Rational therapy for vomiting in dogs and cats
Lauren A. Trepanier, DVM, PhD, Dip. ACVIM, Dip. ACVCP
University of Wisconsin-Madison, School of Veterinary Medicine, Madison, Wisconsin

Vomiting is a common problem in veterinary patients, and can lead to dehydration, weight loss, and reflux esophagitis. There are several clinically effective veterinary anti-emetic drugs. Choosing among these options depends on the likely cause of the vomiting and the mechanisms of action and side effects of each drug.

The first step before considering an antiemetic in a dog or cat is a reasonable work-up to rule out serious underlying disease. Every acutely vomiting animal that is brought to a veterinary clinic deserves two view abdominal radiographs to rule out obstruction. Using antiemetics empirically in animals with unrecognized GI obstruction can delay the diagnosis and worsen the prognosis. If vomiting is severe or persistent, a CBC, biochemical panel, and pancreatic lipase test are indicated.

“If they are sick enough for an antiemetic, they are sick enough for a work-up”

ANTI-EMETICS
Maropitant (Cerenia™):
Neurokinin-1 receptor antagonist.
- Inhibits substance P binding to NK-1 receptors in emetic center, chemoreceptor trigger zone (CRTZ), and enteric plexus of gut.
- Very effective antiemetic.
- May not control actual nausea after some stimuli (for example, after doxorubicin, hydromorphone, and morphine; Rau 2010, Claude 2014, Koh 2014)

Indications:
- Vomiting due to uremia, gastroenteritis, or pancreatitis
- Prevention of vomiting due to motion sickness in dogs and cats
- Pre-treatment of dogs to prevent vomiting prior to cisplatin, doxorubicin, or hydromorphone
- Potent enough to prevent xylazine-induced emesis in cats (Hickman, 2008).
- Has anesthetic-sparing effect during spays in dogs (Boscan, 2011)
  - 1 mg/kg IV, followed by 30 ug/kg/hr CRI

Dosing:
- Dogs: 1 mg/kg IV or SC; 2 mg/kg PO
  - 8 weeks of age and older
  - Dosing limited to 5 days in a row for puppies 2 to 7 months old
  - Longer treatment now label approved for dogs older than 7 months
- Dogs for motion sickness: 8 mg/kg PO once daily for maximum of 2 days
- Cats: 1 mg/kg IV, SC, or PO once daily
  - 16 weeks of age and older

Drug interactions/Contraindications/Side effects:
- Well tolerated and effective treatment for various causes of vomiting.
- Maropitant may not be the best drug to control nausea. Therefore, not indicated for inappetent or nauseous patients without actual vomiting.
- Pain on injection can be decreased by refrigerating vial (Narishetty 2009)

Metoclopramide
Increases release of acetylcholine in GI smooth muscle, leading to increased gastric emptying and net “downstream” intestinal motility, without ileus.
- Antagonizes the actions of dopamine on the chemoreceptor trigger zone in dogs (central antiemetic action in dogs).
- As effective as maropitant in blocking apomorphine-induced emesis in dogs (Selacek 2008)
- Traditionally thought to increase tone in the lower esophageal sphincter (reducing reflux), but
Metoclopramide in cats:
  • Metoclopramide does not appear to be effective as a central D2 antagonist antiemetic in cats. Emesis in cats appears to be mediated through receptors other than D2, particularly alpha2 receptors.
    o This is consistent with the finding that cats are also very insensitive to vomiting induced by apomorphine (a dopaminergic agonist), but are sensitive to emesis from xylazine (an a2 agonist).
    o Further, metoclopramide can decrease xylazine-induced vomiting in cats (Kolahian 2010)
  • Metoclopramide does appear to decrease vomiting in cats clinically, either due to its prokinetic effects or through indirect effects not involving D2 receptors.

Indications:
  • Delayed gastric emptying
  • Nausea associated with ileus
  • Central antiemetic in dogs, especially when ileus is also suspected (e.g. renal failure and pancreatitis)
  • Prevention of GI upset during cyclosporine treatment (anecdotal success)
  • Prevention of nausea due to overdistended stomach during esophagostomy tube feedings

Dosing:
  • 0.2-0.4 mg/kg q. 6 hours SC or PO.
  • May be most effective when given by continuous rate IV infusion (1-2 mg/kg/day). Reduce the dosage in renal failure.

Drug interactions/Contraindications:
  • Rule out intestinal obstruction first
  • Enhances acetaminophen, and ethanol absorption in humans (therefore, should be avoided for treatment of vomiting due to intoxications; may enhance delivery of toxin to small intestine)

Side effects:
  • Tremor, hyperactivity, and anxiety after high doses (Parkinson's-like; stop the drug and treat with diazepam)
  • Decrease dosage in renal failure (decreased metoclopramide clearance may lead to tremor).

Ondansetron (Zofran®)
  Antiemetic with 5HT3 receptor antagonist activity; antagonizes these receptors in both the CNS and GI tract. Particularly effective for vomiting due to peripheral stimulation (Sedlacek 2008)
  Indications:
  • Refractory vomiting in patients with diagnosed visceral disease (e.g. pancreatitis, GI neoplasia, hepatic disease).
  • Prophylaxis of vomiting associated with chemotherapy.
  • Prophylaxis of vomiting from dexmedetomidine in cats (0.22 mg/kg of ondansetron in same syringe as dexmedetomidine, given IM) (Santos 2011)
  • May be more effective for nausea (without vomiting) than maropitant (Kretzing 2011)

Formulations/Dose/Route:
  • 2 mg/ml injectable; 4 mg tablet; oral solution 4 mg per 5ml.
  • Best estimated dosage: 1.0 mg/kg SC q. 12 hours. (Quimby 2014)
    o Marked variability in pharmacokinetics in (beagle) dogs (Baek 2015)
    o Prior recommended dosage of 0.5 mg/kg PO q 12h may be sub-therapeutic in cats (Quimby 2014)
    o SC route in cats is twice as bioavailable and may give longer duration of action than PO or IV (Quimby 2014)

Drug interactions/Contraindications/Side effects:
  • Headache or dizziness in humans
- Increases in ALT reported in humans.
- Ondansetron is a p-glycoprotein substrate in humans but has not been evaluated in dogs—potential for adverse effects in Collies and other dogs with MDR1 mutations
  http://www.vetmed.wsu.edu/depts-VCPL/drugs.aspx

**Dolasetron** (Anzemet):
Another 5HT3 receptor antagonist in both the CNS and GI tract.
- Less frequent dosing than ondansetron in humans.

**Indications:**
- As for ondansetron
- Available as injectable but much more expensive than injectable ondansetron
- Oral formulation is twice as expensive but may allow once daily dosing (?)

**Formulations/Dose/Route:**
- 0.6 – 1.0 mg/kg IV once daily(?)
- Elimination half-life of active metabolite is only 4 hours in dogs (Dow 1996).
- Oral tablets (50 and 100 mg) too large for use without reformulation.

**Drug interactions/Contraindications/Side effects:**
- Headache or dizziness in humans
- Associated with prolongation of QT interval in humans (hypokalemia is a risk factor).

**Prochlorperazine** (Compazine®), **Chlorpromazine** (Thorazine®)
Central antiemetics with multiple mechanisms of action: dopamine antagonist, H1 antagonist, alpha-adrenergic antagonist, and anticholinergic. Inhibit vomiting at chemoreceptor trigger zone and directly at emetic center (therefore, potent antiemetic). **Less effective for peripheral triggers of vomiting** (Sedlacek 2008)

**Indications:**
- Not recommended for empirical outpatient use because of potential for hypotension and sedation (undesirable in a sick patient).
- Prochlorperazine or chlorpromazine may be useful for refractory vomiting in patients with diagnosed underlying disease and a central cause for vomiting (e.g. chemotherapy, uremia), for which IV fluid support can be provided.
- Additional effect of sedation may be beneficial in anxious dogs or fractious cats.
- Inexpensive
- Note: acepromazine (0.05 mg/kg IM) is also effective as an adjunct treatment to prevent nausea in dogs, for example prior to morphine pre-medication (Koh 2014)

**Dosage:** 0.1-0.5 mg/kg SC q. 8 hours.

**Drug interactions/Contraindications/Side effects:**
- Can cause hypotension (alpha-blockade) or tremors (dopaminergic antagonism).
- Can cause sedation and potentiate effects of sedatives, anesthetics, and organophosphates.
- Do not use this drug in dehydrated patients or in those without a diagnosis.
- Do not use formulations that contain anticholinergics such as isopropamide.
- Do not use in combination with metoclopramide (additive antidopaminergic effects).

**ADJUNCTIVE DRUGS FOR VOMITING PATIENTS**

**Famotidine** (Pepcid®)
Famotidine is an H2 blocker that is more potent than ranitidine and unlike cimetidine, has no P450 inhibition. **Famotidine is not an antiemetic, and is overused in vomiting animals,** since hyperacidity is probably a relatively uncommon cause of vomiting in dogs and cats.

**Indications:**
- Persistent vomiting where secondary reflux and esophagitis are a concern
- Vomiting due to hyperacidity (renal failure, mast cell disease).
No direct antiemetic effects.

**Empirical dose:**
- 1 mg/kg twice daily; 8mg/ml suspension available
- However, this dosage suppresses gastric acid (pH > 3-4) for only 14-22% of the day in dogs (Tolbert 2011), which is inadequate by human standards
- Omeprazole is more effective than famotidine at suppressing gastric acid in dogs

**Side effects:**
- Generally well tolerated.
- As for other basic drugs, rapid IV infusion may cause bradycardia.
- Prior anecdotal reports of hemolysis were unsupported in recent study; safe in cats given famotidine IV by slow bolus over 5 minutes (de Brito Galvao & Trepanier, 2008).
- Requires dose reduction in renal failure (shown in humans).

**Ranitidine (Zantac®):**
Also an H₂ blocker; has additional benefit of prokinetic effects (weak anticholinesterase activity)

**Indications:**
- No direct antiemetic effects.
- As an antacid in patients suspected of having both hyperacidity and either gastric atony or megacolon (cats)

**Formulations and dosage:** 75 mg tablets over the counter; Syrup 15 mg/ml available.
- Dosage in cats (based on pharmacokinetics): 2.5 mg/kg IV q. 12 hours, 3.5 mg/kg PO q. 12 hours.
- Typical dosage in dogs: 2 mg/kg PO q. 8-12 h
  - However, ranitidine at 2 mg/kg PO q. 12 h was ineffective in suppressing gastric acid in dogs, compared to famotidine (Bersenas 2005)

**Side effects:**
- As for famotidine, requires dose reduction in renal failure (shown in humans).
- Unlike cimetidine, no clinically significant P450 enzyme inhibition with ranitidine at therapeutic dosages.
- Rapid IV infusion may cause hypotension.

**Omeprazole (Prilosec®; Gastrogard®):**
H+/K+ ATPase pump inhibitor. Blocks the final step in gastric acid secretion.
- More potent than famotidine at acid suppression in dogs (Tolbert 2011)

**Indications:**
- Clinically proven gastroduodenal ulceration
- Erosive esophagitis
- NSAID overdose
- Portal hypertension
- (Gastrinomas)

**Formulations/Dose/Route:** 10 and 20 mg capsules.
- Drug is enteric-coated to prevent degradation.
  - If reformulated, enteric-coated granules can be placed in a gelatin capsule.
  - Split enteric coated tablets are actually effective in cats (Parkinson 2015)
  - Note: equine preparation is much too concentrated to use safely in dogs and cats unless professionally reformulated.

**Empirical dose:**
- 1.0 mg/kg PO BID in dogs and cats (Bersen & Parkinson 2015)
- 1.5-2.6 mg/kg once daily (Tolbert 2011)

**Drug interactions/Contraindications:**
- Omeprazole is a P450 enzyme inhibitor in humans, but not as broad spectrum as cimetidine.
- Can inhibit bioactivation of clopidogrel (Plavix) in humans
- Unnecessary to add famotidine during initial treatment with omeprazole (Tolbert 2015)

**Side effects:**
- Chronic administration of omeprazole is associated with gastric polyps in humans.
- Safety for long-term administration (months to years) not established in dogs/cats.
- Omeprazole does lead to gastric mucosal hypertrophy in dogs at high doses given chronically.

Sucralfate (Carafate®):

- Disaccharide complexed to aluminum hydroxide; at acid pH in stomach, acquires negative charge and adheres to positively charged matrix elements exposed in ulcer beds.
- Also binds pepsin and bile salts (which can otherwise contribute to ulcer formation), and phosphates (useful for renal failure patients with hyperphosphatemia).
- May enhance production by gastric mucosa of cytoprotective prostaglandins (increased blood flow and cell turnover lead to faster ulcer healing).

Indications:
- Gastric ulceration
- Esophagitis
- Gastric or duodenal neoplasia with ulceration
- Post-endoscopic retrieval of gastric or esophageal foreign bodies
- (Disappointing topical efficacy for radiation mucositis in humans)

Note: sucralfate has been shown in an experimental model to prevent acid-induced esophagitis in cats; may be useful prior to surgery when reflux is anticipated (recent meal; megaesophagus; esophageal or gastric foreign body).

Empirical dosage: 1/4 to 1 gram q. 6 to 8 hours. May be crushed and suspended in water; it is stable for 14 days in the refrigerator as a 200 mg/ml suspension.

Drug interactions:
- Very important! Sucralfate binds other drugs and impairs their absorption (tetracycline, digoxin, fluoroquinolones)
- Important to give most other drugs at least 2 hours before sucralfate (not vice versa). This is difficult for many clients to achieve.
- Exception: sucralfate can be given concomitantly with H2 blockers without affecting their overall absorption (Albin, 1986; Mullersman, 1986); therefore, no separation of dosing times is necessary.

Side effects: Constipation, chalky, unpalatable taste

Cisapride

- Prokinetic drug in the same family as metoclopramide; increases release of acetylcholine from myenteric plexus (via effects on serotonin receptors) in smooth muscle of esophagus, stomach, small intestine, and colon; increases lower esophageal sphincter pressure, gastric emptying, small intestinal motility, and colonic motility
- More potent than metoclopramide and no antidopaminergic effects
- Appears to be more effective than metoclopramide at increasing tone in the lower esophageal sphincter (Kempf 2014)

Indications:
- Gastroesophageal reflux
- Sliding hiatal hernias
- Recurrent bloating due to gastroparesis
- Gastroparesis associated with inflammatory bowel disease
- Feline megacolon

Formulations/Dosage: 10 mg tablets. Empirical dose: 0.5 mg/kg PO q. 8 hours (for cats, 2.5 mg q. 8 hours to start); use with lactulose if megacolon present; food enhances absorption in humans

Drug interactions/Contraindications:
- Caution with ketoconazole or itraconazole: these antifungals inhibit cisapride metabolism in humans and can lead to cardiac arrhythmias.
- Contraindicated for mechanical obstructions or for colonic strictures.
- No direct efficacy as an antiemetic.
Side effects:
- Diarrhea, cramping in some humans
- Unlike metoclopramide, no CNS side effects
- In cats, cisapride can also lead to QT prolongation, but at dosages 20 times higher than those used clinically.
  - These same ECG changes (QT prolongation) have been reported for dolasetron. Until more is known in cats, the combination of cisapride and dolasetron may best be avoided.
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