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RESEARCH PAPER

Cardiopulmonary effects and anaesthesia recovery quality in horses anaesthetized with isoflurane and low-dose S-ketamine or medetomidine infusions

M Paula Larenza Menzies*, Simone K Ringer*, Aude Conrot*, Regula Theurillat†, Katharina Kluge*, Annette PN Kutter*, Michelle Jackson‡, Wolfgang Thormann† & Regula Bettschart-Wolfensberger*

*Section of Anaesthesiology, Equine Department, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland

†Clinical Pharmacology Laboratory, Institute for Infectious Diseases, University of Berne, Berne, Switzerland

‡Clinic for Equine Surgery, Equine Department, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland

Correspondence: Regula Bettschart-Wolfensberger, Section of Anaesthesiology, Equine Department, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 260, 8057 Zurich, Switzerland. E-mail: regula.bettschart-wolfensberger@uzh.ch

Abstract

Objectives To evaluate cardiopulmonary effects and anaesthesia recovery quality in horses anaesthetized with isoflurane receiving medetomidine or S-ketamine infusions.

Study design Randomized, blinded, prospective clinical trial.

Animals Fifty horses undergoing elective surgery.

Methods After acepromazine and flunixin meglumine premedication, horses received medetomidine (7 μg kg^{-1}) intravenously (IV). Anaesthesia was induced with midazolam and racemic ketamine (Med treatment group; 2.2 mg kg^{-1}; $n = 25$) or S-ketamine (S-ket treatment group; 1.1 mg kg^{-1}; $n = 25$) IV and maintained with isoflurane in oxygen/air and medetomidine (Med; 3.5 μg kg^{-1} $hour^{-1}$) or S-ketamine (S-ket; 0.5 mg kg^{-1} $hour^{-1}$). All horses were mechanically ventilated. Cardiopulmonary variables were evaluated. Isoflurane end-tidal concentrations (F_E'Iso), dobutamine requirements and thiopental boli were recorded. Plasma samples were collected in six horses to evaluate S-ketamine and S-norketamine concentrations. After surgery, medetomidine 2 μg kg^{-1} was administered IV. Four independent observers scored recovery using a visual analogue scale and a numerical rating scale.

Results Both groups required similar mean F_E'Iso (1%). However, S-ket horses needed more thiopental boli. Median intraoperative cardiac index values were higher with S-ket (4.5 L $minute^{-1}$ m^{-2}) than Med (3.9 L $minute^{-1}$ m^{-2}). Overall, there were no differences in heart rate, blood pressure or dobutamine requirements; however, horses in S-ket showed higher heart rate values at 30 minutes after anaesthesia induction. Compared with Med horses, S-ket horses showed decreased PaO_2 and increased pulmonary venous admixture values estimated with the *F*shunt calculation. Recoveries were shorter and of poorer quality with S-ket. During infusion, S-ketamine and S-norketamine plasma concentrations lay in the ranges of 0.209–0.917 μg mL^{-1} and 0.250–0.723 μg mL^{-1}, respectively.

Conclusions and clinical relevance Despite the higher intraoperative cardiac index with S-ket, both protocols were considered to provide acceptable cardiovascular function. However, recovery quality was significantly better in the Med group.

Keywords anaesthesia, horse, isoflurane, medetomidine, S-ketamine, S-norketamine.

Introduction

Horses are among the species in which high numbers of perianaesthetic fatalities occur, mainly as a result of cardiovascular problems and complications during recovery (Johnston et al. 2002; Bettschart-Wolfensberger & Larenza 2007). Therefore, the selection of anaesthetic agents in equine anaesthesia often aims to preserve intraoperative cardiovascular function and to induce quiet recoveries.

The addition of racemic ketamine to volatile anaesthetics reduces the concentrations of volatile agents required to maintain anaesthesia, minimizing their depressive effects on the cardiovascular system (Muir & Sams 1992). However, racemic ketamine may induce violent emergence reactions during the anaesthetic recovery period if it is infused for more than 1 hour, probably as a result of the cumulative effects of the parent compound and their metabolites (Bettschart-Wolfensberger et al. 1996). A previous study demonstrated that the elimination of S-ketamine, the more potent isomer of the racemic mixture, is faster when it is administered as the single enantiomer (Larenza et al. 2008). Similarly, S-ketamine administered as a constant rate infusion (CRI) proved to be advantageous over a racemic ketamine CRI on the basis of better recovery qualities in horses undergoing surgery (Larenza et al. 2009a). Although there are some reports on the cardiopulmonary effects of S-ketamine in horses (Larenza et al. 2007, 2008, 2009a), most such studies were performed in small populations of clinical or research horses and important information such as the cardiac index (CI) is missing.

Therefore, the present study aimed to evaluate the quality of recovery from anaesthesia and the cardiovascular effects of a CRI of S-ketamine in a clinical population of horses anaesthetized with isoflurane. For comparison, a second group of horses were anaesthetized with a similar balanced anaesthetic technique using a CRI of the α_2-adrenoreceptor agonist medetomidine instead of S-ketamine. Medetomidine was chosen as the comparison drug because it has been shown to provide smooth recoveries in horses (Ringer et al. 2007; Kalchofner et al. 2009).

Materials and methods

Animals and study design

The present study was performed as a randomized, blinded, prospective clinical trial according to the VICH (International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products) Guidelines on Good Clinical Practice. The study was approved by the animal experimentation commission of the canton of Zurich (no.158/2006) and signed owner consents were obtained. A total of 50 client-owned horses undergoing elective surgical procedures were recruited. This number of horses was chosen based on previous experiments using a similar study design, which indicated that significant changes in recovery could be detected using groups of 10–25 animals (Larenza et al. 2007; Ringer et al. 2007). Horses were considered sufficiently healthy to undergo anaesthesia based on physical examination and haematocrit/plasma total protein analysis. Emergency patients (i.e. horses with colic), pregnant mares, horses with systemic diseases or pathological cardiovascular or haemodynamic disorders and horses that required intramuscular (IM) sedation or assisted recovery were excluded from the study. Included animals were randomly allocated into either of two groups, the S-ketamine treatment group (S-ket; $n = 25$) and the medetomidine treatment group (Med; $n = 25$), using the envelope system. Food was withheld for 8–16 hours before surgery. Free access to water was provided until 30 minutes prior to anaesthesia induction. All anaesthetic administrations were performed by the same anaesthetist (MPLM), who was unaware of treatment allocation.

Anaesthesia premedication and induction

Prior to surgery, the skin area over a jugular vein was clipped, scrubbed and a 14 gauge, 16 mm over-the-needle catheter (Secalon T with FloSwitch; Becton Dickinson Critical Care Systems, Switzerland) was introduced percutaneously after the skin had been desensitized with 2 mL of mepivacaine 2% (Mepivacaine 2%; Streuli Pharma AG, Switzerland). A venous blood sample was collected and values for haemoglobin and plasma Na^+ were obtained. At 30–60 minutes before anaesthesia induction, patients in both groups received 35,000 IU kg^{-1} of penicillin Na^+ (Penicilline Natrium Streuli 10 Mio UI; G Streuli & Co AG, Switzerland), 7 mg kg^{-1} of gentamicin (Vetagent Injektionslösung; Veterinaria AG, Switzerland) and 1 mg kg^{-1} of flunixin meglumine (Fluniximin; Dr E Graeub AG, Switzerland) intravenously (IV) and 0.03 mg kg^{-1} of acepromazine (Prequillan; Arovet AG, Switzerland) IM.

