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Exploring The Impact Of Gut Microbiota On The Management Of Epilepsy

Dr.Milagrin xavier[1],Angelin Grace T[2].,Gokula Priya P[3].,Prithiga M[4].,Revathi D[5] , Kaushika S[6]

[1]Assistant Professor,Department of pharmacy practice,Swamy vivekanandha college of pharmacy,Elayampalayam,Tiruchengode,Namakkal District,Tamilnadu,India

[2 to 6]V[th] Pharm D,Swamy Vivekanandha college of pharmacy, Elayampalayam,Tiruchengode,Namakkal District,Tamilnadu,India

ABSTRACT:

One of the most prevalent neurological conditions that has a significant negative impact on the lives of many individuals encyclopedically is epilepsy. Regulatory modulator systems, inhibitory-exitatory pathways, and ion transport in the neural membrane have all been linked to the aetiology of epilepsy. There is a proportion that the brain and the gut communicate in two ways: the brain controls the gastrointestinal tract, while the gut influences behaviour and brain function. The gut microbiome is pivotal to both health and illness, and dysbiosis is linked to a number of neurological conditions. When given in sufficient quantities, probiotics—which are live microorganisms—benefit both people and animals. In this study, we assessed how a combination of probiotic bacteria affected neurobehavioral functioning, gamma-aminobutyric acid (GABA), nitric oxide (NO), malondialdehyde.

Key words: gut microbiota, probiotics, epilepsy

INTRODUCTION:

Epilepsy is a neurological illness that affects over 70 million individuals globally and has a significant social and economic impact. Its mechanisms are complex, with idiopathic 60% of cases and relapses to unprovoked spontaneous seizures as its defining features. Epilepsy diagnosis is difficult in clinical practice. Patients with infrequent seizures may not exhibit the electrical markers needed for diagnosis, whereas patients without seizures may occasionally experience epileptiform discharges. The majority of antiepileptic treatments are pharmacological, encompassing both new and inexpensive pharmaceuticals. Refractory epilepsy, a condition in which medication therapy is ineffective in controlling seizures in more than 30% of epileptic patients, is one such instance[1]. The term "microbiota" refers to the entire population of microorganisms found in a

certain location. Along with bacteria, this population also consists of fungi, viruses, archaea, and protozoa[2]. It is well recognised that the postnatal development of the enteric nervous system depends on the early microbial colonisation of the digestive tract. Therefore, gut microbiota may have an impact on the CNS's growth and functionality[3]. Phytochemicals with strong anti-inflammatory and antioxidant properties can also be released and transformed as a result of microbes breaking down plant cell walls[4].

GUT MICROBIOTA:

- The microbiota present in our bowel is plainly the richest and most important group of bacteria, indeed though it's a subset of the larger microbiota. The four primary bacterial species set up in the mortal gut are Bacteroidetes, Actinobacteria, Firmicutes(including Lactobacillus), and Proteobacteria(including Escherichia)[5].
- •A crucial factor in maintaining mortal health is the gut microbiota. It provides resistance against colonisation by possible infections and boosts impunity. With around 150 times further genes than the mortal genome, it provides a wide range of enzymatic processes. The product of health-promoting metabolites including vitamins and short- chain adipose acids(SCFAs) affects supplemental and gut health through a number of intestinal- organ axes[6].
- •The human genome has about 23,000 genes, whereas the gut microbiota encodes over 3 million genes. Bacteria are categorised taxonomically based on their species, classes, orders, families, genera, and species. The colon contains 2172 species of microorganisms organised into 12 distinct groups, of which six major phyla—Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria, and Verrucomicrobia—have been found. However, Firmicutes and Bacteroidetes make up around 90% of the gut microbiota[7].

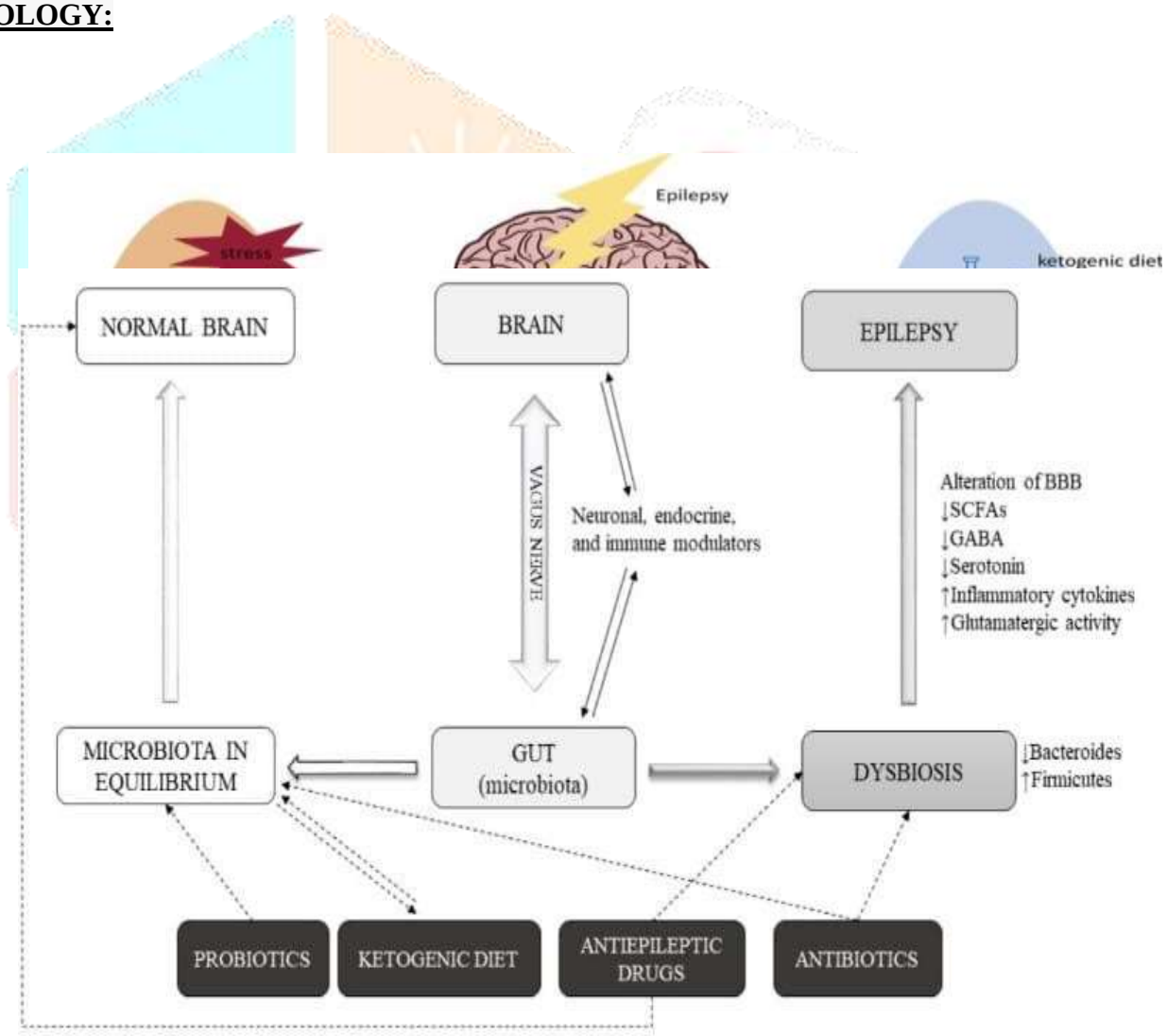
MECHANISM OF KETOGENIC DIET:

- In order to promote ketosis by lowering blood glucose and insulin release, the KD limits daily carbohydrate intake to less than 60 grammes. Free fatty acids (FFAs) and gluconeogenesis in the liver serve as the main energy sources in ketosis when the insulin-to-glucagon ratio falls[8].
- When glucose is limited, the brain uses the ketone bodies from FFAs, which can provide up to 60% of its energy[8]. Distinguished from diabetic ketoacidosis by maintaining constant blood glucose, normal blood gas readings, and high ketone bodies and lipids, nutritional ketosis. Possibly important in human evolution, it is thought to be an adaptive mechanism supporting the energy needs of the brain and muscles[8].Although there may not always be a correlation between seizure control and measurements of ketosis, they do show diet compliance[8]. Theories imply that efficient energy is necessary for brain development and repair, but the precise causes of the KD's neurological advantages are still unknown[8]. More research is necessary to determine how certain factors, such as FFAs and glucose levels, relate to seizure control and how to provide customised care[8].

GUT-BRAIN AXIS:

The Smaller trials have also demonstrated that the KD lowers the frequency and onset of seizures in various pediatric seizure syndromes, including myoclonic-atonic epilepsy, Dravet syndrome, and other illnesses. The KD greatly lowers seizures, as demonstrated by the use of animal models of epilepsy. It also offers insights into possible processes that may contribute to decreased neural excitability. The administration of ketone bodies and KD has been shown to have neuroprotective benefits through a variety of molecular mechanisms. The majority of research reports connections between neuroprotection and biological processes, such as alterations in inflammatory proteins or oxidative stress. Nevertheless, it is still debatable and unclear from many research whether these pathways are changed as a result of the diet's primary or secondary impacts. A number of sophisticated experiments employing inhibitors and mouse knockout strains have recently produce [9].

ETIOLOGY:



PATHOPHYSIOLOGY:

IMMUNE AND INFLAMMATION PATHWAYS:

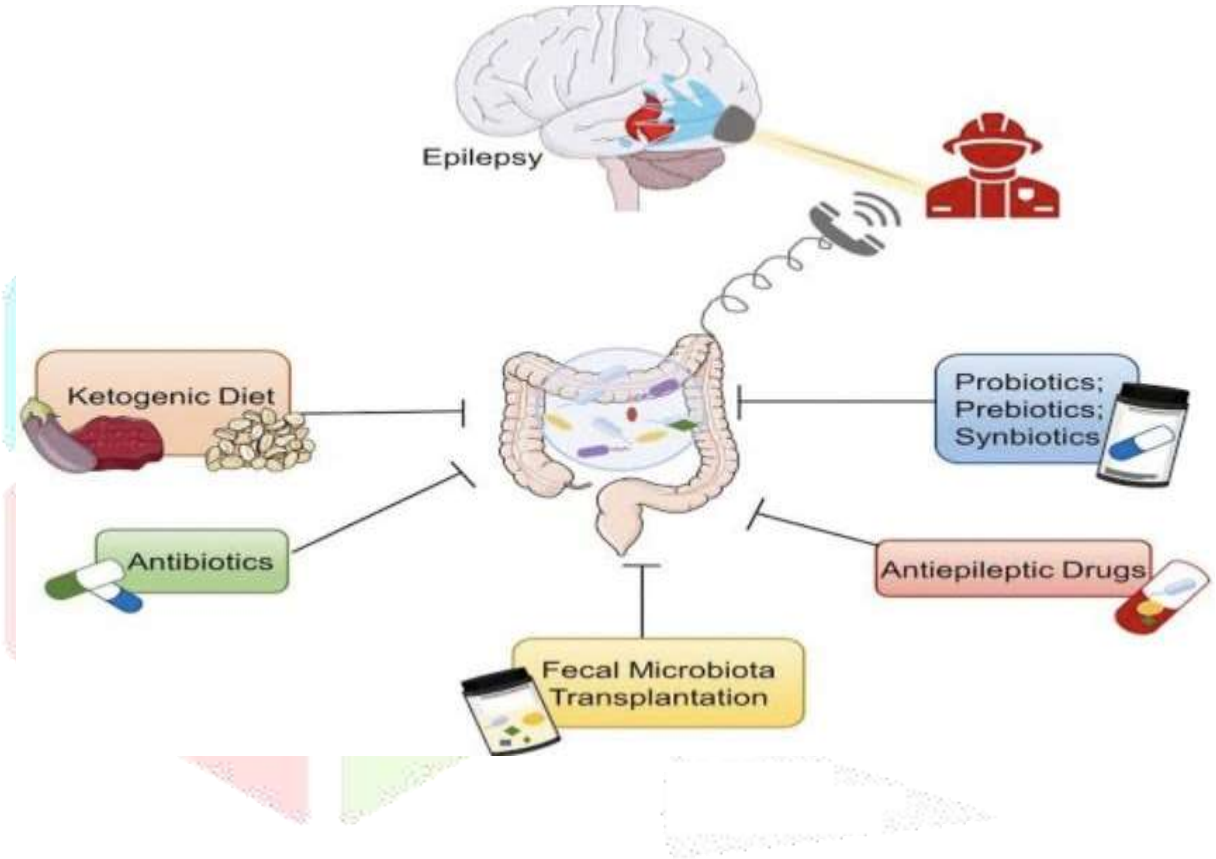
Epilepsy pathophysiology is associated with both neuroinflammation and neuroimmunity [10]. A growing body of research indicates that the brain-gut axis's inflammatory and immunological pathways could have a role in the etiology of epilepsy. The primary inflammatory cells in the central nervous system are microglia and astrocytes, and an inflammatory condition in these cells increases the risk of

epilepsy.[11][12].

GUT IMMUNITY:

Seventy to eighty percent of all immune cells are found in the intestinal mucosa's lymphoid tissue [13]. Immune cells are impacted by GM; germ-free (GF) mice exhibit immunological abnormalities, such as a drop in T and B cell populations and a decrease in cytokine production [14]. Moreover, GM seems to be one of the key elements in the microglial cells' development and the sex- and age-dependent activation of astrocytes [15, 16]. To control the onset of epilepsy, the GM controls innate immunity, adaptive immunity, and inflammatory processes.

TREATMENT:



PROBIOTICS/PREBIOTICS/SYNBIOTICS:

Probiotics are live microorganisms that improve the host's health when taken as directed [17]. Bifidobacterium and Lactobacillus belong to two of the most common probiotics [18]. The International Scientific Association for Probiotics and Prebiotics defined prebiotics as a "substrate that provides a health benefit when selectively utilized by host microorganisms" in 2020 [19]. Synbiotics are referred to as "a substance comprising living microorganisms and substrate(s) selectively metabolized by host microorganisms that confers beneficial effects on the human" [19] Synbiotics are referred to as "a compound comprising live microorganisms and substrate(s) selectively metabolized by host microorganisms that confers a health benefit on the host" [19]. They fall into two categories: synergistic synbiotics, where co-administered living bacteria specifically use the prebiotic, and complementary synbiotics, where each component acts independently. In a prospective study, 28.9% of DRE patients treated with a probiotic mixture experienced a ≥50% reduction in seizure frequency over a four-month period, and four months after

therapy stopped, 76.9% of these improved individuals continued to have fewer seizures [20].Because adjuvant probiotics reduced seizure frequency, as demonstrated by this study [20], they could be used as an adjunctive treatment to antiepileptic medications. Probiotic medication may significantly lessen the severity of seizures, as demonstrated by the higher levels of GABA in mice brain tissue and lack of full kindling in the PTZ-induced chemical kindling mouse model in the probiotic-supplemented group [21]. Using Lactobacillus fermentum MSK 408 or synbiotics to treat PTZ-induced seizures in mice with KD may lessen the negative effects of the disease without sacrificing its antiepileptic qualities. KD and MSK 408 both enhance GABA metabolism by GM control [22].Propionate and butyrate are two SCFAs that have antiepileptic properties. The total SCFAs were dramatically lowered following a month-long intervention with the conventional KD, particularly acetate, propionate, and butyrate. This reduction in total SCFAs may have resulted from a decrease in the consumption of fermentable carbs or from a decrease in fermenting bacteria induced by KD[21]. GM enrichment linked to SCFAs may result from using synbiotics (21). By modifying the GM, MSK 408 may affect SCFAs, restore the serum lipid profile, and mRNA expression of tight junction protein in the gut and brain independently [22]. While larger placebo-controlled trials and more thorough animal testing are needed to confirm theories and investigate mechanisms, these preliminary data on the use of additional probiotics in the treatment of DRE are encouraging. In order to minimise adverse effects, probiotics can be administered in addition to KD therapy as a treatment for refractory epilepsy.

CONCLUSION:

In this study—the first to assess the impact of probiotic supplementation on an animal model of epilepsy—the probiotic bacteria significantly lessen the severity of seizures. Probiotic treatment makes sense because it increases GABA activity and improves the antioxidant/oxidant balance in the kindled rats, even though the imbalance of inhibitory/excitatory neurotransmission and antioxidant/oxidant agents is known to be one of the primary causes of epileptic convulsions. These are only preliminary findings, and more preclinical and clinical studies are required to provide more convincing proof of the probiotics' entire therapeutic potential for the management of epilepsy.

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