When the Hind-Gut Falls Behind

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Introduction

Gastrointestinal (GI) stasis is a common medical problem in domestic rabbits[2]. Rabbits have a unique and highly-specialized GI system, and even small changes to their dietary intake or digestives processes can cause significant disease and dysbiosis[2]. GI stasis is a vague term that refers to decreased motility of the GI tract, decreased appetite and decreased fecal production[4]. The term "GI stasis" is a syndrome[4], and not a diagnosis as there are many etiologies and it is often multifactorial. The cause of an episode GI stasis often remains unidentified and is deemed idiopathic[2]. Clinical signs of GI stasis can include anorexia, decreased or absent fecal production, bruxism, abdominal distention, abdominal pain, decreased or absent gut sounds, dehydration, and the absence of normal behaviors such as grooming or sociability[2,4].

Clinical diagnosis of GI stasis is obtained with a thorough history[2]. Further diagnosis of the etiology relies on physical examination, radiology, ultrasonography, and bloodwork depending on severity[2]. In a majority of cases, GI stasis is treated with supportive care with pain medications, supplemental feedings, subcutaneous or intravenous fluid therapy, GI motility medications, and appropriate husbandry modifications. If a specific etiology for the stasis is identified, such as dental disease, intestinal obstruction, or liver lobe torsion, more specific treatments can be utilized.

History and Presentation

Ollie is an approximately 2 year old, male neutered, Dwarf rabbit who presented to Mississippi State University College of Veterinary Medicine Community Veterinary Services on January 26th, 2021 with a 36 hour history of not eating or drinking. The last known time that Ollie had eaten was January 24th in the evening. His owner reported only minimal fecal output of abnormal

pellets approximately the size of a grain of rice. Ollie's diet consists of unlimited Timothy hay, 1 tablespoon of Oxbow rabbit pellets and spring mix twice a day, and occasional Oxbow apple and banana treats. Ollie also lives with a female spayed rabbit, whom the bonding process is ongoing. His owner had started feeding him Oxbow Critical Care™ the previous day.

On presentation, Ollie was bright, alert, and responsive. He weighed 1430 grams with an ideal body condition of 3/5. His heart rate was 230 beats per minute and his respiration rate was approximately 200 breathes per minute. A temperature was not obtained. His heart and lungs auscultated normally, with no murmurs, arrythmias, crackles or wheezes appreciated. His teeth were examined with an otoscope, and they appeared healthy with appropriate occlusion. His abdomen was soft and doughy, with an enlarged, though non-painful, stomach. No borborygmi was heard on auscultation. The remainder of Ollie's physical exam was within normal limits.

Diagnostic Approach

Radiology is the single most important diagnostic tool used for rabbits with GI stasis[4]. Abdominal radiographs are used to evaluate the size, location, and contents (ingesta and gas) of the GI tract[4]. 2-view full body radiographs were performed on Ollie, which revealed a moderately distended stomach with mottled soft-tissue opaque material. There was not excessive gas present, and the remainder of the abdomen was normal. The soft-tissue opaque material was likely Critical Care™, although foreign material or a trichobezoar could not be ruled out.

An oral exam should be performed on all rabbits presenting with GI stasis. Ollie's teeth were examined very closely with an otoscope. The alignment and occlusal surfaces of his incisors and cheek teeth appeared normal, with no hooks, pins, or wave mouth present, and no ulcers were present on the cheeks or tongue.

Relevant Physiology

Lagomorphs (rabbits) are classified as hindgut (cecum and colon) fermenters[3] and have a very unique and specialized way of obtaining nutrients and energy from their food. As strict herbivores with small body sizes and correspondingly high metabolic rates[1], rabbits are adapted to ingest significant quantities of high-fiber, low-energy density food[3]. However, due to their small size and need to escape predators, rabbits are unable to store large quantities of food in their bodies[1,3], as it would make them heavier and slower. The hindgut allows for high food intake by separating out the easily fermentable and slowly fermentable components of the diet, mostly based on particle size[1,3]. This is accomplished through continuous mixing of the ingesta with normograde and retrograde movement through the cecum and proximal colon termed the "wash back"[3]. The larger, slowly fermentable ingesta, mostly fibrous plant material, accumulates in the center of the hindgut, and is rapidly excreted in a normograde direction[3]. The rapidly eliminated indigestible fiber may not provide much nutrition for the rabbit, but it is the main driving force for GI motility[1]. The more fermentable, smaller particles are moved to the periphery of the colon, where they are moved in a retrograde direction back into the cecum for further fermentation[3]. Periodically, the retrograde peristalsis ceases, and a large quantity of the cecal contents is excreted in a normograde direction[3]. This progress creates two types of feces; a hard and dry, high-fiber stool, and a soft, mucous covered fecal pellet called a cecotroph[3]. Cecotrophs are high in bacteria, amino acids, vitamins, and minerals, and are designed to be immediately re-ingested for continued fermentation[3].

Microbial protein is the main protein source for rabbits[1], which is broken down by the colonic enzyme lysozyme[3]. Just like other animals, protein and amino acids are absorbed in the small intestine. Gut bacteria and microbial protein are excreted in cecotrophs, re-ingested, and

transported to the small intestine for absorption. The mucus covering on the cecotrophs allows for the survival of the bacterial and protein in the acidic environment of the stomach[1,3].

The cecum is the primary location of bacterial fermentation on ingesta, primarily by *Bacteroides spp* and various protozoa[3]. This fermentation process produces volatile fatty acids (VFA), which are the main energy source for rabbits[3]. A portion of the VFAs are directly absorbed in the cecum, while the remainder are excreted in the cecotrophs for re-ingestion and later absorption[3]. The colon is responsible for further absorption of VFAs, as well as water and electrolytes[3].

Pathophysiology

GI stasis can be due to a wide variety of pathologic conditions including inadequate diet, inadequate water intake, dental disease, pain, acute or chronic stress, bacterial/viral/parasitic infections, neoplasia, GI obstructions/impactions, liver disease, pancreatitis, lead toxicity, and drug effects (certain antibiotics, opioids, anesthetics etc.)[2]. In many cases, the cause of GI stasis is not identified[2] and is deemed idiopathic. Whatever the inciting cause is, once initiated the resultant dysmotility can lead to dysbiosis, dehydration of gastric and intestinal contents, impaired fermentation, and gas accumulation with resultant pain, creating further anorexia and worsening GI stasis[2]. Below are some of the most common causes of GI stasis further examined.

<u>Inappropriate Husbandry</u>

A thorough history should always be obtained for a rabbit presenting with signs of GI stasis. Information obtained should include what the rabbit eats and how much, if they have access to unlimited fresh hay and clean water and what enclosure they live in (cage vs x-pen vs free roam vs outdoors). A proper diet for rabbits is 70-75% high-quality, high-fiber grass hay (timothy, orchard, meadow or oat), 15-20% hay-based uniform pellets specific for their life stage, and 5-

15% fresh greens[3]. Hay is not only the key GI motility stimulant, but hay also encourages natural foraging/grazing behaviors which will increase activity, decrease boredom and stress, and create a sense of security[3]. Diets with inadequate hay can lead to decreased GI motility and dental issues, which are discussed next. Due to the large amount of dry material that rabbits should eat, rabbits have a higher daily water requirement than other domestic animals and can drink up to 120ml/kg/day[6]. Restricted water access can cause dehydration, which can lead to decreased intestinal motility and GI stasis.

Dental Disease

Lagomorph's teeth are elodont (continuously growing and erupting), hypsodont (long-crowned), aradicular (open-rooted)[2] and diphyodont (grossly distinct deciduous teeth)[5]. They have 28 teeth with the dental formula I(2/1), C(0/0), P(3/2), M(3/3)[5]. The first incisors are chisel-like and used for grabbing and slicing forage and food material. The much smaller second mandibular incisors (aka peg teeth) sit palatal to the first incisors and are present to protect the hard palate from the sharp mandibular incisors[5]. The premolars and molars (together called the cheek teeth[2,5]) are responsible for chewing. The act of chewing forage is necessary for normal tooth wear, and inappropriate diets can lead to malocclusions and dental disease[2,5]. When eating hay or leafy foods, the cheek teeth move with lateral and horizontal movements, and the occlusal surfaces are worn evenly[5]. When eating pellets or grains, the cheek teeth move with more vertical movements, and the wear on the occlusal surfaces are uneven and reduced[5]. The inadequate wear will allow the teeth to continue to erupt, until they come into contact with the opposing teeth, which prevents further eruption[5]. This will exert pressure on the tooth roots, causing the tooth to bend and curve in a buccal direction under the gumline[5]. The increased curvature of the tooth will lead to incomplete attrition and spikes/hooks of the occlusal surfaces[5]. The increased

pressure on the roots can also affect the apical germinal cells, causing decreased or, in severe cases, cessation of tooth eruption[5].

The resultant malocclusions and dental disease due to a diet low in hay can lead to anorexia, dysphagia, drooling, weight loss/emaciation and changes in fecal production[2]. Severe dental issues can lead to secondary tooth root abscesses with can cause exophthalmos, purulent nasal discharge and excessive lacrimation/ocular discharge[2]. Rabbits with signs of GI stasis should always have a thorough oral examination with a bivalve speculum, otoscope, or similar device. Dental or skull radiographs can be acquired if indicated. Treatment can include shortening any overgrown teeth, extracting diseased teeth and marsupialization of facial abscesses[2].

Stress

Because rabbits are a prey species, they naturally have a strong physiologic response to stress[6], though it does vary between individuals. The autonomic nervous system (ANS) and the adrenal glands play a role in regulating the fusus coli, which is located in the transverse colon[3]. The fusus coli is referred to as the "pacemaker" of the hindgut, as it controls the normograde and retrograde peristaltic movements that create the different types of feces[3]. The close relationship between the ANS and adrenal glands with the hindgut may explain why rabbits are prone to stress-related GI stasis[3]. Environmental stressors, such as temperature, new people or animals, loud/new noises, husbandry issues etc., cause the release of catecholamines[2], which can act on the fusus coli and cause ileus[3].

Trichobezoars and Impactions

Rabbit's groom themselves throughout the day, just like cats, and it is normal for them to ingest their fur. Unlike cats, rabbit's do not have the ability to vomit due to a well-developed cardiac

sphincter[3], so the fur they ingest must come out the other end. Trichobezoars (hairballs) can form due to decreased GI motility or dehydration[1,3] and are not simply due to fur ingestion. Decreased GI motility leads to dehydration of gastric and intestinal contents[3] because water will continually be absorbed, even if the material is not moving. Trichobezoars or food impactions can then worsen the GI stasis by creating a pyloric or intestinal obstruction which could require surgical intervention[3].

Neoplasia can also present as a GI obstruction/impaction[2] and should be on a differential list for an older rabbit with GI stasis. GI tumors in rabbits include gastric adenocarcinoma, papilloma, leiomyoma/sarcoma, and metastatic tumors, especially uterine adenocarcinoma[2].

Liver Lobe Torsion

While a less common etiology, rabbits with a liver lobe torsion normally present with vague signs of GI stasis[2]. Hints towards this condition are cranial abdominal pain, an abnormally placed liver on palpation, and elevated liver enzymes on a chemistry panel[2]. Diagnosis can be made with an ultrasound examination with color flow Doppler and visualizing an area of the liver without blood flow[2]. This is a surgical emergency, and removal of the affected liver lobe is the only treatment.

Treatment

The severity of disease can vary greatly depending on the inciting cause and duration of signs. When a rabbit first presents with GI stasis, it is important to determine if the rabbit is stable enough to be handled and examined. Most domestic rabbits tolerate being handled, though in cases of severe disease or stress, handling can worsen the condition. In debilitated or highly stressed rabbits, sedation should be considered[4]. Midazolam (0.5-2mg/kg alone, 0.25-0.5mg/kg

with opioid[7]) with an opioid such as butorphanol (0.2-0.4mg/kg[7]) or buprenorphine (0.01-0.05mg/kg[7]) given intramuscularly (IM), subcutaneously (SQ), or intravenously (IV) can be used for sedation. Ketamine (1-10mg/kg) can be added via the same routes for additional sedation or analgesia[7]. Midazolam can be reversed with Flumazenil (0.01-0.1mg/kg[7]) IM or IV if needed.

The treatment of GI stasis is largely symptomatic unless an underlying cause is identified. The patient should be kept in a dark, quiet, and warm environment to reduce stress[2]. Symptomatic therapy includes supplemental feedings, fluid therapy, analgesics, and prokinetics. Nutritional supplementation is only contraindicated if you suspect an obstruction, otherwise, all rabbits with GI stasis should be fed as quickly as possible[4]. Most rabbits tolerate hand-feeding quite well. Critical Care™ is an Oxbow product that is formulated specifically for syringe-feeding herbivores[8]. Rabbits should receive 3 tablespoons per kg daily, divided into 4-6 feedings[8]. Fluid therapy with isotonic crystalloids (i.e., Lactated Ringers solution, Plasmalyte etc.) should include deficits, maintenance, and ongoing losses (diarrhea, polyuria etc.). Maintenance fluid rate for rabbits is 100-150ml/kg/day and can be divided into multiple SQ injections given every 6-12 hours[7].

Analgesia is an important component of GI stasis therapy. Meloxicam (0.3-1mg/kg orally Q24) is a non-steroidal anti-inflammatory medication that works well in rabbits. Meloxicam should only be used in well-hydrated patients with normal renal values due to its excretion via the kidneys[7]. Opioids such as buprenorphine (0.01-0.05mg/kg SQ, IV Q6-12) or butorphanol (0.1-0.5mg/kg SQ, IM, IV Q4) can also be used, though prolonged use can cause ileus[2].

Prokinetic medications are frequently used for GI stasis, though they are contraindicated if an obstruction is present. Metoclopramide is a prokinetic that works in the stomach and small intestine and can be given at 0.2-0.5mg/kg orally or SQ Q6-8[7]. Cisapride is a prokinetic that

works in the stomach, small intestine, and large intestine. Cisapride was removed from the human market in 2000, due to the risk of lethal cardiac arrythmias[9]. This has not been shown to occur in animal patients except at doses 20x higher than the recommended dose[9]. Cisapride can be compounded for veterinary use and given at 0.5mg/kg orally Q8-12[7].

Anorexic or stressed rabbits can often get GI ulcers. Omeprazole and Ranitidine can both be used as gastroprotectants. Omeprazole is a proton pump inhibitor and can be given at 20mg/kg SQ Q12. Ranitidine is an H2 blocker and can be given at 2-5mg/kg orally Q12. There is evidence that administering ranitidine and cisapride together can potentiate the effects of both drugs[4].

Simethicone is the active ingredient in Gas-X and infant gas drops, and may be beneficial in rabbit with severe gas accumulation. Simethicone can be given at 65-130mg/animal orally Q1 for 2-3 treatments[7].

Serial abdominal radiographs are the ideal method to determine how the rabbit is responding to treatment[4]. Radiographs can be repeated very 24 hours in more stable patients, while more critical patients may need to be re-evaluated very 3-4 hours[4]. Signs of worsening disease include increased gas accumulation, increased stomach size, and a rounded stomach. Signs of improvement include decreased gas accumulations, changes in the gas pattern ("broken-up" gas, or gas that has moved further along the GI tract), presence of formed stool in the colon, and a less round stomach[4]. Radiographic findings, however, must be evaluated in conjunction with the patient's clinical signs.

Rabbits that are responding well to medical management will begin to eat on their own, have formed stool and will resume normal activities such as grooming[4].

Ollie was prescribed meloxicam 1.5mg/ml oral suspension: 0.4ml (0.4mg/kg) orally Q24h for 7 days, metoclopramide 1mg/ml oral liquid: 0.7ml (0.5mg/kg) orally Q12 for 7 days, and omeprazole 2mg/ml oral suspension: 0.7ml (1mg/kg) orally Q12 for 7 days. Ollie's owner had already purchased Oxbow Critical Care™ and was given instructions to feed Ollie 4 tablespoons a day for a few days until he started eating on his own again. 24 hours later, Ollie's owner reported that Ollie had eaten a small amount of cilantro but nothing else and had not started producing feces. She was told to maintain the treatment plan, and that she could increase the metoclopramide to 3 times a day if able. 48 hours after presentation, Ollie was reportedly doing much better and ate his dinner the previous evening and was producing fecal pellets again. She was told to continue the medications for the full 7 days. Recheck radiographs were recommended after the 7 days, but the owner declined. Ollie's GI stasis was presumed to be due to the stress of another rabbit being in the house, though a definitive reason will never be known. Ollie made a full recovery and was reportedly doing well in June 2021.

Conclusion

GI stasis in rabbits is a common medical issue with many known etiologies, though the inciting cause is not always identified. Critical diagnostic steps include a thorough history of the patient's diet and husbandry, an oral exam, and abdominal radiographs. Symptomatic treatment is often warranted, and rabbits can recovery in a few days if treated appropriately with supplemental feeding, fluid therapy, analgesics and prokinetic medications.

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