Emesis is a common adverse effect associated with administration of α₂-adrenergic agonists and opioids. In cats, the incidence of emesis is approximately 80% following administration of dexmedetomidine, buprenorphine, hydromorphone, or xylazine. The incidence of emesis produced by those agents can be decreased, but not eliminated, by administration of antiemetics. Administration of ondansetron to cats medicated with dexmedetomidine and buprenorphine decreased the incidence of emesis, although a third of the cats still vomited. Similarly, metoclopramide decreased, but did not eliminate, the number of emetic episodes in cats treated with xylazine.

Maropitant, a neurokinin-1 receptor antagonist, is an effective antiemetic in dogs treated with opioids. Emesis is prevented when maropitant is administered to dogs at least 30 minutes before administration of hydromorphone. Information about the antiemetic efficacy of maropitant for the prevention of emesis induced by opioids or α₂-adrenergic agonists in cats is lacking. Therefore, the purpose of the study reported here was to investigate the antiemetic effects of maropitant in cats administered dexmedetomidine and morphine prior to being anesthetized for elective ovariohysterectomy. We hypothesized that the incidence of emesis in cats administered maropitant would be less than that in control cats administered saline (0.9% NaCl) solution. Moreover, because maropitant may cause discomfort in cats when injected SC, we also hypothesized that the aversive behavioral response to the injection for cats receiving maropitant would be more severe than that for control cats injected with isotonic saline solution.

**OBJECTIVE**

To evaluate the effects of maropitant in cats receiving dexmedetomidine and morphine.

**DESIGN**

Randomized controlled trial.

**ANIMALS**

66 healthy female domestic shorthair cats.

**PROCEDURES**

Cats were randomly assigned to receive maropitant (1 mg/kg [0.45 mg/lb], SC; maropitant group; n = 32) or saline (0.9% NaCl) solution (0.1 mL/kg [0.045 mL/lb], SC; control group; 34) 20 hours before IM administration of dexmedetomidine (20 µg/kg [9.1 µg/lb]) and morphine (0.1 mg/kg). Following administration of dexmedetomidine and morphine, the incidences of emesis, retching, and signs of nausea (sialorrhea and lip licking) were compared between the 2 groups. The aversive behavioral response of each cat to injection of maropitant or saline solution was scored on a visual analogue scale by each of 4 observers who were unaware of the treatment administered.

**RESULTS**

Only 1 of 32 cats in the maropitant group vomited, whereas 20 of 34 control cats vomited. The incidences of emesis and retching for the maropitant group were significantly lower than those for the control group. The incidence of signs of nausea did not differ between the 2 groups. Visual analogue scale scores for the maropitant group were significantly higher than those for the control group.

**CONCLUSIONS AND CLINICAL RELEVANCE**

Results of the present study indicated that administration of maropitant to healthy cats approximately 20 hours prior to administration of dexmedetomidine and morphine significantly decreased the incidence of emesis but did not decrease the incidence of signs of nausea. However, maropitant appeared to cause substantial discomfort when injected SC. (J Am Vet Med Assoc 2016;248:1257–1261)

**ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>IQR</td>
<td>Interquartile range</td>
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<tr>
<td>VAS</td>
<td>Visual analogue scale</td>
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</table>
Materials and Methods

Animals
All study procedures were approved by the Institutional Animal Care and Use Committee of Cornell University. Sixty-seven female domestic shorthair cats scheduled for elective ovariohysterectomy were evaluated for inclusion in a randomized controlled trial. To be included in the trial, each cat had to be assigned an American Society of Anesthesiologists physical status of I on the basis of results of a physical examination and abbreviated hematologic and biochemical analyses, which included assessment of Hct and plasma protein, BUN, and blood glucose concentrations. Cats with a history of vomiting, inappetence, or diarrhea or that had signs of abdominal pain elicited during physical examination were excluded from the trial. Each cat was individually housed prior to surgery. Food but not water was withheld from each cat for 12 hours prior to anesthesia. All cats were under the care of an animal shelter at the time of evaluation, and consent was obtained from the shelter for all cats enrolled in the trial.

Study protocol
Cats were allocated to receive an SC injection of either maropitant citrate (1 mg/kg [0.45 mg/lb]) or isotonic saline solution (0.1 mL/kg [0.045 mL/lb]) by block randomization, for which labels were removed from an opaque envelope. Each cat received the assigned treatment between 3 PM and 4 PM on the day prior to surgery following the performance of a physical examination. All syringes containing maropitant or saline solution were prepared by a licensed veterinary technician and labeled in a way that did not reveal their contents. Injections of the assigned treatments were always administered by 1 of 2 investigators (DMS or MMF). Following administration of the assigned treatment, each cat was left undisturbed for 20 hours. At noon the following day, each cat underwent a physical examination and then was administered an IM injection of dexmedetomidine (20 µg/kg [9.1 µg/lb]) and morphine sulfate (0.1 mg/kg). The cat was observed for 30 minutes after administration of dexmedetomidine and morphine, at which time an IV catheter was placed and anesthesia was induced. No further study observations were made after that time.

Assessment of the behavioral response to injection of the assigned treatment
For each cat, the response to injection of the assigned treatment (maropitant or saline solution) was independently evaluated by 4 observers (DMS, MMF, LC, and RDG) who were unaware of (ie, blinded to) the treatment administered. Each observer was asked to place a mark over a 10-cm straight line that reflected the cat’s response to the injection. That line served as a VAS for which the left end represented no response to the injection and the right end represented the most aversive reaction to the injection that the observer could imagine.

Assessment of emesis and signs of nausea
Each cat was observed for emesis, retching, and signs of nausea by veterinary students supervised by licensed veterinary technicians, all of whom were blinded to the assigned treatment, for 15 minutes prior to and 30 minutes after administration of dexmedetomidine and morphine. Emesis, or vomiting, was defined as the forceful expulsion of gastric contents through the mouth, whereas retching was defined as the rhythmic contraction of the diaphragm and abdominal muscles without expulsion of contents. Signs of nausea were considered present when sialorrhea (defined as the collection of clear or frothy fluid around the lips with or without dripping) and excessive licking of the lips were observed.

Statistical analysis
For continuous variables (age, body weight, and time from dexmedetomidine and morphine administration to first episode of emesis or retching [time to emesis or retching]), the D’Agostino-Pearson test was used to evaluate the data distributions for normality. A t test was used to compare body weight between the 2 treatment groups. Mann-Whitney tests were used to compare age, time to emesis or retching, and number of emetic events per cat between the 2 treatment groups. A Mann-Whitney test was also used to compare the VAS scores assigned by each observer between the 2 treatment groups. For each cat, emesis, retching, and signs of nausea were considered all-or-none events (ie, present or absent), and Fisher exact tests were used to compare their respective incidences between the 2 treatment groups. A Fisher exact test was also used to compare the incidence of cats with a VAS score ≥ 7 cm (the top third of the scale, which represented the most aversive reactions) between the 2 treatment groups. Parametric data were summarized as the mean ± SD, and nonparametric data were summarized as the median (IQR [25th to 75th percentiles]). All analyses were performed with statistical software, and values of P < 0.05 were considered significant.

Results
Cats
Of the 67 cats initially evaluated for the trial, 1 was excluded because it was dehydrated and showed signs of inappetence and depression during the physical examination prior to administration of the preanesthetics (dexmedetomidine and morphine). Therefore, 66 cats were enrolled in the trial; 32 cats were administered maropitant (maropitant group), and 34 cats were administered isotonic saline solution (control group). The median age for the cats in the maropitant group (12 months; IQR, 6 to 24 months) did not differ significantly (P = 0.40) from that for cats in the control group (12 months; IQR, 6 to 12 months). Likewise, the mean ± SD body weight for cats in the maropitant group (2.8 ± 0.6 kg [6.2 ± 1.3 lb]) did not differ significantly (P = 0.30) from that for the cats in the control group (2.8 ± 0.5 kg [6.2 ± 1.1 lb]).
Behavioral response to injection of the assigned treatment

The VAS scores for the behavioral response of cats to injection of maropitant or saline solution assigned by each of the 4 observers were summarized (Figure 1). Within each observer and for all observers combined, the VAS scores for cats in the maropitant group were significantly greater than those for cats in the control group. When VAS data for all 4 observers were pooled, a VAS ≥ 7 cm was assigned significantly (P < 0.001) more frequently to cats in the maropitant group (27.3% [35/128 observations]) than to cats in the control group (4% [6/136 observations]).

Emesis, retching, and signs of nausea

The incidences of emesis, retching, and signs of nausea; the times from administration of dexmedetomidine and morphine to emesis and retching (time to emesis and retching); and the number of emetic episodes per cat were summarized (Table 1). Maropitant administration significantly reduced the incidence of emesis (P < 0.001) and retching (P = 0.002) but did not significantly (P = 0.06) affect the incidence of signs of nausea. The number of emetic episodes per cat and the time to emesis were not compared between the 2 treatment groups because only 1 cat in the maropitant group vomited.

Discussion

Results of the present study indicated that administration of maropitant (1 mg/kg, SC) to healthy cats approximately 20 hours prior to administration of dexmedetomidine and morphine significantly decreased the incidence of emesis but did not decrease the incidence of signs of nausea (sialorrhea and excessive licking of the lips). Also, injection of maropitant was associated with substantial aversive behavioral responses.

The antiemetic efficacy of maropitant in the cats of the present study appeared to be greater than the antiemetic efficacy of other antiemetics in cats. When cats receiving xylazine (0.66 mg/kg [0.3 mg/lb], IM),

![Figure 1](image_url)

**Figure 1**—Scatterplots of the VAS scores for the behavioral response of cats to injection of maropitant (1 mg/kg [0.45 mg/lb], SC; n = 32) or saline (0.9% NaCl) solution (0.1 mL/kg [0.045 mL/lb], SC; control; 34) approximately 20 hours prior to IM administration of dexmedetomidine (20 µg/kg [9.1 µg/lb]) and morphine (0.1 mg/kg). Each cat was randomly assigned to receive maropitant or saline solution by a block randomization method and was independently assigned a VAS score by each of 4 observers. A score of 0 represented no reaction to injection of the assigned treatment, and a score of 10 represented the most aversive reaction to injection of the assigned treatment that the observer could imagine. For the scatterplot for each treatment within each observer, the long horizontal line represents the median and the short horizontal lines above and below the median line delimit the first and third quartiles. *Median value is significantly (P < 0.001) greater than that for the control group.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Maropitant group</th>
<th>Control group</th>
<th>P value</th>
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<tbody>
<tr>
<td>Emesis</td>
<td>1 (3)</td>
<td>20 (59)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Time from administration of dexmedetomidine and morphine to emesis (min)</td>
<td>5*</td>
<td>3 (2.25–4.00)</td>
<td>—</td>
</tr>
<tr>
<td>No. of emetic episodes/cat</td>
<td>4</td>
<td>1 (0–1.25)</td>
<td>—</td>
</tr>
<tr>
<td>Retching</td>
<td>6 (19)</td>
<td>19 (56)</td>
<td>0.002</td>
</tr>
<tr>
<td>Time from administration of dexmedetomidine and morphine to retching (min)</td>
<td>4 (2.00–6.20)</td>
<td>3 (2.00–4.00)</td>
<td>0.5</td>
</tr>
<tr>
<td>Signs of nausea</td>
<td>11 (34)</td>
<td>19 (56)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Values represent the number (%) of cats affected or the median (IQR [25th to 75th percentile]). Each cat was observed for emesis, retching, and signs of nausea by veterinary students supervised by licensed veterinary technicians, all of whom were blinded to the assigned treatment, for 15 minutes prior to and 30 minutes after administration of dexmedetomidine and morphine. Emesis was defined as the forceful expulsion of gastric contents through the mouth, whereas retching was defined as the rhythmic contraction of the diaphragm and abdominal muscles without expulsion of contents. Signs of nausea were considered present when sialorrhea (defined as the collection of clear or frothy fluid around the lips with or without dripping) and excessive licking of the lips were observed.

*The IQR was not provided because only 1 cat was affected in this group.

-= Not determined.

Table 1—Descriptive data for various outcomes for healthy cats that were randomly allocated to receive either maropitant (1 mg/kg [0.45 mg/lb], SC; maropitant group; n = 32) or saline (0.9% NaCl) solution (0.1 mL/kg [0.045 mL/lb], SC; control group; 34) approximately 20 hours prior to IM administration of dexmedetomidine (20 µg/kg [9.1 µg/lb]) and morphine (0.1 mg/kg).
an α2-adrenergic agonist with emetic potential, were also administered metoclopramide (0.2 to 1.0 mg/kg [0.09 to 0.45 mg/lb], IM), they had fewer episodes of emesis than when they did not receive metoclopramide, although emesis was not completely prevented.3 The incidence of emesis was not reported for that study1 because only 8 cats were evaluated. In another study,3 the incidence of dexmedetomidine-induced emesis decreased from 78% (22/28) to 33% (10/30) when ondansetron (0.22 mg/kg [0.1 mg/kg], IM) was administered simultaneously with dexmedetomidine (40 µg/kg [18.2 µg/lb], IM) to healthy cats. In a crossover study6 that involved 6 cats, administration of dexamethasone (2 to 8 mg/kg [0.91 to 3.6 mg/lb], IM) delayed the onset of xylazine-induced emesis and reduced the number of emetic episodes but did not completely prevent emesis, even when dexamethasone was administered at the highest dose evaluated. Administration of promethazine (2 to 4 mg/kg [0.91 to 1.8 mg/lb], IM), a first-generation histamine receptor antagonist, to cats 1 hour before administration of xylazine (0.66 mg/kg, IM) also decreased the number of emetic episodes.9 In the present study, 20 of 34 (59%) control cats but only 1 of 32 (3%) cats in the maropitant group vomited, which suggested that maropitant was a more effective antiemetic for cats than metoclopramide, ondansetron, dexamethasone, or promethazine.

In the aforementioned studies,1,3,8,9 the antiemetic was administered to cats within 1 hour prior to the administration of the emetogenic agent. In the present study, maropitant was administered 20 hours before the emetogenic agents (dexmedetomidine and morphine) and still almost completely prevented emesis. Both the high antiemetic efficacy and the long duration of action might make maropitant an appealing antiemetic for cats, at least for the prevention of emesis induced by α2-adrenergic agonists and opioids. Although the antiemetic efficacy of maropitant when administered < 20 hours before administration of the emetogenic agents was not evaluated in the present study, the manufacturer reports that, in cats, the peak plasma concentration of maropitant is achieved at a mean of 0.32 hours after administration and the mean apparent elimination half-life is 16.8 hours.6 Therefore, we believe that the antiemetic efficacy of maropitant will be at least as high as that reported in the present study once the peak plasma concentration is achieved, even when it is administered < 20 hours before the emetogenic agent.

The antiemetic efficacy of maropitant observed in the cats of the present study was similar to that reported in dogs.5,10 In dogs, administration of maropitant (1 mg/kg, IM or SC) between 30 minutes and 1 hour before administration of hydromorphone (0.1 to 0.2 mg/kg, IM) completely prevented emesis.5,5 However, administration of maropitant (1 mg/kg, SC) to dogs < 15 minutes before administration of hydromorphone (0.1 to 0.2 mg/kg, IM) only decreased, but did not prevent, the incidence of emesis.5,10 In those 2 studies,5,10 it is likely that the peak plasma concentration of maropitant (and thus its peak efficacy) was not achieved before the emetogenic agent was administered. In dogs, administration of maropitant does not prevent signs of nausea, even when it completely prevents emesis.5 Likewise, maropitant administration did not eliminate signs of nausea for the cats of the present study despite a significant decrease in the incidence of emesis. Nausea is subjective and difficult to evaluate in veterinary patients; however, signs such as salivation and excessive swallowing and licking of the lips have been used in other studies1,5 to assess nausea in cats and dogs. For the cats of the present study, observation of sialorrhea and lip licking either alone or in combination was considered an indication of nausea. Collectively, the findings of those previous studies5,5 and the present study suggested that the efficacy of maropitant as an antinausea medication is considerably less than its antiemetic efficacy.

In the present study, cats had substantially greater aversive behavioral responses to injection of maropitant than to injection of isotonic saline solution. Those responses were independently evaluated by each of 4 observers on a 10-cm VAS and consisted primarily of vocalization and attempts to escape manual restraint. Although the VAS is a subjective measure, the VAS scores assigned to cats in the maropitant group were significantly higher than those assigned to control cats for all 4 observers. Additionally, when the VAS scores for all 4 observers were combined, the percentage of VAS scores ≥ 7 cm (the top third of the scale, which represented the most aversive reactions) was significantly greater for the maropitant group (27.3% [35/126 observations]) than for the control group (4% [6/136 observations]), which suggested that a severe aversive reaction to injection of maropitant was not an infrequent finding. Moreover, 1 cat in the maropitant group was assigned a VAS score of 10 by 1 observer who thought that animal had the worst reaction imaginable to an SC injection.

Given that injection of maropitant appeared to cause substantial discomfort for the cats of the present study, the quandary becomes whether the antiemetic efficacy of maropitant is sufficient to justify the discomfort caused by its administration. There is no question that decreasing or preventing emesis is very important for patients in which vomiting could result in severe secondary complications, such as those with abnormally increased intracranial pressure, descemeteces, and laryngeal dysfunction. However, the value of antiemetic administration to healthy animals prior to anesthesia for elective surgeries might be debatable. In dogs, although maropitant administration effectively decreases the incidence of emesis, it does not decrease the incidence of gastroesophageal reflux11; therefore, maropitant does not decrease the risk for the development of esophagitis and esophageal strictures or aspiration pneumonitis secondary to gastroesophageal reflux. Alternatively, if the sole purpose of
maropitant administration is to minimize the risk of postoperative emesis, it could be administered while patients are anesthetized to minimize the discomfort associated with its injection.

In the present study, administration of maropitant (1 mg/kg, SC) to healthy cats 20 hours prior to administration of dexamethomidine and morphine effectively decreased the incidence of emesis induced by those emetogenic agents. However, maropitant did not significantly decrease the incidence of signs of nausea, and it appeared to cause substantial discomfort when administered SC.

Acknowledgments
The authors thank Pati Kirch for technical assistance.

Footnotes
   c. Morphine sulfate, Baxter Healthcare Corp, Deerfield, Ill.
   d. GraphPad software, version 6.05, GraphPad, La Jolla, Calif.

References