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RESEARCH PAPER

Minimum end-tidal sevoflurane concentration necessary to prevent movement during a constant rate infusion of morphine, or morphine plus dexmedetomidine in ponies

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Abstract

Objective To compare the effects of a constant rate infusion (CRI) of dexmedetomidine and morphine to those of morphine alone on the minimum end-tidal sevoflurane concentration necessary to prevent movement (MAC_{NM}) in ponies.

Study design Prospective, randomized, crossover, 'blinded', experimental study.

Animals Five healthy adult gelding ponies were anaesthetized twice with a 3-week washout period.

Methods After induction of anaesthesia with sevoflurane in oxygen (via nasotracheal tube), the ponies were positioned on a surgical table (T0), and anaesthesia was maintained with sevoflurane (F_E' SEVO 2.5%) in 55% oxygen. Monitoring included pulse oximetry, electrocardiography and measurement of anaesthetic gases, arterial blood pressure and body temperature. The ponies were mechanically ventilated and randomly allocated to receive IV treatment M [morphine 0.15 mg kg^{-1} (T10-T15) followed by a CRI (0.1 mg kg^{-1} $hour^{-1}$)] or treatment DM [dexmedetomidine 3.5 μg kg^{-1} plus morphine 0.15 mg kg^{-1} (T10-T15) followed by a CRI of dexmedetomidine 1.75 μg kg^{-1} $hour^{-1}$ and morphine 0.1 mg kg^{-1} $hour^{-1}$]. At T60, a stepwise MAC_{NM} determination was initiated using constant current electrical stimuli at the skin of the lateral pastern region. Triplicate MAC_{NM} estimations were obtained and then averaged in each pony. Wilcoxon signed-rank test was used to detect differences in MAC between treatments ($\alpha = 0.05$).

Results Sevoflurane-morphine MAC_{NM} values (median (range) and mean ± SD) were 2.56 (2.01–4.07) and 2.79 ± 0.73%. The addition of a continuous infusion of dexmedetomidine significantly reduced sevoflurane MAC_{NM} values to 0.89 (0.62–1.05) and 0.89 ± 0.22% (mean MAC_{NM} reduction 67 ± 11%).

Conclusion and clinical relevance Co-administration of dexmedetomidine and morphine CRIs significantly reduced the MAC_{NM} of sevoflurane compared with a CRI of morphine alone at the reported doses.

Keywords constant-rate infusion, dexmedetomidine, minimal alveolar concentration, morphine, ponies, sevoflurane.

Introduction

Morphine is a μ-opioid receptor agonist that has been used during equine anaesthesia to provide

analgesia. Its use during anaesthesia is controversial and the evidence for and against has been reviewed by Clutton (2010). Reasons against its use include the potential occurrence of dangerous behaviour, cardiopulmonary disturbances, respiratory depression (Steffey et al. 2003) and a reduction of gastrointestinal motility (Roger et al. 1985). In contrast to experimental work, clinical studies reported minimal haemodynamic and ventilatory changes (Mircica et al. 2003; Clark et al. 2005), improvement of the recovery qualities (Mircica et al. 2003; Love et al. 2006; Clark et al. 2008) and no increased incidence of post surgical colic (Mircica et al. 2003).

With regard to the effects of morphine on anaesthetic agent requirements, horses undergoing elective surgical procedures receiving a morphine constant-rate infusion (CRI) tended to receive fewer and lower doses of additional anaesthetic drugs (Clark et al. 2005). In contrast, IV boluses of morphine at two different doses increased, decreased or did not change the minimum alveolar concentration (MAC) of isoflurane in anaesthetized horses (Steffey et al. 2003). However, the influence of a CRI of morphine on the MAC of volatile agents has not been reported in horses.

Alpha-2 agonists often are combined with low (subanalgesic) doses opioids in standing horses and their combination appear to be 'synergistic', resulting in reliable sedation and stable cardiorespiratory function (Solano et al. 2009; Clarke et al. 2014). During anaesthesia, alpha-2 agonists reduce the MAC of the volatile agent. However, the concurrent IV bolus administration of two doses of morphine failed to further reduce the MAC of halothane compared to xylazine alone in adult horses (Bennett et al. 2004). An IV dexmedetomidine CRI decreased the mean ± SD MAC of sevoflurane in ponies from 2.42 ± 0.55 to 1.07 ± 0.21% (Gozalo-Marcilla et al. 2013) but, to date, the effect on MAC of adding a dexmedetomidine CRI to a morphine infusion has not been studied.

Traditionally, the concept of the MAC is defined as the alveolar concentration of volatile anaesthetic agent at which 50% of the patients do not respond with purposeful movement to a supramaximal noxious stimulus (Merkel & Eger 1963). Differentiation between purposeful *versus* nonpurposeful movement is sometimes difficult and subjective. Derivatives of the traditional MAC such as the minimum end-tidal concentration of sevoflurane necessary to prevent movement (MAC_{NM}), therefore have been described in the literature. From a clinical standpoint, MAC_{NM} may be more relevant than the traditional MAC (Seddighi et al. 2011, 2012).

The main objectives of this study were to determine and compare the MAC_{NM} values of sevoflurane in experimental ponies receiving a CRI of morphine alone or combined with dexmedetomidine.

Materials and methods

This study was approved by the Ethical Committee of the Faculty of Veterinary Medicine of the University of Ghent (2011/168).

Animals and instrumentation

Five healthy gelding ponies, aged 13 ± 3 years, weighing 294 ± 57 kg with body condition scores of 4 out of 5 (Carroll & Huntington 1988) were included in this trial.

Food, but not water, was withheld for 12 hours. Induction and maintenance of anaesthesia, fluid therapy and monitoring were as described by Gozalo-Marcilla et al. (2013). Briefly, anaesthesia was induced in the recovery box with sevoflurane (Sevorane, Abbott, Belgium) in oxygen via a nasotracheal tube with inflated cuff. After induction, the ponies were positioned on a surgical table in right lateral recumbency. General anaesthesia was maintained with sevoflurane in oxygen/air [inspired oxygen fraction (FiO_2) of 55%] via the nasotracheal tube. The ponies were mechanically ventilated [intermittent positive pressure ventilation (IPPV) with tidal volume of 10 mL kg^{-1} and positive end-expiratory pressure (PEEP) of 0.49 kPa (3.7 mmHg)] to maintain the arterial partial pressure of carbon dioxide ($PaCO_2$) between 6.67 and 8.00 kPa (50–60 mmHg). Lactated Ringer's solution (Hemofiltratie BH 504, Dirinco, The Netherlands) was infused IV (3 mL kg^{-1} $hour^{-1}$) and a urinary catheter was placed.

Monitoring included electrocardiography, pulse oximetry, anaesthetic gas monitoring, invasive (transposed carotid artery) and non-invasive (right metacarpal artery) blood pressure and body temperature by a nasal probe. The multiparameter monitoring device (S/5 D-LCC15-03, Datex Ohmeda, OR, USA) was calibrated before every procedure (QUICK CAL Calibration gas, GE Healthcare Finland Oy, Finland) and the pressure transducers were zeroed to atmospheric pressure and placed at the level of the right atrium. Arterial blood samples were withdrawn for immediate blood gas analysis [pH,