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Management of Obesity and Other Metabolic Disorders Through Faecal Microbiota Transplant Technology

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Abstract

The microbiota regulates health and many diseases both infectious and metabolic. The makeup and density of intestinal microbiota can be influenced by diet and therefore, they play a major role in the development of obesity by regulating energy metabolism. Recent evidence, primarily from investigations from animal models, suggests that the gut microbiota affects nutrient acquisition and energy regulation. Gut microbiota regulates obesity by regulating energy absorption, central appetite, fat storage, chronic inflammation, and circadian rhythms. Several members of Proteobacteria were the most consistently reported obesity-associated phylum. Non antibiotic therapeutic method, the Faecal Microbiota transfer technology, seems to be one of the effective therapeutic and management techniques to treat and/or manage some of the metabolic disorders in particular obesity.

Keywords: Faecal Microbiota; Energy Absorption; Obesity; Circadian Rhythms; Bacteriocins; Bacteriophages; Polycystic Ovary Syndrome; Clostridium Leptum; Bacteroides Fragilis; Bifidobacterium Catenulatum; Lactobacillus; Clostridium Coccoides; Bifidobacteriu; Muciniphila

Abbreviations: NG: Nasogastric; FMT: Faecal Microbiota Transplant Technology; CDI: Clostridioides Difficile Infection; CRE: Carbapenem-Resistant Interobacteriaceae; SCFAs: Short-Chain Fatty Acids; BA: Bile Acids; FXR: Farnesoid X Receptor; NAFLD: Non-Alcoholic Fatty Liver Disease; NASH: Non-Alcoholic Steatohepatitis; RYGB: Roux-En-Y Gastric Bypass; SREBP-1: Liver Sterol Response Element Binding Protein Type-1

Introduction

In order to avoid the ill effects of antibiotics scientists were in search of alternative therapies for infectious diseases [1]. Antimicrobial Proteins, Bacteriocins, Bacteriophages, Plant-Derived Antimicrobial Compounds, Probiotics and Prebiotics have been identified to suit the requirements as an efficient alternative for antibiotics [2]. Faecal microbiota transplant technology (FMT) delivers the faecal matter of a healthy human to a patient via colonoscopy, enema, nasogastric (NG) tube, or in capsule. FMT is a highly effective, safe, and cost-effective treatment option at least for recurrent Clostridioides difficile infection (CDI) with a success rate of around 90%. From animal models and human trials this technique is also proved to be effective in diseases such as Carbapenem-resistant Interobacteriaceae (CRE), Alzheimer's, arthritis, diabetes mellitus, inflammatory bowel disease, autism, polycystic ovary syndrome and obesity [3-5].

Obesity is a public health issue, due to disequilibrium in energy balance, with energy intake exceeding energy expenditure resulting in a state of chronic inflammation. Obesity also proves to be a triggering factor for the prognosis of metabolic diseases such as type 2 diabetes, cardiovascular diseases, osteoarthritis, and certain cancers. Globally, the prevalence of obesity is increasing at an alarming rate. Further to increasing the onset of metabolic imbalances, obesity is one of 9 contributory factors for aging as well as for reducing the life span. The increasing rate of aging due to obesity affects all aspects of physiology and thus shortening life span and health span [6]. Obesity is also associated with depression, suffering from sleep issues, insomnia, and increased risk for developing asthma. At present, there are more than 500 million adults worldwide who are considered to be overweight [body mass index (BMI) of 25.0-29.9 kg/m^2] and 250 million people saluted as obese (BMI ≥30 kg/m^2) globally [7].

Out numbering the human genome by 150:1, bacteria is involved in the development and evolution of human beings with a constant turnover from birth till death. Diversity as well as adaptability of these organisms and their by-products change drastically throughout life in human beings [8-10]. The bacterial

populations residing in the digestive system are observed to co-develop along with the human host and depend on the mode of birth [11], breastfeeding and early diet and nutrition, environmental and other factors including antibiotic exposure ultimately leading to bacterial disequilibrium and variations in prognostic outcomes. Gut microbes are involved in polysaccharide breakdown, nutrient absorption, inflammatory responses, gut permeability, and bile acid modification. In addition to changes in energy balance discussed earlier, other defined factors are also identified to be responsible for the increased incidence of obesity and related metabolic diseases worldwide. One such crucial factor is the dysbiosis of the gut microbiota due to their capability to utilize more energy from the diet [12-14].

Role of Gut Microbiota in Obesity

In depth studies provide concrete proof for the close association between the microorganism present inside the digestive system and obesity as well as obesity-associated abnormalities. Elevated energy harvest from the diet, fatty acid regulation within the tissues, chronic as well as low-grade inflammation are linked as causal factors to induce obesity [7]. When these bacteria and their metabolites interfere with the host carbohydrate metabolism, obesity and imbalance of their number ultimately results in metabolic syndrome [4,15]. There exists a drastic difference between the bacterial population of the digestive system of lean and obese individuals which came to limelight only from metagenomic studies [16]. The altered microbiota found in obese individuals could be responsible for redisposing them to obesity through increased energy extraction, or possibly through an interaction with the gut–brain access leading to decreased energy output or through influencing fullness [17].

The hypothesis for the involvement of the intestinal bacteria to induce obesity could through increasing dietary energy harvest, increase adipose tissue formation, altering the locomotor activity of the host, having central effects on a feeling of fullness, and triggering systemic inflammation [7]. Reports are available for the high fat diet to induce chronic systemic inflammation. As a result, shifts in the balance of gut microbiota composition toward high in unfavorable bacterial species may predispose an individual to weight gain [11].

Decrease in the fractional proportion of Bacteroidetes species relative to Firmicutes in obese subjects compared with lean individuals was a valid observation but vice versa could be observed regarding the relative proportion of Bacteroidetes species and microbial diversity. Similarly, diversity of the genes was decreased in obese compared with lean individuals [7].

Many studies have given a clue that the methanogenic Archaea may contribute to altered metabolism and weight gain in the host. In fact, the point to be focused is that there may be difference between the content of the stool or colonic samples with which Studies are performed compared to the metabolically active small intestine [6]. In depth studies has proved that alterations in intestinal bacterial population is capable of reducing intestinal barrier integrity but to increase the oxidative stress and mucus degradation by reducing the production of butyrate (known to be associated with obesity and pain sensation and plays an important role in colonic function). Akkermansia muciniphila was reported to reduce the insulin resistance index, control fat storage, adipose tissue metabolism, intestinal levels of acylglycerols, and glucose homeostasis. When the diet was altered increase in *Clostridium leptum*, *Bacteroides fragilis*, and *Bifidobacterium catenulatum* and decreased abundance of *Lactobacillus*, *Clostridium coccoides*, and *Bifidobacterium* was noticed. Only quality of the diet and not the quantity hardly had the impact in the experiment. Zhang et al. [18] also reported that the gut of obese subjects had more H2-producing bacterial groups. These bacteria are capable of absorbing H2 rapidly by Methanogens resulting in the fermentation of carbohydrates and increasing the hydrolysis efficiency of usually indigestible organic matter [18-20]. It is interesting to note that pure form of lipopolysaccharide, endotoxin, the only bacterial product when subcutaneously infused into mice, obesity and insulin resistance could be induced via an inflammation-mediated pathway.

To ensure efficacy during obesity treatments, alterations of intestinal bacteria are essential. With good knowledge gained about the influence of the commensal microbes, obesity could be therapeutically treated by changing bacteria in the gut accordingly [7]. Not all bacterial strains have the capacity to induce obesity since some pros and some are anti-obesity depending on the fibre utilization (Anti-obesity) like *A. muciniphila* commonly linked to anti-obesity characteristics [21,22]. Metabolic syndrome is due to altered gut barrier function and leakage of bacteria and/or bacterial components into the circulatory system resulting in an inflammatory state. For example, endotoxemia is an indication for translocation of gram-negative bacteria contributory factor in many diseases, including metabolic syndrome [23]. Inflamed gut that allows fatty acids into the circulatory ultimately gets esterifies into triglycerides and stored within the adipocytes. Some strains of gut bacteria can influence ANGPTL4 levels that decrease triglyceride storage and increase circulating plasma triglyceride levels.

Other Metabolic Diseases

Some strains of bacteria can harvest energy from specific monosaccharides through specialized proteins resulting in the imbalance of host's weight and metabolic energy [16]. Liver sterol response element binding protein type-1 (SREBP-1), a transcriptional regulator of lipogenic gene expression is found to have a close association with bacteria in the digestive system to involve in bacteria-induced lipogenesis as well as remodeling of adipose tissue storage. Indeed, treatment with specific bacteria

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strains such as A. muciniphila, probiotics or prebiotics has been shown to down regulate high-fat diet or high cholesterol-induced SREBP-1c expression in the liver. Conclusion can be drawn that metabolic imbalance seen in obese subjects could possibly be linked to the nutritional manipulation of these energy-extracting, lipogenic bacteria and their respective proteins [11].

Along with inflammatory mechanisms they are capable of producing signaling molecules anticipated to affect gut integrity, the immune system and may influence host metabolism. Short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate, are small molecules metabolized by gut microbes from dietary fibers. The location of receptors in the human body for these SCFAs is still an enigma and therefore may induce complex effects.

Bile acids (BA) are identified to aid in microbiota-host communication through nuclear receptor farnesoid X receptor (FXR) to maintain metabolic health. This interesting conclusion was drawn from a study where FXR-deficient mice fed with high-fat diet, or those mice genetically predisposed toward obesity have better glucose regulation than control mice with normally functioning FXR. This observation in human trials is still pending. Association among fatty liver disease (non-alcoholic fatty liver disease [NAFLD] and non-alcoholic steatohepatitis [NASH]), the intestinal microbiota, and obesity is not surprising because NAFLD and NASH are associated with obesity and insulin resistance. Data from human studies also support the concept that changes in the intestinal microbiota contribute to the development of fatty liver diseases. Increase in intestinal permeability, LPS-binding peptide levels in the plasma, endotoxemia, and numbers of Gammaproteobacterial, reduced numbers Bacteroidetes compared with healthy subjects could be noticed in patients with NAFLD. Microbiota strains differ in subjects with non-alcoholic steatohepatitis (NASH) or non-alcoholic fatty liver disease (NAFLD), compared with healthy controls. More human trials are wanting to ascertain the functional role of microbiota in all aspects of the metabolic syndrome including insulin resistance, dyslipidemia, atherosclerosis, hepatic steatosis, and elevated blood pressure. Nevertheless, confirmation on the effect of FMT in NASH or NAFLD in human studies is wanting [23].

FMT Therapy/Management for Obesity

Obesity can happen for a number of reasons, including diet, a sedentary lifestyle, genetic factors, a health condition, or the use of certain medications. A number of treatment options can help people to achieve and maintain a suitable weight. However, recent experiments performed by microbiologists have demonstrated that alteration in the relative level of the two dominant bacterial populations (Bacteroidetes and Firmicutes) could be associated with obesity, namely, the population of Bacteroidetes was lower, while Firmicutes was higher in obese individuals. These Firmicutes are better in efficiency to absorb energy from diet compared to the bacteria from lean subjects. Turnbaugh et al [16] from his in-depth study in which the fecal microbiota of obese C57BL/6J donors was transplanted into germ-free C57BL/6J recipients. Germ-free mice colonized with an bacterium from obese subjects exhibited a significant increase in total body fat compared with germ-free mice colonized with a microbiota from lean subjects suggesting that intestinal bacteria could be an additional contributing factor to the pathos-physiology of obesity. In their human trials patients with metabolic syndrome were randomly assigned to groups and given small intestinal infusions of allogenic or autologous microbiota to study the effect of FMT. Patients who received an infusion of microbiota from lean donors were observed to have a significant increase in insulin sensitivity and butyrate producing intestinal microbiota (e.g., *Eubacterium hallii* or *Roseburia intestinalis*). Interestingly in subjects with high microbial gene richness at baseline and when FMT donors that are metabolically compromised are used, no metabolic improvement is seen.

Roux-en-Y gastric bypass (RYGB) an effective therapeutic agent in treating obesity also ultimately induces a significant alteration in the intestinal bacteria profiles. In obese subjects the caecal concentrations of butyric acid and iso-butyric acid were significantly lower indicating altered microbial activity Evidence from studies unequivocally establish the beneficial effects of FMT treatment in obesity and the metabolic syndrome function [7].

In addition to examining the role of FMT in metabolic disorders, scientists focused their attention towards testing the efficacy of FMT in other disease processes that have similar pathogenicity as metabolic syndrome including allergen-related GI disease like Celiac disease. The complex relationship between different bacterial populations depends on individual conditions, disease status, dietary habits, development, physiological status, gut microbial composition, and other. Since effective colonization using FMT depends on the microbiota profile of the recipient that differs between patients suffering with metabolic syndrome [24]. The gut microbiota is also susceptible to alteration due to change in the external environment as a result of industrialization and modern lifestyle. Engineering a customized bacterial population to restore microbial profile through FMT might represent a future remedy to restore a healthy gut microbiota. FMT in therapeutics has to go a long way although; new discoveries will continue to fill up the lacuna in our understanding of how effectively FMT can be used to improve metabolic disorders related to gut dysbiosis like obesity and metabolic syndrome [24]..

References

1. PD Gupta, AK Asha (2018) The Price we Pay for Overdose of Antibiotics: Is there any Alternative? COJ Tech Sci Res 1(2): 000509.

2. Łojewska E, Sakowicz T (2021) An Alternative to Antibiotics: Selected Methods to Combat Zoonotic Foodborne Bacterial Infections. Curr Microbiol 78(12):4037-4049.

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3. Gupta PD, Pushkala K Fecal. Transplant Technology: An Effective Therapeutic Method for Many Diseases' Journal of Clinical and Medical Case Reports and Reviews.
4. Gupta PD, Pushkala K (2005) Human syndromes. 1st ed. Oxford & IBH Publishing, India.
5. Pushkala K, Gupta PD (2023) Polycystic Ovarian Syndrome Managed by Faecal Transplant Therapy. J of Gyne Obste & Mother Health 1(2): 1-4.
6. Salvestrini V, Sell C, Lorenzini A (2019) Obesity May Accelerate the Aging Process. Front Endocrinol (Lausanne) 10: 266.
7. Kang Y, Cai Y (2017) Gut microbiota and obesity: implications for fecal microbiota transplantation therapy. Hormones (Athens) 16(3): 223-234.
8. Barlow GM, Yu A, Mathur R (2015) Role of the Gut Microbiome in Obesity and Diabetes Mellitus. Nutr Clin Pract 30(6): 787-797.
9. Kootte RS, Vrieze A, Holleman F, Thie GMD, Zoetendal EG, et al. (2012) The therapeutic potential of manipulating gut microbiota in obesity and type 2 diabetes mellitus. Diabetes Obes Metab 14(2): 112-120.
10. Wisnewsky JA, Clément K, Nieuwpoort M (2019) Fecal Microbiota Transplantation: A Future Therapeutic Option for Obesity/Diabetes? Curr Diab Rep 19(8): 51.
11. Napolitano M, Covasa M (2020) Microbiota Transplant in the Treatment of Obesity and Diabetes: Current and Future Perspectives. Front Microbiol 11: 590370.
12. P D Gupta (2021) The Mighty Microbiota: Regulator of the Human Body. Clinical Research and Clinical Trials 3(5).
13. Gupta PD (2018) Bacteria: The Powerful Creatures: A Mini Review. Cell Tissue Res 18: 6555-6558.
14. Gupta PD (2021) C- section babies are easy target for corona infection. J Cell tissue research 21(2): PV 4.
15. Lee P, Yacyshyn BR, Yacyshyn MB (2019) Gut microbiota, and obesity: An opportunity to alter obesity through faecal microbiota transplant (FMT). Diabetes Obes Metab 21(3): 479-490.
16. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, et al. (2006) An obesity-associated gut microbiome with increased capacity for energy harvest. Nature 444(7122): 1027-1031.
17. Kelly C, Khan S, Kashyap P, Laine L, Rubin D, et al. (2015) Update on fecal microbiota transplantation 2015: indications, methodologies, mechanisms, and outlook. Gastroenterology 149(1): 223-227.
18. Zhang H, DeBiase JK, Zuccolo A, Kudrna D, Braidotti M, et al. (2009) Human gut microbiota in obesity and after gastric bypass. Proc Natl Acad Sci USA 106(7): 2365-2370.
19. Kang Y, Cai Y (2018) Gut microbiota and metabolic disease: from pathogenesis to new therapeutic strategies. Clin Res Hepatol Gastroenterol 42(2): 110-117.
20. Fei N, Zhao L (2013) An opportunistic pathogen iso-lasted from the gut of an obese human cause's obesity in germfree mice. ISME J 7(4): 880-884.
21. Santos JG, Alves BC, Hames To, Dall 'Alba V (2019) Dietary interventions, intestinal microenvironment, and obesity: a systematic review. Nutr Rev 77: 601-613.
22. Okubo H, Nakatsu Y, Kushiyama A, Yammotoya T, Matsunaga Y, et al. (2018) Gut microbiota as a therapeutic target for metabolic disorders. Curr Med Chem 25(9): 984-1001.
23. De Groot PF, Frissen MN, de Clercq NC, Nieuwdorp M (2017) Fecal microbiota transplantation in metabolic syndrome: History, present and future. Gut Microbes 8(3): 253-267.
24. Li SS, Zhu A, Benes V, Costea PL, Hercog R, et al. (2016) Durable coexistence of donor and recipient strains after fecal microbiota transplantation. Science 352 (6285): 586-589.

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