Original Article

JVC Journal of Veterinary Clinics

pISSN 1598-298X • eISSN 2384-0749
J Vet Clin 2024;41:150-156
https://doi.org/10.17555/jvc.2024.41.3.150

Fecal Microbiota Transplantation via Commercial Oral Capsules for Chronic Enteropathies in Dogs and Cats

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Abstract This retrospective case series assessed the effectiveness of commercially available oral fecal microbiota transplantation (FMT) for treating chronic enteropathies in eight animals, five dogs, and three cats, between 2020 and 2023 at the Seoul National University Veterinary Medical Teaching Hospital. Chronic enteropathies, often resistant to conventional therapies, present a significant challenge in veterinary medicine. To assess oral capsule FMT's effectiveness (Doggybiome® one capsule daily for dogs and Kittybiome® one capsule daily for cats) as a universal adjunctive therapy for chronic enteropathies across species not responding to traditional treatments. This retrospective case series applied a uniform evaluation of gastrointestinal symptoms and treatment efficacy, utilizing established scoring systems (Canine Inflammatory Bowel Disease Activity Index [CIBDAI] and Canine Chronic Enteropathy Clinical Activity Index [CCECAI] for dogs, Feline Chronic Enteropathy Activity Index [FCEAI] for cats) before and one month after FMT. This approach ensured consistency in hypothesis testing across the study population. Results revealed significant improvements in clinical indices post-FMT, with notable reductions in the CIBDAI, CCECAI, and FCEAI scores ($p < 0.05$). Additionally, symptoms such as anorexia, lethargy, diarrhea, vomiting, and weight loss showed marked improvement, with normalization of appetite and activity levels observed in most cases. No adverse effects were reported, indicating the safety and tolerability of this treatment. This study highlights the potential of oral capsule FMT as a viable therapeutic option for dogs and cats with chronic enteropathies unresponsive to conventional treatments, providing a new avenue for clinical management. Further research is warranted to expand these findings and explore the microbiome changes associated with FMT in veterinary patients.

Key words fecal microbiota transplantation, oral capsule, chronic enteropathy, canine, feline.

Received June 5, 2024 / Revised June 12, 2024 / Accepted June 13, 2024

Introduction

Chronic enteropathy (CE) is a common complaint during veterinary visits. CE is diagnosed according to chronic gastrointestinal signs for more than three weeks, histopathological confirmation of inflammatory changes, exclusion of infectious diseases, and exclusion of other extra-gastrointestinal underlying causes (11). It is sub-classified into food-responsive, antibiotic-responsive, steroid-responsive (or immunosuppressant-responsive), and non-responsive enteropathies according to the response to therapy (7).

Among dogs and cats diagnosed with steroid- or immunosuppressant-responsive enteropathy, some are categorized as non-responsive enteropathy (NRE) and have a poor prognosis (11). Researches have also investigated the effects of probiotics, prebiotics, fecal microbiota transplantation (FMT), stem cell therapy, and other approaches for improving CE in dogs and cats (2,17,19,20).

Fecal microbiota transplantation, which is a CE treatment, is an emerging method for altering the gastrointestinal microbiota via transferring gut microbiota from a healthy donor to the recipient's gut (4). Literature on FMT can be traced back to the 4th century, wherein it was utilized as mainstream medicine for treating *Clostridioides difficile* infection (CDI) from the 1950s onward (21,23). Subsequent to the revelation of the diverse roles played by the microbiome within the human

Table 1. Scoring system for chronic enteropathy

CIBDAI (12)	
Attitude/activity	0 = normal; 1 = slight decrease; 2 = moderate decrease, 3 = severe
Appetite	0 = normal; 1 = slight decrease; 2 = moderate decrease, 3 = severe
Vomiting	0 = normal; 1 = mild (1/week); 2 = moderate (2-3/week); 3 = severe (>3/week)
Stool consistency	0 = normal; 1 = slightly soft feces; 2 = very soft feces; 3 = watery diarrhea
Stool frequency	0 = normal; 1 = slightly increased(2-3/day) or fecal blood, mucus or both; 2 = moderately increased (4-5/day); 3 = severely increased (>5/day)
Weight loss	0 = none; 1 = mild (<5%); 2 = moderate (5-10%); 3 = severe (>10%)
CCECAI (1)	
Attitude/activity	0 = normal; 1 = slight decrease; 2 = moderate decrease, 3 = severe
Appetite	0 = normal; 1 = slight decrease; 2 = moderate decrease, 3 = severe
Vomiting	0 = normal; 1 = mild (1/week); 2 = moderate (2-3/week); 3 = severe (>3/week)
Stool consistency	0 = normal; 1 = slightly soft feces; 2 = very soft feces; 3 = watery diarrhea
Stool frequency	0 = normal; 1 = slightly increased(2-3/day) or fecal blood, mucus or both; 2 = moderately increased (4-5/day); 3 = severely increased (>5/day)
Weight loss	0 = none; 1 = mild (<5%); 2 = moderate (5-10%); 3 = severe (>10%)
Albumin levels	0 = albumin>20 g/L; 1 = albumin 15-19.9 g/L; 2 = albumin 12-14.9 g/L; 3 = albumin <12 g/L
Ascites and peripheral edema	0 = none; 1 = mild ascites or peripheral edema; 2 = moderate amount of ascites/peripheral edema; 3 = severe ascites/pleural effusion and peripheral edema
Pruritus	0 = none; 1 = occasional episodes of itching; 2 = regular episodes of itching, but stops when dog is asleep; 3 = dog regularly wakes up because of itching
FCEAI (10)	
Attitude/activity	0 = normal; 1 = slight decrease; 2 = moderate decrease, 3 = severe
Appetite	0 = normal; 1 = slight decrease; 2 = moderate decrease, 3 = severe
Vomiting	0 = normal; 1 = mild (1/week); 2 = moderate (2-3/week); 3 = severe (>3/week)
Diarrhea	0 = well-formed feces; 1 = slightly soft feces, fecal blood, mucus, or slightly increased frequency (2–3/day); 2 = very soft feces or moderately increased frequency (4–5/day); 3 = watery diarrhea or severely increased frequency (>5/day)
Weight loss	0 = none; 1 = mild (<5%); 2 = moderate (5-10%); 3 = severe (>10%)
Endoscopic lesions	0 = none; 1 = yes
Total protein	0 = normal; 1 = increased
ALT/ALP	0 = normal; 1 = increased
Phosphorus	0 = normal; 1 = decreased

ALT, alanine transaminase; ALP, alkaline phosphatase; CIBDAI, chronic inflammatory bowel disease activity index; CCECAI, canine chronic enteropathy clinical activity index; FCEAI, feline chronic enteropathy activity index.

body, FMT has been attempted and confirmed to be effective not only in CDI but also in various other diseases including inflammatory bowel disease, type 2 diabetes mellitus, idiopathic thrombocytic purpura and multiple sclerosis (21). FMT can be administered through various routes, and recently, the oral capsule form of FMT has received approval from the FDA for use in humans. While there are some researches about the effects of FMT on chronic diarrhea in dogs (2,6,15,16,22), and cats (8,18) there is currently a lack of literature in veterinary medicine discussing the use of commercially available oral capsule FMT, which is already on the market. In this case series, we aim to introduce the effects of oral capsule FMT, readily available in the market, in dogs and cats diagnosed of CE.

Materials and Methods

Case selection

A retrospective review of medical records encompassing dogs and cats that underwent oral commercial FMT was conducted (Oral capsule fecal microbiota transplant [OCFMT]; Doggybiome® for dogs and Kittybiome® for cats) from 2020 to 2023 at Seoul National University Veterinary Medical Teaching Hospital. The hospital board of the Seoul National University Veterinary Medical Teaching Hospital approved the study design and use of the medical records of the dogs. The owners of the dogs provided informed consents for participation and data publication. Dogs and cats were included if they received OCFMT for chronic enteropathy, defined as gastrointestinal signs lasting for more than three weeks. OCFMT was administered when standard treatments (dietary changes, antibiotics, steroids) failed to yield positive responses.

To evaluate the outcomes of OCFMT, a comprehensive examination of the medical records was conducted. All dogs and cats underwent a thorough assessment, including physical examinations, complete blood counts, serum chemistry, urinalysis, blood smear, fecal smear, fecal polymerase chain reaction (PCR), abdominal X-ray, and ultrasound to identify the root cause of chronic enteropathy. For patients with chronic enteropathy, detailed history-taking focused on gastrointestinal signs, including attitude/activity, appetite, vomiting frequency, diarrhea frequency, and stool characteristics, along with a broader assessment of overall systemic history. Some of the animals underwent endoscopy to elucidate the underlying cause. Medical records were analyzed for sequential data, including body weight, activity/attitude, appetite, vomiting and diarrhea frequency, stool characteristics, serum chemistry (with emphasis on albumin levels in dogs and alanine transaminase [ALT], alkaline phosphatase [ALP], total protein, and phosphorus levels in cats), physical examination findings, abdominal ultrasound results, and any reported skin-related complaints.

Outcome measures

A scoring system was utilized for chronic enteropathy before and after OCFMT to assess its effectiveness in chronic gastrointestinal disorders. In dogs, we utilized the Canine Inflammatory Bowel Disease Activity Index (CIBDAI) (12) and Canine Chronic Enteropathy Clinical Activity Index (CCECAI) (1), whereas, the Feline Chronic Enteropathy Activity Index (FCEAI) was used for cats (10) (Table 1). The pre-treatment score was based on the assessment taken just prior to initiating OCFMT (day 0), whereas the post-treatment score was determined one month after initiating OCFMT.

Statistical analysis

Statistical analyses were conducted using GraphPad Prism version 10 (GraphPad Software Inc., La Jolla, California, USA). Statistical significance was set at $p < 0.05$. A paired t-test was utilized for analyzing the CIBDAI, CCECAI, and FCEAI scores before and after treatment. All data are presented as mean ± SEM, except for patient signalment, including age and weight that are presented as medians and ranges.

Results

Animals

Eight animals, comprising five dogs (D1-5) and three cats (C1-3), met the selection criteria, and the breeds were diverse (see Table 2 for each animal's signalment). The dogs included three castrated males, one spayed female, and one intact female. For cats, two were spayed females and one was a castrated male.

History and Clinical Findings

Eight animals had a history of chronic diarrhea (3-15 months) prior to initiating OCFMT (Table 2). One dog (D3) was managed for hyperadrenocorticism and diabetes mellitus for six months before showing gastrointestinal signs. The other dogs and cats did not have any other concurrent diseases or other significant findings regarding the overall examination described in the Materials and Methods section.

Before FMT, all animals underwent food (median: 115 days), antibiotic (median: 50 days), and steroid trials (median: 90 days). Five dogs received secondary immunosuppressants, while three cats did not. Clinical signs included anorexia (6/8), lethargy (5/8), weight loss (6/8), diarrhea (8/8), and vomiting (4/8). Four dogs had hypoalbuminemia, and one dog (D3) had ascites. Ultrasound revealed intestinal wall thickening

Table 2. Signalment, history and final diagnosis of the eight animals with chronic diarrhea

Patient	Signalment	CE-period	US finding	Hypo-albumin-emia	FMT period (days)	Food trial	Antibiotics trial	Prebiotics	PDS	Immune-suppressant
D1	Pomeranian 6 yrs MC 4.25 kg	15 months	Jejunum; severe mucosal striation	o	100	Hydrolyzed protein diet, low fat diet	Tylosin	o	o	Cyclosporin
D2	Maltese 14 yrs FS 2.2 kg	7 months	Ileum; increased thickness and echogenicity of muscular layer	x	21	Hydrolyzed protein diet, low fat diet	Tylosin, metronidazole, amoxicillin-clavulanate, doxycycline, dewormer (praziquantel, pyrantel pamoate, febantel)	o	o	Leflunomide
D3	Poodle 14 yrs IF 2.3 kg	8 months	Small intestine: striation, ascites, enlargement of jejunal L/N	o	100	Low fat diet	Tylosin, metronidazole, amoxicillin-clavulanate, sulfasalazine	o	o	Cyclosporin, MMF, leflunomide
D4	Cocker Spaniel 13 yrs MC 7.2 kg	4 months	Small intestine: speckles	o	1st: 14/ 2nd: 28	Low fat diet	Tylosine, metronidazole, doxycycline, dewormer (praziquantel, pyrantel pamoate, febantel)	o	o	Cyclosporin, azathioprine
D5	Cocker Spaniel 13 yrs MC 8.95 kg	100 days	Small intestine: speckles and striation	o	50	Hydrolyzed protein diet, low fat diet	Tylosin	o	o	MMF
C1	Ragdoll 3 yrs MC 6.34 kg	6 months	Small ascites, abdominal lymphadenopathy, mild thick ICC wall	x	30	Hydrolyzed protein diet	Metronidazole, amoxicillin-clavulanate, tylosin	o	o	x
C2	Sphinx 3 yrs FS 3.84 kg	10 months	None	x	30	Hydrolyzed protein diet, gastro-intestinal diet	Fenbendazole, metronidazole	o	o	x
C3	Exotic Short-hair Cat 6 yrs FS 3.25 kg	4 months	Cecal wall hypertrophy, mild enlargement of colic L/N	x	30	Hydrolyzed protein diet	Fenbendazole, tylosin, metronidazole, amoxicillin, clindamycin	o	o	x

CE, chronic enteropathy; FMT, fecal microbiota transplantation; FS, female spayed; IF, intact female; ICC, ileocecocolic junction; L/N, lymph node; MC, male castrated; MMF, mycophenolate mofetil; PDS, prednisolone .

with an intact layer (3/8), mucosal striation (4/8), and enlarged intestinal lymph nodes (3/8).

FMT regimens and Efficacy

For eight animals diagnosed with chronic enteropathy, traditional treatments including food, antibiotics, and steroids failed to alleviate persistent clinical symptoms. After discussing with the owners, FMT was incorporated as a supplementary approach to the standard therapeutic regimens. The treatment involved administering one capsule orally each day, with Doggybiome® and Kittybiome® were prescribed for dogs and cats, respectively. The OCFMT was administered on an empty stomach before a meal, either in the morning or in the evening. Treatment durations varied among the dogs, ranging from 14 to 100 days, whereas the cats received treatment for a fixed period of 30 days.

Significant improvements in clinical indices were observed in all eight animals one month after FMT, as illustrated in Fig. 1. The mean CIBDAI score revealed a notable change from 9 ± 1.70 before FMT to 3 ± 1.52 after FMT ($p = 0.0385$, paired t-test). Similarly, the mean CCECAI score presented a significant shift from 10.6 ± 2.14 to 4.4 ± 1.86 following FMT ($p = 0.0327$, paired t-test). Furthermore, the mean FCEAI score had a substantial decrease from 10.67 ± 1.45 to 1 ± 0.00 after FMT ($p = 0.0181$).

Following FMT, appetite was normalized in five out of six animals with anorexia, and all five animals displaying lethargy revealed normalization in attitude and activity levels. Diarrhea improved in all eight animals, with 6 returning to normal bowel movements. Vomiting was reduced in three of four animals, and weight loss improved in four of six animals. For the dogs, hypoalbuminemia improved with increased albumin levels in one out of four cases. The elevated ALT/ALP levels were normalized in both cats after FMT. These outcomes, particularly the scores one month post-FMT as illustrated in Fig. 1, underscore FMT efficiency in significantly improving the health status of animals with chronic enteropathy.

Discussion

This retrospective case series demonstrates the efficacy of commercially available OCFMT in dogs and cats with chronic enteropathies. Excluding extraintestinal issues and ruling out infectious diseases, commercially available OCFMT were prescribed to patients with chronic diarrhea that persisted despite food, antibiotics, steroids, and a second immunosuppressant trial. Symptom improvement was observed in all eight animals in this cohort.

There are various routes of FMT administration, including colonoscopy, enema, nasoduodenal route, nasojejunal route, oral capsule, esophagogastroduodenoscopy, transendoscopic enteral tubing, and percutaneous endoscopic cecostomy (9). Among these, only the oral capsule method permits self-administration, whereas other methods necessitate anesthesia in dogs and cats. When comparing FMT effectiveness between oral capsule administration and other methods in humans, it was confirmed that the oral capsule method is similarly effective for colonoscopy, esophagogastroduodenoscopy, and gastric tubes (13,14). Nearly all case studies applying FMT to chronic enteropathies in veterinary medicine utilized rectal enemas (2,6,15,16,22), and one study demonstrated oral transplantation of frozen capsules (5). This case report revealed that

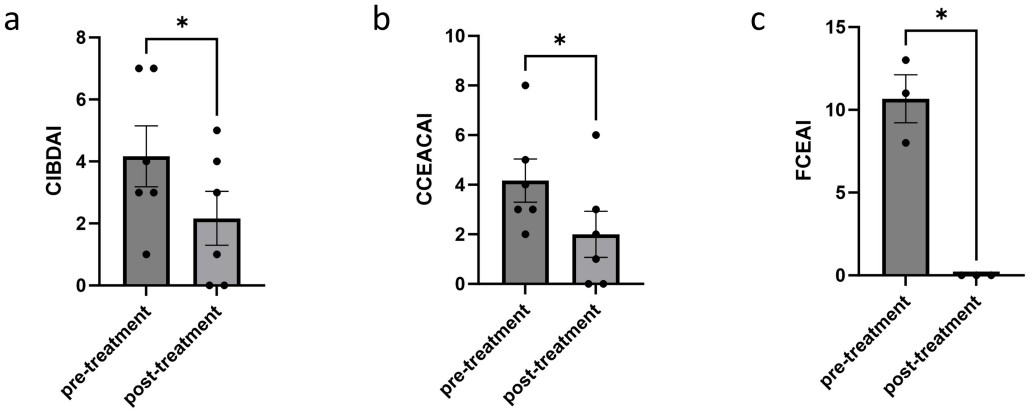

Fig. 1. Changes in CIBDAI, CCEACAI, and FCEAI score following administration oral capsule type FMT. (a, b) CIBDAI and CCEACAI score of canine patients. N = 6. (c) FCEAI score of feline patients. Quantitative data are presented as a mean ± S.E.M. A paired t-test was conducted in Figure 1a-1c. *indicates $p < 0.05$ versus pre-treatment. CE, chronic enteropathy; CIBDAI, chronic inflammatory bowel disease activity index; CCECAI, canine chronic enteropathy clinical activity index; FCEAI, feline chronic enteropathy activity index; FMT, fecal microbiota transplantation.

the efficacy of FMT was similar between oral and endoscopic procedures. In cats, rectal enema was utilized in one case report (8). In a recent study involving 46 cats undergoing FMT, researchers used freeze-dried donor feces to generate a powder, encapsulate it, and administer it orally (18). To the best of our knowledge, no reported cases or studies utilizing non-frozen, commercially available oral capsules of FMT was reported for treating chronic enteropathy in dogs and cats. Likewise, this is a pioneering study in this area.

Although OCFMT has received FDA approval for preventing recurrent CDI in humans (3), a commercially available oral capsule formulation for dogs and cats is currently available. Despite the prevalence of chronic enteropathies across patients seen at veterinary clinics, some do not respond to conventional therapy and FMT application in standard clinical settings is challenging. In this case report, we highlighted the efficacy of an accessible and commercially available oral capsule FMT formulation for dogs and cars. Results demonstrate an effectiveness comparable to that of traditional FMT methods.

This study had certain limitations. Due to its retrospective case series nature, we confirmed the efficacy of commercial oral capsule FMT using limited number of animals. Consequently, additional studies involving a larger number of animals are warranted for further validation. Furthermore, although investigating the microbiome changes before and after FMT would have been beneficial, this was not addressed in this study. A recent FMT study involving 46 cats revealed alterations in the relative abundances of Clostridium, Collinsella, Megamonas, Desulfovibro, and Escherichia post-FMT (18). Similar improvements in dysbiosis were observed among dogs with CE after FMT (6). Despite not conducting microbiome analysis, it was hypothesized that similar alterations in microbiome composition occurred after FMT based on previous studies. It is speculated that these changes may have contributed to improved clinical symptoms, consistent with observations from prior research.

In conclusion, this retrospective case series explored the effectiveness of commercially available OCFMT for treating CE in dogs and cats. When administered to patients with chronic diarrhea unresponsive to conventional treatments, oral capsule FMT demonstrated symptom improvement in all eight animals. Despite limitations including small sample size and lack of microbiome analysis, it highlighted the potential of this accessible FMT method in veterinary practice. Further research with larger cohorts and microbiome assessments are necessitated to deepen our understanding of its therapeutic mechanisms and broaden its application in CE management.

Acknowledgements

We would thank the veterinary clinicians and staff at Seoul National University. We would also like to acknowledge the Research Institute for Veterinary Science at the College of Veterinary Medicine.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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