Randomized Trial to Evaluate Two Dry Therapeutic Diets for Shelter Dogs with Acute Diarrhea

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ABSTRACT

Acute diarrhea is common in dogs housed in animal shelters and is often managed by dietary manipulation. The objective of this randomized study was to compare the effect of PURINA VETERINARY DIETS Canine EN® and Hill's® Prescription Diet i/d® Canine on acute diarrhea in a population of young, otherwise healthy shelter dogs. Shelter dogs (n=24) were eligible for inclusion in the study if diarrhea without blood or tenesmus had been noted for at least 2 days. Qualifying dogs were randomly assigned to be fed EN or i/d beginning on Day 0 with fecal scores, appetite, and overall health status monitored daily for the next 14 days. A total of 14 dogs fed EN and 10 dogs fed i/d completed the study at least through Day 11. Between Days 1 - 7, dogs fed i/d were 2.3 times (95% CI 1.1-5.0) more likely to have diarrheic stools than dogs fed EN (p =0.042). Although both diets were well tolerated and apparently effective, dogs with acute diarrhea fed PURINA VETERINARY DIETS Canine EN were less likely to have diarrheic stools between Days 1 - 7 than dogs fed Hill's Prescription Diet i/d Canine.

INTRODUCTION

Acute diarrhea is common in dogs housed in animal shelters, and is often managed by dietary manipulation. Acute diarrhea may result from many different factors, including diet change, stress, and viral, bacterial, or parasitic agents. Diet change is typically inevitable in the shelter environment, as often the previous diet is unknown, and resources

typically dictate the use of particular diets. Stress may play a significant role amongst the population of dogs housed in animal shelters, as exposure to novel environment and routine and social isolation are common, both of which have been documented to cause stress in the dog. Viral, bacterial, and parasitic agents are also common in the shelter environment. For example, a recent study that evaluated the prevalence of enteropathogens in dogs with and without diarrhea entering a Florida shelter found hookworms in 58% and 48%, Giardia spp in 22% and 16%, and canine enteric coronavirus in 2% and 18%, respectively.

Regardless of the underlying cause, the development of acute diarrhea negatively impacts both the individual dog and shelter resources. The adoption process is often delayed in these cases, which can further limit already strained shelter resources. In rare cases, intractable diarrhea may even result in the euthanasia of the dog.

Dietary therapy has long been used as a sole or adjunctive therapy for acute diarrhea in dogs. Depending on the underlying cause, dietary therapy may be successful as the lone treatment in many cases. The standard dietary recommendations for acute gastroenteritis traditionally include fasting for 24 to 48 hours, followed by feeding small amounts of a highly digestible, or "bland" diet multiple times a day. However, the old dogma of "resting the gut" has been questioned in recent years, especially in cases of acute diarrhea.

The presumed ideal diet for dogs with acute diarrhea contains highly digestible protein and carbohydrate sources, and is lower in fat than typical diets. Additionally, ingredients known to be associated with intolerances should be avoided in these diets, and these diets should contain large amounts of readily available electrolytes and vitamins.[3] Many diets are commercially available for this purpose, including PURINA VETERINARY DIETS Canine EN® (EN) and Hill's® Prescription Diet i/d® Canine (i/d), both highly digestible and low in fat, but differing in some specific nutritional components. The main differences include that EN contains inulin as a prebiotic source, whereas the prebiotic source in i/d is beet pulp. Additionally, EN contains long chain omega-3 fatty acids, and a larger percentage of medium chain fatty acids.

The objective of this study was to compare clinical responses to EN or i/d when fed to otherwise healthy shelter dogs experiencing acute small bowel diarrhea. Based on differences in the composition of the diets, the primary hypothesis was that dogs fed EN would have a faster resolution to normal stools than dogs fed i/d.

MATERIALS AND METHODS

Animals

The experimental design was approved by the Board of Directors at the five participating animal shelters in north-central Colorado (3 shelters) or southern Wyoming (1 shelter), and by the Institutional Animal Care and Use Committee at Colorado State University. The study dogs were stray, owner-relinquished, or transfers from other shelters. All observers were trained to objectively assign a fecal score using a visual guide resulting in a standardized number associated with the stool characteristics (7 = watery puddles; 6 = texture but no shape; 5 = moist piles; 4 = moist log shape; 3 = normal). All dogs had small bowel diarrhea (fecal score $\geq$ 4) that had been recognized for at least 2 days between Day -2 and Day 1 of the study.

The other inclusion criteria stipulated that the dogs weigh greater than 10 pounds, were greater than 3 months, but less than 3 years of age (estimated by the attending veterinarian for strays), and were eligible for adoption after resolution of clinical signs, based on behavioral assessment. A complete physical examination was completed by a study veterinarian when each dog was admitted to the study. Exclusion criteria eliminated dogs with clinical evidence of systemic infectious disease (eg, parvovirus, canine distemper virus), protracted vomiting (> 4 episodes on days -2 through 0) requiring pharmaceutical intervention, hemato-

chezia, tenesmus, and physical examination findings of dehydration > 3%, abdominal masses, or skin changes consistent with food allergic dermatitis.

Experimental Design

Dogs meeting the inclusion criteria had a fecal sample collected and were administered a combination of febental, pyrantel, and praziquantel (Drontal Plus Taste Tabs; Bayer Animal Health) according to manufacturer's instructions beginning on Day -3, -2 or -1, and continued for 3 doses. Feces were also collected on Days 7 and 14. Blood (3 ml total volume) was collected on Day – 2 or 0 depending on the original source of the dog. The dogs were either housed at the participating shelter (n=6) in isolation runs or transported to a Colorado State University research room (n=18) on Day -1. Once the final housing was determined, the dog stayed in that run for the duration of the study. At the end of the study, intact dogs were neutered and all were adopted to private owners by the participating shelter.

On Day 0, qualifying dogs were assigned to be fed either EN or i/d kibble for 14 days by coin flip (shelter housed dogs) or by alternating the diets for each new case entry (research room). The specified diet was fed exclusively, and the staff was instructed to not offer treats or other food, until after the study was completed. The amount of ration to be fed was based on the dog's weight and the manufacturer feeding instructions and was offered twice daily. Appetite was scored (once daily) after the food had been with the dog for 30 minutes according to the following criteria:

- 0 = all food consumed
- 1 = ½ food consumed
- 2 = ¼ food consumed
- 3 = no food consumed.

The feces passed during the first defecation of the day were objectively scored using the visual guide as described above. Body weight and body condition score (using a 1 - 9 scale) were assessed on Day -2, -1 or 0, and again on Days 7 and 144. Dogs were exercised a minimum of twice daily, and vomiting or other concerns were assessed and recorded by the study veterinarian.

Assays

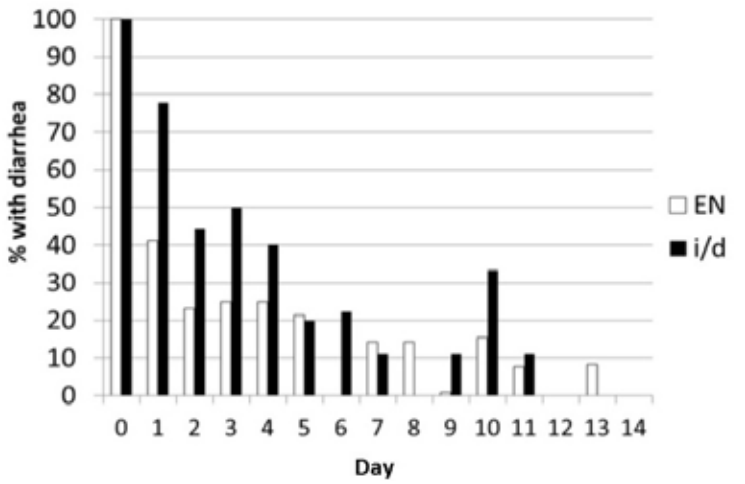
Fecal samples from Days -2, 7, and 14 underwent zinc sulfate centrifugation, and were examined microscopically at 100X for parasite eggs, oocysts, and cysts (Center for Companion Animal Studies, Colorado State University). In addition, each sample was evaluated for Giardia spp cysts and Cryptosporidium spp oocysts by use of a commercially available immunofluorescent assay (Merifluor Giardia/Cryptosporidium, Meridian Diagnostics). A complete blood count and serum biochemical panel (Clinical Pathology Laboratory, Colorado State University) were performed on blood collected on Day – 2 or Day 0 with results to be used in the general health assessment if progression of clinical illness was noted during the study.

Statistical Analysis

This randomized trial was considered a pilot study. The daily fecal score data were grouped into Days 1 - 7, Days 8 - 14, and Days 1 - 14 analyses. The data from one dog in the i/d group was not included in the Day 8 - 14 and Day 1 – 14 analyses because feeding was inadvertently delayed on Day 7, which may have influenced subsequent clinical scoring. Statistical differences between diets in proportions of diarrheic stools on Days 1 - 7, Days 8 - 14, and Days 1 - 14 were analyzed using logistic regression. Parasitism as a factor associated with diarrhea was analyzed using logistic regression. Median day to return to normal stool (fecal score < 4 for 2 consecutive days) was calculated for each diet and assessed using the Wilcox rank-sum test. Kaplan-Meier curves showing time to recovery were drawn, and a log-rank test for equality of survivor functions used to determine difference between diets in time to recovery. All statistical analyses were performed using Stata 11.2. Significance was defined as $P < 0.05$ for all analyses.

RESULTS

Figure 1. *Percentages of dogs being fed EN (n = 14) or i/d (n = 10) with diarrhea by day of the study. When controlling for day in the period Days 1 - 7, stools from dogs fed i/d 2.3 times (95% CI 1.1–5.1) more likely to be diarrheic than those fed EN (p = 0.032). When controlling for diet in the period Days 1 - 7, there was a significant difference in occurrence of diarrhea on Days 5 (p = 0.009), 6 (p = 0.002), 7 (p = 0.002) compared to Day 1.*



Between June 2012 and November 2013, approximately 115 dogs were screened by the participating shelters and the study veterinarian for entry into the study. Of those dogs, 52 dogs met the entry criteria and were entered into the study. A total of 28 of the 52 dogs were subsequently excluded for various reasons including: behavioral problems, adoption, or having their fecal scores normalize by the morning of Day 1 or 2. The remaining qualifying dogs were randomized to be fed EN (14 dogs) or i/d (10 dogs). Six dogs completed the study while housed at Shelter 1. Eighteen dogs were transported from their respective shelters (Shelter 2, n = 8; Shelter 3, n = 7; Shelter 4, n = 3) to the facility research room for completion of the study.

On Day 0, 7 of 14 dogs fed EN and 4 of 10 dogs fed i/d ate < 100% of the ration offered at the morning feeding; this result was not significantly different. Of the 14 dogs fed EN, one dog refused to eat the diet on Days 0 – 2, but then ate the entire ration offered from Days 3 – 14. Of the 10 dogs fed i/d, one dog refused to eat the diet on Days 0 – 2, but then ate 100% of the ration offered from Days 4 – 14. When body weights were compared between Day 7 and Day 14, some dogs lost weight (EN = 7 dogs; i/d = 7 dogs), some dogs gained weight (EN = 5 dogs; i/d = 2 dogs), and there was no change in weight for some dogs (EN = 2 dogs; i/d = 1 dog). For dogs fed EN that lost weight, the range was 1.1% to 10.3%, with a median of 3.2%. For dogs fed i/d that lost weight, the range was 1.3% to 6.0% with a median of 3.2%. None of the dogs had diarrhea on Day 12 or Day 14 of the study and all were successfully adopted.

Gastrointestinal parasites were detected in the Day – 2 samples of 6 of 14 dogs (42.9%) fed EN and 5 of 10 dogs (50%) fed i/d, but the differences between groups were not significantly different (P = 1). Dogs fed EN were parasitized with Giardia spp alone (4 dogs), Ancylostoma caninum alone (1 dog), or Giardia spp and Cryptosporidium spp (1 dog). Dogs fed i/d were parasitized with Giardia spp alone (3 dogs), Giardia spp and A caninum (1 dog), or Giardia spp and Cryptosporidium spp (1 dog). When controlling for diet and day, dogs that were parasitized at Day -2 were more likely to have diarrheic stools over time than those who were not parasitized on Day -2 (p = 0.006). Giardia spp cysts were still detected in the feces collected on Day 7 and Day 14 from 2 of the 10 dogs (20%) parasitized with Giardia spp on Day -2; the other 8 dogs were negative. Both dogs initially parasitized by A caninum and both dogs initially parasitized by Cryptosporidium spp on Day-2 were

negative on Day 7 and Day 14.

The median values for the first day of normal stool (fecal score < 4) for dogs fed EN or i/d were Day 3 and Day 5, respectively. However, this difference was not significantly different (P = 0.13). In addition, when the speed to recovery was compared using the log-rank test, there was no significant difference between the groups (P = 0.15). However, when controlling for day in the period Days 1 - 7, stools from dogs fed i/d were 2.3 times (95% CI 1.1–5.1) more likely to be diarrheic than those fed EN (Figure 1; P = 0.032). When controlling for diet in the period Days 1 - 7, there was a significant difference in occurrence of diarrhea on Days 5 (P = 0.009), 6 (P = 0.002), and 7 (P = 0.002) compared to Day 1 suggesting diarrhea was resolving in both groups. Diarrhea was uncommon in any dog during Days 8 – 14, and statistical differences between the groups were not noted in this period (Days 12 and 14 were omitted from this analysis because no dogs had diarrhea on these days) (Figure 1).

DISCUSSION

Both gastrointestinal diets studied here are

Table 1. *Nutrient analyses of the diets studied.*

Nutrients	Hill's ®Prescription Diet i/d® Canine Dry	PURINA VETERINARY DIET® EN® Canine Dry
	dry matter	dry matter
Protein : %	25.72	26.06
Fat : %	13.67	11.57
Carbohydrate: %	51.87	54.64
Crude fiber: %	2.66	1.83
Ash : %	6.09	5.90
Total Dietary Fiber : %	10.03	9.29
Insoluble Dietary Fiber : %	9.23	7.41
Soluble Fiber : %	0.79	1.87
Calcium : ppm	10803	11408
Phosphorus : ppm	8513	8126
Potassium : ppm	8015	5902
Sodium : ppm	4195	3546
Chloride : %	0.98	1.08
Copper : ppm	12.24	13.49
Iron : ppm	306	403
Magnesium : ppm	981	682
Manganese : ppm	27	66
Zinc : ppm	186	181
	% in fat	% in fat
Medium-chain fatty acids (C8:0-C12:0): %	0.56	19.91
Eicosapentaenoic acid (C20:5n3): %	ND*	0.52

**ND = non-detectable.*

formulated to provide complete and balanced nutrition, and the nutrient analyses of both diets are shown in Table 1. Overall, this study demonstrated that feeding diets formulated specifically for gastrointestinal disorders benefits dogs with acute diarrhea. Although we did detect a difference between the diets, this study was limited by multiple factors.

The high spontaneous resolution rate reported in this study emphasizes how difficult it can be to perform controlled studies on dogs with acute diarrhea. This study was also limited by its small sample size. Because of the difficulty of obtaining appropriate candidates from the shelter population, the dogs were obtained from multiple different shelters, and some dogs were housed in their shelter environment, while others were transported to CSU to complete the study. Although these variables may have contributed to stress in these patients, we feel that stress is ubiquitous in this population, and would likely play a role no matter where the study was carried out. Another major potential limitation of this study related to fecal scoring. While the majority of stools were scored by masked observers, some were not. The diets are visually different and so masking was difficult in this study design. However, we believe that the objective use of the visual guide lessened the potential for bias.

Despite the limitations, and the fact that both diets are very well suited for dogs with acute diarrhea, we did find that diarrhea was less common in the dogs fed EN during the Day 1 –7 treatment period. These results might be explained by the lower fat content, higher percentage of total fat derived from medium-chain fatty acids, higher percentage of soluble fiber including inulin, a prebiotic, and increased levels of eicosapentaenoic acid (C20:5n3) found in the EN diet.

Whether the differences in fat content of the diets studied herein contributed to the results of the study is unknown (Table 1). Some believe that increased levels of dietary fat can reduce digestibility by delaying gastric emptying.[5] Additionally, undigested fats that reach the ileum or colon may contribute to the creation of pro-inflammatory hydroxyl fatty acids, which may be damaging to the mucosa, and may also result in diarrhea.[5] Furthermore, medium-chain fatty acids are hydrolyzed and absorbed faster than long-chain fatty acids, and require less enterocyte reprocessing, contributing to increased digestibility when compared to diets containing a higher percentage of long-chain fatty acids.[6] Human studies have also indicated that MCT's may be beneficial in patients with pancreatitis[7] and children with acute diarrhea.[8] In summary, the lower fat content, and higher percentage of fat supplied by medium-chained fatty acids, may have contributed to the EN group having less diarrheic stools than the i/d group during Days 1-7 of the study.

The soluble fiber source in EN is inulin-derived from chicory root which is a well-known prebiotic that promotes digestive health.[9] Multiple previous studies have demonstrated that when fed to dogs, purified inulin or chicory increases the amount of bifidobacteria in feces when compared to controls.[10,11,12] The presence of bifidobacteria in the feces has long been used as a gauge of gastrointestinal health and prebiotic potential.[9] Additionally, chicory has been demonstrated to reduce the amount of fecal clostridia in dogs, when compared to controls.[10] A recent paper describing the fecal microbiome of dogs with acute diarrhea demonstrated a significant increase in Clostridium perfringens when compared to healthy dogs.[13] Therefore, it is possible that the inulin content in EN contributed to the findings reported in our study. However, i/d provides soluble fiber from beet pulp that presumably would have a similar benefit in this group of dogs.

Eicosapentaenoic acid is a long chain omega-3 fatty acid with anti-inflammatory effects.[14] Studies that specifically evaluate the ability of omega-3 fatty acids to reduce intestinal inflammation in dogs and cats are lacking. However, in humans with ulcer-

ative colitis, the addition of fish oil, which is rich in long chain omega-3 fatty acids EPA and DHA, to the diet allowed for diminished usage of anti-inflammatory medications, and demonstrated a reduction in inflammatory mediators.[15] Consequently, many in the veterinary field feel that their use is justified for patients with presumed or biopsy-demonstrated intestinal inflammation, and their presence in the EN diet may have been in a factor in the studies reported findings. Some veterinary internists are concerned about gastrointestinal side effects that could develop when supplementing omega-3 fatty acids. However, vomiting or diarrhea in one study of different supplementation levels showed side-effects were uncommon and variable.[16]

As is common in the shelter environment, many of the dogs in this study were parasitized. Parasitized dogs were more likely to have diarrhea. However, there were similar percentages of parasitism between groups prior to instituting dietary therapy. All dogs were administered febantel-pyrantel-praziquantel, regardless of parasitism status. Dogs were most commonly parasitized with Giardia spp or Ancylostoma caninum, both of which would be expected to respond to febantel-pyrantel-praziquantel. While this drug is not a treatment for Cryptosporidium spp, both dogs parasitized by this organism developed normal stools over the course of the study. Additionally, both dogs with Giardia spp cysts noted in their feces on both Day 7 and Day 14 had normal stools by Day 6 and Day 10, respectively, suggesting that dietary manipulation likely contributed to the improvement in their fecal scores. The dog that developed a normal fecal score by Day 6 was in the EN group; the dog that developed a normal fecal score by Day 10 was in the i/d group. The Giardia spp results demonstrated that not all treated dogs will have negative test results in the short term which is similar to what has been shown in other studies.[17] Thus, the primary goal of Giardia spp treatment should be normalization of the stools, and dietary manipulation can be beneficial in these cases.

It is unknown exactly why some of the dogs lost weight on the fed diets; however, it is suspected that this was simply due to patient variability and the fixed amount fed. This is a good reminder that although feeding guidelines are very valuable, they do not apply uniformly to the patient, as energy requirements can vary significantly in individuals of the same weight class. It is therefore important to remind pet guardians that feeding guidelines are averages, and may need to be adjusted based on their individual pet's response to the diet, with help from their veterinary practitioner.

CONCLUSIONS

In conclusion, this study demonstrates that dogs with acute diarrhea can benefit from being fed diets formulated specifically for gastrointestinal disorders. The results presented indicate that PURINA VETERINARY DIET Canine EN and Hills Science Diet i/d canine are well suited for the speedy resolution of acute diarrhea in dogs.

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CONFLICT OF INTEREST STATEMENT

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