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Prevalence of Gastroesophageal Reflux in Cats During Anesthesia and Effect of Omeprazole on Gastric pH

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Background: Gastroesophageal reflux (GER) is poorly characterized in anesthetized cats, but can cause aspiration pneumonia, esophagitis, and esophageal stricture formation. Objective: To determine whether pre-anesthetic orally administered omeprazole increases gastric and esophageal pH and increases serum gastrin concentrations in anesthetized cats, and to determine the prevalence of GER using combined multichannel impedance and pH monitoring. Animals: Twenty-seven healthy cats undergoing elective dental procedures. Methods: Prospective, double-masked, placebo-controlled, randomized clinical trial. Cats were randomized to receive 2 PO doses of omeprazole (1.45–2.20 mg/kg) or an empty gelatin capsule placebo 18–24 hours and 4 hours before anesthetic induction. Blood for measurement of serum gastrin concentration was collected during anesthetic induction. An esophageal pH/impedance catheter was utilized to continuously measure esophageal pH and detect GER throughout anesthesia. Results: Mean gastric pH in the cats that received omeprazole was 7.2 ± 0.4 (range, 6.6–7.8) and was significantly higher than the pH in cats that received the placebo 2.8 ± 1.0 (range, 1.3–4.1; \( P < .001 \)). Omeprazole administration was not associated with a significant increase in serum gastrin concentration (\( P = .616 \)). Nine of 27 cats (33.3%) had ≥1 episode of GER during anesthesia. Conclusions and Clinical Relevance: Pre-anesthetic administration of 2 PO doses of omeprazole at a dosage of 1.45–2.20 mg/kg in cats was associated with a significant increase in gastric and esophageal pH within 24 hours, but was not associated with a significant increase in serum gastrin concentration. Prevalence of reflux events in cats during anesthesia was similar to that of dogs during anesthesia. Key words: Esophagitis; Feline; Gastric pH; Impedance; Reflux.
overt clinical signs, and the need for advanced diagnostic equipment including esophageal pH catheters or pH capsules, endoscopes, and videofluoroscopic units that are not readily available to many veterinarians. Videofluoroscopy also is challenging to complete in nonseated cats given the temperament of the animals during restraint and the reluctance of cats to readily swallow barium-soaked food. Esophageal pH monitoring was considered the gold standard for documenting GER in people and animals, but mounting evidence has documented that esophageal pH probes underestimate the frequency of reflux events (RE) because of their insensitivity to nonacid reflux and subtle changes in pH that can be associated with many reflux events. Combined multichannel intraluminal impedance (MII)/pH-metry uses impedance technology to determine the type (liquid, gas) and incidence of reflux independent of its acidity. Combined MII/pH-meter also allows for detection of weakly acidic reflux (4.0 < pH < 7.0) and weakly alkaline (pH ≥ 7.0) reflux events that have been associated with esophagitis and respiratory symptoms in people.

Previous studies evaluating GER in anesthetized cats exclusively have evaluated the incidence of reflux under anesthesia using esophageal pH probes. Omeprazole has been evaluated in humans and dogs to decrease GER under anesthesia, but most studies have documented no effect of proton pump inhibitors (PPIs) on frequency of reflux. Proximal exposure of the esophageal mucosa to refluxed acid is an important cause of esophagitis and potential stricture formation, particularly when pH is <4.0 because the proteolytic pH range for the conversion of pepsinogen to pepsin is between 1.5 and 3.5. Efforts to neutralize gastric acid by PO administration of PPIs within 24 hours of anesthesia induction and determination of the effects of 2 PO doses of a PPI on serum gastrin concentrations have not been determined in cats to date. Long-term PPI therapy induces moderate hypergastrinemia and enterochromaffin-like (ECL)-cell hyperplasia in most patients, and hypergastrinemia has been used as an surrogate marker of gastric acid suppression efficacy. Gastrin concentrations therefore may be a comparably accurate measure of pharmacodynamic antisecretory effects vs. measurements of gastric acid secretion.

We hypothesized that pre-anesthetic administration of omeprazole in cats undergoing elective periodontal procedures would increase gastric and esophageal pH as well as serum gastrin concentrations. In addition, we hypothesized that the prevalence of GER in cats during anesthesia was significantly lower than that of dogs given the higher prevalence of clinically apparent esophagitis and postanesthesia stricture formation in dogs.

Materials and Methods

Animals

Client-owned cats admitted to the William R. Pritchard Veterinary Medical Teaching Hospital (VMTH) at the University of California, Davis, for elective dental procedures were recruited for inclusion into this prospective, randomized, masked, placebo-controlled study. All cats <6 years underwent a comprehensive physical examination, followed by a minimum database consisting of measurement of hematocrit and plasma protein concentration, semiquantitative assessment of blood urea nitrogen by dipstick, and urine specific gravity (USG) with a refractometer. In addition, a CBC, biochemistry panel, urinalysis, and serum concentration of total T4 were performed on all cats ≥6 years old. Cats with a history of GER, regurgitation, vomiting, esophagitis, and coughing or cats that had received a gastric acid suppressant drug or prokinetic medication within 2 weeks of anesthesia were excluded. Hyperthyroid cats or cats with renal disease (IRIS stage 1 or higher) also were excluded from the study. All laboratory testing must have been completed within 1 month of the procedure date. A sample size of 10 cats in each group, assuming a standard deviation (SD) of 1.0, a 2-sided test, and a probability of type 1 error equal to 0.05 had a power of 0.92 to detect a mean difference in pH of 1.5. We chose to enroll 13 cats in each group to account for attrition and achieved the desired level of power. The study protocol was evaluated and approved by the University of California, Davis, School of Veterinary Medicine Animal Care and Use Committee (IACUC), and owners of all cats signed an informed consent form before enrollment of the pet in the study.

Treatment Groups

Each cat was randomized by an Excel software program random number generator into 1 of 2 treatment groups to receive either 2 PO doses of omeprazole sodium (1.45–2.20 mg/kg) or a placebo of an empty gel cap (size # 4) followed by 10 mL of water administered PO by syringe. Omeprazole capsules (20 mg) containing enteric-coated omeprazole granules were opened and the contents evenly divided by weight to formulate 10 mg capsules that again were placed into empty gel caps (size # 4). All treatments were administered by 1 of the investigators who was not involved in the interpretation of the pH/impedance results. A first dose of omeprazole or placebo was given PO 18–24 hours before induction, and a second dose was administered PO 4 hours before induction.

Gastrin Assay

Blood was collected into a serum tube (without serum separator gel) from the cephalic or medial saphenous vein at the time of IV catheter placement within 15 minutes of anesthetic induction. Serum samples were stored at −80°C until being batch-mailed for determination of serum gastrin concentrations at Michigan State University Diagnostic Center for Population and Animal Health. Serum gastrin concentration was determined with a commercially available radioimmunoassay kit according to the manufacturer’s protocol. The laboratory reported the following percentage cross-reactivity with related compounds: gastrin 17-1 (100%), gastrin 17-II (77%), gastrin 34-I (42%), gastrin 5–17 (54%), cholecystokinin-PZ (<0.1%), and cholecystokinin-8 (10.9%). The laboratory-reported limit of detection was 3 ng/L. For intra-assay repeatability (10 replicates), the coefficient of variation (COV) for a feline sample with a gastrin concentration of 45 ng/L was 8.6%. For interassay repeatability (10 replicates), the COV for a feline sample with a gastrin concentration of 54 ng/L was 9.2%.

Anesthetic Protocol

All cats were fasted for at least 12 hours before induction. The anesthetic protocol was identical in each cat, consisting of premedication with oxymorphone (0.05 mg/kg SC) and atropine...
(0.02 mg/kg SC), followed by induction of anesthesia with propofol (4 mg/kg IV) and midazolam (0.2 mg/kg IV), titrated to effect to produce a lack of palpebral reflex, ventromedial rotation of the eyes, and jaw muscle relaxation. Anesthesia was maintained in all cats with isoflurane (1-3%), titrated to maintain appropriate procedural anesthetic depth. All cats were endotracheally intubated and maintained in dorsal recumbency, and lactated Ringer’s solution (10 mL/kg/h IV) was administered throughout anesthesia. Esophageal temperature probes and stethoscopes were avoided during anesthetic monitoring to minimize artifact during recording. The anesthetist responsible for administering and monitoring anesthesia was masked to the treatment group assignment.

**Measurement of Reflux**

Immediately after induction of anesthesia, a 6.4-French (2.13-mm) esophageal multi-use pH/impedance catheter was attached to an electrical external reference pad that was placed in the axillary region of the cat. All of the pH/impedance catheters had 7 impedance sensors, each in the form of a 4-mm cylindrical ring and spaced 2 cm apart, as well as 1 pH sensor located approximately 2 cm from the tip of the catheter (Fig 1). The segment between each pair of sensors, known as the impedance sensor spacing, corresponds to 1 recording impedance channel, thus resulting in 6 corresponding impedance channels along the length of the catheter.

The pH electrode of the MII-pH catheter was calibrated within 10 minutes of use in buffer solutions of pH 4.0 and 7.0 according to the manufacturer’s instructions. The esophageal catheter was coated with a water-based lubricant and introduced into the left or right naris and passed through the ventral nasal meatus into the oropharynx where it was reflected rostrally with the aid of a spay hook. Any residual lubricant was removed from the catheter with a saline-moistened gauze, and the catheter then was guided aborad into the esophagus by use of a loop snare passed through the biopsy channel of a video endoscope. Catheter placement was performed in all cats by 1 of 3 investigators (SLM, RSG, or ADM) skilled in endoscope handling to ensure consistency in the positioning of the catheter. The catheter was advanced into the greater curvature region of the stomach in 32 cats to record gastric pH for 2 minutes before the catheter was retracted into the distal esophagus so that the pH sensor on the catheter was positioned 6 cm proximal to the gastroesophageal junction (GEJ) in all cats with all of the catheter’s impedance rings and channels located within the esophagus. Deionized water was used to rinse any residual gastric acid from the pH catheter, and air introduced into the stomach and esophagus during catheter placement was carefully suctioned. The catheter then was secured in place using butterfly tape wrapped around the catheter and secured to the skin with skin staples lateral to the naris and ventrolateral to the ipsilateral zygomatic arch. The catheter was attached to a recording device from which data were uploaded to a computer by proprietary software. The reasons for placing the catheter transnasally (in contrast to transorally) were 2-fold: (1) to minimize interference (movement and displacement) of the catheter during the dental procedure, and (2) to avoid interference with the dentist’s procedure and field of vision in the oral cavity. The oropharynx was suctioned throughout the procedure to minimize fluid entering the hypopharynx and esophagus and contaminating the distally located pH sensor or impedance channels. Esophageal pH and impedance were recorded throughout the dentistry procedure until the catheter was removed immediately before extubation of the cat. Data analysis was performed by proprietary software from the manufacturer by 1 of the investigators (JO) who was masked to the treatment group assignment.

**Defining Reflux by Impedance**

A reflux episode was defined as a 50% decrement in ohms seen in 2 consecutive impedance channels in the distal esophagus for >2 seconds from the pre-episodic esophageal baseline recording. Impedance (Z) technology relies upon the principle of resistance to the passage of flow of an electrical current and is inversely related to conductivity. Impedance is influenced by the physical characteristics of intraluminal substrates, and gastric refluxate has high electrical conductivity, or low impedance, whereas intraluminal air has a low conductivity, or high impedance. Interpretation of the waveform generated by the computer can be used to determine whether the refluxate originated orally or aborally. In addition, the demarcated concentric impedance rings and impedance channels located along the length of the catheter allow the investigator to determine the distance the refluxate travels up the esophagus by assessing the length of the waveform generated (Fig 2).

The pH of the refluxate was classified as strongly acidic (pH < 4.0), weakly acidic (4.0 < pH < 7.0), or weakly alkaline (pH ≥ 7.0). The mean acid clearance time was defined as the duration of each acid RE, beginning at the moment the pH decreased to <4.0 and ending when the pH increased to ≥4.1. All cats were monitored during the dentistry procedure for regurgitation or reflux events by the anesthesiologist, and all events were recorded in the anesthesia record of the animal.

**Statistical Analysis**

All data were coded and recorded into SPSS 22.0 for the Macintosh computer. Differences between group means were assessed by the independent-samples t-test. All results were confirmed with the nonparametric Mann-Whitney U-test. Statistical significance was ascertained at a probability of type I error (α) of 0.05. A
Bonferroni correction was utilized to adjust for multiple comparisons (1 primary and 3 secondary endpoints).

### Results

#### Animals

Thirty-six cats were evaluated for enrollment in the study, and 9 cats ultimately were excluded: 4 cats were excluded because of small patient size (<4.0 kg) precluding transnasal passage of the esophageal catheter. Three additional cats were excluded because of failure of pH/impedance catheter calibration or failure of pH/impedance data to be recorded. Two cats were excluded post-procedure because of histories of chronic vomiting (1) and chronic kidney disease (1) that were not apparent at the time of enrollment. Of the 27 cats that completed the study, 14 were assigned to the placebo group and 13 were assigned to the omeprazole group. Drying of the pH sensor on the catheter precluded accurate determination of gastric and esophageal pH in 4 of the 27 cats, but this did not affect impedance function, which allowed determination of RE in all cats. Seventeen cats had a CBC, biochemistry panel, urinalysis, and serum T4 concentration performed. Of the remaining 10 cats (all <6 years of age), 8 did not have serum T4 concentration measured, 4 had a hematocrit/plasma protein performed instead of a CBC, and 2 had semiquantitative assessment of blood urea nitrogen by dipstick and measurement of urine specific gravity (USG) instead of a biochemistry panel and complete urinalysis.

The age of the cats ranged from 1.7 to 16.9 years (mean ± SD, 8.6 ± 3.8 years). Body weight ranged from 4.5 to 7.7 kg (mean ± SD, 5.5 ± 0.8 kg). Castrated male cats (18 of 27; 67%) represented the largest sex grouping; the remaining 9 cats were spayed females. No significant differences in age (P = .35), body weight (P = .43), or sex distribution (P = .17) were identified between the treatment groups. Domestic shorthaired cats represented the most common breed (n = 19/27; 70%), with domestic longhaired cats (n = 4/27; 15%), Maine Coon (n = 2/27; 7%), Himalayan (n = 1/27; 4%), and Burmese (n = 1/27; 4%) breeds also represented. The dosage of omeprazole administered to the cats assigned to the omeprazole group ranged from 1.45 to 2.20 mg/kg (mean ± SD, 1.85 ± 0.23 mg/kg). No diarrhea was noted by owners of any cat in the omeprazole group after administration.
of the drug. The dentistry procedure time ranged from 1.4 to 5.1 hours (mean ± SD, 2.8 ± 0.9 hours) and no significant difference in procedure time was identified between treatment groups (P = .65). All cats underwent periodontal treatment under anesthesia, and 17 of 27 cats (63%) also required dental extractions. There was no difference in the procedures performed between groups (P = .88). No morbidity or death was associated with anesthesia or the study procedures. No visual evidence of reflux or regurgitation was recorded in any of the enrolled cats during the dentistry procedure.

**Gastrin**

Serum gastrin concentrations were measured in all 27 cats enrolled in the study. Gastrin concentrations in the placebo group (34.3 ± 10.8 ng/L; range, 22–64 ng/L) and omeprazole group (45.7 mean ± 37.2 ng/L; range, 16–135 ng/L) were not significantly different (P = .62).

**Gastric pH**

Gastric pH was recorded in all 27 cats, but pH readings were invalid for 1 cat in the placebo group and for 3 cats in the omeprazole group because of drying of the pH sensor. The drying of the pH sensor did not affect the functioning of the impedance channels that allowed the continued determination of RE throughout the procedure in these cats. Gastric pH readings were valid in 23 of 27 cats, representing 13 cats in the placebo group and 10 in the omeprazole group. Mean gastric pH in the cats that received omeprazole was 7.2 ± 0.4 (range, 6.6–7.8) and was significantly higher than the pH in cats that received the placebo 2.8 ± 1.0 (range, 1.3–4.1; P < .001; Fig 3).

**Esophageal pH**

Esophageal pH was measured in the same 23 cats as gastric pH, and results of esophageal pH testing were not valid in the other 4 cats. Mean esophageal pH for the omeprazole group was 6.8 ± 0.4 (range, 6.3–7.6) and was significantly higher (P < .001) than mean pH for the placebo group 5.3 ± 0.9 (range, 3.8–6.6). An esophageal pH < 4.0 was documented in 3 of 13 cats in the placebo group and in none of the cats in the omeprazole group. In these 3 cats, the mean time of esophageal pH < 4.0 was 106.5 ± 107.2 minutes (range, 7.1–220.0 minutes), or 48.8% of total procedure time. The mean percentage of total procedural time that the esophageal pH was < 4.0 was 14.2% for the entire placebo group. Mean percentage of procedural time that the esophageal pH was < 4.0 for the omeprazole group could not be calculated because a pH < 4.0 was not recorded.

**Gastroesophageal Reflux Events**

Nine of 27 cats (33.3%) had at least 1 episode of GER during anesthesia, representing 7 of 14 cats (50.0%) in the placebo group, and 2 of 13 cats (15.4%) in the omeprazole group. In total, 14 individual REs were documented in the 9 cats (Table S1). Of the 9 cats in which reflux was identified, 6 cats each had a single reflux event (5 placebo, 1 omeprazole), a single cat had 2 reflux events (placebo), and 2 cats each had 3 separate reflux events (1 placebo, 1 omeprazole; Table S1).

The height of the refluxate in the esophagus was determined by impedance data for all 14 REs in the 9 cats that experienced reflux (Table S1). No cat was noted to have visual evidence of reflux or regurgitation during or immediately after anesthesia. The mean ± SD number of RE was 0.71 ± 0.94 for the placebo group (n = 14) and 0.31 ± 0.86 for the omeprazole group (n = 13). The administration of omeprazole did not significantly decrease the number of RE in comparison with the placebo group (P = .057). The odds ratio of the placebo group having at least 1 reflux event was 2.75 times the likelihood of a reflux event in the omeprazole group (95% confidence interval [CI] = 0.77–9.86; P = .069).

**Mean Acid Clearance Time**

The mean acid clearance time was calculated for cats in the placebo group (106.5 ± 107.2 minutes; range, 7.1–220 minutes). Cats in the omeprazole group had no strongly acidic reflux documented, precluding calculation of mean acid clearance time.

**Discussion**

Gastroesophageal reflux (GER) during anesthesia is a common and well-documented phenomenon in people and dogs and has been associated with esophagitis, esophageal stricture formation, and aspiration pneumonia.1,3 In contrast, GER has been documented
to occur less frequently in endotracheal-intubated cats compared to non-intubated cats, and the refluxate reached the pharynx in 7% of cats compared to nearly 25% of dogs. Several pre-anesthetic and anesthetic agents decrease LES tone and possibly increase the risk of GER in cats. These include commonly used drugs such as atropine, acepromazine, propofol, ketamine, and xylazine. Atropine and acepromazine administration to cats was shown to decrease LES pressure to 13.2% of baseline, and ketamine administration was shown to decrease LES pressure considerably less compared to administration of propofol, thiopental, and a combination of xylazine, ketamine, and atropine in 40 cats undergoing elective castration or ovariectomy procedures. Although not investigated in cats, inhalant anesthetics also have been shown to decrease LES tone in other species.

Transient lower esophageal sphincter relaxations (TLESRs) have been found to be the main mechanism for all types of RE in humans and provide an alternate mechanism for GER in cats. These TLESRs are variously classified as reflex-mediated, prolonged relaxations of the LES that occur independent of swallowing. They occur as a normal physiologic response to gastric distention, but not gastric pH, and allow venting of gastric gas in the anesthetized cats overall and in 50% of cats that had continuous gastric and esophageal pH measurements throughout their procedures had a gastric pH < 4.0, with 2 cats having pH < 4.0 for over 90 minutes (92.3 and 220.0 minutes, respectively). In vivo studies in several domestic species, including cats, have shown that acute esophagitis can be induced by bathing the esophagus in a combination of HCI and pepsin or HCl alone for protracted periods (up to 1 hour) does not result in macroscopic or microscopic changes consistent with acute esophagitis. Despite the established risk of pepsin, other enzymes (e.g., trypsin) and bile salts can cause esophagitis. These compounds often have maximal proteolytic or solubilizing activities at a pH that can be found in the esophagus after weakly or nonacid RE. This further highlights the importance of characterizing all types of RE, not just strongly acidic RE. Anesthesia increases the risk of esophagitis and stricture formation in part because clearance of esophageal reflux does not occur under anesthesia.

Omeprazole was evaluated at a slightly higher dosage than has been used in previous studies of cats, although the dosage is consistent with studies in dogs showing the efficacy and safety of a higher dosage of omeprazole. Twice-daily dosing of omeprazole in cats recently was shown to cause significant acid suppression in contrast to once-daily administration of the drug.

Administration of omeprazole did not significantly decrease the number of RE in comparison with the placebo group (P = .057), consistent with previous impedance/pH-metry studies in humans and dogs that failed to find a decrease in the incidence of reflux with pre-anesthetic administration of omeprazole or esomeprazole (the active S-enantiomer of omeprazole) compared to controls. A single study in dogs found that pre-anesthetic administration of omeprazole decreased the incidence of reflux, but that study was hampered by the use of pH monitoring only to detect reflux events. The mechanism responsible for the increased frequency of reflux episodes was not definitively known, but omeprazole and esomeprazole have been shown to decrease gastric volume in both people and cats and could have decreased the number of TLESRs.

Based on the results of our study showing a relatively high prevalence of reflux events in cats during anesthesia and a significant effect of omeprazole on technology allows for weakly acidic or weakly alkaline RE, which are characterized by subtle changes in pH, potentially to be missed, resulting in an underestimation of the frequency of reflux. If traditional pH-metry without impedance technology had been utilized in our study, only 3 strongly acidic REs would have been documented out of a total of 14 reflux events.

The PO administration of omeprazole was associated with a significant increase in both gastric and esophageal pH, and none of the 10 cats in the omeprazole group that had continuous gastric and esophageal pH measurements throughout their procedures had a gastric or esophageal pH < 4.0 at any measured time point. This marked effect was noted despite administration of 2 PO doses of the PPI within only 24 hours of anesthesia. In the placebo group, 3 cats had periods of time during which esophageal pH was < 4.0, with 2 cats having pH < 4.0 for over 90 minutes (92.3 and 220.0 minutes, respectively). In vivo studies in several domestic species, including cats, have shown that acute esophagitis can be induced by bathing the esophagus in a combination of HCl and pepsin or HCl alone for protracted periods (up to 1 hour) does not result in macroscopic or microscopic changes consistent with acute esophagitis. Despite the established risk of pepsin, other enzymes (e.g., trypsin) and bile salts can cause esophagitis. These compounds often have maximal proteolytic or solubilizing activities at a pH that can be found in the esophagus after weakly or nonacid RE. This further highlights the importance of characterizing all types of RE, not just strongly acidic RE. Anesthesia increases the risk of esophagitis and stricture formation in part because clearance of esophageal reflux does not occur under anesthesia.

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Administration of omeprazole did not significantly decrease the number of RE in comparison with the placebo group (P = .057), consistent with previous impedance/pH-metry studies in humans and dogs that failed to find a decrease in the incidence of reflux with pre-anesthetic administration of omeprazole or esomeprazole (the active S-enantiomer of omeprazole) compared to controls. A single study in dogs found that pre-anesthetic administration of omeprazole decreased the incidence of reflux, but that study was hampered by the use of pH monitoring only to detect reflux events. The mechanism responsible for the increased frequency of reflux episodes was not definitively known, but omeprazole and esomeprazole have been shown to decrease gastric volume in both people and cats and could have decreased the number of TLESRs.

Based on the results of our study showing a relatively high prevalence of reflux events in cats during anesthesia and a significant effect of omeprazole on
gastric and esophageal pH, future studies should determine the clinical impact of GER in anesthetized cats and whether pre-anesthetic administration of PPIs is warranted. Modification of gastric and esophageal pH by omeprazole might decrease the risk of esophagitis and esophageal stricture formation based on experimental studies performed in rabbits and cats.19,35,37

The lack of an increase in serum gastrin concentrations after 2 PO doses of omeprazole to the cats in our study was unexpected in light of the findings of increases in serum gastrin concentrations within 24 hours of PPI administration in dogs and humans.44,45 Serum gastrin measurements in healthy controls in a previous study showed a seemingly wide range of concentrations (17–94 pg/mL) in cats and dogs, with many dogs having serum gastrin concentrations within the normal reference interval 24 hours after PPI administration.45,46 It took 4–5 days for serum gastrin concentration to peak in dogs, although gastrin concentrations did increase to a level of significance 24 hours after initiation of omeprazole therapy.45 A recent study evaluating the long-term effects (8 weeks) of twice-daily omeprazole orally administered to 6 healthy adult cats showed a significant increase in serum gastrin concentrations at 4 weeks and 8 weeks after initiation of omeprazole administration compared to placebo, but serum gastrin concentrations were not determined within the first 24 hours of omeprazole administration.44 It is plausible that the relatively brief period after administration of omeprazole and collection of serum for gastrin determination provided insufficient time for removal of negative-feedback inhibition of gastrin secretion as has been documented in humans.46 The gastrin assay we used has been validated for cats and has been used in other studies and is not suspected to be a source of error.45 Further studies with larger numbers of animals given omeprazole for a longer duration are indicated to assess the effects of PPIs on serum gastrin concentrations in cats.

Our study had several limitations. The relatively small study numbers of cats in both groups increased the probability of a type II error. A further limitation of the study was the loss of pH data from several cats, which was unexpected in light of the findings of increases in serum gastrin concentrations within 24 hours of PPI administration.45,46 It took 4–5 days for serum gastrin concentration to peak in dogs, although gastrin concentrations did increase to a level of significance 24 hours after initiation of omeprazole administration compared to placebo, but serum gastrin concentrations were not determined within the first 24 hours of omeprazole administration.44 It is plausible that the relatively brief period after administration of omeprazole and collection of serum for gastrin determination provided insufficient time for removal of negative-feedback inhibition of gastrin secretion as has been documented in humans.46 The gastrin assay we used has been validated for cats and has been used in other studies and is not suspected to be a source of error.45 Further studies with larger numbers of animals given omeprazole for a longer duration are indicated to assess the effects of PPIs on serum gastrin concentrations in cats.

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Conflict of Interest Declaration: Sandhill Scientific Inc. employed Jean Osborn at the time of the study. She has advanced expertise in interpreting esophageal pH/impedance recordings and interpreted all recordings in a masked fashion.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

Footnotes

a Azostix® Reagent Strips, Siemens Healthcare Diagnostics Inc., Tarrytown, NY
b Reichert® Vet 360 Refractometer, Reichert Analytical Instruments Inc., Depew, NY
c Microsoft® Excel® for Mac 2011, Version 14.4.8
d Omeprazole delayed-release capsules USP, Apotex Inc., Toronto, ON, Canada
e Gastrin [125I] Radioimmunoassay Kit, MP Biomedicals, Diagnostics Division, Orangeburg, NY
f Osmomyrophosphate hydrochloride injection (1 mg/mL), Endo Pharmaceuticals Inc., Malvern, PA
g Atropine, Baxter Healthcare Corporation, Deerfield, IL
h Propofol, Diprivan, Abbott Laboratories, North Chicago, IL
i Midazolam injection USP, West-Ward Pharmaceuticals, Eatontown, NJ
j Isolurane USP, Piramal Critical Care, Inc., Bethlehem, PA
k Lactated Ringer’s Solution, Baxter Healthcare Corporation, Deerfield, IL
l Esophageal impedance/pH catheters, model ZP-BS-46E, Sandhill Scientific, Inc., Highlands Ranch, CO
m PDI lubricating jelly II, Orangeburg, NY
n Vet Oval Loop “Grabber” snare, 2.5 cm loop, Endoscopy Support Services Inc., Brewster, NY
o Olympus GIF-P140 gastroscope, Olympus America Inc., Center Valley, PA
p Vet One® surgical skin staples, MWI, Boise, ID
q ZepHr® Impedance/pH reflux recorder, Sandhill Scientific, Inc., Highlands Ranch, CO
r Sandhill Patient Import/Export Utility software version 5.3.0, Sandhill Scientific, Inc., Highlands Ranch, CO
s Sandhill BioVIEW Analysis software version 5.5.4.1 and Sandhill pH Analysis software version 4.0.1, Sandhill Scientific, Inc., Highlands Ranch, CO
t IBM SPSS version 22.0 software for the Macintosh, IBM Corporation, Armonk, NY

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

Table S1. Table illustrating the mean esophageal and gastric pH, and the frequency, type, and height of the reflux events in 9 of 27 apparently healthy cats that had ≥ 1 reflux event during anesthesia for an elective dental procedure.