Rational Therapy for Vomiting in Dogs and Cats

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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. All acutely vomiting animals that are brought to a veterinary clinic deserve an abdominal radiograph 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. Try to reserve repeated dosing of antiemetics for those patients that have this baseline completed.

Anti-emetics

Maropitant (Cerenia™)

Neurokinin-1 receptor antagonist.

- Inhibits substance P binding to NK-1 receptors in emetic center, CRTZ, and enteric plexus of gut.

Indications

- Vomiting due to uremia, gastroenteritis, or pancreatitis
- Prevention of motion sickness in dogs and cats
- Prevents emesis from cisplatin and doxorubicin in dogs
- Prevents 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 on label due to drug accumulation
- 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 for treatment of various causes of 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).
- Also increases tone in lower esophageal sphincter, reducing reflux.

It is unclear whether metoclopramide is effective as a central antiemetic in cats. Emesis in cats appears to be mediated though receptors other than D2, particularly alpha2 receptors. 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). However, metoclopramide does appear to decrease vomiting in some cats, possible due to its prokinetic effects.

Indications

- Delayed gastric emptying
- Nausea associated with ileus
- Reflux esophagitis
- Central antiemetic in dogs (esp. renal failure and pancreatitis)
- Prevention of nausea 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.

Indications

- Refractory vomiting in patients with diagnosed underlying disease (e.g. pancreatitis, GI neoplasia, hepatic disease).
- Prophylaxis of vomiting associated with chemotherapy.
- Prophylaxis of vomiting associated with dexmedetomidine in cats (0.22 mg/kg of ondansetron in same syringe as dexmedetomidine, given IM) (Santos 2011)
- Useful for severe refractory vomiting when cost is not an issue.

Formulations/dose/route

2 mg/ml injectable; 4 mg tablet; oral solution 4 mg per 5ml. Empirical dosage: 0.5 mg/kg q. 12 hours.

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; 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®)

Central antiemetic with multiple mechanisms of action: dopamine antagonist, H1 antagonist, alpha-adrenergic antagonist, and anticholinergic. Inhibits vomiting at chemoreceptor trigger zone and directly at emetic center (therefore, potent antiemetic). May be more effective than metoclopramide, especially in cats.

Indications

- Not recommended for empirical outpatient use because of potential for hypotension and sedation (undesirable in a sick patient).
- Prochlorperazine is useful for refractory vomiting in patients with diagnosed underlying disease (e.g. pancreatitis, GI neoplasia, chemotherapy), for which IV fluid support can be provided.
- Cats appear to be more sensitive than dogs to the emetic effects of alpha-2 agonists (e.g. xylazine), and therefore might be expected to respond well to alpha-2 antagonist antiemetics such as prochlorperazine. Adjunctive fluid support is strongly recommended.
- Used for migraines in human patients
- Inexpensive

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®)

An H2 blocker; more potent than ranitidine and cimetidine; longer duration of action than ranitidine or cimetidine, and unlike cimetidine, 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 reflux and esophagitis are a concern
- Vomiting due to hyperacidity (renal failure, mast cell disease).
- Prophylaxis of gastroduodenal ulceration in dogs with portal hypertension
- No direct antiemetic effects.

Empirical dose

1.0 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)

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 H_2 blocker; has additional benefit of prokinetic effects (weak anticholinesterase activity)

Indications

- Persistent vomiting where reflux and esophagitis are a concern
- Vomiting due to hyperacidity (renal failure, mast cell disease).
- 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 in one study (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
- Prevention of NSAID induced ulceration? (efficacy shown in humans)
- Effective in decreasing incidence of exercise-induced gastric erosions in sled dogs (Williamson 2010)

Formulations/dose/route

10 and 20 mg capsules. Drug is enteric-coated to prevent degradation.

- If reformulated, enteric-coated granules need to be replaced in a gelatin capsule.
- Note: equine preparation is much too concentrated to use safely in dogs and cats.

Empirical dose

0.7 - 1.0 mg/kg PO once daily is typical

- Twice daily administration of omeprazole suspension (1 mg/kg b.i.d) was superior to once daily tablets in suppressing acid in dogs (Bersenas 2005)
- Recent study showed that 1.5-2.6 mg/kg once daily suppressed gastric acid (pH > 3-4) for 50-60% of the day (Tolbert 2011)

Drug interactions/contraindications

- Omeprazole is a P450 enzyme inhibitor in humans, but not as broad spectrum as cimetidine.
- Use caution when administering omeprazole with other drugs (interactions reported in humans with diazepam or warfarin).
- Depending on the drug, omeprazole can also act as a P450 inducer.

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, doxycycline, 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

Indications

- Gastroparesis associated with inflammatory bowel disease
- Feline megacolon
- Gastroesophageal reflux unresponsive to metoclopramide and antacids

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.

Underlying disease	Clinical approach to vomiting
Renal failure	Metoclopramide or maropitant Hydration, treat hypokalemia if present Famotidine or ranitidine for maintenance
Hepatic insufficiency	Famotidine to prevent gastric ulceration (if portal hypertension suspected) Treat encephalopathy (lactulose, hydration) Treat hypokalemia Avoid metronidazole if GI upset already present Metoclopramide or maropitant if still vomiting
Inflammatory bowel disease	Treat underlying inflammation (novel protein diet, glucocorticoids) Metoclopramide if still vomiting
Pancreatitis	Metoclopramide and/or maropitant acutely Prochlorperazine (e.g. fractious cat) If painful, buprenorphine, butorphanol, or fentanyl CRI for visceral analgesia
Intoxication	Gastric lavage; then consider metoclopramide or maropitant only after toxins removed from stomach
Hairballs	Petrolatum products If no response, cisapride or metoclopramide
Motion sickness	Dogs: dimenhydrinate (Dramamine) or maropitant Cats: maropitant
Megacolon with vomiting	Treat megacolon (SC fluids, lactulose, cisapride) If also in renal failure, add ranitidine
Parvoviral enteritis	Maropitant; add metoclopramide if ileus suspected Palpate daily for possible intussusception
Post operative ileus	Metoclopramide or cisapride