

Treatment of Reproductive Diseases Via Fecal Microbiota Transplantation (FMT): A Scientific Mini-Review

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Abstract

Reproductive diseases, including infertility, polycystic ovary syndrome (PCOS), and endometriosis, represent a growing global health burden. Emerging evidence suggests that the gut microbiome plays a critical role in regulating reproductive health, opening new avenues for therapeutic interventions. Fecal microbiota transplantation (FMT), a procedure involving the transfer of healthy donor microbiota to a recipient, has shown promise in treating a range of conditions, from metabolic disorders to gastrointestinal diseases. This mini-review explores the potential of FMT as a novel treatment for reproductive diseases, highlighting its mechanisms, efficacy, and future directions.

Keywords: Fecal Microbiota Transplantation, Gut-Reproductive Axis, PCOS, Endometriosis, Microbiome

Introduction

Reproductive diseases — infertility, polycystic ovary syndrome (PCOS), endometriosis, etc. — are experienced by millions of people across the globe; they carry a huge physical, psychological and economic cost (1). While medical science has made great strides many of today's treatments still have limited effect or come with adverse side effects (2). The gut microbiome has been shown to impact systemic health and affect reproduction in recent literature (3). The gut-reproductive axis, due to its interactions with microbial metabolites, immune modulation, and hormonal regulation, provides a strong rationale for investigating microbiome-based therapeutic approaches (4).

Fecal microbiota transplantation (FMT) has emerged as a therapeutic option that restores gut microbial balance via healthy donor microbial transfer (5), and FMT has been shown helpful for treating infectious diseases such as *Clostridioides difficile* infection, inflammatory bowel disease and metabolic syndrome (6). This mini-review outlined the potential use of FMT as a therapeutic strategy for human reproductive diseases, clarifying its mechanisms, clinical applications, and limitations.

1. The Gut-Reproductive Axis

The gut microbiome impacts reproductive health via several modalities (3). Gut microbes influence levels of estrogens by regulating enterohepatic circulation of estrogen metabolites (7). Dysbiosis may cause estrogen imbalance, which is why it is implicated in conditions like endometriosis and PCOS (8). They play a crucial role in immune modulation: the microbiome has an important influence on the immune system, hence contributing to

systemic inflammation and autoimmunity, involved in reproductive diseases (9). Gut microbiota are integral to energy metabolism and insulin sensitivity, processes that are impacted in the setting of PCOS and infertility (10).

2. FMT: Mechanisms and Applications

FMT entails transferring processed fecal material from a healthy donor recipient with the goal of restoring microbial diversity and function (11). Supportive therapeutic potential of FMT in reproductive diseases is offered by efficacy of FMT in replenish beneficial bacteria, modulate inflammation and generalize metabolic health (12). Healthy gut microbiome community can be restored by fecal microbiota transplantation (FMT) capable to restore the species of *Lactobacillus* and *Bifidobacterium* which were frequently depleted in reproductive disorders (13). FMT can help restore the gut barrier, down regulate systemic inflammation which may help ease symptoms of endometriosis and PCOS (14). Evidence suggests FMT may improve insulin sensitivity and assist with obesity, both risk factors for PCOS and infertility (15).

3. Clinical Evidence

While studies on FMT for reproductive diseases are still nascent, initial studies and case reports are promising (16). A study showed that FMT improved insulin sensitivity, reduced androgens, and restored menstrual regularity in women with PCOS (17). This research reveal that in PCOS, androgen-induced gut dysbiosis has been shown to cause disrupts in glucose and lipid metabolism, along with endocrine functions (17).

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Moreover, a study revealed that fecal microbiota transplantation from PCOS patients led to metabolic disorders and ovarian dysfunction in germ-free mice (18), providing further evidence for the important role of gut microbiota in PCOS pathophysiology.

Recent animal research has focused on the effect of the gut microbiome on endometriosis development and the potential roles of fecal microbiota transplantation (FMT) in treating this condition (19). Studies have shown that gut microbiome plays an important role in the pathogenesis and expansion of endometriotic lesions. Similarly, antibiotics treatment to deplete mouse endometrial microbiome has been shown to reduce endometriotic lesions growth (20). But when these microbiota-depleted mice were given fecal transplants from mice that had endometriosis, the growth of lesions (courtesy of the already-inhabited gut microbiota) was restored. This means that gut bacteria participate in promoting the progression of endometriotic lesions, and that reconfiguring intestinal bacteria through FMT will affect the progression of disease.

4. Challenges and Limitations

FMT has important hurdles to overcome standardization and safety concerns (21). Variability in donor selection, processing methods, and routes of administration can impact outcomes. FMT is generally safe but can cause infection, immune reactions, and long-term changes to the microbes in the gut. The absence of standardized protocols for FMT in reproductive pathologies hinders clinical implementation.

5. Future Directions

In order to explore the full potential of FMT in the treatment of reproductive diseases, future researches should concentrate on mechanistic studies, conducting randomized controlled clinical trials and individualized strategies (22). They helped understanding and identifying specific microbial taxa and metabolites in the gut-reproductive axis; evaluating the efficacy, safety of FMT in reproductive disorders and defining microbiome-based diagnostics and individualized FMT protocols per patient (23).

Conclusion

FMT is a novel and preventive therapeutic strategy for reproductive diseases, which extends the modulation effects of GM on female reproductive diseases through the gut-reproductive axis and its underlying dysbiosis, inflammation and metabolic dysfunction. Even though there are still some hurdles to overcome, clinical trials and continued research may soon be able to solidify the use of FMT as safe and effective for the treatments of infertility, PCOS, endometriosis, and more. As research progresses, FMT might change the face of reproductive medicine, signaling hope for millions of patients around the globe.

References

- Sharma A, Shrivastava D. Psychological Problems Related to Infertility. *Cureus*. 2022;14(10):e30320.
- Assidi M, Buhmeida A, Budowle B. Medicine and health of the 21st Century: Not just a high biotech-driven solution. *NPJ Genomic Medicine*. 2022;7(1):67.
- Qi X, Yun C, Pang Y, Qiao J. The impact of the gut microbiota on the reproductive and metabolic endocrine system. *Gut Microbes*. 2021;13(1):1-21.
- Zhang Y, Chen R, Zhang D, Qi S, Liu Y. Metabolite interactions between host and microbiota during health and disease: Which feeds the other? *Biomedical Pharmacotherapy*. 2023;160:114295.
- Onifade IA, Sunbare-Funto OJ, Mbah CE, Ajibade OA, Oyawoye OM, Aborode AT, et al. Faecal microbial transplant. *Advances in Biomarker Sciences and Technology*. 2024;6:20-34.
- Boicean A, Birlutiu V, Ichim C, Anderco P, Birsan S. Fecal Microbiota Transplantation in Inflammatory Bowel Disease. *Biomedicines*. 2023;11(4).
- Lephart ED, Naftolin F. Estrogen Action and Gut Microbiome Metabolism in Dermal Health. *Dermatology Therapy (Heidelberg)*. 2022;12(7):1535-50.
- Liang Y, Zeng W, Hou T, Yang H, Wu B, Pan R, et al. Gut microbiome and reproductive endocrine diseases: a Mendelian randomization study. *Frontiers in Endocrinology (Lausanne)*. 2023;14:1164186.
- Belkaid Y, Hand TW. Role of the microbiota in immunity and inflammation. *Cell*. 2014;157(1):121-41.
- Sun Y, Gao S, Ye C, Zhao W. Gut microbiota dysbiosis in polycystic ovary syndrome: Mechanisms of progression and clinical applications. *Frontiers in Cellular and Infection Microbiology*. 2023;13:1142041.
- Yan H, Ren J, Liu G-H. Fecal microbiota transplantation: A new strategy to delay aging. *hLife*. 2023;1(1):8-11.
- Hamamah S, Gheorghita R, Lobiuc A, Sirbu IO, Covasa M. Fecal microbiota transplantation in non-communicable diseases: Recent advances and protocols. *Frontiers in Medicine (Lausanne)*. 2022;9:1060581.
- Quaranta G, Guarnaccia A, Fancello G, Agrillo C, Iannarelli F, Sanguinetti M, et al. Fecal Microbiota Transplantation and Other Gut Microbiota Manipulation Strategies. *Microorganisms*. 2022;10(12).
- Quaranta G, Sanguinetti M, Masucci L. Fecal Microbiota Transplantation: A Potential Tool for Treatment of Human Female Reproductive Tract Diseases. *Frontiers in Immunology*. 2019;10:2653.
- Singh S, Pal N, Shubham S, Sarma DK, Verma V, Marotta F, et al. Polycystic Ovary Syndrome: Etiology, Current Management, and Future Therapeutics. *Journal of Clinical Medicine*. 2023;12(4).
- Choi HH, Cho YS. Fecal Microbiota Transplantation: Current Applications, Effectiveness, and Future Perspectives. *Clinical Endoscopy*. 2016;49(3):257-65.
- Han Q, Wang J, Li W, Chen ZJ, Du Y. Androgen-induced gut dysbiosis disrupts glucolipid metabolism and endocrinal functions in polycystic ovary syndrome. *Microbiome*. 2021;9(1):101.
- Huang F, Deng Y, Zhou M, Tang R, Zhang P, Chen R. Fecal microbiota transplantation from patients with polycystic ovary syndrome induces metabolic disorders and ovarian dysfunction in germ-free mice. *BMC Microbiology*. 2024;24(1):364.

19. Chadchan SB, Naik SK, Popli P, Talwar C, Putluri S, Ambati CR, et al. Gut microbiota and microbiota-derived metabolites promote endometriosis. *Cell Death Discovery*. 2023;9(1):28.
20. Martinelli S, Nannini G, Cianchi F, Staderini F, Coratti F, Amedei A. Microbiota Transplant and Gynecological Disorders: The Bridge between Present and Future Treatments. *Microorganisms*. 2023;11(10):2407.
21. Belotserkovsky I, Stabryla LM, Hunter M, Allegretti J, Callahan BJ, Carlson PE, et al. Standards for fecal microbiota transplant: Tools and therapeutic advances. *Biologicals*. 2024;86:101758.
22. Zheng L, Ji YY, Wen XL, Duan SL. Fecal microbiota transplantation in metabolic diseases: Current status and perspectives. *World Journal of Gastroenterology*. 2022;28(23):2546-60.
23. Ianiro G, Puncocchar M, Karcher N, Porcari S, Armanini F, Asnicar F, et al. Variability of strain engraftment and predictability of microbiome composition after fecal microbiota transplantation across different diseases. *Nature Medicine*. 2022;28(9):1913-23.