Veterinary
Anaesthesia and Analgesia
Formerly the Journal of Veterinary Anaesthesia

Veterinary Anaesthesia and Analgesia, 2014, **41**, 365–371 doi:10.1111/vaa.12128

RESEARCH PAPER

Antinociceptive and selected physiological effects of morphine and xylazine on tiletamine-zolazepam anesthesia in llamas

Reza Seddighi*, Sarah B Elliot†, Brian K Whitlock*, Christine M Egger‡ & Thomas J Doherty*

*Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Tennessee, Knoxville, TN, USA

†Department of Biomedical and Diagnostic Sciences, College of Veterinary Medicine, University of Tennessee, Knoxville, TN, USA

‡Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Tennessee, Knoxville, TN, USA

Correspondence: Reza Seddighi, Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Tennessee, 2407 River Dr., C247 Veterinary Medicine Building, Knoxville, TN 37996, USA. E-mail: mrsed@utk.edu

Abstract

Objective Evaluate antinociception, anesthesia, and recovery in llamas given tiletamine-zolazepam (TZ) with either morphine, xylazine, morphine and xylazine, or saline.

Study design Randomized crossover experimental study.

Animals Six healthy, adult intact male llamas.

Methods Llamas were given each of four treatments intramuscularly with a 1-week washout: TZ (2 mg kg^{-1}) combined with either morphine (0.5 mg kg^{-1}; M), xylazine (0.15 mg kg^{-1}; X), morphine (0.5 mg kg^{-1}) and xylazine (0.15 mg kg^{-1}) (MX), or saline (C). Llamas breathed room air during the experiment. Characteristics of anesthesia, recovery, and selected cardiopulmonary variables were recorded. Antinociception was assessed by clamping a claw at 5-minute intervals. Data were analyzed using a mixed-model ANOVA and Tukey-Kramer test, and are expressed as least squares mean ± SEM. Significance was set at $p < 0.05$.

Results No llama in the control group demonstrated antinociception. Antinociception was longest with treatment MX, followed by treatments X and M, respectively. Heart rates in llamas given treatments X and MX were significantly lower than with other treatments. The respiratory rate in llamas given treatment C was greater ($p < 0.05$) than for all other treatments, however, the respiratory rate was not significantly different among treatments X, M and MX. The PaO_2 for llamas given MX remained <60 mmHg throughout the 20 minute period of blood gas analysis. Mean arterial blood pressure in llamas in treatment MX was less than for treatments M or C.

Conclusion and clinical relevance The combination of morphine (0.5 mg kg^{-1}) and xylazine (0.15 mg kg^{-1}) increased the duration of antinociception compared with xylazine alone, in TZ-anesthetized llamas. Treatments X, M and MX were associated with hypoxemia (PaO_2 < 60 mmHg).

Keywords antinociception, llama, morphine, tiletamine-zolazepam, xylazine.

Introduction

Llamas (*Lama glama*) frequently undergo general anesthesia for a variety of surgical procedures. Due to difficulties of venipuncture in llamas, intramuscular (IM) drug protocols are more

practical than intravenous (IV) protocols for inducing anesthesia of short duration or under field conditions. Combinations of xylazine and ketamine are commonly used to induce anesthesia in llamas, but these combinations are short-acting (DuBois et al. 2004). In a previous study, xylazine combined with tiletamine-zolazepam (TZ) increased the duration of antinociception in a dose-dependent manner, however, hypoxemia occurred when greater doses of xylazine were used (Seddighi et al. 2013).

Morphine, a μ opioid agonist, is used as an analgesic in ruminants (Carroll & Hartsfield 1996; Greene 2003) and morphine induced antinociception and sedation in awake llamas (Uhrig et al. 2007). Morphine did not increase the duration of antinociception in llamas anesthetized with xylazine and ketamine (Queiroz-Castro et al. 2006), however, morphine decreased the MAC (minimum alveolar concentration) of isoflurane in goats (Doherty et al. 2004).

The aim of this study was to determine the antinociceptive and selected clinical effects of morphine alone and in combination with xylazine, in TZ-anesthetized llamas. It was hypothesized that co-administration of either xylazine or morphine would increase the duration of antinociception of TZ, and that the combination of morphine and xylazine with TZ would increase the duration of antinociception over either drug alone.

Materials and methods

Animals

Six adult, intact male llamas (113 ± 30 kg) were used in the study. The llamas were determined to be in good health on the basis of history and physical examination. Llamas were dewormed and vaccinated, and were acclimated to their new premises for 14 days prior to study commencement. The study was approved by the Institutional Animal Care and Use Committee (Protocol No. 1980-1210), and was in accordance with institutional guidelines for humane animal treatment.

Experimental design

Each llama was studied on four occasions, using a randomized crossover design (SAS, version 9.1; SAS Institute, NC, USA), with a minimum of 7 days between experiments.

Anesthesia

The experiment was performed in a laboratory with a barometric pressure of approximately 740 mmHg. Prior to each experiment, food was withheld for 18 hours and water was withheld for 12 hours. Each llama was brought into a quiet room approximately 1 hour before the start of the experiment. The treatments consisted of TZ injectable formulation (2 mg kg^{-1}; Telazol; Zoetis, NJ, USA) with either morphine (0.5 mg kg^{-1}; Baxter Healthcare Corporation, IL, USA) (M), xylazine (0.15 mg kg^{-1}; 100 mg mL^{-1}; AnaSed; Alkorn, IL, USA) (X), morphine (0.5 mg kg^{-1}) combined with xylazine (0.15 mg kg^{-1}) (MX), or a saline control (C). The individual drug doses were combined, and the injectate volume was made up to 6 mL by addition of normal saline solution. Drugs were injected into a semitendinosus or semimembranosus muscle. When the llama assumed sternal recumbency with its neck resting on the floor, it was rolled into left lateral recumbency on a padded surface.

Monitoring and data collection

Recording of selected cardiopulmonary data began after the llama was rolled into lateral recumbency, and was continued until the recording of the variables was no longer tolerated by the animal. Heart rate (HR) was monitored continuously with base-apex electrocardiograph leads (1100 Patient Monitor; Criticare Systems, WI, USA). Systolic (SAP), diastolic (DAP), and mean (MAP) arterial blood pressures were measured with an oscillometric device (Dinamap Veterinary Blood Pressure Monitor 8300; Critikon, FL, USA), and recorded at 5-minute intervals. A pressure cuff of appropriate size (a cuff width of approximately 40% of limb circumference–neonatal No. 4 or 5) was placed over the metacarpal artery of the nondependent thoracic limb, and the limb was positioned with the cuff approximately at the level of the base of the heart. Respiratory rate (f_R) was assessed every 5 minutes on the basis of the number of observed thoracic excursions during a 1-minute period. Rectal temperature was measured with a temperature probe (1100 Patient Monitor; Criticare Systems). Cardiopulmonary data were collected immediately prior to delivery of the noxious stimulus.

A sample of arterial blood (1 mL) for blood-gas analysis was collected percutaneously from a femoral artery at 5, 10, 15, and 20 minutes after