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Probiotics in the Management of Surgery- Induced Diarrhea: Efficacy and Clinical Applications

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Abstract:- Surgery-induced diarrhea (SID) is a frequent consequence of gastrointestinal procedures that is frequently brought on by disruptions to the microbiota, modifications to gut permeability, and changes in gut motility. It may cause severe morbidity, hindered healing, prolonged hospital stays, and higher medical expenses. Probiotics are live bacteria that, when given in sufficient quantities, offer health advantages. As a result, they have gained attention as a possible treatment strategy to lessen SID. Probiotics may reduce SID through a number of methods, including altered gut microbiome, improved mucosal barrier function, and pathogen suppression. In numerous clinical trials, probiotics like Lactobacillus, Bifidobacterium, and Saccharomyces boulardii have shown encouraging outcomes in lowering the frequency, length, and severity of postoperative diarrhea. Probiotics have also been linked to decrease inflammatory responses and enhanced immunological function, both of which are crucial in the post-surgical context. However, a number of variables, like the particular strains utilized, the dosage, the length of time of administration, and the patient's initial state of health and microbiome composition, affect how well probiotics work to manage SID. Even though the available data points to a positive safety profile for probiotics, especially in patients who are immunocompetent, more extensive randomized controlled trials are required to create standard recommendations for their application in clinical practice. This review examines the effectiveness of probiotics and their clinical uses in the treatment of Surgery induced diarrhea.

Keywords:- *Probiotics, Surgery, Diarrhea, Gut-Microbiome.*

I. INTRODUCTION

A. Probiotics

Probiotic literally translates from Greek to mean "for life." Lilley and Stillwell originally used the term in 1965 to characterize compounds released by one microbe that promote the growth of another. [1] The term "human microbiome" refers to the whole set of microbial genes associated with the human body. These microorganisms include various types of bacteria and archaea, as well as numerous viruses that can infect humans or other pathogens directly. [2] Human health and the constitutive interaction between the host and their microbiota may be related. The microbiome is influenced by a wide range of variables, such as psychological stress, the circadian rhythm, and cultural and ethnic influences. The microbiome is influenced by dietary choices as well, especially the gut flora. [3]

B. Surgery Induced Diarrhea

Diarrhea is defined by the World Health Organization (WHO) as experiencing three or more loose or liquid feces in the form of a container in a 24-hour period. According to Anonymous (1988), diarrhea is categorized as acute if it began fewer than 14 days ago and as persistent if it has persisted 14 days or more. Infectious diarrhea is a type of diarrhea that is caused by an infectious agent. [4] The most frequent nosocomial infection, Clostridium difficile, is responsible for 10–20% of cases of antibiotic-associated diarrhea and the majority of cases of antibiotic-associated colitis. In the US, C. difficile-associated diarrhea (also known as CDAD) is becoming more common and more severe. It is believed that abdominal surgery increases the incidence of CDAD, and postoperative CDAD. [5] Following colorectal cancer (CRC) surgery, postoperative diarrhea is a common complication that can have a detrimental impact on patients' nutritional condition and clinical outcome. Bowel stenosis brought on by a large tumour, surgical procedures, and perioperative pharmaceutical treatment are some of the causes of postoperative diarrhea. Another frequent nosocomial enteritis that causes diarrhea is Clostridioides difficile infection (CDI). [6]

C. Gut Microbia Modulation:

The imbalances or aberrations of microbiota, commonly referred to as dysbiosis, have been shown to play a significant role in FGIDs and allergies such infectious and antibiotic-associated diarrhea, highlighting the relevance and significance of the gut microbiota in the host's health.[7] The ability of individual probiotic strains or combinations of probiotic strains to prevent, displace, or obstruct the adhesion process of pathogenic bacteria is a prerequisite for the probiotic processes influencing gut microbiota.[8] But this is just one of the processes; the article also discusses other mechanisms, such as bacteriocins. The heterogeneity of the strain, species, and genus is crucial in influencing the probiotics' amount of adherence and adhesion-competing characteristics. [9] Another important way that probiotics influence the gut microbiota is via producing various antimicrobial compounds such bacteriocins, SCFAs, and de-conjugated bile acids. The chemicals that remain after probiotic bacteria break down carbohydrates are called short-chain fatty acids (SCFAs), and they include butyric, propionic, lactic, and acetic acids. These SCFAs reduce the pH of the small intestine generally and prevent the formation of harmful bacteria. [10] Additionally, probiotic bacteria can produce bile acid derivatives called de-

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conjugated bile acids, which have a higher antibacterial action than their bile salt counterparts. However, the probiotic cell' defensive mechanism against these substances is yet understood. [11]

II. BARRIER

Probiotics can affect mucosal cell-cell interactions and cellular "stability" in addition to inhibiting the growth of "conventional" organisms or potential pathogens. They can improve intestinal barrier function by modulating the phosphorylation of cytoskeletal and tight junctional proteins.[12] Tight junction proteins connect epithelial cells together at their apical junctions, secretion of water and chloride, and mucus production are among the interrelated mechanisms that ensure the operation of the intestinal barrier.[13] In intestinal epithelial cell models, Lactobacillus rhamnosus GG was able to stop cytokine-induced apoptosis by blocking tumor necrosis factor (TNF).[14] It has been demonstrated that lactobacillus species enhance mucin expression in human intestinal epithelial cells in vitro, preventing pathogenic E. coli. Both adhesion and invasion. [15] According to Lactobacillus rhamnosus GG, to stop the lining's planned cell loss and inflammation gut epithelial cells and demonstrated to have mitogenic properties promoting the regeneration of mucosa. [16]

A. Probiotic Strains and Their Benefits:

The gut microbiota is mostly dominated by the two groups Bacteroidetes and Firmicutes; Actinobacteria, Proteobacteria, and Verrucomicrobia are also present, but to a considerably lesser extent. Lactobacillus, Sacchromyces, and Bifidobacterium are the three probiotic genera that are most commonly used. [17] Lactobacillus, Lactococcus (Lactococcus lactis), Bifidobacterium, Streptococcus (Streptococcus thermophilus), and Enterococcus (Enterococcus faecium, Enterococcus faecalis) are the currently approved probiotics mentioned by the Health Functional Foods Act. It has also been demonstrated that the effects of these probiotics vary depending on the strain. Taking note of this, the Joint Probiotics Expert Committee, the Food and Agriculture Organization of the United Nations (FAO), and the World Health Organization have suggested utilizing Bifidobacterium and Lactobacillus for both functional and safety reasons. [18]

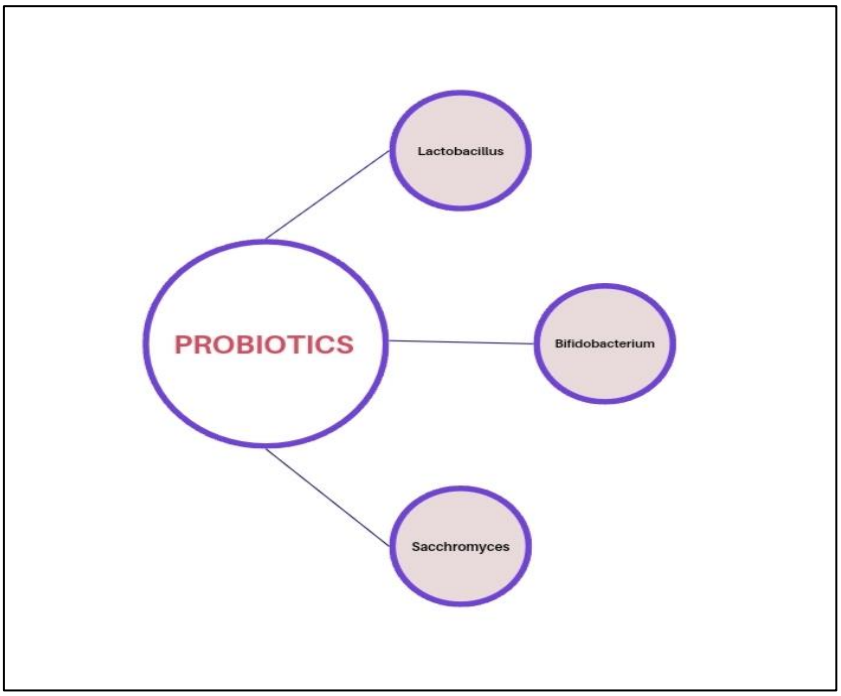

Fig. 1: Probiotic Strains

B. Intestinal Homeostasis and Function: The Role of Gut Microbiota

The fermentation of carbohydrates into short-chain fatty acids (SCFAs) like butyrate, acetate, and propionic acid occurs when certain bacteria, including Bacteroides, Roseburia, Bifidobacterium, Fecalibacterium, and Enterobacteria, fail to absorb the carbohydrates from the small intestine. This process is carried out by the gut microbiota. [19]

C. Effects of Probiotics in Postoperative Complications in Surgical Patients:

Postoperative ileus is a typical outcome of abdominal surgery that has been linked to several mechanisms, such as inhibition of neural reflexes, inflammation, and neurohormonal peptides. It has been demonstrated that Lactobacillus reuteri DSM-17938 microvesicles can increase the frequency of colonic propagation contractions. The bacterium Bifidobacterium lactis HN019 ferments carbohydrates and modifies intestinal motility. After 14 days of treatment, oral administration of L. plantarum PS128 was found to significantly increase the small intestine transit

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rate. This is because L. plantarum PS128 alters the expression of genes related to serotonin signal transduction, increasing the production and storage of 5-HT in entero-chromaffin cells in the ileum, according to immune-histochemical pathways. [20]

D. Effects of Probiotics in Postoperative Pain:

Analgesic receptor expression can be promoted by lactobacilli and Bifidobacteria. It was found that L. acidophilus NCFM and L. salivarius Ls-33 both prolonged increased the expression of OPRM1 mRNA (μ-opioid) in human HT-29 epithelial cells; however, only Lactobacillus acidophilus NCFM also increased the expression of CNR2 mRNA (cannabinoid).After 15 days of oral NCFM treatment (109 cm/d), subjects had a 20% rise in pain threshold or a nociceptive response comparable to subcutaneous 0.1 mg/kg morphine administration due to a reduction in normal visceral perception. [21]

E. Effects of Probiotics in Immuno-Modulatory Action:

- The balance of the Th1-Th2 immune response was discovered to be impacted by the oral administration of Lactobacillus strains; however, this effect appears to be species-, strain-, dose-, and most likely time-specific. [22]
- In addition to producing anti-inflammatory cytokines like IL-10, Lactobacillus strains can also create pro-inflammatory cytokines like IL-12 and IFN-γ. In general, Bifidobacterium strains are more effective in producing IL-10 than Lactobacillus strains. [23]

F. To Prevent Antibiotic-Associated Diarrhea

Based on an analysis of 42 studies with 11,305 participants, the most current one indicates that probiotics can reduce adult risk of antibiotic-associated diarrhea by 37%. It was discovered that the Lactobacillus and Bifidobacteria genera worked well. [24]

Table 1: Probiotics Strains and its Indications

INDICATIONS	PROBIOTIC STRAINS
Postoperative ileus	*Lactobacilli plantaram*
Postoperative pain	*Lactobacilli* *Bifidobacteria*
Immunomodulatory actions	
Th_1 , Th_2 – Immune response	*Lactobacillius*
Interleukin – 10	*Bifidobacterium*
Antibiotic – associated diarrhea	*Lactobacillius* *Bifidobacteria*

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III. ADVERSE EFFECTS: [25, 26, 27]

There are a few potential negative effects of probiotic use in humans that have been brought up. The potential for transmigration and the possibility of adverse effects on gastrointestinal physiology and function, including metabolic and physiological processes, are among these putative hazards associated with probiotic colonization.

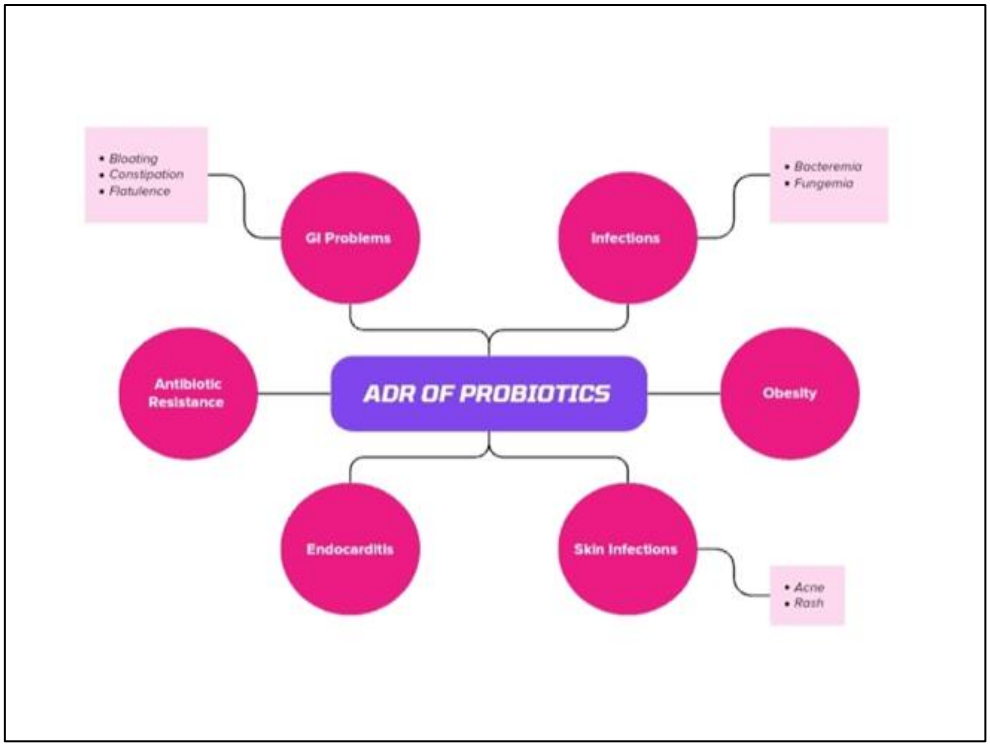

Fig. 2: Adverse Drug Effects

A. Transmigration Potential

Probiotics reduce pathogen transmigration while they are being used. Human research indicates that probiotic-using patients have a decreased risk of transmigration compared to non-users. Instead of probiotic bacteria migrating into the bloodstream, there may be a decrease in the translocation of other bacteria, according to research from animals. Population-based research has not shown that taking probiotics increases the risk of bacteraemia or endocarditis. Additionally, research done on humans and animals has not shown any detrimental effects on the permeability of gut proteins.

B. Bacteraemia and Endocarditis Potential

There have been reports of two cases of bacteraemia in children with central venous catheters, three cases of bacteraemia linked to Lactobacillus GG in children with short gut syndrome, one case of endocarditis, and one case of liver abscess associated with sepsis linked to probiotics.

C. Gastrointestinal Toxicity Studies

One potential effect of probiotic administration on gastrointestinal physiology is the generation of potentially unwanted metabolites, particularly in those with short small bowel syndrome.

D. Antibiotic-Resistance Transfer

The possibility of antibiotic-resistant bacteria transferring from probiotics to pathogenic bacteria in the gastrointestinal tract has been a major source of concern. Plasmids containing antibiotic-resistant genes, such as those encoding resistance to tetracycline, erythromycin, chloramphenicol, and macrolide-lincosamide streptogramin, are present when lactic acid bacteria are examined for the possibility of transferable antibiotic resistance. In raw meat, silage, and animal excrement, these resistance plasmids have been detected in L. reuteri, L. fermentum, L. acidophilus, and L. plantarum. In addition to the other possible toxicities, lactic acidosis development may theoretically lead to the generation of d-lactate.

IV. FUTURE DIRECTIONS IN PROBIOTIC RESEARCH FOR POST-SURGICAL CARE

A. Efficacy Based on Specific Probiotic Strains:

Probiotics are live bacteria that provide the host with health advantages when consumed in sufficient doses. These beneficial bacteria are essential for recovery after surgery, as they help maintain a balanced gut microbiota, regulate immune responses, and strengthen the intestinal barrier. Research shows that probiotics can reduce the risk of postoperative complications, such as infections and inflammation, which can lead to quicker recovery times. By populating the gastrointestinal tract with these advantageous

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microorganisms, probiotics enhance the digestion and absorption of nutrients, facilitating the rapid restoration of bowel function. Fermentation of dietary fibre can yield short-chain fatty acids (SCFAs) including butyrate, acetate, and propionate, thanks to specific probiotic bacteria, like Lactobacillus and Bifidobacterium. These SCFAs are crucial energy sources for the cells lining the colon and are vital for maintaining gut health. They nourish intestinal epithelial cells, support their growth and differentiation, and help maintain the integrity of the intestinal barrier. Additionally, SCFAs possess anti-inflammatory properties and assist in modulating immune responses, thereby promoting overall gut health. Through the promotion of the growth of helpful bacteria and the suppression of dangerous pathogens, they can also change the composition of the gut microbiota. The metabolites generated by specific probiotic strains influence various aspects of gut function, including energy metabolism, gut barrier maintenance, immune regulation, and the overall composition of gut microbiota. However, the precise role of these metabolites in enhancing bowel function after surgery is still not fully understood. Thus, it is crucial to explore the effectiveness of these interventions in the context of abdominal surgery to improve patient outcomes and enhance surgical care. [28]

B. Combination Therapies

The gut microbiome is a dynamic ecosystem that can be rapidly altered by supplements containing probiotics or prebiotics. In fact, changes in dietary fibre intake can modify the microbiome's composition within just 24 hours. Synbiotics, which combine prebiotics and probiotics—often found in fermented foods—work synergistically to enhance health. In this review, we have explored the inflammatory effects of surgery and highlighted the significance of the host-microbiome relationship in influencing surgical outcomes. Numerous studies have shown that synbiotics can effectively reduce various negative post-surgical outcomes during the perioperative period. Future research should focus on developing evidence-based formulations that are specific to certain strains and determining the optimal duration for treatment. [29]

V. SAFE USE OF PROBIOTICS: [30, 31]

Record the history of isolation and taxonomic classification of the probiotic. Cross-contamination between batches is one of the manufacturing precautions used to keep the probiotic free of bacteria and other contaminants. No relationship was seen between the probiotic and strain-level toxicity or infectivity assessments. Genes not transferable for resistance to antibiotics. The population's physiological condition and consumption patterns. Use with caution in vulnerable populations, including critically ill patients and infants. The amount administered oral or via another mode of administration Allergenic elements (such as dairy proteins) are not present in items intended for the allergic population.

Considering this, it is imperative to realize that an assessment of whether or not "probiotics are safe" can never be made generally; rather, it can only be done in relation to the many conditions mentioned above.

A. Probiotic Safety:

European Food Safety Authority (EFSA): By virtue of Regulation No. 178/2002, EFSA was founded in 2002 to address the growing importance and complexity of scientific and technical issues related to the safety of food and feed. The European Union's Novel Food Regulation (9258/1997 EEC), which addresses novel foods and food additives that were not commonly used for human consumption within the Community before 1997, governs probiotics. [32]

B. Qualified Presumption of Safety (QPS):

"Qualified Presumption of Safety" is a safety method that was proposed by the Scientific Committee on Animal Nutrition. Four phases are involved in establishing QPS: The taxonomy of the microbe must be defined; the scientific literature, usage history, industrial applications, ecological data, and data on human intervention must be gathered in sufficient quantities to support the QPS status; pathogenicity must be ruled out; and the end use must be defined. [33]

C. FAO/WHO:

In 2002, an effort was made to develop standards for the use of probiotics in foods, and as part of that effort, a group of professionals proposed a basic method for describing a probiotic. The group believed that the previously indicated set of criteria would be useful in demonstrating safety overlapped with the PROSAFE results. [34]

VI. CONCLUSION

Growing research indicates that probiotics can enhance mucosal barriers, regulate gut microbiota, and lower inflammatory responses—all of which are important adjuncts in the therapy of surgery-induced diarrhea (SID). Extensive research on probiotic strains—including Lactobacillus, Bifidobacterium, and Saccharomyces boulardii—has demonstrated their ability to lower the frequency and intensity of SID, which could lead to better patient outcomes and lower healthcare costs. Large-scale, randomized controlled studies are still required to provide standardized methods, even though recent research highlights the safety and potential advantages of probiotics, especially in immunocompetent patients. For the purpose of maximizing therapeutic effects, future research should concentrate on improving probiotic formulations, dosing schedules, and patient selection standards. In summary, probiotics are a potential approach to controlling SID; however, additional research is necessary to ensure their safe and effective usage to enhance patient outcomes in postoperative care and to completely integrate them into clinical practice.

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