Motility Modification

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Many gastrointestinal diseases in companion animals are associated with disturbances in gastrointestinal motility. Inflammatory, infectious and neoplastic diseases of the gastrointestinal tract can result in these alterations through production of local inflammatory mediators, distension, obstruction, infiltration of smooth muscle, altered intestinal secretory/absorptive functions, interference with regional blood flow and changes in smooth muscle responsiveness. The vast majority of these disruptions can be addressed through direct intervention against the primary disease process. However selected cases may benefit from pharmacologic manipulation of gastrointestinal motility.

Primary motility disturbances of the bowel are poorly understood group of disease processes in veterinary medicine.

Diagnosis of altered motility

Alterations in gastrointestinal motility are difficult to document because of the differences between solids vs. liquids and low sensitivity of testing.

Radiography

- Retention of food or fluid >16-17hrs after a meal is considered to be consistent with delayed gastric emptying
- Radiographic distension of the esophagus is consistent with esophageal hypo/dysmotilty; can be focal
- Colonic distension/obstipation with extreme dilation/colonic diameter may suggest altered colonic motility
- Radiographic distension of intestinal segments with gas or fluid may be observed

It is important to comment that retention of food in the stomach may represent hypomotility but this may not be the primary concern. In otherwords, normal transit times can be altered in patients with local gatstrointestinal disease.

Barium studies

- Traditionally, barium studies have been used to confirm delayed gastric emptying
  - 30% Barium: stomach should empty within 15-60 min in cats and 1-2hrs in dogs
  - Barium meal: stomach should empty within < 10-15hrs
- Delayed intestinal transit times
  - Colonic introduction of barium should occur in 3-5 hours in dogs and ~1 hour (30 min -5 hours) in cats

These studies provide limited information about gastric emptying as they do not critically evaluate food substrates and consistencies that will affect emptying in an individual patient.

Abdominal ultrasound

Has been used in our patients to evaluate gastric empyting by measuring the number of pyloric contractions observed over time. As expected, this is limited by experience of the ultrasonagrapher. Additional findings, the may be seen on ultrasound include dilation of the stomach or bowel segments without evidence mechanical obstruction.

Sonagraphic evaluation is most helpful in exploring potential organic or structural causes of altered motility.

Wireless pH and motility capsules

The smart pill has been used in human medicine and recently been used in small animals to evaluate gastric empyting time and intestinal transit times. These pills are capable of measuring real time pH and therefore detecting an abrupt change in pH from the acidic gastric milieu to the almost alkaline duodenum which signifies the movement out of the stomach. Availability, cost and lack of standardization to patient size/meal limit the clinical utility at this time in companion animals. Further work will likely help this to become more useful in our patients in the future.

Gastric emptying scintigraphy

Considered the gold standard in people for assessment of gastric emptying. Utilizes the addition of ^{99m}Tc sulfur colloid to a standard meal and the acquiring images with a gamma camera over time to assess the overall radioactivity within the stomach. The availability and feasibility of this in our patients is limited at this time. Standardization of meal, positioning, colloid and normals have not been rigorously evaluated in clinical companion animals.

Additional testing

Breath testing, manometry and advanced imaging (MRI) are considered in a people but are limited by availability and logistical/patient considerations between animals and people.

Medications

Dopaminergic D2 antagonists

These medications have both promotility and anti-emetic properties. They have been show to reverse gastric relaxation induced by dopamine infusions and abolish vomiting induced by apomorphine. The prokinetic effects are not explained by the dopamine receptor antagonism as the role of dopaminergic inhibitory neurons for altering motility. It is suspected that alternative properties contribute to there effect on motility. These include antagonism of adrenergic receptors A2, B2), antagonisim of 5HT3 (serotonergic) receptors and/or agnoistic activity on 5HT4 (serotonergic) receptors.

These medications regulate gastroespophageal sphincter tone via dopaminergic inhibition. Gastric motility is altered by increasing the amplitude and frequency of pyloric contractility, inhibiting receptive relaxation and coordinating gastric/duodenal motility. The effect on gastric motility is modest when compared to direct serotonergic agonists. While metoclopramide does have an effect on small intestinal motility by enhancing antopyloroduodenal coordination it is considered minimal.

Metoclopramide	
Dose	0.2-0.4 mg/kg q 6 PO, SQ, IM, IV 1-2 mg/kg/day CRI (Give loading dose 0.2 mg/kg IV)
Indications	Delayed gastric empyting Gastroesophageal reflux disease Hiatal hernias Small intestinal transit disorders
Non-motility indications	Anti-emetic
Side effects	

Motilin-like drugs

Motilin is an endocrine hormone released from endocrine cells of the proximal small intestine. This hormone is released in response to H+ and lipid during the fed state but plays a major role during the interdigestive (fasting state). It acts on the stomach, duodenum and jejunum to increase gastroesophageal sphincter pressure and stimulates propulsive motility. Addiitonally, it stimulates gastric, pancreatic and biliary secretion.

Erythromycin and other macrolides have been noted to have activity similar to motilin by stimulating migrating motility complexes and antegrade peristalsis. The effects on sphincter tone have been documented in cats and dogs. The strong gastric contractility is observed (typically of MMC phase III) following administration. One study documented stimulation of colonic motility in dogs but not cats.

Erythromycin	
Dose	0.5-1 mg/kg PO, IV q 8
Indications	Gastroesophageal reflux Delayed gastric empyting Constipation (D)
Non-motility indications	Antibiotic (only at higher doses)
Side effects	Minimal

Other motilin like drugs with higher potency and selectivity may be developed in the future.

Serotoninergic agonists

Drugs that at on 5HT4 receptors have significant effects on motility. Cholinergic neurons within the ENS induce depolarization and contraction of gastrointestinal smooth muscle. These medications have been shown to increase gastroesophageal sphincter pressure, stimulate distal esophageal peristalsis (cats), improve gastric emptying, stimulate small intestinal and colonic motility. Cisapride has alternative effects on serotoninergic receptors (5HT1 agonism, 5HT3 antagonism, 5HT2a antagonism). Other drugs in this class include mosapride, prucalopride and tegaserod. Currently, these medications are not commercially available in the US but may be available in the future.

Cisapride	
Dose	0.25-1 mg/kg PO q 8 Anecdotally can be rectally
Indications	Gastroesophageal reflux Delayed gastric empyting Hiatal hernias Small intestinal motility disorders Constipation
Non-motility indications	Weak 5HT3 effects for emesis
Side effects	Torsades des Pointes?
Contraindications	Mechanical obstruction Prolonged QT????

Acetylcholinesterase inhibitors

These medications stimulate gastrointestinal motility by inhibiting acetycholinesterase activity. As a result, the enhanced parasympathetic activity improves gastric emptying and both small intestinal and colonic motility.

Ranitidine	
Dose	1-2 mg/kg PO, IV, SQ q 8-12
Nizatidine	
Dose	2.5-5 mg/kg PO q 24
Indications	Delayed gastric emptying Small intestinal motility disorders (proximal > distal) Constipation
Non-motility indications	H2 inhibition

Cholinomimetic agents

Bind to muscurinic cholinergic receptors throughout the gastrointestinal tract. At usual doses has negligible nicotinic activity. It is more resistant to hydrolysis than acetylcholine by cholinesterase and, therefore, has an increased duration of activity

Bethanecol	
Dose	5-15 mg/dog q 8
Indications	Canine idiopathic megaesophagus
Non-gastrointestinal properties	Detrusor contractility
Side effects	Vomiting, diarrhea, salivation, and anorexia Toxicity results in cardiovascular or respiratory effects
Contraindications	Urinary obstruction Questionable urinary integrity

Additional considerations

Nitric oxide donors

In some conditions in people loss of neuronal nitric oxide synthase is responsible for reduced NO production and failure of the stomach to relax/altered gastric motility. Novel therapies are being developed in people with diabetic gastroparesis and may play a role in our patients in the future.

Ghrelin analogues

Ghrelin has emerged as a multifunctional hormone with important effects on energy homeostasis but also on gastrointestinal motility. Like motilin, it induces hunger contractions in the fasting state and acts postprandially to accelerate gastric emptying. The generation of novel ghrelin like medications may be clinically useful in our patients. Capromorelin is currently being investigated as an appetite stimulants in feline patients and could have clinical utility in the future.

Prostaglandin E1 analogues

These medicaitions have been shown to initiate a giant migrating complex pattern and increase colonic propulsive activity. Therefore, the use of misoprostol could be considered in dogs and cats with refractory constipation (2-5 ug/kg q 6-8)

Opiod antagonism

Opiods can impair gastric empyting and intestinal transit time. This is particularly important in post operative patients in humans. Minimization of opiods and occasionally the utilization of opiod antagonists can help to mitigate the altered intestinal motility. Oral naloxone has been utilized in people with post operative ileus and patients treated with opiods. Newer medications in people including

methlynaltrexone and alvimopan (which are peripherally acting mu opioid receptor antagonists) may prove beneficial in our patients In the future.

Acupuncture/electroacupuncture

Electroacupuncture has been shown to enhance intestinal contractions during Phase I of the migrating motor complex and glucagon-induced hypomotility in the fed state, and accelerates intestinal transit via the opioid and cholinergic pathways in dogs. Additionally both mechanical and electrical accupunture enhance gastric or duodenal motility, and the reflex at work is supra-spinal and involves the vagal nerve; the peripheral stimulation activates type III afferent fibers. In addition to the reflexes that are activated, the effects of acupuncture may be mediated via centers in the limbic system, the hypothalamus and the brain stem. This may have benefit in select patients in the future.

Patient ambulation has been anectodally associated with improvements in postoperative ileus. The effect of ambulation may not be a true effect but is worthwhile to consider in hospitalized patients.