بسم الله الرحمن الرحيم

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HANAA ALY

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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HANAA ALY

Efficacy and safety of probiotic versus conventional treatment of Irritable bowel syndrome

A Thesis

Submitted for the Partial Fulfillment of the Requirements of Master degree In Internal Medicine & Gastroenterology

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بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

قَالُوا

سُبْحَانَكَ لَا عِلْمَ لَنَا

إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ

الْعَلِيمُ الْحَكِيمُ

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Ahmed Salem Elmetwally.

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List of Abbreviations

Abbreviation	Full name
IBS	Irritable bowel syndrome
FGID	functional gastrointestinal disorder
FODMAPs	fermentable oligosaccharides, disaccharides, monosaccharides and polyols
IBD	inflammatory bowel disease
ENS	enteric nervous system
CNS	central nervous system
HPA	hypothalamic pituitary axis
EC	enterochromaffin cells
CBT	cognitive behavioral therapy
TCAs	tricyclic antidepressants
SSRIs	selective serotonin reuptake inhibitors
GI	gastrointestinal
GRAS	Generally Regarded As Safe
FDA	Food and Drug Administration
QPS	Qualified Presumption of Safety
SCFA	short-chain fatty acid
CDCP	Centers for Disease Control and Prevention
UTI	urinary tract infection
BV	bacterial vaginosis

Introduction

Irritable bowel syndrome (IBS) is a frequent functional gastrointestinal disorder, alterations in the gut microbiota composition contributes to symptom generation. calculated to affect around 11.2% of the world's population (**Dale, Rasmussen et al. 2019**).

Symptoms include bloating, flatulence, abdominal pain, or discomfort associated with a change in bowel habits (diarrhea, constipation, or mix). The pathophysiology of IBS is not well understood, but most likely involves multiple causes. IBS has been associated with abnormal gastrointestinal motor function, visceral hypersensitivity, psychosocial factors, autonomic dysfunction, and inflammation. In a subgroup of patients, IBS develops after an acute bacterial infection of the bowel (**Saha et al. 2014**).

Suggested mechanisms include visceral hypersensitivity, dysfunction in the gut–brain axis, disturbances in the epithelial barrier integrity causing abnormal change in intestinal permeability, altered gastrointestinal motility, immune activation, abnormal enteroendocrine signaling, as well as dysbiosis in the gut microbiota (**Kemppinen, Howell et al. 2020**). Increased numbers of inflammatory cells, such as mast cells and lymphocytes in the colonic mucosa of IBS patients suggest an ongoing state of inflammation in these patients (**Barbara, Cremon et al. 2011**).

The diagnosis of IBS is based on exclusion of other severe gastrointestinal disorders and fulfilling of the Rome criteria, a collection

of symptom-based diagnostic criteria for IBS and other FGIDs (**Lacy and Patel et al. 2017**).

Medical treatment of IBS is most commonly based on targeting the predominant symptom experienced by the patient. In addition, a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) has been shown to improve IBS symptoms and is currently a recommended dietary strategy. Although IBS is a non-fatal condition, the symptoms are experienced as troublesome for those affected and the condition is associated with increased rates of depression and anxiety, as well as economic challenges, hence often leads to severe reduction in quality of life (QoL) (**Lea and Whorwell et al. 2003**). Neither pharmacological treatment nor diet changes tend to completely eliminate symptoms, therefore alternative approaches to improve symptoms and better life for those affected are of great need (**Holtmann, Ford et al. 2016**).

Alteration in the gut microbiome is suggested as a likely contributor to IBS, a concept arisen from clinical observations of symptoms developing after an infection, commonly described as post-infectious IBS . Small intestinal bacterial overgrowth often causes symptoms similar to those of IBS, in particular bloating in relation to food intake (**Klem, Wadhwa et al. 2017**)

Probiotics are defined as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" . They can influence immune functions, motility, and the intraluminal milieu. The concept of probiotics was, for the first time, suggested in 1908 by Elie Metchinkoff, a Russian Noble Laureate who observed that consumption of fermented foods containing lactic acid bacteria had a

beneficial effect on human health. Based on his own theory that lactic acid could prolong life, he consumed sour milk every day, and was the one to first name it yoghurt Since then, the effects of probiotics have been widely investigated in a broad spectrum of diseases and are currently suggested as a possible treatment or prevention in several gastrointestinal disorders (**Brown and Valiere et al. 2004**).

Efficacy of Probiotics good response in many trials; (**Pineton de Chambrun et al., 2015; Spiller et al., 2016; Sun et al., 2018**)

Probiotics have been shown to have a beneficial effect in acute infectious diarrhea and inflammatory bowel disease and thus could presumably be of potential benefit in postinfectious IBS. Another rationale for using probiotics in IBS is their potential to influence fermentation processes and diminish gas production by changing the colonic flora (**Enck, Aziz et al. 2016**).

The exact mechanisms of probiotics in the human body are currently only partly known. Probiotics have been suggested to act through inhibition of pathogenic bacteria overgrowth and prevention of pathogenic invasion of the host, improvement of gut barrier function and receptor interactions, as well as production or secretion of substances such as short chain fatty acids (SCFAs) and neurotransmitters (**Dale, Rasmussen et al. 2019**).

Studies in both animals and humans have suggested that different strains of probiotics may improve abdominal pain and reduce visceral hypersensitivity by modulation of expression of neurotransmitters and receptors involved in the modulation of pain, such as the opioid receptor or the cannabinoid receptor (**Kemppinen, Howell et al. 2020**).

In addition, probiotics have been shown to reduce intestinal cytokine secretion and improve epithelial barrier function in a mice model of intestinal inflammation, and reduction of IBS symptoms in response to probiotic supple Identification of specific bacterial strains or probiotic supplements with beneficial effects on IBS symptoms may lead to more effective therapy strategies(**Dale, Rasmussen et al. 2019**).

The theory that probiotic supplements improve IBS symptoms through modulation of the gut microbiota, or its metabolic pathways needs further mechanistic evidence. Hence, the aim of this study is to assess the effect of probiotic supplementation on symptoms in IBS patient.

Safety of Probiotics in IBS: many studies show therse is no adverse effect of propiotics in treatment of IBS (**Yoon et al., 2014; Pineton de Chambrun et al., 2015; Spiller et al., 2016; Preston et al., 2018**) .

The side effect of conventional treatment :Antispasmodic (dizziness – drowsiness –dry mouth – nausea – constipation –abdominal bloating),Polyethylene glycol (nausea – abdominal cramping – upset stomach –bloating – dizziness),Chloride channel activator (constipation – abdominal pain – distention – nausea – anorexia),Opiate agents (nausea – vomiting – constipation –pruritus – dizziness – dry mouth – sedation),5-HT3 receptor antagonist (constipation or diarrhea – headache – dizziness – nausea - vomiting) (**Camilleri M, Andresen V.et al 2009**)

Aim of the Work

The aim of this study is to investigate the efficacy of probiotics in irritable bowel syndrome (IBS) patients.