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RESEARCH PAPER

Effects of acepromazine–morphine and acepromazine–methadone premedication on the minimum alveolar concentration of isoflurane in dogs

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Abstract

Objective To evaluate the effects of premedication with acepromazine–morphine or acepromazine–methadone on the minimum alveolar concentration of isoflurane (ISO_{MAC}) and the incidence of bradycardia and hypotension in dogs.

Study design Prospective randomized clinical study.

Animals Thirty-two female dogs undergoing elective ovariohysterectomy.

Methods Dogs were randomly assigned to one of three groups: no premedication (CONTROL group; $n = 9$); acepromazine (0.02 mg kg^{-1}) and morphine (0.5 mg kg^{-1}) (ACPMOR group; $n = 11$); and acepromazine (0.02 mg kg^{-1}) and methadone (0.5 mg kg^{-1}) (ACPMET group; $n = 12$). All drugs were administered intramuscularly. Twenty minutes later, anesthesia was induced with propofol administered intravenously to effect. Determinations of the ISO_{MAC} were conducted by use of the up-and-down method using a quantal study design to determine the MAC for the population. Cardiovascular variables were registered immediately before noxious stimulation that was performed approximately 30 minutes after anesthetic induction. The occurrence of bradycardia (heart rates ≤ 70 beats $minute^{-1}$ in dogs ≤15 kg and ≤60 beats $minute^{-1}$ in dogs >15 kg) and hypotension (mean arterial pressure < 60 mmHg) were registered.

Results The ISO_{MAC} in CONTROL was 1.20 ± 0.11%. Compared with CONTROL, the ISO_{MAC} was reduced by 33.3% and 68.3% in ACPMOR and ACPMET, respectively ($p < 0.001$). The ISO_{MAC} was lower in ACPMET than in ACPMOR ($p < 0.001$). Bradycardia was observed in 0%, 45% and 50% of dogs and hypotension was observed in 56%, 55% and 67% of dogs in CONTROL, ACPMOR and ACPMET, respectively.

Conclusions and clinical relevance The percentage reduction of the ISO_{MAC} in ACPMET was approximately twice that in ACPMOR. Premedication with acepromazine–morphine or acepromazine–methadone increased the incidence of bradycardia. Hypotension was observed in most dogs during isoflurane anesthesia regardless of premedication.

Keywords inhalation anesthesia, opioid, phenothiazine, sedative.

Introduction

The minimum alveolar concentration (MAC) is the concentration of an inhalation anesthetic required to prevent gross purposeful movements in 50% of patients in response to noxious stimulation (Quasha et al. 1980). The MAC is a measure of potency used to compare two or more inhalation anesthetics (Steffey & Mama 2007). Drugs which possess sedative and/or analgesic properties generally reduce the MAC of inhalation anesthetics (Murphy & Hug

1982; Heard et al. 1986; Webb & O'Brien 1988; Ko et al. 2009; Credie et al. 2010) and the ability of different anesthetic adjuncts to reduce MAC can be used to compare the efficacy and potency of drugs of a same class (e.g. comparing different opioids) (Michelsen et al. 1996).

Phenothiazine derivatives, such as acepromazine, are often used as premedication in dogs for their tranquilizing or sedative properties. Because acepromazine is generally considered to be devoid of clinically significant analgesic properties, it is commonly administered with an opioid analgesic agent. Sedation and analgesia appears to be improved with the combination, compared with use of either drug alone (Monteiro et al. 2008), and this effect facilitates handling and preparation of dogs for diagnostic and surgical procedures.

Morphine has been the opioid of choice by many veterinary practitioners for providing preemptive analgesia in dogs, but methadone has gained popularity for this purpose as it does not induce vomiting (Monteiro et al. 2008, 2009), and it was associated with a more profound degree of sedation than morphine when both drugs were used in combination with acepromazine (Monteiro et al. 2009).

Premedication with a sedative-opioid combination can reduce the MAC of an inhalation agent (Hellyer et al. 2001). Although the effects of acepromazine (Heard et al. 1986; Webb & O'Brien 1988) and opioids (Murphy & Hug 1982; Michelsen et al. 1996; Ko et al. 2009; Credie et al. 2010) on the MAC of inhalation anesthetic agents have been extensively studied in dogs, the majority of studies were performed with each agent administered alone. Nevertheless, the use of a combination of drugs, such as in neuroleptanalgesia, may result in additive or synergistic effect (Monteiro et al. 2008, 2009). Because the combination of acepromazine–methadone provided more intense sedation in more dogs (6/6 dogs) compared with the combination acepromazine–morphine (1/6 dogs; Monteiro et al. 2009), a greater decrease in the MAC of inhalation anesthetics might be expected in dogs given acepromazine–methadone. The present study aimed to evaluate the effects of intramuscular (IM) premedication with acepromazine–morphine or acepromazine–methadone on the MAC of isoflurane (ISO_{MAC}) in dogs. The hypothesis was that the combination of acepromazine–methadone would result in a greater decrease in the ISO_{MAC} than the combination of acepromazine–morphine. A further aim of this study was to evaluate the incidence of bradycardia and hypotension in isoflurane-anesthetized dogs given each of the combinations.

Materials and methods

Animals

This study was approved by the Institutional Animal Care Committee of the University of Vila Velha, Brazil (protocol 203/2011). Thirty-two client-owned female dogs scheduled for elective ovariohysterectomies were enrolled in the study after informed owner consent was obtained. Health status was assessed by means of a physical examination, an electrocardiogram (ECG), and a complete blood count and serum chemistry. Any dog having clinical signs of systemic disease, abnormal laboratory data, or aged <6 months or >10 years was excluded from the study.

Study design and treatments

The dogs were randomly assigned to one of three groups according to the premedication used, as follows: no premedication (CONTROL group); acepromazine (0.02 mg kg^{-1}, Acepran 0.2%; Vetnil, Brazil) and morphine (0.5 mg kg^{-1}, Dimorf; Cristália, Brazil) (ACPMOR group); and acepromazine (0.02 mg kg^{-1}) and methadone (0.5 mg kg^{-1}, Mytedon; Cristália) (ACPMET group). Randomization was performed by drawing one of three pieces of paper with each treatment identification from a bag. On all occasions, premedication was injected into the semitendinosus muscle. The drugs were mixed in a single syringe in the ACPMOR and ACPMET groups.

Experimental procedure

Food but not water was withheld for 12 hours prior to anesthesia. A 20 or 22 gauge catheter was placed in a cephalic vein. All animals were administered lactated Ringer's solution at 10 mL kg^{-1} $hour^{-1}$. Approximately 20 minutes after premedication (ACPMOR and ACPMET), anesthesia was induced by administering propofol (Propovan; Cristália) intravenously (IV) to effect to allow endotracheal intubation. Dogs were positioned in dorsal recumbency on an electrical heating pad throughout anesthesia to maintain the body (esophageal) temperature between 37 °C and 38 °C. Anesthesia was