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FEACAL MICROBIOTA TRANSPLANTS IN CLOSTRIDIUM DIFFICILE INFECTION, INFLAMMATORY BOWEL DISEASE, OBESITY, METABOLIC SYNDROME

***K. Rishitha, L. Divya Bhargavi, P. Deepthi, Dr. G. Ramesh, Satheesh S. Gottipati and Dr. P. Srinivasa Babu**

Vignan Pharmacy College, Vadlamudi.

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***Corresponding Author**
K. Rishitha
Vignan Pharmacy College,
Vadlamudi.

ABSTRACT

Fecal microbiota transplantation (FMT) has been shown to be more effective in treating relapsing or refractory Clostridium difficile infection (CDI) and, potentially, inflammatory bowel disease (IBD). In clinical setting, the FMT was noted to significantly lower the risk of recurrent CDI, likely by increasing microbial diversity and altering the metabolic environment in the intestinal tract of recipients. The efficacy of FMT in the treatment of IBD appears to be influenced by a number of factors, including donor microbial profiles, inflammatory burden, and the microbial diversity of the recipient. The administration of a solution of fecal matter from a donor into the intestinal tract of a recipient in order to directly change the recipient's gut microbial composition and confer a health benefit is fecal microbiota transplantation (FMT). It may also carry therapeutic potential for other conditions such as inflammatory bowel disease, obesity, metabolic syndrome, and functional gastrointestinal disorders.

KEYWORDS: Fecal bacteriotherapy, Clostridium difficile infection, Inflammatory bowel disease, gutmicrobiome, Probiotics.

INTRODUCTION

Fecal Microbiota Transplant (FMT) is a procedure in which the fecal matter is collected from a tested donor, processed and depending on where the fecal matter is to be transplanted using colonoscopy, upper GI endoscopy or enema to recipient. In humans, the procedure is referred to as fecal microbiota transplantation and in animal models, the procedure include transfer of

unprocessed stool by feeding or oral gavage of fecal matter. Through microfiltration, spore fractionation, and density gradients the microbial portion of human stool can be highly enriched from other fecal material.[1] Here, we tentatively emphasize that viable bacteria may not be the only player in donor feces that affect the recipient's biology, but also viruses, archaea, fungi, animal colonocytes, protists, and a number of metabolites that commensal bacteria make or are dependent upon can potentially occur in unprocessed feces. The prevalence of obesity and its related metabolic disorders, such as type 2 diabetes (T2D), non-alcoholic fatty liver disease, hypercholesterolemia, have increased dramatically. While these diseases are recognised to play an emerging role in metabolic health and disease that are linked to human genetics and lifestyle changes, the human gut microbiome, or the microorganisms living in the gut and their collective genomes emerging role. There are many ways to alter the gut microbiota, including probiotics, prebiotics, and fecal microbiota transplantation (FMT). Though beneficial effects of probiotics have been reported in many studies, none show an alteration in fecal microbiota composition on other hand, FMT causes significant changes in fecal microbiota composition.[2] For the treatment of severe diarrhoea the successful practice of altering gut microbiota with FMT from a healthy to diseased individual was first recorded in the 4th century. Recently the evidence from animal and human models suggests that FMT could also be used as a therapeutic intervention against obesity and metabolic syndrome.[3,4]

PROCEDURE

The collection of microorganisms that live in the stomach and intestines is the gut microbiota. Due to antibiotic use or chronic gut disease like severe steroid refractory IBD, the healthy gut microbiota is altered, Clostridium difficile may proliferate and cause an infection that is difficult to cure; recent studies have also reported its beneficial effect in patients suffering from severe alcoholic hepatitis. Stool is made into a liquid mixture from a healthy donor is filtered and transferred to a patient with recurrent C.difficile infection, severe inflammatory bowel disease or alcoholic hepatitis. It’s a simple procedure and is performed usually by colonoscopy and less commonly by naso-duodenal tube.[5,6]

FECAL COMPOSITION

Human fecal composition has not been intensively studied and have examined composition are mostly from the 1970s and 1980s and report varying results, perhaps because of variation in diet and health. On average, adult fecal matter is estimated to be 75% water and 25% solid

matter and the majority of solid matter is organic material, whose make up consists of 25%–54% microbial cells (with a slight portion likely consisting of viruses) that may be alive or dead. As microbial counts were based on light microscopy and a modification of the Gram stain, the microbial cells were presumed to be mostly bacteria, and several other components are found in significant concentration, including archaea, fungi, and microbial eukaryotes.[7,8] 95.7% of patients spanning infants, adults, and the elderly, was detected with one particular metanoarchaeon species, Metanobrevibacter and it can comprise up to 10% of all fecal anaerobes. Viable colonocytes are also isolated from newborn and adult feces. There is no analysis of potential contribution to the success of fecal transplants has been reported. There is also a risk of contamination by environmental microbes during the collection, storage, and handling of donor stool. To standardize laboratory protocols and enhance stability of fecal matter, one option is to use frozen donor material and several studies compared the efficacy of frozen versus fresh stool on recurrent or refractory CDI and reported little to no difference.[9,10]

CLOSTRIDIUM DIFFICILE

This colitis occurs when antibiotic therapy is given and may be associated with diarrhoea, abdominal cramps and fever. It is diagnosed by a stool DNA test that detects the bacteria. Initially, this is treated with metronidazole, vancomycin and fidaxomicin and if the infection keeps recurring, fecal transplantation is considered.[11,12]

INFLAMMATORY BOWEL DISEASE

IBD is an chronic inflammation of the gastrointestinal tract that includes ulcerative colitis (UC) and Crohn's disease (CD). During disease activity (colloquially termed 'flares'), patients may present with diarrhea, nausea, weight loss, loss of appetite, fever, and abdominal pain. The pathophysiology is unknown, but the cause is multifactorial, due to imbalances in the intestinal microbiota, gut epithelium, and immune system in genetically susceptible individuals. IBD is hypothesized to occur due to continuous inappropriate antigenic stimulation of gut mucosa-associated lymphatic tissue by commensal microbes and Dysbiosis of the gut has been considered as a possible pathologic contributor to IBD development. The antibiotics such as amoxicillin/clavulanic acid and rifaximin can reduce intestinal inflammation and induce remission in some patients.[13,14]

OBESITY AND METABOLIC SYNDROME

The disorder that is characterized by excessive adipose tissue deposition is obesity. Signs such as central obesity, hypertension, dyslipidemia, and hyperglycemia that increases one's risk for developing heart disease and diabetes mellitus is characterised as metabolic syndrome. Recent metagenomic studies characterized that the gut microbiome in lean and obese individuals, and reported marked differences between the two. Transfer of the gut microbiota from human for obesity into germ-free mice led to greater adiposity and body mass in the mice transplanted with the obese microbiota. Recent studies of a small double-blind, randomized, controlled study found that the fecal transplants from lean to obese (with metabolic syndrome) individuals resulted in improved insulin sensitivity, increased gut-microbial diversity, and increased butyrate-producing bacteria (Roseburia intestinalis) in the obese recipients. This study shows a proof for the future study of FMT for the treatment of obesity, metabolic syndrome, and diabetes mellitus. When choosing candidate donors for FMT the body mass index of the donor may need to be taken into consideration for the potential of the gut microbiota to affect weight gain.[15,16]

DONOR REQUIREMENTS

Donor should not have

- any antibiotics in the last 3 months
- immune-compromised
- any tattooing or body piercing in the last 6 months
- a history of drug abuse
- a history of high risk sexual behaviour
- a history of any incarceration
- travelled to endemic areas
- any other gastro intestinal disorder such as IBD.[17,18]

DONOR SCREENING INCLUDES

- The blood tests such as Hepatitis A, B, C and E serology, HIV serology, should all be negative
- For ova and cysts of parasites, C. difficile PCR, culture and sensitivity, giardia antigen stool culture should be done.[14,15]

PREPARATION OF A RECIPIENT FOR FMT

- 24 hrs before procedure recipient should be on empty digestive system.
- Advised a bowel cleansing liquid. This is avoided by those suffering from severe infection, IBD, colitis, pseudomembranous colitis (infection in the colon; overgrowth of Clostridium difficile bacteria) or toxic megacolon.
- Advised tablet loperamide to reduce intestinal motility and thereby hold the transplanted bacteria.[19]

PREPARATION OF THE DONOR

- Five days before the transplant donors should avoid any foods that the recipient is allergic to.
- If donor has fever, diarrhoea or vomiting donation should be postponed.
- The previous night may be given a laxative.

If the recipient has no relapses for eight weeks then FMT is considered as success. Some patient's may require several sittings to get a successful outcome.[20]

CONCLUSION

Larger studies are needed to confirm the results and to evaluate long-term safety and effectiveness. In the short term FMT is a safe and effective option to prevent recurrent CDIs in patients with IBD, and will likely remain an important tool in the future. In IBD populations although the cure rate for CDI may be lower than in non-IBD populations, the impact of CDI on the course of IBD warrants FMT intervention. Physicians should understand the alteration of FMT microbial diversity as a general intervention and which species and/or strains are amenable to colonizing the recipient's intestine in both CDI and IBD. It is important to determine when microbial interventions might be most effective in the disease course, and in what manner and dosing they would need to be provided to sustain beneficial effects. The controlled clinical studies currently testing FMT for metabolic syndrome we should have a clear indication in the next few years. Also similar procedures will provide new therapeutic options for obesity and its associated metabolic disorders.

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