ISSN: 1813-4890

Advances in Fecal Microbiota Transplantation for Treatment of Animal Diseases

Xiaomin Shi, Yajing Xie, Liping Zhu*

School of Bioengineering, Shandong Provincial Key Lab of Bioengineering, Qilu University of Technology (Shandong Academy of Sciences), Jinan 250353, China

*zhuliping2012@aliyun.com

Abstract

Gut microbes have an important impact on the health of the host, and quickly into sight and open a research boom. Fecal microbiota transplantation (FMT) has been legally treated human diseases in recent years, meanwhile, FMT has also been applied to cure animal diseases. This paper focuses on a comprehensive review of FMT for applications in livestock animals, domestic pets and wildlife.

Keywords

Intestinal Flora; Faecal Microbiota Transplantation; Animal Disease.

1. Introduction

The gut microbiota is a complex 'organ' in humans and animals, containing a wide range of bacteria, fungi, viruses and protozoa. The adult gut microbiota consists of over 2,000 species of bacteria, the density and diversity of which increases progressively from the stomach to the colon. The microbiota provides many benefits to the host through a range of physiological functions including enhancing intestinal integrity or shaping the intestinal epithelium, harvesting energy,

The gut microbiota defend against pathogens and modulating host immunity[1]. Fecal transplantation is a form of treatment in which the faecal microbiota of a healthy human is transplanted into the patient. the use of FMT around the world dates back to the 40th century in China when it was used to treat gastroenteritis and diarrhoea in humans. in 1958 Eisman et al. published an early case series documenting four human cases of pseudomembranous small bowel colitis associated with Staphylococcus aureus cases, who treated the disease by performing FMT via colonic enemas. In recent years, FMT has become more widely used in the treatment of human disease and is commonly used to treat Clostridioides difficile infection (CDI)[2]. Although FMT is currently used primarily for the treatment of relapsing Clostridium difficile infections in developed countries, many experimental FMTs have shown positive effects in other diseases such as inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), multiple sclerosis (MS), hepatic encephalopathy (HE) and metabolic syndrome. For the vast majority of diseases, the exact mechanism of FMT efficacy is not known, but may be due to increased microbial diversity, increased populations of beneficial microorganisms, and regulation of the immune system. Although the exact mechanism of the efficacy of FMT in humans and animals is not yet known for most diseases, several possibilities have been identified. One of the commonly accepted mechanisms of action is that FMT restores the gut microbes to normal by repopulating the gut with an intact complex microbial community. For example, in human patients with recurrent Clostridium difficile infections treated with FMT, the dysbiosis of the gut flora is normalised, followed by a reduction in symptoms and a significant reduction in recurrence rates[3]. In addition, the increased microbiota diversity increases the host's ability to metabolise complex carbohydrates, thereby improving digestion.

FMT is also thought to play a role in the competitive elimination of gastrointestinal pathogens through the repopulation of normal microbes, with beneficial microbes outperforming pathogens in terms of adhesion, attachment and infection. A recent clinical study has shown that FMT significantly reduces drug resistance in patients infected with multidrug-resistant bacteria with no other adverse effects on the body[4]. It is well known that fecal transplants and normal gut flora have the ability to modulate immune responses, for example, mice with a germ-free or pathogen-free immune system are less developed, have fewer cells and respond less well than mice with a normal gut microbiota[5]. The gut-associated lymphoid tissue (GALT) is considered a major organ of immune function and the impact of the gut microbiota on systemic immunity should not be underestimated[6]. FMT has also been described as a mechanism for altering microbial populations at the phylum or family level to achieve phenotypic outcomes. For example, when FMT from obese donors were transplanted into lean donors, an increase in the thickwalled bacterial phylum was associated with subsequent weight gain, which was thought to be primarily due to an increased ability to gain energy. Phenotypes associated with extragastric systems can also be transferred via FMT. For example, Kelly et al. described behaviour consistent with depression and anxiety via FMT transfer. Overall, the mechanisms of FMT efficacy are likely to be complex, multifactorial and dependent on the disease, type and age of the recipient and donor.

2. Applications of FMT in Animals

2.1. Application of FMT in Livestock Animals

FMT enhances the immunity and disease resistance of young mammals by transplanting gut microorganisms from adults, as this is a critical period for the colonisation of the intestinal tract. For example, the weaning period of piglets is a period of high incidence of diarrhoea, which in addition to the obvious disease of diarrhoea also leads to reduced growth and feed intake, increased morbidity and mortality. Piglets receiving FMT in adult pigs can significantly improve diarrhoea[7]. This transformation may be due to the fact that FMT partially reverses the imbalance in the intestinal flora of diarrhoeic piglets and improves their resistance to disease, thus alleviating the symptoms of diarrhoea in piglets. However, a previous trial showed that early transplantation of faecal microbiota from Yorkshire and Rongchang pigs to 3-day-old lactating piglets disrupted intestinal flora balance, thereby compromising intestinal health[8]. Calf diarrhoea is also a relatively common condition and is also associated with intestinal infections. Hyun et al. conducted FMT on 57 growing calves and followed calves for up to 24 months and showed that FMT improved diarrhoea caused by altered intestinal microbiota in preweaned calves and that FMT may have a potential role in improving growth performance[9]. There are no systematic trials in the treatment of horses, but FMT may be an effective treatment for acute and chronic diarrhoea and inflammatory bowel disease (IBD) in horses[10]. In poultry, transplantation of cecum contents from healthy adult chickens into chicks infected with C. jejuni reduced the spread and colonization of Campylobacter jejuni and improved the composition of the intestinal flora. Sina used high feed-utilizing chickens as donors for FMT of ground feed-utilizing chickens, but FMT had only a modest effect, while modulating early microbial colonization led to long-term changes in bacterial taxonomy and metabolite composition as well as host gut development[11].

2.2. Application of FMT in Domestic Animals

Although FMT is rarely used in domestic pets, recent trials of FMT in both dogs and cats have shown positive effects. Acute hemorrhagic diarrhoea syndrome (AHDS), caused by microviral infection, is a common disease in dogs, but conventional treatment is slow and the prolonged duration of treatment is likely to increase mortality.Pereira et al. treated 66 puppies with AHDS in two separate ways The results showed that the pups receiving FMT as an adjunctive treatment recovered more quickly, that FMT was well tolerated and that the clinical course was significantly improved, with 61.5% of the pups receiving FMT having their diarrhoea disappear within the first 48 hours, compared to 4.8% of the pups receiving only standard treatment. 4.8%. In addition, FMT reduced the average length of hospital stay by approximately 2.3 days and mortality was lower[12]. In a domestic cat case report from Israel, the successful use of FMT was documented in a cat with chronic ulcerative colitis, characterised by bleeding, mucus and odorous colonic diarrhoea. For approximately one year prior to FMT administration, the cat did not respond to multiple medications, diet changes and probiotic treatments. Although the diarrhoea improved rapidly after the first transplant, the clinical signs recurred and a second FMT transplant was required for eventual long-term resolution of the clinical condition[13]. However, a recent paper states that there was no clinically significant benefit from treating eight dogs with AHDS with FMT and that gut microbial alpha diversity was not significantly improved in FMT-treated patients compared to normally treated patients, but there was a significant increase in short-chain fatty acid-producing colonies within 30 days of a single FMT, and that the increase in these bacteria was beneficial[14].

2.3. Application of FMT in Wildlife

Animals living in zoos have a very different environment and diet to those in the wild. For example, there is less food diversity, less contact with other species, a reduced range of habitats and less interaction with different habitat types[15]. In addition, human contact, antibiotic administration and other veterinary interventions will affect all aspects of the animals living in zoos. Changes in diet and living environment may alter the gut microbiota of captive mammals. Captive animals moving from a captive to a natural environment will gradually acquire a gut microbiota more similar to that of wild individuals, accompanied by an increase in gut microbial diversity. This suggests that the wild environment reshapes the gut microbiota of animals released into the wild as they adapt to their natural environment and diet. Wild animals can alter their gut microbiota to facilitate adaptation to dietary and environmental shifts. FMT has also been successfully tested in wildlife, for example, an Australian hospital has successfully treated diarrhea in young kangaroos by transplanting fecal bacteria from healthy individuals over the past 50 years with a 100% success rate [16]." Blyton et al. found that koalas' gut microflora did not change with diet during the month of experimentation, and that koalas receiving FMT had a stable gut flora within 9-18 days, which was more similar to the donor koala's gut flora composition. The authors concluded that FMT could help koalas adapt to the new environment and the change in diet, and thus could better protect them[17].

3. Constraints and Prospects for FMT Development

The use of FMT in animal diseases is still subject to a number of constraints, such as the selection of the faecal donor, the mode of administration, the dose administered, economic factors, etc. FMT is a cumbersome process, and the complexity and specialisation of the technique may limit its use in animal husbandry. Certain flora in donor faeces may determine the success of FMT treatment, but its effectiveness is still unpredictable due to the lack of effective assessment tools and techniques. The safety of FMT needs to be further investigated, for example, whether the recipient may experience uncomfortable reactions after transplantation, such as low fever, abdominal pain, diarrhoea, gastrointestinal distention, easy fatigue,etc[18], and whether similar side effects are also manifested in the recipient animal and whether their severity threatens The effects of metabolites and other substances in faeces on the recipient and its intestinal flora are not yet known, and considering that livestock and poultry are the main source of food for humans, there is no final word on whether there are safety risks for livestock products after FMT in animals. Therefore, on the one hand, more careful donor and donor faecal screening criteria should be developed when FMT is applied to livestock production to reduce cross-transmission of pathogenic bacteria and conditional pathogens during FMT, and it is preferable that donors are selected without a history of antibiotic or residueprone drug use to avoid potential contamination of recipients with antibiotic and drug residues. On the other hand, the intestinal flora is a complex group of many components that have not yet been characterised and the effects of transferring flora from one individual to another cannot yet be fully elucidated. It is necessary to systematically collect information on the efficacy of FMT, including long-term or short-term safety data, and to document and define clinically relevant responses, including benefits and drawbacks, in recipients following FMT. and monitoring. This is an importan reference for the retrospective safety and efficacy of FMT transplantation, and for the study of potential mechanisms.

Acknowledgments

This work was funded by the Key Research and Development Program of Shandong Province (grant number 2019GNC106154, 2014GGB01661).

References

[1] Thursby E, Juge N. Introduction to the human gut microbiota[J]. Biochemical Journal, 2017, 474(11): 1823-1836.

[2] Frederik E. Juul , Kjetil G, Michael B et al. Fecal Microbiota Transplantation for Clostridium difficile Infection[J]. N Engl J Med, 2018, 378: 2535-2536.

[3] Raghavendra P, Joel P. Fecal Microbiota Transplantation for the Management of Clostridium difficile Infection[J]. Surg Infect, 2018, 19(8): 109-118.

[4] Catarina G, Carlos P, Patrícia P, et al. Fecal Microbiota Transplant in a Patient Infected with Multidrug-Resistant Bacteria: A Case Report[J]. GE Port J Gastroenterol, 2021, 28:56-61.

[5] Willyard, C. Squeaky clean mice could be ruining research[J]. Nature, 2018, 556:16-18.

[6] Chattha, K.S, Roth, J.A, Saif, L.J, et al. Strategies for design and application of enteric viral vaccines[J]. Annu Rev Anim Biosci. 2015. 3:375-395.

[7] Y Su, X L Li, D Y Li, et al. Fecal Microbiota Transplantation Shows Marked Shifts in the Multi-Omic Profiles of Porcine Post-weaning Diarrhea[J]. Front Microbiol, 2021, 12, 3-9.

[8] H. Diao,H. L. Yan,Y. Xiao,B, et al. Modulation of intestine development by fecal microbiota transplantation in suckling pigs[J]. RSC Adv, 2018, 8: 8709-8715.

[9] HS Kim, TW Whon, H Sung, et al. Longitudinal evaluation of fecal microbiota transplantation for ameliorating calf diarrhea and improving growth performance[J]. Nat Commun, 2021, 12(161): 2-13.

[10] KR Mullen, K Yasuda, TJ Divers et al. Equine faecal microbiota transplant: Current knowledge, proposed guidelines and future directions[J]. Equine Vet Edu, 2018, 30(3): 152-158.

[11] Sina C S, Renée, M P, Elizabeth M, et al. Fecal Microbiota Transplant from Highly Feed-Efficient Donors Shows Little Effect on Age-Related Changes in Feed-Efficiency-Associated Fecal Microbiota from Chickens[J]. Appl Environ Microb, 2017, 84(2): 3-13.

[12] Pereira G Q , Gomes L A , Santos I S, et al. Fecal microbiota transplantation in puppies with canine parvovirus infection[J]. J Vet Intern Med, 2018, 32(2);707-711.

[13] Z He , B T Cui, T Zhang, et al. Fecal microbiota transplantation cured epilepsy in a case with Crohn's disease: The first report[J]. World J. Gastroenterol, 2017, 23(19): 3565-3568.

[14] Gal A, Barko P C , Biggs P J , et al. One dog's waste is another dog's wealth: A pilot study of fecal microbiota transplantation in dogs with acute hemorrhagic diarrhea syndrome[J]. PLoS ONE, 2021, 16(4): e0250344.

[15] W Guo, K Ren, R Ning, C Li, et al. Fecal microbiota transplantation provides new insight into wildlife conservation[J]. Glob Ecol Conserv, 2020, 24:2-9.

ISSN: 1813-4890

[16] E J T Milliken. Fifty years of faecal microbiota transplant in Central Australia[J]. Gut, 2018, 1.
[17] Blyton M, Soo R M, Whisson D, et al.Faecal inoculations alter the gastrointestinal microbiome and allow dietary expansion in a wild specialist herbivore, the koala[J]. Animal Microbiome, 2019, 1 (1): 1-18.
[18] Kunde S, Pham A, Bonczyk S, et al. Safety, tolerability, andclinical response after fecal transplantation in children and youngadults with ulcerative colitis[J]. J Pediatr Gastroenterol Nutr, 2013, 56(6):597-601.