SHORT COMMUNICATION

Evaluation of the antiemetic efficacy of maropitant in dogs medicated with morphine and acepromazine

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Abstract

Objective To evaluate whether maropitant (1 mg kg\(^{-1}\)) injected subcutaneously (SC), administered simultaneously or 30 minutes prior to intramuscular (IM) administration of morphine (0.5 mg kg\(^{-1}\)) and acepromazine (0.05 mg kg\(^{-1}\)), reduces the incidence of salivation, retching and emesis in dogs.

Study design Randomized, controlled, prospective clinical trial.

Animals Sixty dogs scheduled for an ovariohysterectomy as part of a population control program.

Methods Dogs were randomly allocated to be administered maropitant (1 mg kg\(^{-1}\)) SC simultaneously (group M0) or 30 minutes prior to (group M30) administration of morphine (0.5 mg kg\(^{-1}\)) and acepromazine (0.05 mg kg\(^{-1}\)) IM. A control group was administered normal saline (C) at T-30 and T0. Dogs were observed for 30 minutes after morphine–acepromazine administration. The occurrence of retching, retching and salivation were recorded, as well as the time to first emesis and the number of emetic events per dog.

Results The occurrence of salivation was not different between the groups. Retching and vomiting occurred significantly less frequently in M30 than in the other two groups (\(p < 0.02\)). The number of emetic events was also significantly less for M30 than for the other two groups (\(p = 0.01\)). When emesis occurred, the time to the first emetic event was similar among the groups.

Conclusions and clinical relevance Maropitant (1 mg kg\(^{-1}\)) SC reduced the frequency of morphine-induced emesis by as much as 70% when administered 30 minutes in advance. Simultaneous administration of maropitant and morphine–acepromazine produced no measurable effect on the frequency of retching or vomiting.

Keywords acepromazine, dogs, maropitant, morphine, vomiting.

Introduction

Morphine is commonly administered for preanesthetic medication and postoperative analgesia in canine veterinary patients; however, it is not devoid of undesirable side effects. The gastrointestinal effects include salivation, nausea, vomiting, defecation and constipation (Lamont & Mathews 2007). Nausea and vomiting might not only produce discomfort, but prevention of vomiting might be particularly desired in patients with an increased risk of aspiration, such as dogs with surgical correction of laryngeal paralysis (MacPhail & Monnet 2001), or those in which increases in intraocular or intracranial pressures are to be avoided (Claude et al. 2014).
The incidence of morphine-induced vomiting in dogs approaches 50–75% after doses of 0.5 mg kg$^{-1}$ (Valverde et al. 2004; Koh et al. 2014). Acepromazine exerts an anti-emetic effect through dopamine D2 receptor antagonism. When acepromazine is administered at least 15 minutes prior to morphine, the frequency of vomiting decreased from 75% to 25% (Valverde et al. 2004). Maropitant is a neurokinin-1 receptor antagonist with central and peripheral antiemetic activity via substance P receptor antagonism (Benchaoui et al. 2007). Maropitant administration completely prevented emesis induced by hydromorphone when injected at least 30 minutes (Hay Kraus 2014) or 45–60 minutes before administration of hydromorphone (Johnson 2014). However, Koh et al. (2014) reported a reduction of emesis from 75.7% to 37.8% when maropitant was administered 20 minutes before morphine (0.5 mg kg$^{-1}$).

The objective of this investigation was to evaluate whether maropitant could reduce or eliminate the occurrence of emesis when administered simultaneously or 30 minutes prior to morphine. Our hypothesis was that subcutaneous (SC) administration of maropitant (1 mg kg$^{-1}$; Cerenia; Pfizer PGM Poce sur Cisse, France) SC 30 minutes prior (T-30) to morphine and acepromazine. Group M0 was administered maropitant (1 mg kg$^{-1}$) SC at T0, simultaneously with morphine and acepromazine. In order to ensure that the observers were unaware of the group to which each individual was assigned, a saline injection was given at T0 in group M30 and T-30 in group M0. For the same reason, a control group (group C) was administered injections of normal saline instead of maropitant at both T-30 and T0. Treatments were prepared by an investigator (AML) using labeled syringes that did not reveal the content. The solutions were then administered by a single investigator (MAH) unaware of group allocation. Dogs were observed for 30 minutes after the administration of morphine and acepromazine. The presence of salivation, retching and vomiting was recorded by veterinary students in their final year, supervised by one of two investigators (NJL, MPZ); all were blinded to group allocation. Salivation was monitored by simple observation of ptyalism. Vomiting was recorded when there was expulsion of stomach contents through forceful contractions of the abdominal muscles, and retching was considered as a nonproductive act of vomiting with no expulsion of gastric contents from the mouth. The time from injection until the first emesis and the number of emetic events per dog were also recorded.

**Materials and methods**

**Animals**

This study was approved by the Committee on Bioethics and Animal Welfare of the Universidad Católica de Córdoba, Argentina. Sixty adult mixed-breed dogs, American Society of Anesthesiology (ASA) classification I, scheduled for an ovariohysterectomy as part of a population control program, were enrolled in this study. Owner’s consent was acquired prior to the inclusion of each animal. Food was withheld for 12 hours prior to the administration of the study agents. Dogs had free access to water until 1 hour before the beginning of the study. Dogs with a history of vomiting, inappetence, diarrhea, or abdominal pain in the last month were excluded.

**Study design**

This randomized, blinded, prospective controlled trial was completed within a 4-week period. All dogs were sedated with morphine (0.5 mg kg$^{-1}$; Amidiaz; Laboratorios Richmond, Argentina) and acepromazine (0.05 mg kg$^{-1}$; Acedan; Laboratorios Hollyday, Argentina) administered IM at time zero (T0). By extracting tokens from an opaque envelope, the dogs were assigned randomly to three groups of 20 animals each. Group M30 was administered maropitant (1 mg kg$^{-1}$; Cerenia; Pfizer PGM Poce sur Cisse, France) SC 30 minutes prior (T-30) to morphine and acepromazine. Group M0 was administered maropitant (1 mg kg$^{-1}$) SC at T0, simultaneously with morphine and acepromazine. Group M0 was administered maropitant (1 mg kg$^{-1}$) SC at T0, simultaneously with morphine and acepromazine. In order to ensure that the observers were unaware of the group to which each individual was assigned, a saline injection was given at T0 in group M30 and T-30 in group M0. For the same reason, a control group (group C) was administered injections of normal saline instead of maropitant at both T-30 and T0. Treatments were prepared by an investigator (AML) using labeled syringes that did not reveal the content. The solutions were then administered by a single investigator (MAH) unaware of group allocation. Dogs were observed for 30 minutes after the administration of morphine and acepromazine. The presence of salivation, retching and vomiting was recorded by veterinary students in their final year, supervised by one of two investigators (NJL, MPZ); all were blinded to group allocation. Salivation was monitored by simple observation of ptyalism. Vomiting was recorded when there was expulsion of stomach contents through forceful contractions of the abdominal muscles, and retching was considered as a nonproductive act of vomiting with no expulsion of gastric contents from the mouth. The time from injection until the first emesis and the number of emetic events per dog was also recorded.

**Statistical analysis**

Data were analyzed using commercial software (InfoStat 2008; Grupo InfoStat, FCA, Argentina). Distribution of age and weight was nonparametric (Shapiro–Wilk test), and was compared among groups with the Kruskal–Wallis one-way ANOVA. The distribution of gender and the incidence of salivation, retching and vomiting were compared with chi-square tests. Time from injection until first emesis and the number of emetic events per dog was also compared between groups with Kruskal–Wallis one-way ANOVA. Results are reported as median (minimum – maximum). Significance was set at 5% throughout.