Therapeutic Potential of Gut Microbiome Manipulation: Concepts in Fecal Microbiota Transplantation

Dr Vinod Nikhra M.D.
Hindu Rao Hospital & NDMC Medical College,
New Delhi, India

ABSTRACT

MICROBIAL ALTERATIONS AND DYSBIOSIS: The composition and diversity of gut microbiota is an indicator of health and various groups of commensal bacteria provide health advantages as they enhance metabolism, the immune system, cancer resistance, endocrine signaling and brain function. In general, the gut microbiome remains relatively resilient over time, however, antibiotic use, erratic diet, illness and other factors can lead to alterations and dysbiosis, which weaken various elements of the barrier, causing collapse of the mucus layer that separates epithelial cells and microbiota and reduced expression of antimicrobial peptides which control bacteria including *C. difficile*.

FMT - INVASIVE GUT MICROBIAL MANIPULATION: FMT is administration of a form of fecal material from the donor into the intestinal tract of the recipient in order to directly modify the recipient's gut microbial composition suitably to confer health benefits. FMT has been used to successfully treat recurrent *Clostridium difficile* infection (DCI). There are preliminary indications to suggest that it may also carry therapeutic potential for other conditions such as inflammatory bowel disease, obesity, metabolic syndrome and functional gastrointestinal disorders.

MECHANISMS AND EFFECTS OF FMT: FMT involves administration of the whole microbiota from healthy donor stool into the recipient's intestinal tract to normalize or modify intestinal microbiota composition and function. FMT has restorative potential for both composition and functionality of gut microbiota and results in normalization of microbial diversity and community profile in patients by multiple mechanisms including competition for nutrients among *C. difficile* and other microbiota, direct suppression by antimicrobial peptides, bile-acid-mediated inhibition of spore germination and vegetative growth; and activation of immune-mediated colonization resistance.

POSSIBLE SCOPE OF FMT INTERVENTIONS: FMT is be considered for recurrent or relapsing CDI when there is failure to respond to conventional antibiotic therapy. For a moderate CDI, FMT is indicated when there is no response to standard therapy for at least 1 week. For severe CDI, it is indicated when there is no treatment response after appropriate maximal therapy for 48 h. FMT leads to a significant change in microbial diversity in patients with recurrent CDI and complete resolution of symptoms. However, the trials to treat ulcerative colitis (UC) with FMT have shown conflicting results. Further, the patients with Crohn's disease (CD) and ulcerative colitis (UC) have increased incidence of CDI, and presence of CDI commonly complicates the course of these underlying diseases.

LIMITATIONS, REGULATIONS AND COMPLICATIONS: The occasional adverse effects of FMT are diarrhoea, abdominal cramping, belching and nausea, which are self-limiting and resolve in a variable period. An increased risk of IBD flare, fever and elevation in inflammatory markers following FMT may occur. Some serious adverse effects are upper GI bleeding, enteritis and peritonitis, which vary with the administration method and may be related to complications of the method itself rather than FMT. FMT is regulated in Canada as a 'new biologic drug', specifying the indications, patient's consent, preparing the FMT from a known solitary donor and screening for potential pathogens prior to administration. The US Food and Drug Administration (FDA) considers stool as a biological product and drug, and mandates physicians to maintain similar precautions to administer FMT. FMT, so far is not regulated in West by the European Medicines Agency, or elsewhere in Asia, Africa or Australia.

FUTURE DIRECTIONS AND DEVELOPMENTS: There is increasing acceptance for the therapeutic use of FMT. However, the risks and benefits remain poorly defined because the published FMT experience remains limited. In future, FMT can be a pauci-strain type or multi-strain type depending on the fecal microbiota analysis of the recipient. The suitable strains can be picked-up from donor fecal sample, grown in cultures and transplanted through an appropriate route. Depending on the recipients' microbiota diagnostic analysis, the FMT using suitable pauci-strains may be a promising development in near future. FMT using frozen sample is another prospective development and may lead to autologous FMT using the sample preserved from the healthy state in a microbiota bank similar to stem cells bank.

IMAGE

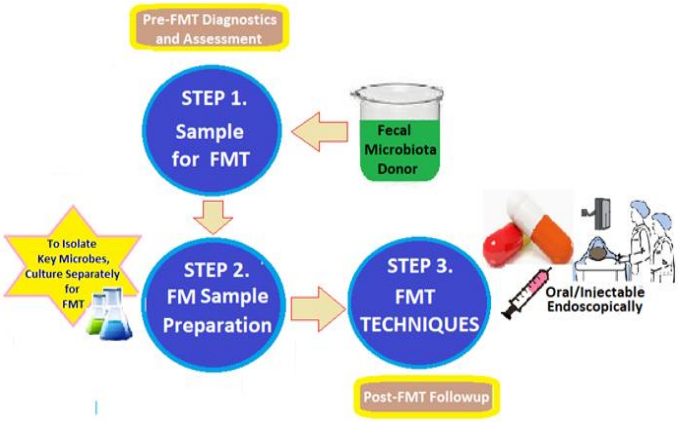
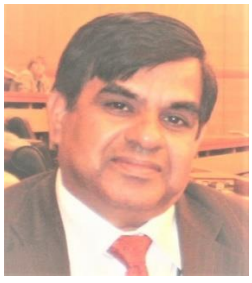


Fig. Steps for Fecal Microbiota Transplantation

REFERENCES

1. Peterson CT, Sharma V, Elmén L, Peterson SN. 2015. Immune homeostasis, dysbiosis and therapeutic modulation of the gut microbiota. *Clin Exp Immunol*. 179:3; 363-77.
2. Petersen C, Round JL, Huttenhower C, et al. 2014. Defining dysbiosis and its influence on host immunity and disease. *Cell Microbiol*. 16:7; 1024-33.
3. Moayyedi, P, Surette, MG, Kim, PT et al. 2015. Fecal microbiota transplantation induces remission in patients with active ulcerative colitis in a randomized, controlled trial. Gastroenterology. 149; 102–09.
4. Weingarden AR, Chen C, Bobr A, Yao D, et al. 2014. Microbiota transplantation restores normal fecal bile acid composition in recurrent Clostridium difficile infection. Am J Physiol Gastrointest Liver Physiol. 306; G310–19.
5. Brandt LJ, Aroniadis OC. 2013. An overview of fecal microbiota transplantation: techniques, indications, and outcomes. Gastrointest Endosc. 78; 240–49. (Contd.)

KEYWORDS: Clostridium difficile infection, Fecal microbiota transplantation, Frozen sample FMT, Gut microbial diagnostics, IBD, IBS, MetS, Microbial Dysbiosis, Pauci-strain and multi-strain FMT, Microbiota bank.



Photograph

Dr Vinod Nikhra is a Senior Consultant Physician and Faculty at NDMC Medical College and Hindu Rao Multi-speciality Public Hospital, New Delhi, India. He is a healthcare administrator, academician and clinician. He has been a Visitor at Cleveland Clinic Foundation, Cleveland and an Observing Physician at Alabama Medical Center – a tertiary care hospital in Opelika, Alabama, USA. He has been elected a Fellow by International Medical Sciences Academy and the Royal Society of Medicine, London. He has been Editor of 'Madhya, the midage', the official Journal of Association for Health in Middle Age during 2003-2006. He has been on Reviewer panel of, among others, the Family Practice, an Oxford University medical journal and International Journal of Obesity. His published books include, 'Aging slowly, Living longer' and 'The Anti-obesity Guide'. Over the years he has contributed about hundred papers in leading national and international medical journals.

Email: drvinodnikhra@gmail.com Alt.email: drvinodnikhra@rediffmail.com