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Is Fecal Transplant Sense?

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ABSTRACT

FMT (Fecal Microbial Transplant) has been introduced in an attempt to restore the gut microbial balance and firstly to treat C. difficult. It appears to be the most efficient method to effectively change and sustain the gut microbial composition with low side effects for the time being.. FMT is still a difficult idea to accept within the pediatric scientific community and parents of patients as atherapy. FMT may be a treatment of many difficult diseases and could be adjuvant for the treatment of non-communicable diseases.

Keywords: *fecal transplant, dysbiosis, C. dificili, microbial flora*

INTRODUCTION

FMT approach has already been used for treating micro biome diseases such as Clostridium difficile resistant infection .In many aspects, FMT is simpler to perform than other organ transplants, without the need for immunological matching of donor and recipient or the need for immune suppression after the procedure. Most feacal donors have been healthy family members or spouses/significant partners who have common genetic and/or environmental factors. .

As a definition, fecal transplant orfecal microbiota transplantation (FMT) is the transfer of stool from a healthy donor to a recipient believed to harbor an altered colonic microbiome resulting in disease [1].Altered microbiome means dysbiosis which is an imbalance of the gut flora caused by a decrease in beneficial bacteria and an increase in harmful bacteria, yeast, and/or parasites, which is associated with a various diseased state [2].The goal of FMT is to restore eubiosis, equilibrium, or a healthy microbial flora microbiome. This procedure is often referred to as: stool transplantation, fecal transplantation, fecal flora reconstitution, fecal bacterio-therapy, or human probiotic infusion [1, 3].

The rationale of using FMT has been confirmed because of its successful use in treating recurrent C. difficile infection. [4]. Fecal transplant was first recognized in the 4th century in China. It was known as “yellow soup”. The Chinese used it for treating severe diarrhea and food poisoning [5].Fresh warm camel feces were used by Bedouins as a treatment for bacterial dysentery [6].In 1959, another successful fecal transplant for ulcerative colitis was done by Bennet and colleagues [7].

What is being transferred by FMT is not only viable bacteria but other components as well such as colonocytes, archaea, viruses, fungi, protists, and metabolites [8].It is the complex nature of feces where each of its relative components has a potential role in therapy. In reality the main goal of using FMT is the treatment and suppression of Clostridium difficile infection and potentially eliminate this bacteria in the diseased gut and allow commensal bacteria to flourish and normalize in diversity and content. Moreover, colonocytes prevent bacterial translocation into internal tissues and organs. It transplants the healthy viable colon stem cells to repair the damage in superficial colon cells. Metabolites help to nourish the colonocyte barrier and intestinal bacteria [8].

The hypothesis behind FMT relies on the concept of bacterial interference, such as using harmless bacteria to displace pathogenic organisms and to restore missing components of the dysbioticflora (Bacteroidetes and Firmicutes) [9]. The restored colon microbial community could inhibit C. difficult by several mechanisms such as by bile-acid-mediated inhibition of spore germination

and vegetative growth by activation of immune-mediated colonization resistance; competing for nutrients; direct suppression by antimicrobial peptides; and decreasing bacteria with genes resistant antibiotics [10]. The FMT mechanism of action could be explained in various ways such as by triggering mucosal immune responses depending on the microbiota composition and the recipient's genotype [11]. Another mechanism could be byrapid production of anti-inflammatory mediators that may counteract pro-inflammatory cytokines [12]. A third way is by producing antimicrobial agents (Bacteriocins) by the colonic flora to eradicate C. difficile and other pathogens. [10, 13]. In this way it restores the gut barrier integrity by providing the necessary tonic signals for epithelial regeneration and production of mucins and antimicrobial peptides [12].This will help in healing the mucosal injury by the production of mucin, Transforming Growth Factor B, and keratinocyte growth factor. The new transfused gut microbial flora "microbiome" appears to be stable in the recipients for at least 22 weeks [13]. The dose of at least 50 g of stool is needed to have better results than lesser doses [3].

Studies have utilized different delivery methods that include: nasogastric tube, nasojejunal tube, enemas, colonoscopy (ileocecal or rectal), and capsule form of the product. The delivery to the ileocecal area guarantees delivery of the transplanted microbiome to the entire colon [14]. Rectal enemas are limited to the delivery of FMT to the rectum and left colon so this would limit their efficacy beyond those areas [15].

Children who are highly sensitized to some types of food may develop anaphylactic reaction when in contact with antigens from the transplant feces. The question then arises when such a child needs to undergo fecal transplant? Could the food antigen ingested by the donor trigger anaphylactic reaction upon FMT? These questions must be investigated and taken into consideration [14]. Side effects are usually not serious but there could be some potential risks. Short-term adverse events include abdominal discomfort, bloating, flatulence, diarrhea, constipation, vomiting, and transient fever. There could be some serious adverse events due to the procedure as complications of endoscopy (perforation, bleeding),adverse effects related to sedation (aspiration), transmission of enteric pathogens if not well prepared, peritonitis in a patient undergoing peritoneal dialysis, pneumonia, and inflammatory bowel disease (IBD) flares. Moreover, induction of chronic diseases based on alterations in the gut microbiota could happen such as obesity, diabetes, atherosclerosis, nonalcoholic fatty liver disease, asthma and autism [14, 16, 17].

The therapeutic potentials of FMT innon-gastroenterologicconditionsisbeingstudied.Theseconditionsinclude: autoimmune disorders, obesity, food allergy, metabolic syndrome, diabetes, neurological conditions, multiple sclerosis, Parkinsons disease, and chronic fatigue syndrome [18-20]. For treatment of slow transit constipation, the efficacy of FMT remains unknown and more studies are needed. For treatment of IBD, the efficacy of FMT shows substantial promise. A few randomized trials have shown clear benefit of FMT in the treatment of ulcerative colitis, while the effectiveness of FMT for Crohn's remains unknown due to a lack of studies [4].

The future field of research is to manipulate the microbiota environment to treat or prevent obesity in humans especially children, IBS, atopy and inflammation since they all have disturbed microbiome and are fairly common and difficult to treat [21, 22]. More research is needed to investigate the concept of tailoring the micro-organism transferred to specific diseases or to optimize microbiota to prevent infections or to reconstitute the microbiota following antibiotic treatment. Further research is needed to know the optimal duration and quantity of FMT.

Some questions arise such as do we have to take into consideration the host's diet, genotype, or environment? Do we have to consider some specific commensal bacterial species which might cause improper immune responses in different individuals? To what extent can dietary changes optimize the intestinal microbiota, and how will this influence the immune system, after the transplant?

As a conclusion, FMT has been introduced several decades ago in an attempt to restore the gut microbial balance and firstly to treat C. difficult. It appears to be the most efficient method to effectively change and sustain the gut microbial composition with low cost and side effects. Till now FMT is still difficult for the pediatric scientific community to embrace and to accept this therapy as there are only sporadic reports in children. FMT may be a treatment of many difficult diseases and could be adjuvant for the treatment of non-communicable diseases. More randomized controlled studies are required

to determine the safety and efficacy of FMT in children. The last piece of thought …Will FMT be the future treatment and replace antibiotics? [3].

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