Veterinary
Anaesthesia and Analgesia
Formerly the Journal of Veterinary Anaesthesia

Veterinary Anaesthesia and Analgesia, 2011, **38,** 310–319 doi:10.1111/j.1467-2995.2011.00618.x

RESEARCH PAPER

Determination of the sevoflurane sparing effect of methadone in cats

Tatiana H. Ferreira*, Eugene P Steffey†, Khursheed R. Mama†, Marlis L Rezende† & Antonio JA Aguiar‡
*Department of Anesthesiology, Botucatu Medical School, São Paulo State University – UNESP, Botucatu, SP, Brazil
†Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO, USA
‡Department of Veterinary Surgery and Anesthesiology, School of Veterinary Medicine and Animal Science, São Paulo State University – UNESP, Botucatu, SP, Brazil

Correspondence: Khursheed R. Mama, Department of Clinical Sciences, Colorado State University, Fort Collins, CO 80523, USA.
E-mail: kmama@colostate.edu

Abstract

Objective To determine the magnitude and duration of sevoflurane minimum alveolar concentration (MAC) reduction following a single intravenous (IV) dose of methadone in cats.

Study design Prospective experimental study.

Animals Eight (four females and four males) healthy mixed-breed adult (1–2 years) cats weighing 5.82 ± 0.42 kg.

Methods Anesthesia was induced and maintained with sevoflurane. Intravenous catheters facilitated administration of methadone and lactated Ringer's solution. After baseline MAC determination in triplicate using a tail clamp technique, 0.3 mg kg^{-1} of methadone was administered IV. End-tidal sevoflurane concentration (E′SEVO) was reduced and MAC was redetermined. In an effort to determine the duration of MAC reduction, measurements were repeated in a stepwise manner until MAC values returned to baseline. After the last stimulation, the E′SEVO was increased to 1.2 individual MAC for 15 minutes, then sevoflurane was discontinued and cats were allowed to recover from anesthesia.

Results Baseline sevoflurane MAC was 3.18 ± 0.06%. When compared with baseline the sevoflurane MAC after methadone administration was significantly reduced by 25, 15 and 7% at 26, 76 and 122 minutes, respectively. The final MAC value (3.09 ± 0.07%) determined 156 minutes after methadone administration was not significantly different from baseline.

Conclusions and clinical relevance Intravenous methadone (0.3 mg kg^{-1}) significantly decreased MAC of sevoflurane in cats but the effect was short-lived.

Keywords cat, methadone, minimum alveolar concentration, sevoflurane.

Introduction

Methadone is a synthetic opioid whose chemical structure is unrelated to any of the opium-derivative alkaloids (Fishman et al. 2002). This drug is an agonist at MOP (μ) opioid receptors and antagonist at N-methyl-D-aspartate (NMDA) receptors (Gorman et al. 1997). It also inhibits the reuptake of serotonin and norepinephrine (Codd et al. 1995; Gorman et al. 1997; Fishman et al. 2002) and promotes the blockade of nicotinic cholinergic receptors (Xiao et al. 2001). The use of methadone in cats may present an advantage over other opioids as it does not undergo glucuronidation and so is less likely to accumulate (Court & Greenblatt 2000).

Sevoflurane is among the newer inhalational anesthetics available for use in veterinary clinical practice. One of its advantages is its low blood:gas partition coefficient which facilitates rapid changes in anesthetic depth and a rapid recovery. Although it is reported to be a safe and effective anesthetic in healthy cats (Hikasa et al. 1996), sevoflurane is also reported to cause dose-dependent cardiovascular depression in this species (Pypendop & Ilkiw 2004). Hence in cats, as with other species, opioids are often administered in combination with inhalational anesthetics to facilitate a reduction in dose and improve hemodynamic stability (Ilkiw 1999).

Minimum alveolar concentration (MAC), the index of potency of inhalant anesthetics, represents the end-tidal partial pressure of the anesthetic (expressed as a percent) required to prevent movement in 50% of individuals exposed to a supramaximal noxious stimulus (Quasha et al. 1980). In animal studies the MAC is usually determined in each individual as the average of the highest concentration that allows movement and the lowest concentration that prevents it in response to the supramaximal noxious stimulus. The sparing effect of opioids on MAC has been described in a wide range of species (Hall et al. 1987; Steffey et al. 1994, 2003; Criado & Segura 2003; Credie et al. 2010). In cats, remifentanil, alfentanil, fentanyl, morphine, buprenorphine, and butorphanol decrease the MAC of isoflurane (Ilkiw et al. 1997, 2002; Yackey et al. 2004; Ferreira et al. 2009) and hydromorphone, tramadol and butorphanol decrease the MAC of sevoflurane (Ko et al. 2008). To the authors' knowledge, there are no studies evaluating the effects of methadone on the MAC of inhalational anesthetics in cats. As observed with other opioids in this species, we hypothesized that methadone would significantly decrease sevoflurane MAC in cats.

The reported dose range for methadone is variable. Racemic methadone has been administered to cats in doses ranging from 0.1 to 0.6 mg kg^{-1} (Dobromylskyj 1993; Rohrer Bley et al. 2004; Steagall et al. 2006). We elected to use a dose of 0.3 mg kg^{-1}, IV based on our experience in awake cats with this dose (Ferreira et al. 2010) where we observed analgesic efficacy without side effects. The purpose of this study was to determine the magnitude and duration of effect of intravenous methadone on the MAC of sevoflurane in cats.

Materials and methods

Cats

Eight healthy adult (1–2 years) neutered mixed-breed cats (four females and four males), weighing 5.82 ± 0.42 kg were studied following approval by the Institutional Animal Care and Use Committee. Cats were group-housed, with fresh water *ad libitum* and fed a commercial dry cat food. They were not fasted prior to anesthesia.

Anesthesia and instrumentation

Depending on the temperament of the individual cat, induction of anesthesia was initiated using either an acrylic chamber or mask with 6% sevoflurane (SEVOFLO; Abbott Laboratories, North Chicago, IL, USA) in oxygen (5 L $minute^{-1}$) delivered with an out-of-circuit vaporizer (Drägerwerk Ag Lübeck, Vapor 19.1; Lübeck, Schleswig-Holstein, Germany) and a non-rebreathing (Bain) circuit. The four cats induced using the chamber were removed as soon as they became recumbent and induction was completed by face-mask delivery of sevoflurane. In all cases, induction was considered complete upon orotracheal intubation with a cuffed endotracheal tube and the time from first breath of sevoflurane to intubation was recorded. Quality of induction was scored using criteria provided in Table 1. Cats were then positioned in right lateral recumbency and the end-tidal sevoflurane concentration ($F_E'SEVO$) recorded directly from the analyzer (uncorrected for calibration or barometric pressure) were maintained between 3.8 and 4.5% during instrumentation. Time from intubation until the end of instrumentation was recorded.

Anesthesia was maintained with sevoflurane in oxygen administered using a non-rebreathing (Bain) circuit connected to a standard small animal anesthesia machine and out-of circle vaporizer. The oxygen flow-rate was maintained at 2 L $minute^{-1}$ for the duration of the study. Ventilation was controlled (Bird Mark 7 – Respirator, Bird Corporation – Viasys Healthcare, Palm Springs, CA, USA) to maintain end-tidal partial pressure of carbon dioxide ($P_E'CO_2$) between 25 and 35 mmHg.

A catheter was placed through the lumen of the endotracheal tube so that the tip of the catheter was positioned at the distal end of the tube within the thoracic trachea. This catheter was connected to the gas analyzer (BCI International – 9100 Multigas

