Low incidence of postoperative nausea, vomiting, regurgitation, and aspiration pneumonia in geriatric dogs receiving maropitant, famotidine, and fentanyl as part of an anesthesia protocol

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OBJECTIVE
To determine the incidence of and potential risk factors for postoperative regurgitation and vomiting (PORV), postoperative nausea and vomiting (PONV), and aspiration pneumonia in geriatric dogs using premedication with maropitant and famotidine, intraoperative fentanyl, and postoperative fentanyl as part of an anesthetic protocol.

ANIMALS
105 client-owned geriatric dogs that underwent general anesthesia for a major surgical procedure between January 2019 and March 2020.

PROCEDURES
Medical records were reviewed to collect data on signalment, historical gastrointestinal signs, American Society of Anesthesiologists (ASA) score, indication for surgery, duration of anesthesia and surgery, patient position during surgery, mode of ventilation, and perioperative administration of maropitant, famotidine, anticholinergics, opioids, colloidal support, NSAID, corticosteroids, and appetite stimulants. The incidence of postoperative regurgitation, vomiting, nausea, and aspiration pneumonia was calculated, and variables were each analyzed for their association with these outcomes.

RESULTS
2 of 105 (1.9%) dogs regurgitated, 1 of 105 (1.0%) dogs developed aspiration pneumonia, 4 of 105 (3.8%) dogs exhibited nausea, and no dogs vomited. Identified possible risk factors included older age (≥13 years old) for postoperative regurgitation, regurgitation for postoperative aspiration pneumonia, and high ASA score (≥4) for both regurgitation and aspiration pneumonia.

CONCLUSIONS AND CLINICAL RELEVANCE
The use of an antiemetic protocol including maropitant, famotidine, and fentanyl in geriatric dogs resulted in very low incidences of PORV, PONV, and aspiration pneumonia. Future prospective studies are warranted to further evaluate and mitigate postoperative risks.
revealed an incidence of PONV in 50% of dogs undergoing routine ovariohysterectomy, and there is an emerging clinical interest in reducing PONV in veterinary patients. However, most previous studies have focused on PORV due to the objective nature of these events.

Aspiration pneumonia is another known complication of general anesthesia, with a variable incidence reported. Ovbay et al reported a 0.17% overall incidence of postoperative aspiration pneumonia, and geriatric patients > 8 years of age were predisposed. Other studies have yielded incidences of aspiration pneumonia as high as 5% to 7% in patients undergoing laparotomy and those undergoing general anesthesia without any other concurrent risk factors. A previous study demonstrated a significant decrease in the risk of aspiration pneumonia from 13% to 1.3% with repeated anesthesia episodes by using an antiemetic drug protocol that included decreased anticholinergic use, decreased μ-opioid use, and prophylactic use of maropitant and metoclopramide for nausea or vomiting. In addition to age and recent anesthesia, other published risk factors for aspiration pneumonia include a history of vomiting or regurgitation, esophageal disease, laryngeal dysfunction, neurological disorders, upper airway surgery, laparotomy, and neurosurgery. The mortality rate from aspiration pneumonia postanesthesia approaches 25% in the general veterinary population, and increasing patient age is associated with nonsurvival.

Veterinarians and owners may be hesitant to anesthetize geriatric dogs because of higher odds of anesthetic and postanesthetic complications. Specifically, vomiting and regurgitation can negatively impact patient comfort and increase hospitalization time and cost, and they are known risk factors for aspiration pneumonia, especially in older dogs and when associated with recent anesthesia. The objective of the present study was to retrospectively determine the incidences of PORV, PONV, and aspiration pneumonia in geriatric dogs using an anesthetic protocol with antiemetic effects that included premedication with maropitant citrate and famotidine as well as intraoperative and postoperative fentanyl administration. A secondary objective was to identify potential risk factors for PORV, PONV, and aspiration pneumonia in this population of dogs. We hypothesized that using this drug protocol would lead to low incidences of PORV, PONV, and aspiration pneumonia in a geriatric population of dogs.

Materials and Methods

Case selection criteria

Medical records for geriatric dogs having surgery between January 2019 and March 2020 with the Surgical Oncology Service at VCA West Coast Specialty and Emergency Animal Hospital were reviewed. Dogs were included if they were ≥ 8 years of age at presentation, underwent a major surgical procedure under general anesthesia, and the specified anesthetic protocol was used. A major surgical procedure was defined as any surgical procedure that required admission to the hospital, entry into the operating room to perform the procedure, and postanesthesia recovery in the hospital for a minimum of 24 hours. The anesthesia protocol included premedication with maropitant citrate (1 mg/kg, IV; Cerenia, Zoetis) and famotidine (1 mg/kg, IV; West-Ward Pharmaceuticals) prior to induction with propofol (PropoFlo, Zoetis) and maintenance of anesthesia using a fentanyl citrate (West-Ward Pharmaceuticals) constant rate infusion (CRI; 4 to 24 μg/kg/h) and isoflurane anesthesia (Fluriso, MWI Veterinary Supply Co). A fentanyl CRI (1 to 6 μg/kg/h) was administered to all patients postoperatively for pain management. To reduce variability in medication doses and protocols, all cases were selected from a single service and were under the care of the same board certified surgeon (AV).

Patients with preexisting laryngeal dysfunction, esophageal disease, or aspiration pneumonia and patients undergoing esophagostomy tube placement were excluded. Patients were also excluded if an antiemetic was administered postoperatively without documented signs of nausea, vomiting, or regurgitation.

Medical records review

Data retrieved from the medical records included age, body weight, breed, sex and neuter status; prior history of vomiting, regurgitation, anorexia, or hypoxemia; and NSAID and corticosteroid administration prior to surgery. The dosage, time, and route of administration of maropitant and famotidine were recorded.

Each surgical procedure was subcategorized as intra-abdominal, intrathoracic, head and neck, or any other noncavity location, including the limbs or trunk (Supplementary Appendix S1). Each surgery was also categorized as whether or not the procedure was emergent. If multiple surgeries were performed under a single anesthetic event, all procedures were considered in the analysis.

Additional data collected included the duration of anesthesia and surgery, intraoperative anticholinergic administration, intraoperative colloidal support, changes in laterality or recumbency for multiple surgical procedures during a single anesthetic event, intraoperative mode of ventilation and change in ventilation mode, ASA score, and occurrence of clinically identifiable regurgitation under anesthesia or during recovery. Subclinical (silent) episodes of regurgitation were not evaluated in this study. Administration of opioids, NSAIDs, corticosteroid drugs, maropitant, other antiemetics, and appetite stimulants within the first 24 hours postoperative was noted. The number of episodes each of vomiting, regurgitation, diarrhea, and nausea (lip licking, lip smacking, ptalynia) was
recorded for each patient within the first 24 hours postoperatively.

The medical records were searched for clinical signs of aspiration pneumonia including coughing, pyrexia, lethargy, and increased respiratory rate or effort. Aspiration pneumonia was diagnosed when there was radiographic evidence with appropriate clinical signs. The duration of hospitalization and overall outcome were recorded when aspiration pneumonia was diagnosed.

**Statistical analysis**

Variables analyzed included body weight, age, duration of anesthesia, duration of surgery, time (minutes) of maropitant administration prior to induction of anesthesia, number of hours postoperatively that food was eaten, and the number of meals consumed within 24 hours after anesthesia. These variables were normally distributed. Additional variables analyzed included sex, neuter status, history of hyporexia or anorexia, history of vomiting, NSAID administration pre- or postoperatively, corticosteroid administration pre- or postoperatively, surgical location within (specifically intraabdominal or intrathoracic) or outside (head and neck or other location) a body cavity, gastrointestinal surgery, emergency surgery, anticholinergic administration intraoperatively, mode of ventilation and change in mode of ventilation, change in position of the patient during surgery, ASA score, administration of a rescue antiemetic, and food consumption within 12 or 24 hours postoperatively.

Analysis of variance, the χ² test (when all cells in the 2 X 2 table included > 10 observations), and the Fisher exact test (n ≤ 10/cell) were used to evaluate the association between each variable and aspiration pneumonia, PORV, PONV, regurgitation, and nausea, without controlling for other factors. All statistical analyses were performed with commercially available software (Statview 5.0), and a *P* value ≤ 0.05 was considered statistically significant.

**Results**

Of 137 cases of dogs ≥ 8 years old that were anesthetized using the evaluated drug protocol, 123 (89.8%) met the induction criteria. Eighteen cases were excluded due to concurrent esophagostomy tube placement (n = 7); suspected or confirmed laryngeal paralysis (2); postoperative antiemetic administration without documented nausea, vomiting, or regurgitation (2); and the same patient undergoing multiple anesthetic events within the study period (7), leaving 105 dogs for inclusion in the statistical analysis.

Mean age of the 105 dogs was 10 ± 1.8 years (median, 10 years; range, 8 to 14 years). There were 42 (40%) male dogs (41 castrated and 1 sexually intact) and 63 (60%) female dogs (59 spayed and 4 sexually intact). The most breed categories were mixed breed (n = 41 [39%]), followed by Golden Retriever (9 [9%]), Boxer (6 [6%]), Labrador Retriever (6 [6%]), and German Shepherd Dog (4 [4%]).

Maropitant was administered a median of 17 minutes (range, 3 to 342 minutes) prior to induction of anesthesia. No clinical regurgitation was noted intraoperatively. Two (19%) dogs regurgitated within 24 hours after surgery. One (1.0%) dog developed aspiration pneumonia 60 hours postoperatively, and this dog also regurgitated within 24 hours after surgery. No dogs vomited within 24 hours postoperatively; however, signs of nausea were noted in 4 (3.8%). A rescue antiemetic was administered to 1 (1.0%) dog, and this dog also displayed signs of nausea (ie, ptyalism and lip licking). No dogs had evidence of both nausea and regurgitation. The overall incidence of PONV was 19%, and the overall incidence of PONV was 3.8%.

Possible risk factors identified on bivariable analysis included increasing age (≥ 13 years) for regurgitation (*P* = 0.02), regurgitation for aspiration pneumonia (*P* = 0.02), and ASA score ≥ 4 for regurgitation (*P* < 0.001) and aspiration pneumonia (*P* < 0.001). Variables with no significant association with these outcomes included body weight, sex, neuter status, history of hyporexia or anorexia, history of vomiting, NSAID or corticosteroid administration pre- or postoperatively, time of maropitant administration, duration of anesthesia or surgery, surgical location within or outside a body cavity, gastrointestinal surgery, emergency surgery, anticholinergic administration intraoperatively, mode of ventilation and change in mode of ventilation, change in position of the patient during surgery, administration of a rescue antiemetic, food consumption within 12 or 24 hours postoperatively, number of hours postoperatively that food was eaten, and the number of meals consumed within 24 hours after anesthesia were not associated with postoperative nausea, vomiting, regurgitation, or aspiration pneumonia.

**Discussion**

Geriatric dogs anesthetized using a protocol including premedication with maropitant citrate and famotidine as well as intraoperative and postoperative fentanyl CRI had very low incidences of postoperative regurgitation (1.9%) and postoperative nausea (3.8%). No vomiting occurred. These results are within the previously reported range for all ages of dogs regarding postoperative regurgitation (0.96% to 6.6%) and lower than the previously reported risks of postoperative vomiting (6% to 7%), overall PORV (12.3%), and PONV (50%) in the general population of dogs, despite older age being a potential risk factor. The incidence of aspiration pneumonia in geriatric dogs in our study was 1.0%, which was also comparable to previously reported incidences of aspiration pneumonia in all ages of dogs. Data from our study showed that use of the evaluated
anesthesia protocol may lead to a low risk of postoperative regurgitation, vomiting, and aspiration pneumonia in geriatric dogs, making for a safer anesthesia recovery.

The anesthesia protocol in our study was selected based on the potential and known antiemetic properties of each drug. Maropitant citrate is a potent neuropeptidin-1 (NK-1) receptor antagonist, famotidine is a histamine H2-receptor antagonist, and fentanyl is a lipid-soluble μ-opioid receptor agonist. NK-1 receptor antagonists are a group of potent antiemetics that act by inhibiting the binding of substance P and are effective in the prevention of vomiting in both dogs and humans. In human medicine, PONV affects 20% to 40% of surgical patients overall, and up to 80% of high-risk patients (e.g., women, nonsmokers, those with a previous history of PONV or motion sickness, and those receiving opioids). Numerous human studies have demonstrated that NK-1 receptor antagonists are effective in the prevention and treatment of postoperative nausea and superior to other antiemetics in the prevention and treatment of postoperative vomiting. Due to its favorable efficacy profile and superiority, treatment with an NK-1 receptor antagonist has been recommended for human patients at risk for PONV and for whom PONV may cause serious adverse outcomes, such as aspiration pneumonia.

Maropitant citrate has been shown to act both centrally and peripherally in the prevention of vomiting in dogs. A few veterinary studies have indicated that preoperative administration of maropitant (when used as a single agent) can be effective in preventing or significantly decreasing opioid-induced nausea and vomiting. Several studies have also revealed the benefits of maropitant as an adjunctive analgesic agent due to substance P inhibition and in reducing the minimum alveolar concentration of inhalant anesthesia, providing further evidence for its use as a premedicant in veterinary patients. The potential benefit of preoperative maropitant administration on postoperative regurgitation, vomiting, and the risk of aspiration pneumonia has not been as widely studied. Extrapolation from human literature suggests that preoperative administration of an NK-1 receptor antagonist would confer a similar benefit in dogs.

Histamine H2-receptor antagonists (H2-blockers) are known to decrease gastric acid secretion in both dogs and people and are routinely used to treat esophagitis and gastritis. Preoperative administration of an H2-blocker significantly reduces the incidence of PONV in people, particularly for high-risk patients such as women. Similarly brachycephalic dogs premedicated with famotidine and an antiemetic, in conjunction with an antiemetic protocol, have been shown to have a decreased incidence of postoperative regurgitation after anesthesia, thus providing further evidence for perioperative use of famotidine in dogs. The μ-opioid receptor agonists are known to have both emetic and antiemetic effects, and the degree of nausea and vomiting elicited has been associated with the lipid solubility of the drug. Highly lipid-soluble drugs such as fentanyl can readily cross the blood-brain barrier to reach centrally located μ-opioid receptors and mediate antiemesis. Conversely, μ-opioids that are less lipid soluble such as morphine tend to activate peripheral μ-opioid receptors and trigger emesis. In people, fentanyl is less emetogenic than morphine and tends to reduce intraoperative and PONV. In dogs, fentanyl has even been shown to reduce the emetic effects of morphine and apomorphine. Thus, fentanyl was chosen in this study for both pain management and for its lower association with nausea and vomiting, compared with other μ-opioids.

A secondary objective of the present study was to identify potential risk factors for aspiration pneumonia in geriatric dogs undergoing anesthesia for major surgical procedures. Identified factors included older age for regurgitation, regurgitation for aspiration pneumonia, and ASA score ≥ 4 for regurgitation and aspiration pneumonia. While these factors were statistically significant on bivariate analysis, a larger-scale prospective study is needed to further investigate these associations because only 2 dogs regurgitated and only 1 developed aspiration pneumonia in this study.

Although no vomiting occurred in our population, nausea was noted in 4 dogs postoperatively. No risk factors for nausea were identified; however, 2 dogs did have several previously identified risk factors for PONV, including a prior history of vomiting, gastrointestinal surgery, emergency surgery, and an ASA score of 4. Nausea is a recognized prodromal sign that may or may not result in vomiting. It is possible that our drug protocol ultimately prevented vomiting in these dogs. Furthermore, dogs that displayed classic signs of nausea (lip licking, lip smacking, and ptyalism) were more likely to be given a rescue antiemetic, which would further suppress potential emetic events. An interesting finding in our study was that no dogs had both postoperative regurgitation and nausea. This provided further evidence that regurgitation and nausea are not biologically linked; a patient does not need to display signs of nausea to regurgitate, and if a patient regurgitates, it does not necessarily show signs of nausea.

Many risk factors for PORV and aspiration pneumonia in the general dog population have been reported, including historical clinical signs of surgery performed, change in position during surgery, ventilation mode, anesthetic duration, and perioperative NSAID or corticosteroid administration. In our study, only a few factors, including advanced age (≥ 13 years) and ASA status of ≥ 4, were statistically significant and may represent potential risk factors for regurgitation and aspiration pneumonia in this geriatric canine population. Significant
risk factors may have become apparent with a larger total case number or if more patients had developed regurgitation or aspiration pneumonia.

The present study had limitations inherent to its retrospective nature. Only patients with complete medical records were considered for inclusion; however, the number of patients experiencing postoperative nausea, regurgitation, and vomiting could have been underrepresented if an event was unobserved or unrecorded. Although possible, the likelihood of this was considered low due to the consistent high level of detail present in records that were available for review. For several years, it has been common practice at the authors’ institution to premedicate nearly all patients undergoing anesthesia with maropitant due to its known benefits in reducing perioperative nausea and vomiting, association with a reduced minimum alveolar concentration of anesthetic, and role as an adjunctive analgesic.2,11,20,28–30,45 Thus, a control group of geriatric dogs that had not received maropitant as a premedicant was not available for comparison within a similar timeframe as our study population. The lack of control group in this study limits the conclusions that can be drawn from our results. Nonetheless, the potentially serious risk of morbidity and mortality in geriatric dogs from PORV, PONV, and aspiration pneumonia warrants the use of a carefully selected anesthetic protocol to mitigate these risks.

Another limitation to the present study was the exclusion of patients with preexisting diseases that have been associated with a higher risk for aspiration pneumonia. These patients were excluded to allow evaluation of this drug protocol in a uniform geriatric population. However, inclusion of dogs with preexisting diseases could potentially significantly change the incidence of aspiration pneumonia and represents an area for future research.

In conclusion, use of an anesthetic protocol including premedication with maropitant citrate and famotidine as well as intraoperative and postoperative fentanyl administration in geriatric dogs undergoing general anesthesia for a surgical procedure led to a good overall outcome and may potentially decrease the risk of adverse events in similar populations. Prospective studies are warranted to further investigate and mitigate the risk of PORV, PONV, and aspiration pneumonia in dogs.

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References


**Supplementary Materials**

Supplementary materials are posted online at the journal website: avmajournals.avma.org

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