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Antiepileptic Drugs and the Relationship with the Intestinal Microbiota

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Summary- This review of the literature examines the use of antiepileptic medications and how they relate to gut microbiota. Relationships exist between the makeup of the intestinal microbiota and the development and execution of the most fundamental physiological processes. Additionally, it affects the functioning of the central nervous system (CNS) by interacting with the microbiota-intestine-brain axis. The use of pharmaceutical medication is one of the factors that can alter the composition of the gut microbiota. When treating epilepsy, various drug types are used, each with a different mechanism of action. Among the medications in question are topiramate, primidone, phenytoin, carbamazepine, and phenobarbital. The similarity in structure and function between enteric and nerve cells establishes the connection between the brain and the gut.

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ANTIEPILEPTIC DRUGS AND THE RELATIONSHIP WITH THE INTESTINAL MICROBIOTA

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Antiepileptic Drugs and the Relationship with the Intestinal Microbiota

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Summary- This review of the literature examines the use of antiepileptic medications and how they relate to gut microbiota. Relationships exist between the makeup of the intestinal microbiota and the development and execution of the most fundamental physiological processes. Additionally, it affects the functioning of the central nervous system (CNS) by interacting with the microbiota-intestine-brain axis. The use of pharmaceutical medication is one of the factors that can alter the composition of the gut microbiota. When treating epilepsy, various drug types are used, each with a different mechanism of action. Among the medications in question are topiramate, primidone, phenytoin, carbamazepine, and phenobarbital. The similarity in structure and function between enteric and nerve cells establishes the connection between the brain and the gut. Valproic acid significantly reduced intestinal inflammation in research involving rats with colitis. Its limited ability to treat seizures in these circumstances may be due to the enterocytes limited ability to absorb this medicine. The study came to the conclusion that colitis patients and people with healthy gut, brain, and microbiota interaction typically respond better to antiepileptics and anticonvulsants than people with imbalances in this axis. These imbalances can result in a lower seizure threshold and an increased frequency of epileptic seizures.

I. INTRODUCTION

Through the gut-brain axis, the gut microbiota has the capacity to regulate events involving the Central Nervous System (CNS) as well as fundamental physiological development and function. Communication pathways between the gut microbiota and the brain system aid data communication. Important participants in this interaction include the Central Nervous System (CNS), Enteric Nervous System (ENS), Autonomic Nervous System, and neuroendocrine channels. The connection between the brain and the intestines has been identified based on the shared physiology of nerve and enteric cells, which show important similarities in their forms and functions. Drug therapy is one thing that has the potential to alter the gut microbiota's composition. The several drug classes that are used to treat epilepsy will be the main topic of this study. Each of these drug classes has a different mechanism of action.

II. METHODOLOGY

The current study is a literature review in which the databases were taken from the SciELO (Scientific Electronic Library Online) and PubMed platforms. The research was carried out in July 2023, meeting the inclusion criteria of articles from 2019 to 2023 in Portuguese, Spanish, and English, online texts and full texts, theses, master's dissertations, book chapters, monographs, and literature in magazines and scientific journals. The following health descriptors (DeCS) were used as strategies to evaluate the texts: "Antiepileptics," "gastrointestinal microbiome," and "nervous system."

III. RESULTS AND DISCUSSION

The microbiota-intestine-brain axis relates the intestinal microbiota to the operation and growth of fundamental physiological functions, but it can also have an impact on CNS processes. Based on several studies, the microbiome has a significant role in the etiology of epilepsy and in controlling seizures. Therefore, numerous interventions like food, supplements, and even medicine can disrupt the axis involving the central nervous system, microbiota, and gut. To better understand the markers, pathophysiology, and treatment of epilepsy, it is beneficial to look into the outcomes of various therapies. [1]

The afferent and efferent pathways of the nervous system facilitate communication with the intestinal microorganisms. The central nervous system (CNS), enteric nervous system (ENS), autonomic nervous system, and neuroendocrine pathways are in charge of controlling this direct interaction. This connection originates due to the enteric system's regulation of the upper system, which subsequently affects the enterocytes' physiological processes. According to some studies, afferent neurons activated by some of the afferent pathways mentioned above excite brain cells through inflammatory pathways when the gut microbiota isn't functioning correctly due to changes in the enteric system.

Drug therapy is one of the factors that can modify the intestinal microbiota. There are several different types of medications that are used to treat epilepsy, including phenytoin, carbamazepine, phenobarbital, primidone, valproic acid, and topiramate.[3,5]

Phenytoin and primidone seem to have similar effects on the body, as they act by altering ionic conductance, blocking sodium channels, and inhibiting the generation of repetitive action potentials. In addition to reducing the number of times a neuron fires and blocking sodium channels, carbamazepine slows nerve impulse transmission before synapses. According to a recent study, this could intensify the effects of GABA at synapses. Phenobarbital stops the excitatory effects of glutamate, especially those caused by the activation of AMPA receptors, by binding to a GABA receptor site and making it take longer for chloride channels to open. High levels of valproic acid suppress high-frequency neuron firing by inhibiting the GABA-T enzyme, which is responsible for decomposing GABA. Topiramate partly blocks Na⁺ channels while stimulating postsynaptic GABA-A receptors. [3, 5].

The physiology of neuronal and enteric cells, which are highly similar in structures and functions, is the basis for the established link between the brain and the intestine. This study found that people with colitis or a healthy gut-brain-microbiota axis respond to antiepileptics and anticonvulsants better than those without these conditions. In a study with rats that had been made to get colitis, valproic acid reduced intestinal inflammation by a lot. However, it was less effective at treating epilepsy in these rats, likely because the enterocytes were less able to absorb this drug. As a result, it is thought that restoring balance to the gut flora can alleviate epileptic seizures. [4,6]

Due to the many factors that affect how the disease develops, research on the gut-brain-microbiota axis and the role of intestinal supplements in epilepsy has become more complex. Because of this, the studies that have already been conducted are restricted, and furthermore, a more thorough investigation is required to clarify the actual impacts and the best course of action in these situations. It is crucial to stress that the intestine and its pathological condition can contribute to the illness and should even be treated with medication for the anticonvulsant effects to be satisfactory. Additionally, to better understand this point of view, it is essential to elucidate additional mediators in addition to those already known. [3,6]

IV. FINAL CONSIDERATION

According to the study in the text, valproic acid can dramatically lower intestinal inflammation in rats with colitis. However, it was shown that under these situations, the drug's efficacy in treating epilepsy was

reduced, maybe due to its limited absorption by the enterocytes. The authors of the study came to the conclusion that individuals with colitis or those who have a good interaction between the gut, brain, and microbiota react to antiepileptic and anticonvulsant drugs more favorably than individuals who have some type of imbalance in this system. As a result, there may be a reduced seizure threshold and more epileptic seizures. To manage epileptic seizures and enhance treatment effectiveness, restoring the gut microbiota has therefore emerged as a feasible and promising therapeutic approach. Due to the limitations of the present studies, more precise and detailed investigations are required to understand the true effects and the best treatments. Research into the gut-brain-microbiota axis and the role of gut supplements is difficult because of the many factors that affect epilepsy. The disease's gastrointestinal status can serve as a factor, and it may be necessary to treat it to enhance anticonvulsant effectiveness. A more profound comprehension of this perspective requires investigating new mediators.

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