Fecal Microbiota Transplantation in Dogs and Cats

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Fecal Microbiota Transplantation (FMT) is a procedure in which fecal matter is collected from a tested donor, mixed with a saline or other solution, strained, and placed in a patient, by colonoscopy, endoscopy, sigmoidoscopy, or enema. The purpose of fecal transplant is to replace good bacteria that have been killed or suppressed. (Source: The Fecal Transplant Foundation)

FMT procedures originally gained popularity in Western medicine and spawned several research studies to treat *Clostridium difficile* Infection (CDI), a common hospital-acquired bacterial infection in humans. Nowadays, the FMT procedure for CDI is considered standard in human medicine.

The explosion of FMT research in human medicine is truly remarkable, as microbiota dysbiosis has been correlated with autoimmune diseases, numerous gastrointestinal such as inflammatory bowel disease (IBD), multiple sclerosis, autism, obesity, ulcerative colitis, pancreatitis, and type 2 diabetes – just to name a few.

In holistic veterinary medicine, the practice of FMT has been used for years. Since clinical trials or pilot studies were not completed, these FMT procedures are considered anecdotal. However, there is nothing wrong with anecdotes because they can encourage the medical community to conduct clinical trials that give us more concrete and definitive answers as well as point us in proper directions.

Indeed, a small but important FMT study was recently conducted on dogs with IBD at the University of Helsinki, Faculty of Veterinary Medicine, at the Department of Equine and Small Animal Medicine.

Before discussing the study, it is necessary to review IBD in dogs and cats. The root cause of an individual dog or cat having IBD is often unknown, but is generally believed to be an abnormal interplay between altered intestinal microbiota, genetic susceptibility, immune system health, and dietary and/or environmental factors. These causes are similar to those resulting in human symptoms of IBD, even including the gluten-intolerance becoming so prevalent today.

However, we should not presume *de facto* that bad or good bacteria or fungi are the same across all mammals. For instance, bacteria can switch roles between two species.

Additionally, it is unknown if *Clostridium difficile (C. diff)* causes diarrhea in dogs and cats. In some studies, *C. diff* was considered the primary cause of diarrhea in 10-20% of dogs. Other studies have shown that this bacterium is shed or is present in up to 58% of healthy dogs and cats.

The same can be said for the bacterium, *C. perfringens,* which is a part of the normal canine intestinal microflora and is cultured from more than 80% of diarrheic and non-diarrheic dogs. Of course, all of the factors mentioned above play a role in bacterial diarrhea in dogs and cats.

The First FMT Study in Dogs with IBD

Study: Give dogs with antibiotic-responsive diarrhea a Fecal Microbiota Transplantation.

Donor Dog: The team first set out to find a minimum of two donor dogs. After adapting protocols from human FMT trials to accommodate canine-specific factors, the team sought dogs with the best indicators for microbiota health and low-risk for disease transmission. The donor dogs had to have no history of gastrointestinal (GI) diseases or sign, and never used systemic antibiotics. They needed to be naturally born and breast-fed. Finally, they had to present with no immune-compromised conditions,

malignancies or atopic diseases. Now, this is where the study criteria became interesting. The team started off with nine potential donor dogs. Via the process of elimination for giardia, certain other parasites, as well as the pathogens *Salmonella spp., Yersinia enterocolitica, Campylobacter, C. perfringens* and *C. diff*., all but one dog were eliminated. Even though the impact of *C. diff.* and *C perfringens* on dogs is still being debated, the researchers did not want these to add to the recipient burden or add an additional variable.

Recipients: The three FMT-recipient dogs left in the study were being, or had been, treated with tylosin (an intestinal antibacterial) to alleviate their GI symptoms. Tylosin was stopped one week prior to the procedure. They were also treated with fenbendazole (antiparasitic) for three days one week prior to the FMT procedure.

All three dogs had additional clinical signs.

The little white terrier, Idefix, scored 10 (indicating severe IBD) on the **Canine Inflammatory Bowel Disease Activity Index**. The variables that affect this index are:

1. Activity/Attitude
2. Appetite
3. Vomiting
4. Stool Consistency
5. Stool Frequency

Recipient, Sisu, had a history of pancreatitis as well as vomiting and diarrhea.

Jassu, the third dog, had a history of gallstones.

Canine Dysbiosis Index: The Canine Dysbiosis Index (also abbreviated as CDI) is a PCR (DNA)-based assay that measures the abundance of eight bacterial groups found in canine feces and summarizes them into one number. The CDI is one of several tests that can indicate the amount of good or bad bacteria in a gut, but is less invasive.

Prior to the FMT procedure, Idefix and Jassu scored high on the dysbiosis index, whereas Sisu landed in the negative range.

After the FMT Procedure – Home Observation:

Caregivers were asked to fill out questionnaires following the FMT survey.

For one month after the procedure, Idefix showed increased energy, general well-being and improvement of GI signs. After that, however, Idefix's condition deteriorated, but it was not as bad as prior to FMT.

Sisu also improved in well-being and energy as well as exhibited less GI signs for the two-month post-procedure observational period. Then, Sisu's diet was changed to a raw diet, which naturally affected the microbiota composition in the GI tract.

After repeated failed contact attempts, the caregiver reported that Jassu did not improve in any observable way. Although studies have shown that FMT can restore the fecal bile acid composition in

humans by restoring microbiota bile acid metabolism, and since Jassu had a history of gallstones, the researchers were hopeful for a similar result. However, of note is the fact that bile in dogs has a lower cholesterol saturation than in humans.

After the Procedure – CDI Scores: During the first two weeks after the FMT procedure, all three dogs' fecal samples per the CDI test dipped to a negative number and closer to the values of the donor dog. Idefix and Sisu mostly maintained a dysbiosis index below zero for the eight-week observational period. Jassu's dysbiosis rebounded to a clinically significant value around the fourth week and then leveled off. The researchers noted that Jassu might have had more beneficial effects from an FMT of a different donor or additional FMT procedures.

Conclusion

While this was a small study, these results are encouraging and will hopefully lead to larger scale trials.

Another area of research being investigated is targeted, synthesized microbiota which could provide higher control of viability and reproducibility.

However, we must remember that several synthesized or natural FMT treatments may be warranted to achieve a symbiotic state in the GI tract. Additionally, the positive effects of FMT treatments may be transient or more permanent depending upon the underlying disease process.

Questions that need to be addressed include: “What is happening to the microbiota if the FMT procedures are consistently producing only transient beneficial effects ? Is the body killing them off? Are they oxidizing at a higher rate in the gut than their reproduction can keep up with? Are they being absorbed into the body? Are they being shed? “ If we can also focus on the causes of why the body can or cannot maintain a symbiotic microbiota state, we may reach a more definitive answer to treat autoimmune and other diseases known to be affected by microbiota.

References

Gerbec, Ziga. "Evaluation of Therapeutic Potential of Restoring Gastrointestinal Homeostasis by a Fecal Microbiota Transplant in Dogs." (n.d.): n. pag. 2016. Web. 23 Apr. 2017. http://www.ffa.uni-lj.si/fileadmin/datoteke/Knjiznica/magistrske/2016/Gerbec_Ziga_mag_nal_2016.pdf.

Honneffer, Julia B., Yasushi Minamoto, and Jan S. Suchodolski. "Microbiota Alterations in Acute and Chronic Gastrointestinal Inflammation of Cats and Dogs." World Journal of Gastroenterology 20.44 (2014): 16489-6497. Baishideng Publishing Group Inc, 28 Nov. 2014. Web. 23 Apr. 2017. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4248192/.

Jergens, Albert E., C. Alan Schreiner, Dagmar E. Frank, Yosiya Niyo, Franklin E. Ahrens, P.D. Eckersall, Tammy J. Benson, and Richard Evans. "A Scoring Index for Disease Activity in Canine Inflammatory Bowel Disease." Journal of Veterinary Internal Medicine17.3 (2003): 291-97. ACVIM, 28 June 2008. Web. 23 Apr. 2017. http://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2003.tb02450.x/abstract.

Marks, S.L., S.C. Rankin, B.A. Byrne, and J.S. Weese. "Enteropathogenic Bacteria in Dogs and Cats: Diagnosis, Epidemiology, Treatment, and Control." Journal of Veterinary Internal Medicine 25.6 (2011):

1195-208. ACVIM, 01 Nov. 2011. Web. 23 Apr. 2017. http://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2011.00821.x/full.

Minamoto, Yasushi, Cristiane C. Otoni, Samantha M. Steelman, Olga Büyükleblebici, Jörg M. Steiner, Albert E. Jergens, and Jan S. Suchodolski. "Alteration of the Fecal Microbiota and Serum Metabolite Profiles in Dogs with Idiopathic Inflammatory Bowel Disease." Gut Microbes 6.1 (2015): 33-47. Taylor & Francis, 7 Jan. 2015. Web. 23 Apr. 2017. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4615558/.

Suchodolski, Jan. "Canine Microbiota Dysbiosis Index." Texas A&M Veterinary Medicine & Biomedical Sciences, n.d. Web. 23 Apr. 2017. http://vetmed.tamu.edu/gilab/service/assays/canine-microbiota-dysbiosis-index.

Suchodolski, Jan S., Melissa E. Markel, Jose F. Garcia-Mazcorro, Stefan Unterer, Romy M. Heilmann, Scot E. Dowd, Priyanka Kachroo, Ivan Ivanov, Yasushi Minamoto, Enricka M. Dillman, Jörg M. Steiner, Audrey K. Cook, and Linda Toresson. "The Fecal Microbiome in Dogs with Acute Diarrhea and Idiopathic Inflammatory Bowel Disease." PLOS ONE. Public Library of Science, 26 Dec. 2012. Web. 23 Apr. 2017. http://journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0051907.