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RESEARCH ARTICLE

UNRAVELING THE IMPACT OF THE FECAL MICROBIAL TRANSPLANT IN COLO-RECTAL CANCER: INSIGHTS INTO TREATMENT AS AN ADJUVANT - A LITERATURE REVIEW

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Abstract

Background and Objective: Fecal Microbial Transplantation (FMT) can be used as an adjuvant therapy for colorectal cancer (CRC) treatment. The current literature review aimed to determine the effectiveness of FMT in improving treatment outcomes in CRC patients, particularly in conjunction with conventional therapies such as chemotherapy, Radiation and immunotherapy. The underlying mechanisms by which FMT influences immune modulation and gut microbiota composition, thereby impacting CRC progression and treatment outcomes is also discussed. After examining the data, FMT as an adjuvant with conventional therapies has better outcomes in colorectal cancer patients.

Methodology: Using online search engines and databases like PubMed and Google scholar that were published between 2009 and 2024, the most relevant published research, including original papers, was assessed, and critically examined throughout the course of a scientific literature search. This article offers valuable insights into the various treatment options of colorectal cancer and implication of FMT as an adjuvant.

Results: Clinical trials showed that combining FMT with chemotherapy improved treatment effectiveness in colorectal cancer. FMT was well-tolerated and enhanced chemotherapy's effects. Another study highlighted FMT's potential in influencing gut microbiota, important in cancer development and treatment response. These findings suggest a growing interest in using FMT alongside other therapies for colorectal cancer.

Conclusion: In comparison to treatment with traditional strategies alone**,** Fecal microbial transplantation, along with chemotherapy, immunotherapy or radiation, improves the prognosis of colon cancer treatment.

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Introduction:-

Colorectal cancer is the second leading cause of cancer-related fatalities in the United States, affecting both men and women. [1] The decrease in colorectal cancer incidence is primarily due to people over the age of 65; the age demographic of cancer patients is shifting from older to middle-aged, with much longer life expectancies and thus more opportunities to experience treatment-related late effects, including subsequent cancers. [2] The human body is home to a wide variety of microorganisms, which are generally referred to as the microbiome. Together, these microbes play an important part in the process of preserving overall health. [3] Rather than colonizing our digestive tract passively, this intricate ecology engages in a variety of interactions with the host, supporting functions including immunology, metabolism, nutritional absorption, tissue growth, and carcinogenesis. [4] The microbiome is thought to influence colorectal cancer development through various mechanisms, such as the production of carcinogenic metabolitesimmune system regulation, and intestinal epithelial barrier disruption. [5,6] Furthermore, the gut microbiota has received growing attention for its possible influence on the effectiveness and toxicity of CRC therapies. For instance, emerging research shows that specific microbial signatures may impact how CRC patients respond to immunotherapy and chemotherapy. [7] This review aims to offer an in-depth understanding of the dynamic relationship between gut microbiota treatment and CRC, with implications for precision medicine techniques and therapeutic treatments. [8] Furthermore, the microbiome has been demonstrated to have a critical role in determining an individual's response to cancer therapies such as immunotherapy and chemotherapy. Specific microbial communities can either increase or reduce the efficiency of various therapies, emphasizing the need for a better understanding of microbiome-cancer association.

Review:

Understanding Colorectal Cancer: Current Treatment Landscape:

Colorectal cancer (CRC) is one of the most frequent malignancies in the world in terms of incidence and death, therefore it poses a significant danger to global health. [9]Recognizing the variety of causes of CRC which includes genetic, environmental, and lifestyle factorsis essential to analyze the current therapeutic landscape [10]. Most current CRC treatment strategies are based on tumor staging, and include adjuvant chemotherapy, targeted medicines, and surgical resection as well as other treatments. [11] For individuals with localized colorectal cancer, surgery remains the primary treatment option, which aims to completely remove the tumor while minimizing side effects and maintaining intestinal function. [12] Adjuvant therapy is necessary to enhance long-term results since a significant percentage of patients experience disease recurrence despite advancements in surgical methods and perioperative care. [13] Adjuvant chemotherapy has been shown to be very effective in decreasing the chance of recurrence and improving survival rates in patients with third-stage colorectal cancer. [14] This chemotherapy often consists of fluoropyrimidine-based regimens like 5-fluorouracil (5-FU) or capecitabine. Furthermore, treatment results have been further improved by the inclusion of oxaliplatin in fluoropyrimidine-based regimens, especially in high-risk second and third stage illness. [15] Systemic chemotherapy remains the mainstay of treatment for metastatic colorectal cancer, with a range of cytotoxic drugs and targeted treatments used either as monotherapy or in combination regimens. [16] Following the development of biologic medications that target the VEGF and EGFR pathways, the treatment of metastatic colorectal cancer has experienced a revolution. These medications have been demonstrated to increase response rates and extend the lifespan for certain patient populations. [17] Despite these therapeutic advances, resistance to chemotherapy and targeted medications remains a key problem in the management of CRC, emphasizing the need for novel treatment methods and customized care. [18] The dynamic character of the treatment landscape is highlighted by the potential of emerging modalities including FMT, immunotherapy, and molecularly targeted medicines to improve outcomes and overcome treatment resistance in CRC. [19]

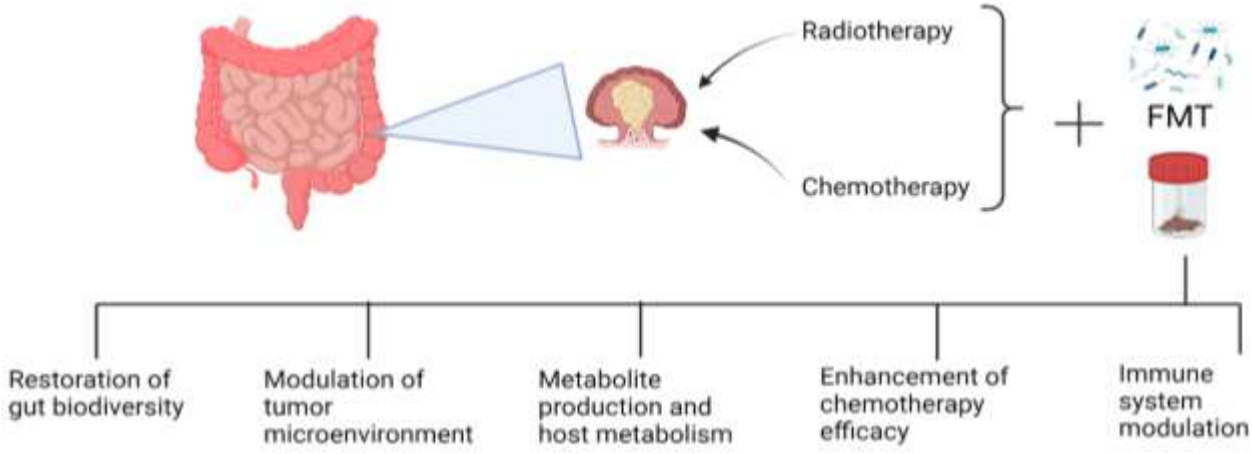
Mechanisms of Action: How Fecal Microbiota Transplantation (FMT) Influences Colorectal Cancer Treatment

Following several studies, FMT has emerged as a potentially useful therapeutic technique for the treatment of colorectal cancer (CRC), providing insights into the mechanisms of action. Recent research highlights several key mechanisms by which FMT influences CRC treatment.

Restoration of Gut Biodiversity:

The immune system and intestinal homeostasis are both significantly impacted by the gut flora. Patients with colorectal cancer usually have dysbiosis, that is defined as a disturbance in intestinal microbial ecosystems and FMT

has been demonstrated to increase immune surveillance and responsiveness to cancer cells by reinstalling helpful bacteria and restoring microbial diversity.[20]



Modulation of Tumor Microenvironment:
The composition of the intestinal microbiota can have an influence on the local cancer microenvironment. The tumor microenvironment's inflammatory cytokine profiles and immune cell recruitment have been linked to FMT-mediated modifications in the microbial composition. This alteration could lead to increased anti-tumor immunity and a better reaction to traditional cancer treatments. [21]

Metabolite Production and Host Metabolism:
Short-chain fatty acids (SCFAs) are metabolites generated by intestinal microbes that influence immune response and host metabolism. It has been established that FMT promotes an increase in SCFA production in CRC patients. This may have anti-inflammatory properties and assist regulate the proliferation and death of gut epithelium.[22]

Enhancement of Chemotherapy Efficacy:
Gut microbiota may have an impact on the chemotherapy's effectiveness in treating colorectal cancer. FMT has been studied as a possible supplemental treatment to increase the effectiveness of anti-tumor drugs. Research indicates that, FMT-induced changes in the makeup of the gut microbiota may affect medication metabolism and bioavailability, influencing treatment outcomes. [23]

Immune System Modulation:
The intestinal microbiome influences systemic immune responses. FMT has been shown to modulate immune cell populations and functions, potentially enhancing anti-tumor immune responses in CRC patients. The immunomodulatory impact of FMT may lead to longer illness-free survival and higher overall rates of survival. [24]

Key Microbial Influences on Colorectal Cancer Treatment
Fusobacterium nucleatum:
This bacterium has been widely studied for its association with CRC.Fusobacterium nucleatum is commonly found in CRC patients, particularly those with recurrence following treatment.Its presence is associated with resistance to treatment, suggesting that targeting this microbe could enhance therapeutic efficacy. Furthermore, studies have shown that Fusobacteriumnucleatum can promote inflammation and tumorigenesis, indicating its dual role as both a pathogenic agent and a potential therapeutic target. [25]

Prevotellaspp:
Prevotella species are prevalent in the intestinal microbiota of CRC patients. The study found that these microbes are involved in modulating immune responses, which could influence tumor progression and treatment outcomes. The presence of Prevotella was associated with a more favorable immune environment, potentially enhancing the effectiveness of immunotherapies in CRC patients. [26]

Lactobacillus spp:
Probiotics, particularly Lactobacillus casei variety rhamnosus, have shown promise in preclinical models for their protective effects against chemotherapy-induced intestinal injury. Probiotics might reduce the side effects of 5-fluorouracil and oxaliplatin in a syngeneic colorectal cancer model, demonstrating probiotics potential to improve treatment tolerance and patient outcomes. [27]

Inclusion Criteria:
Confirmed CRC Diagnosis:
Patients must have a confirmed diagnosis of CRC, which can be verified through histopathological examination or imaging studies. This ensures that the intervention is being tested in a relevant patient population. [28]

Microsatellite Instability-High (MSI-H) Tumors:
Research suggests FMT may be particularly effective for MSI-H tumors, potentially due to their distinct immune microenvironment. [29]

Specific Genetic Mutations:
Patients with specific genetic mutations, like BRAF V600E, may benefit from FMT, as these mutations are associated with distinct microbial signatures. [30]

Informed Consent:
Informed consent is mandatory, understanding the possible risksof FMT as part of their treatment plan. This is a fundamental ethical requirement for any clinical intervention. [31]

Refractory or Recurrent Disease:
FMT may be considered for individuals with CRC that are resistant to traditional treatments or those experiencing recurrence, as it offers an alternative therapeutic approach.[32]

Exclusion Criteria:
Pregnancy or Breastfeeding:
FMT is generally not recommended for pregnant or breastfeeding women due to the lack of safety data in these populations.[31]

Active Infections:
Active infections, particularly gastrointestinal infections, are contraindications for FMT due to the risk of pathogen transmission.[34]

Immunosuppression:
Severely immunocompromised patients are not ideal candidates for FMT due to the heightened risk of infection from donor stool.[33]

Severe Comorbidities:
Severe comorbidities that could escalate FMT-related risks (e.g., uncontrolled heart or lung disease) may necessitate exclusion.[35]

Available evidence for this study:
A recent clinical experiment looked at the combination of FMT and chemotherapy. In this experiment, patients were given FMT capsules from healthy donors. FMT was initially delivered alone for one week before chemotherapy was added for six cycles. It was revealed that FMT was well tolerated by patients and improved chemotherapy effectiveness.[36]Another study demonstrated the potential of FMT in modulating the intestinal microbiota composition, which plays an important role in the development of cancer and treatment response. This review indicated a growing interest in using FMT alongside other therapeutic strategies in patients with gastrointestinal cancers, including CRC.The authors emphasized the need for more research to determine FMT's usefulness in clinical settings. [37] Further research is needed to completely understand the mechanisms and optimize the use of FMT in CRC management.

Conclusion:-

In conclusion, Fecal microbiota transplantation is emerging as a feasible option for colorectal cancer management. The rising amount of data from both preclinical and clinical studies indicates that FMT can profoundly affect the intestinal microbiota composition, which is crucial for modulating immune responses and enhancing the efficacy of conventional cancer therapies. For instance, studies have shown that FMT can restore microbial diversity and improve treatment outcomes in patients undergoing chemotherapy and immunotherapy, particularly those exhibiting dysbiosis. FMT for colorectal cancer is still largely experimental, with most research confined to preclinical studies in mice. Human clinical trials are limited, emphasizing the need for more study in this area.

Limitations:

Fecal microbiota transplantation as an adjuvant for colorectal cancer (CRC) faces several limitations, including methodological variability in study design, donor selection, and administration protocols, which can lead to inconsistent outcomes. Most of the available research is limited to mice trails. Biological challenges arise from the unique composition of each patient's microbiome, resulting in unpredictable responses to FMT and potential risks of introducing pathogenic bacteria. Regulatory uncertainties regarding FMT's clinical use and ethical concerns about donor screening further complicate its implementation. Furthermore, the long-term consequences of FMT on gut health and cancer development are mostly unknown, necessitating further research to optimize its application in CRC management.

Abbreviations –

FMT – Fecal Microbial Transplantation

CRC – Colorectal Cancer

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