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RESEARCH PAPER

The effect of maropitant on intraoperative isoflurane requirements and clinical signs of postoperative nausea and vomiting in dogs undergoing ovariohysterectomy: a randomized clinical trial

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Abstract

Objective To establish if preoperative maropitant significantly reduced intraoperative isoflurane requirements and reduced clinical signs associated with postoperative nausea and vomiting (PONV) in dogs.

Study design Randomized clinical trial.

Animals Twenty-four healthy, client-owned dogs undergoing routine ovariohysterectomy.

Methods Premedication involved acepromazine (0.03 mg kg^{-1}) combined with methadone (0.3 mg kg^{-1}) intramuscularly 45 minutes before anaesthetic induction with intravenous (IV) propofol, dosed to effect. Meloxicam (0.2 mg kg^{-1}) was given intravenously. Dogs were randomly assigned to receive either saline (group S; 0.1 mL kg^{-1}, $n = 12$) or maropitant (group M; 1 mg kg^{-1}, $n = 12$) subcutaneously at time of premedication. Methadone (0.1 mg kg^{-1} IV) was repeated 4 hours later. Anaesthesia was maintained with isoflurane in oxygen, dosed to effect by an observer unaware of group allocation. The dogs were assessed hourly, starting 1 hour postoperatively, using the short form of the Glasgow Composite Pain Score (GCPS), and for ptyalism and signs attributable to PONV [score from 0 (none) to 3 (severe)] by blinded observers. Owners completed a questionnaire at the postoperative recheck.

Results Overall mean ± standard deviation end-tidal isoflurane percentage was lower in group M (1.19 ± 0.26%) than group S (1.44 ± 0.23%) ($p = 0.022$), but was not significantly different between groups at specific noxious events (skin incision, ovarian pedicle clamp application, cervical clamp application, wound closure). No cardiorespiratory variables or postoperative GCPS differed significantly between groups. Overall, 50% of dogs displayed signs attributable to PONV, with no difference in PONV scores between groups ($p = 0.198$). No difference in anaesthetic recovery was noted by owners between groups.

Conclusions Maropitant reduced overall intraoperative isoflurane requirements but did not affect the incidence of PONV.

Clinical relevance Maropitant provided no statistically significant benefits to dogs undergoing ovariohysterectomy with this anaesthetic and analgesic protocol, although clinically significant reductions in isoflurane requirements were noted.

Introduction

Maropitant citrate (maropitant) is an antiemetic drug licensed for use in dogs. It acts by antagonising the neurokinin-1 (NK-1) receptor which is found in multiple locations throughout the body. Normally, NK-1 is activated by substance P to produce a variety of effects including pain, nausea and vomiting.

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In humans, NK-1 receptor antagonists are widely used for their beneficial effects including improved postoperative anaesthetic recovery (Lee et al. 2012). Use of the NK-1 receptor antagonist aprepitant has been associated with a reduction in postoperative analgesia requirements in women following gynaecological surgery alongside a reduced incidence of postoperative nausea and vomiting (PONV) (Kakuta et al. 2011).

Previously in dogs, Alvillar et al. (2012) reported a 16% reduction in the minimum alveolar concentration (MAC) of sevoflurane after the administration of maropitant, which was determined by a tail-clamp technique. Those authors proposed central nervous system or peripheral NK-1 receptor antagonism as a possible mechanism of MAC reduction. In a canine ovariohysterectomy study, the MAC of sevoflurane was reduced by 24% after administration of 1 mg kg^{-1} maropitant intravenously, followed by intravenous (IV) infusion of 30 μg kg^{-1} $hour^{-1}$; and by 30% when 5 mg kg^{-1} was administered intravenously followed by IV infusion at 150 μg kg^{-1} $hour^{-1}$ (Boscan et al. 2011). This study concluded that maropitant had a potential role in the management of ovarian pain. Similarly, Marquez et al. (2015) reported that dogs undergoing ovariohysterectomy benefited from reduced intraoperative isoflurane requirements, lower heart rates (HR) and systolic arterial blood pressure and had reduced pain scores on tracheal extubation after premedication with maropitant 1 mg kg^{-1} subcutaneously (SC), when compared to morphine (0.5 mg kg^{-1} SC), although this difference in isoflurane requirement was not thought to be clinically significant. Dogs receiving maropitant were also more likely to eat within 3 hours of tracheal extubation (64.7% of dogs compared to 15.3%), but factors relating to PONV were not evaluated and the authors concluded that further research was warranted. Finally, Okano et al. (2015) concluded that maropitant reduced the intraoperative isoflurane requirements in a dose-dependent manner when combined with morphine (0.5 mg kg^{-1} SC) for premedication in dogs undergoing ovariohysterectomy.

Despite being widely recognised in humans, PONV has been poorly documented in dogs. In a retrospective observational study, being sexually intact and the use of sevoflurane were identified as significant risk factors for postoperative regurgitation and vomiting following nonelective surgery in dogs. Other risk factors were also identified (Davies et al. 2015).

To date, there are no published studies evaluating the role of maropitant in reducing inhalational anaesthetic requirements when used alongside methadone and acepromazine premedication in a clinical setting or investigating the prevalence of clinical signs attributable to PONV following ovariohysterectomy in dogs. The primary aim of the present study was to investigate whether there was a significant isoflurane sparing effect associated with the preoperative administration of maropitant in dogs undergoing routine ovariohysterectomy, in addition to that afforded by acepromazine and methadone. Secondary aims were to investigate whether dogs displayed clinical signs attributable to PONV in the recovery period and whether these were reduced by preoperative maropitant. Another secondary aim was to determine whether preoperative maropitant reduced postoperative pain scores. Our first hypothesis was that maropitant would reduce the end-tidal isoflurane concentration at predetermined intraoperative event points, compared to saline control. The second hypothesis was that dogs receiving maropitant would display fewer clinical signs attributable to PONV than dogs receiving saline and that they would also have lower postoperative pain scores.

Materials and methods

A sample size of 24 dogs was calculated, for a statistical power of 90% with an alpha value of 5% and based on an expected difference of 16% in isoflurane requirement between groups, with a standard deviation of 0.25% (Alvillar et al. 2012). Dogs presenting to two first opinion practices for routine ovariohysterectomy were enrolled. Informed owner consent was obtained and an animal test certificate (ATC type S 2015/00229) was obtained from the Veterinary Medicines Directorate following ethical approval from the University of Liverpool Veterinary Ethics Committee (VREC221a). Eligible dogs were entire females, aged 0.4−8.0 years and otherwise healthy [American Society of Anesthesiologists (ASA) physical status classification 1−2]. Dogs were excluded if pregnant, exhibiting signs of pseudocyesis or displaying signs of oestrus at the time of presentation for surgery.

Animals were randomly assigned to one of two groups by asking a veterinary nurse to remove one card from an envelope containing 24 cards. This was done privately, without the surgeon or anaesthetist present. Of these cards, 12 assigned a dog to group S and the remaining 12 to group M. After selection, the

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