



Significance of Fecal Microbiome in Treatment of Bowel and Gastric Disease

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Abstract

Increased interest in understanding of role of the human gut microbiome for elucidation the therapeutic potential of its manipulation. Fecal microbiota transplantation (FMT) foe administration of a solution of fecal matter from the donor into the intestine of recipient in order to directly change the recipient's gut microbial composition and confer a health benefit. FMT has been used to successfully treated of *Clostridium difficile* infection. There are preliminary indicated for suggestion that it carry therapeutic potential for other conditions such as inflammatory bowel disease, obesity, metabolic syndrome, and functional gastrointestinal disorders.

Keywords: Bacteriotherapy; *Clostridium difficile* Infection; Fecal Microbiota Transplantation; Gut Microbiome; Inflammatory Bowel Disease

Fecal microbiota transplantation

Fecal microbiota transplantation (FMT) is 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 microbial composition and confer a health benefit [Bakken., *et al.* 2011; Smits., *et al.* 2013] [1]. The first known description of the use of feces as therapy was described by Ge Hong in fourth-century China for the treatment of a variety of conditions including diarrhea [Zhang., *et al.* 2012]. In 1958, Eiseman and colleagues described the use of fecal enemas as a treatment for pseudomembranous colitis, marking the introduction of FMT into mainstream medicine [Eiseman., *et*

al. 1958] [2]. The process usually involves first selecting a donor without a family history of autoimmune, metabolic, and malignant diseases and screening for any potential pathogens. The feces are then prepared by mixing with water or normal saline, followed by a filtration step to remove any particulate matter. The mixture can be administered through a nasogastric tube, nasojejunal tube, esophago gastroduodenoscopy, colonoscopy, or retention enema. Most clinical experience with FMT has been derived from treating recurrent or refractory *Clostridium difficile* infection (CDI) [3].

Clostridium difficile infection

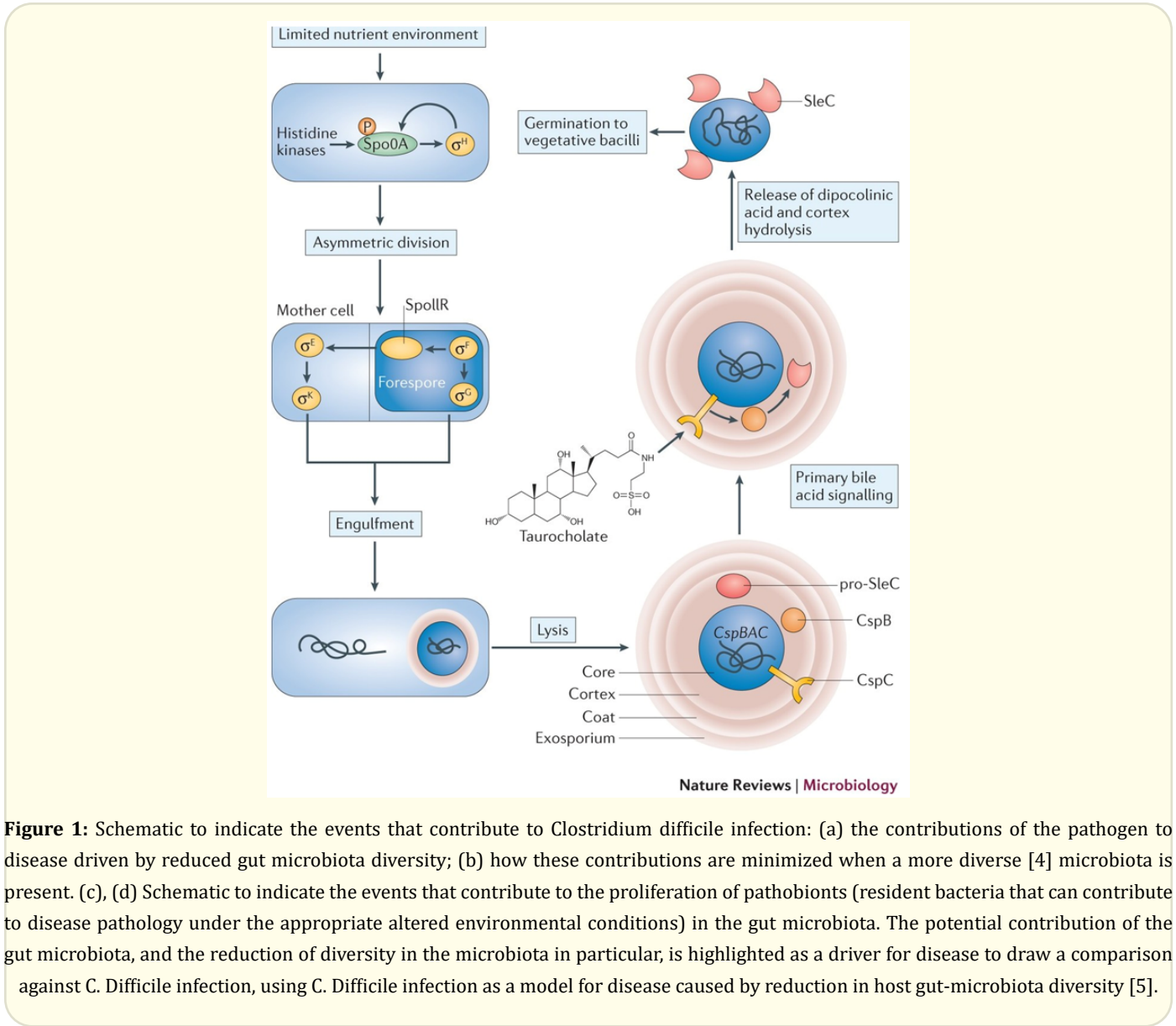


Figure 1: Schematic to indicate the events that contribute to *Clostridium difficile* infection: (a) the contributions of the pathogen to disease driven by reduced gut microbiota diversity; (b) how these contributions are minimized when a more diverse [4] microbiota is present. (c), (d) Schematic to indicate the events that contribute to the proliferation of pathobionts (resident bacteria that can contribute to disease pathology under the appropriate altered environmental conditions) in the gut microbiota. The potential contribution of the gut microbiota, and the reduction of diversity in the microbiota in particular, is highlighted as a driver for disease to draw a comparison against *C. Difficile* infection, using *C. Difficile* infection as a model for disease caused by reduction in host gut-microbiota diversity [5].

Inflammatory bowel disease

IBD is an intestinal disorder that includes ulcerative colitis (UC) and Crohn's disease (CD). IBD is character of chronic inflammation of the gastrointestinal tract, and has a cyclic nature of disease progression and remission. During periods of disease activity (colloquially termed 'flares'), patients may present with diarrhea, nausea, weight loss, loss of appetite, fever, and abdominal pain. The precise 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 [6] hypothesized to occur due to continuous inappropriate antigenic stimulation of gut mucosa-associated lymphatic tissue by commensal microbes. Dysbiosis of gut have recently been considered possible pathologic contributor to IBD development [7].

M. Biopsy specimens from patients with CD were found to have a reduced population of the Clostridium cluster IV species are associated with anti-inflammatory characteristics in patients with CD, and increase of levels of the bacterium are maintenance of clinical remission. Overall, the IBD microbiome were discovered to be inflammation promoting, by indications of increased [8] oxidative stress, increased type II toxin secreted, and increase of virulence-related bacterial genes. Recently, it was observed that the transplantation of fecal ecosystems from patients with UC to germ-free mice increased sensitivity to dextran sodium sulfate-induced colitis, thus supporting the use of microbiota modification for the treatment of UC.

The evidence linked gut microbial dysbiosis for IBD had led to the exploration of FMT as therapy for the disease. A recent systematic review and meta-analysis looked at 18 studies including 122 patients with IBD treated with FMT, and found overall clinical remission rates of 36.2%. Subgroup analyses showed that the clinical remission rate in UC patients was 22%, whereas younger patients (aged 7-20 years) had a rate of 64.1%, and patients with CD had a rate of 60.5%. It appeared that FMT have been more effective for CD and in younger patients than for UC infection, however it is difficult to draw definitive conclusions due to the small sample sizes, short follow-up times, and heterogeneous results. Two randomized controlled trials exploring the use of FMT for treatment were published, with mixed results. The first study enrolled 75 pa-

tients with active UC and randomized them to weekly FMT or water enema for 6 weeks, and found remission (defined by Mayo score < 3 and complete mucosal healing) in 24% of patients [9] treated with FMT compared with 5% treated with water control. The other study randomized 50 patients with mild to moderately active UC to donor or autologous FMT via nasoduodenal tube, which were administered once at the start of the trial and again 3 weeks later. Of the 37 patients that completed follow up, there was no difference in clinical and endoscopic remission between the two groups. These differing results may be due to differences in routes of administration, stool donors, dosing schedules, or concomitant therapies. In addition, the study by Rossen and colleagues may have been too underpowered to detect differences between the two groups. In the trial by Moayyedi and colleagues, the patients that benefitted most from FMT were those with a recent history of disease onset. This may indicate that FMT may be useful only in certain subsets of patients with UC [10].

Although no serious adverse events were noted during the short-term follow up of the IBD patients treated with FMT, some were reported to have developed fevers, chills, bloating, flatulence, vomiting, diarrhoea, and abdominal tenderness. Also, there have been some reports of patients' conditions worsening after FMT. Therefore, FMT should be used with caution until more high-quality, adequately powered trials assessing its efficacy in IBD are completed. However, it is clear that FMT is not as effective in IBD as it is in CDI, and this is probably due to the multifactor pathophysiology of IBD.

Functional gastrointestinal disorders

Functional gastrointestinal disorders (FGID) are commonly diagnosed gastrointestinal (GIT) disease in the Western hemisphere. They presented by gastrointestinal symptoms with absence of any identifiable anatomic or biochemical abnormality. Irritable bowel syndrome (IBS) is the most common form of FGID, and affects 5-15% of the population and 25% of the North American population. IBS has a deleterious affect on a patient's quality of life and places an economic burden on the healthcare system. There are four subtypes of IBS, based on the dominant symptoms experienced by the patient. IBS-D is diarrhea-predominant, IBS-C is constipation predominant, IBS-M is mixed diarrhea and constipation,

and IBS-U is for those who are unsubtype [Yao., *et al.* 2012]. The pathophysiology is not well defined, but involves visceral hypersensitivity, altered barrier function, altered gastrointestinal motility, and an altered gut-brain axis. These changes may be related to changes in the gut microbiota [Pinn., *et al.* 2015]. There have been small, limited case series published demonstrating the use of FMT to treat FGID. One study administered FMT to 45 patients with chronic constipation via colonoscopy and a subsequent retention enema, and found 89% of patients to have immediate symptom relief whilst 60% sustained benefit at 9-19 months. Another study performed on FMT to 13 patients with IBS (9 with IBS-D, 3 with IBS-C, 1 with IBS-M) via esophagogastroduodenoscopy and found 75% had symptom relief at 6-18 months. It appears that FMT may have a therapeutic effect for the treatment of FGID, however, conclusions cannot be made because the available data are extremely limited and susceptible to bias. Well-designed trials should be pursued to determine whether there is indeed a link between the gut microbiota and FGID.

Discussion

Discussed about the fecal transplantation and its microbiota composition and treatment and benefit of fecal microbiome transplantation and benefits in irritation bowel syndrome and various gastric disease like severe diarrhoea and gastritis.

Conclusions

Microbiome is alternative for the treatment of various gastric disease and can be used to restore normal human microfolra.

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