Veterinary
Anaesthesia and Analgesia
Formerly the Journal of Veterinary Anaesthesia

Veterinary Anaesthesia and Analgesia, 2016 doi:10.1111/vaa.12394

RESEARCH PAPER

Comparison of medetomidine–morphine and medetomidine–methadone for sedation, isoflurane requirement and postoperative analgesia in dogs undergoing laparoscopy

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Abstract

Objective To compare the effects of intravenous (IV) medetomidine–morphine and medetomidine–methadone on preoperative sedation, isoflurane requirements and postoperative analgesia in dogs undergoing laparoscopic surgery.

Study design Randomized, crossover trial.

Animals Twelve adult Beagle dogs weighing 15.1 ± 4.1 kg.

Methods Dogs were administered medetomidine (2.5 μg kg^{-1}) IV 5 minutes before either methadone (MET) or morphine (MOR) (0.3 mg kg^{-1}) IV. Anaesthesia was induced with propofol, maintained with isoflurane in oxygen, and depth was clinically assessed and adjusted by an anaesthetist blinded to the treatment. Animals underwent laparoscopic abdominal biopsies. Sedation and nausea scores, pulse rate (PR), respiratory rate (f_R), noninvasive systolic arterial blood pressure (SAP), rectal temperature (RT) and pain scores were recorded before drug administration, 5 minutes after medetomidine injection and 10 minutes after opioid administration. Propofol dose, PR, f_R, SAP, oesophageal temperature (T_{OES}), end-tidal carbon dioxide and end-tidal isoflurane concentration (F_E'Iso) were recorded intraoperatively. Pain scores, PR, f_R, SAP and RT were recorded 10 minutes after extubation, every hour for 6 hours, then at 8, 18 and 24 hours. The experiment was repeated with the other drug 1 month later.

Results Nine dogs completed the study. After opioid administration and intraoperatively, PR, but not SAP, was significantly lower in MET. F_E'Iso was significantly lower in MET. Temperature decreased in both treatments. Pain scores were significantly higher in MOR at 3 hours after extubation, but not at other time points. Two dogs required rescue analgesia; one with both treatments and one in MOR.

Conclusion and clinical relevance At the dose used, sedation produced by both drugs when combined with medetomidine was equivalent, while volatile anaesthetic requirements and PR perioperatively were lower with methadone. Postoperative analgesia was deemed to be adequate for laparoscopy with either protocol, although methadone provided better analgesia 3 hours after surgery.

Keywords anaesthesia, dogs, laparoscopy, methadone, morphine.

Introduction

Opioids are commonly used in the clinical management of acute pain in veterinary patients. Their analgesic effects are mainly attributed to the stimulation of μ- and κ-opioid receptors located in the brain and in the dorsal horn of the spinal cord (Wagner 2002). Morphine is the μ-agonist that other opioids are compared with (KuKanich et al. 2005). It is a well known and less expensive drug with relatively few side effects when administered at clinical dosages (KuKanich & Wiese 2015). Its effects are species-specific, dose-dependent and depressant of the central nervous system in dogs. Methadone is a synthetic full μ-agonist. Its analgesic potency and pharmacokinetics are similar to those of morphine, but, in addition, methadone has antagonistic activity on *N*-methyl-D-aspartate (NMDA) receptors and inhibitory effects on the reuptake of noradrenaline and serotonin (KuKanich & Papich 2009; KuKanich & Wiese 2015). Methadone administration has been reported to produce mild sedation in dogs (Monteiro et al. 2008).

Theoretical advantages offered by methadone over morphine include an affinity for NMDA receptors and the fact that it does not induce emesis in dogs (Blancquaert et al. 1986). There are marketing authorizations in multiple European countries for veterinary use of methadone in dogs and cats. There is evidence that methadone is more potent than morphine in the mouse and rat (Peckham & Traynor 2006; Miranda et al. 2014). Recent studies suggest that greater sedation and isoflurane-sparing effects are achieved when acepromazine is combined with methadone than when it is combined with morphine (Monteiro et al. 2009, 2016). This finding and the various mechanisms of action of methadone raise doubts about the supposed equivalence of methadone and morphine for analgesia.

The purpose of the present study was to compare, in a clinical setting, the effects of IV medetomidine–morphine and IV medetomidine–methadone when used as premedication in dogs undergoing laparoscopic surgery. Our hypothesis was that both drug combinations would result in a similar degree of sedation, and similar isoflurane requirement and perioperative analgesic effects.

Materials and methods

The experimental protocol received approval from the local ethical committee of ONIRIS, Ecole Nationale Vétérinaire, Agroalimentaire et de l'Alimentation, Nantes Atlantique, France.

Animals

In all, 12 adult research Beagle dogs (eight males, four females), aged 4–6 years and weighing [mean ± standard deviation (SD)] 15.1 ± 4.1 kg, were included in this study. As part of a larger research protocol, the dogs were anaesthetized twice, with a 4 week interval, to facilitate laparoscopy for liver and abdominal fat biopsies. The dogs were judged to be healthy (American Society of Anesthesiologists physical status classification 1 or 2) on the basis of a complete physical examination and minimal blood analysis (packed cell volume and total solids).

Study design

This study was a randomized, blinded, crossover trial. For the first stage, dogs were randomly allocated into two treatments, medetomidine–morphine (MOR) or medetomidine–methadone (MET), using the online program at www.randomization.com. Surgery was repeated 4 weeks later using the other treatment.

Animal preparation

Animals were weighed the day before anaesthesia. Syringes containing the opioid treatments (premedication and rescue analgesia) were prepared and labelled for each animal by one anaesthetist not involved in the clinical management of the dogs. Methadone (10 mg mL^{-1}; Comfortan; Sogeval, France) and morphine (10 mg mL^{-1}; Morphine chlorhydrate 1%; Cooper, France) were administered at the same dosage (0.3 mg kg^{-1}).

Food was withheld from the night before the procedure and water from the time of premedication. A 20 gauge intravenous (IV) catheter was inserted into one cephalic vein before any treatment. Once the IV catheter had been placed, the dogs were left undisturbed in a quiet area for at least 15 minutes before the start of experiment.

Sedation and nausea scores of the unrestrained and undisturbed dogs were obtained before

