the head region, no rope-assisted recovery required). Food, but not water, was withheld for 10−16 hours prior to anaesthesia. Each patient was randomly assigned to either group DEX (dexmedetomidine) or MED (medetomidine) at the beginning of the experiment, using previously prepared opaque envelops opened by a person who was not involved in the study. Demographic data and body condition score (BCS), adapted from Carroll & Huntington (1988), were recorded on a separate data sheet (MS). All anaesthetic procedures were performed by the same experienced anaesthetist (MS), who was unaware of the treatment at any time until the end of the study, including the recovery phase.

Study protocol

Sixty minutes prior to sedation, a jugular catheter was placed following desensitisation of the insertion

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