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RESEARCH PAPER

Influence of ketamine or xylazine supplementation on isoflurane anaesthetized horses- a controlled clinical trial

Nina Pöppel*, Klaus Hopster*, Florian Geburek* & Sabine Kästner*,†

*Equine Clinic, University of Veterinary Medicine Hanover, Foundation, Hanover, Germany

†Center for Systems Neuroscience Hanover, University of Veterinary Medicine Hanover, Hanover, Germany

Correspondence: Klaus Hopster, Equine Clinic, University of Veterinary Medicine Hanover, Foundation, Bünteweg 9, 30559 Hanover, Germany. Email: klaus.hopster@tiho-hannover.de

Abstract

Objectives To determine the influence of ketamine or xylazine constant rate infusions on isoflurane requirements, cardiovascular parameters and quality of anaesthesia in horses undergoing elective surgery.

Study design Prospective, matched paired clinical trial.

Animals Fifty four adult Warmblood horses.

Methods After premedication with acepromazine, xylazine and butorphanol, anaesthesia was induced with ketamine-midazolam and maintained with isoflurane alone (I), isoflurane with either 1 mg kg^{-1} $hour^{-1}$ ketamine (IK) or same dose of xylazine (IX). End tidal concentration of isoflurane ($F_E'Iso$) was adjusted by the same anaesthetist in all horses according to a scoring system. Dobutamine was infused to maintain mean arterial pressure (MAP) ≥70 mmHg. Arterial blood gases, heart rate (HR), respiratory rate, MAP and cardiac output (lithium dilution) were measured. Groups I and IK received xylazine before recovery. Recovery quality was scored.

Results Mean ± SD averaged $F_E'Iso$ (volume%) was significantly lower in IX (0.95 ± 0.07) and IK (0.97 ± 0.08) than in I (1.16 ± 0.13). In group IX, HR was significantly lower and averaged MAP (90 ± 13 mmHg) significantly higher than in groups I (71 ± 7 mmHg) and IK (76 ± 7 mm Hg). Differences in other cardiopulmonary variables did not reach statistical significance. All horses recovered well with best score in group IX.

Conclusions Both CRIs of xylazine and of ketamine resulted in pronounced reduction of isoflurane requirements and blood pressure support based on routinely monitored parameters. Cardiac output appeared well maintained in all three protocols, but lithium dilution induced errors mean the results are untrustworthy. The work requires repetition with another mode of measurement of cardiac output.

Clinical relevance All three protocols provided good clinical anaesthesia with clinically acceptable cardiovascular effects.

Keywords balanced anaesthesia, constant rate infusion, equine, ketamine, xylazine.

Introduction

Anaesthesia in horses carries a much higher risk of mortality than in humans and small animals (Johnston et al. 2002; Bidwell et al. 2007; Brodbelt 2009;). In Johnston et al. (2002)'s survey, 30.4% of deaths occurred in the recovery period, mainly due to fractures, and to myopathies. A major risk factor for post-anaesthetic myopathy is reduced muscle perfusion during anaesthesia (Weaver et al. 1984; Lindsay et al. 1989), which is closely related to mean arterial blood pressure (MAP) and cardiac output($\dot{Q}t$) (Richey et al. 1990; Lee et al. 1998; Edner et al. 2002). Therefore, to reduce periopera-

tive morbidity and mortality in horses it is crucial to maintain cardiovascular function during general anaesthesia.

Inhalational agents such as isoflurane, allow easy control of anaesthetic depth and fast recovery (Steffey et al. 1977), but they are accompanied by dose-related cardiovascular depression affecting $\dot{Q}t$, blood pressures and muscle perfusion (Steffey & Howland 1978, 1980). Ideally concentrations of inhalation anaesthetics should be kept as low as possible, and reduction of minimal alveolar concentration (MAC) can be achieved by additional administration of sedatives and/or analgesics during inhalation anaesthesia (Bettschart-Wolfensberger & Larenza 2007). However, this does not necessarily mean that overall cardiovascular performance is improved compared to isoflurane alone.

Ketamine is a dissociative anaesthetic agent with analgesic, anaesthetic and central sympathomimetic properties (Muir 2010), usually resulting in an increase of heart rate (HR), MAP and $\dot{Q}t$ in a plasma concentration-related way (Muir et al. 1977; Muir & Sams 1992). It is also known to reduce the MAC of inhalation agents in horses (Muir & Sams 1992). However, ketamine and its metabolites accumulate with time (Lankveld et al. 2006) leading to a prolonged elimination time and to effects such as muscle tremor and rigidity, excitation and ataxia during recovery.

Xylazine is an alpha-2 adrenoreceptor agonist with sedative, analgesic and muscle relaxant effects (Daunt & Steffey 2002). Xylazine's potential to reduce the MAC of inhalation agents has been demonstrated in horses (Steffey et al. 2000), but xylazine produces bradycardia and blood pressure changes in horses (Kerr et al. 1972; Wagner et al. 1992; England & Clarke 1996), and therefore the cardiopulmonary effects might be additive to those of the inhalation anaesthesia when the two agents are given in combination (Teixeira Neto et al. 2004).

The aim of this study was to compare the influence of ketamine or xylazine constant rate infusion (CRI) on cardiopulmonary function, anaesthetic requirements and recovery in horses in which anaesthesia was maintained by isoflurane in a controlled clinical trial.

Materials and methods

Animals

Fifty-four client-owned horses of various ages (1–19 years), breeds (49 Warmbloods, two Friesian, two German Riding Ponies and one Polo Pony) and a minimum body weight of 300 kg scheduled for elective surgery with an anticipated anaesthetic duration between 90 and 180 minutes were selected for the study. The horses were determined to be healthy based on clinical examination before inclusion into this study. Surgeries where the eyes were covered were excluded. The experimental protocol was approved by the State Office for Consumer Protection and Food Safety in accordance to the German Animal Welfare Law. Informed consent by the owners was obtained for inclusion of their animals in the study.

Anaesthetic protocol and instrumentation

The horses were assigned to one of three treatment groups, by the method of matched pairs according to type of surgery and positioning: isoflurane alone (I), isoflurane in combination with a CRI of either ketamine (IK) or xylazine (IX). This method of assignment meant, for example that the first horse for arthroscopy in lateral recumbency was allocated to randomly group IK, then next horse with arthroscopy in lateral recumbency allocated to group I or IX and the third horse with same recumbency and comparable surgery to the remaining group. Food was withheld for at least six hours, but horses had free access to water. A catheter was placed into a jugular vein (EquiCath Fastflow; Braun Vet Care; Germany) under local anaesthesia (mepivacaine; Scandicain; AstraZeneca; Germany). Thirty minutes before induction of anaesthesia all horses were premedicated with acepromazine (Vetranquil; Albrecht; Germany) (0.03 mg kg^{-1} intramuscularly), flunixin meglumine (Flunidol; CP-Pharma; Germany) (1.1 mg kg^{-1} intravenously (IV)) and antimicrobial agents depending on the surgical case.

Horses were sedated with xylazine (Xylazin 2%; CP-Pharma; Germany) (0.5 mg kg^{-1}) and butorphanol (Alvegesic; CP-Pharma; Germany) (0.025 mg kg^{-1}) IV. If sedation was inadequate additional boli of 0.15 mg kg^{-1} xylazine were given to effect and the final dose recorded. Anaesthesia was induced IV with ketamine (Narketan; Vetoquinol) and midazolam (Midazolam-ratiopharm; Ratiopharm; Germany) at a dose of 2.2 mg kg^{-1} and 0.06 mg kg^{-1} respectively. Once the horse was laterally recumbent, the trachea was intubated, the horse hoisted onto the operating table and positioned in lateral or dorsal recumbency.

