Cannabinoids for the treatment of autism and childhood epilepsy

Canabinoides no tratamento do autismo e epilepsia infantil

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ABSTRACT

BACKGROUND AND OBJECTIVES: Epilepsy and autism spectrum disorder (ASD) are diseases with neuropsychiatric impairment, which, depending on their clinical presentation, can be treated with medical cannabis. The objective of this work is to present a brief review of the literature on the use of cannabinoids (CNB) in the management of ASD and epilepsy.
CONTENTS: The elaboration of this review was made from search and selection. Searches were carried out in the following databases: LILACS, Medline via Pubmed, Scielo and Cochrane Library, published from January 2010 to December 2022.
CONCLUSION: The use of CNB, both for epilepsy and for ASD, has been shown to be safe, however actual effectiveness has yet to be proven.

Keywords: Autism, Cannabidiol, Cannabis, Epilepsy.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A epilepsia e o transtorno do espectro do autismo (TEA) são doenças com comprometimento neuropsiquiátrico, os quais, dependendo da sua apresentação clínica, podem ser tratados com a cannabis medicinal. O objetivo deste estudo foi apresentar uma breve revisão da literatura sobre o uso de canabinoides (CNB) no manejo do TEA e da epilepsia.
CONTEÚDO: A elaboração desta revisão foi feita a partir de busca e seleção. Foram realizadas buscas nas bases de dados: LILACS, Medline via Pubmed, Scielo e Cochrane Library, publicados no período de janeiro de 2010 a dezembro de 2022.
CONCLUSÃO: O uso dos CNB, tanto para epilepsia quanto para o TEA, tem se mostrado seguro, porém a real eficácia ainda não foi comprovada.

Descritores: Autismo, Canabidiol, Cannabis, Epilepsia.

INTRODUCTION

In recent years, the use of cannabinoids in children with epilepsy and autism has expanded in Brazil and worldwide. The present study will address the use of cannabinoids in developing brains, according to the severity of symptoms. It is known that drug-resistant epilepsy[1] has not only epileptic seizures as symptoms, but also its comorbidities, which are cognitive and behavioral disorders[2,3]. In autism spectrum disorder (ASD), the symptoms of irritability, anxiety, repetitive and restrictive behavior, and self and hetero-aggressiveness may be disconcerting, not only for patients, but also for their family and social companions.
Despite pharmacological advances, epilepsy remains refractory in up to 36% of cases, regardless of mono- or polytherapy treatments and the insertion of new drugs[4]. As for ASD, the most commonly prescribed drugs are risperidone and aripiprazole, which are antipsychotics that have considerable effects, such as weight gain and metabolic syndrome, and that may be ineffective in a considerable number of patients for controlling symptoms[5].
The present study's objective was to present a brief review on the use of CNB in epilepsy and ASD.

CONTENTS

The preparation of this review was based on search and selection. The following databases were searched: LILACS, Medline via Pubmed, Scielo and Cochrane Library using the descriptors: ("Cannabidiol" OR "Cannabis") AND "Epilepsy" AND ("Treatment" OR "Therapeutics") AND Autism

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HIGHLIGHTS
- Epilepsy is a neurobiological disorder that occurs in any age group and features persistent, recurrent, and long-lasting epileptic seizures that can lead to cognitive, social, and behavioral impairment.
- Autism spectrum disorder (ASD) is a neurodevelopmental disorder with impaired communication, socialization, and restrictive behavior. The prevalence of epilepsy is higher in patients with ASD when compared to the general population, just as the occurrence of ASD is higher in patients with epilepsy.
- The endocannabinoid system is composed of several enzymes, molecules, and two endogenous cannabinoid receptors, CB1 and CB2, the former being more abundant in the central nervous system, and the use of phytocannabinoid derivatives in epilepsy and ASD is an alternative option, especially in cases of resistance to pharmacological treatment.

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Spectrum Disorder; associated to titles, abstracts or keywords. The articles searched were published from January 2010 to December 2022.

CANABIDIOL

Cannabidiol, a non-psychoactive derivative of cannabis, has demonstrated its efficacy and safety, and has been approved by the Food and Drug Administration (FDA) for the treatment of some epileptic syndromes, such as Dravet[6-8], Lennox-Gastaut[9,10] and tuberous sclerosis complex[11,12].

The most common adverse effects, which usually occur early in the treatment, are drowsiness, nausea, vomiting, diarrhea, and change in appetite[13]. A transient increase in liver enzymes may occur, especially when the use is concomitant with valproic acid derivatives, as well as thrombocytopenia. Another effect observed was an increase in the serum dosage of clobazam and other benzodiazepines, with potentiation of their adverse effects, such as drowsiness and increased secretion, which normalized after the reduction of clobazam[6,7].

Therefore, it is suggested that the control of serum dosage of anti-crisis drugs, blood count, liver enzyme and bilirubin dosage be performed before and during treatment with CNB.

Regarding the choice of product, it should be emphasized that full spectrum formulations seem to be more effective than isolated cannabis components, due to the entourage effect[14,15], but there is still no full spectrum product approved by the FDA for pediatric use[16]. Thus, the management of CNB in the pediatric age group has to be different from that of adults, due to the deleterious effects of THC on the developing brain. The choice should be made considering the peculiarities of each case, exposing the family about the risks versus benefits of each presentation[17].

In ASD, non-pharmacological treatment, which includes parents training together with a multidisciplinary approach by specialists, is the method of choice. However, many patients require drugs in order to control signs and symptoms such as aggressiveness, irritability, restrictive and repetitive behavior, anxiety, and sleep disorders. So far, for ASD, the scientific evidence for pharmacological treatment converges on managing irritability with risperidone and aripiprazole; and the use of methylphenidate, atomoxetine, and guanfacine for attention deficit hyperactivity disorder, as well as melatonin for sleep disorders[18,19].

However, many cases of ASD are refractory, regardless of therapies and drug use. Phytocannabinoids seem to occupy a prominent place, according to some research, but more robust studies are still needed in order to prove their real effectiveness.

There are several observational studies on the use of cannabinoids in ASD. It is worth mentioning the research developed in Israel, whose results were published in the Nature journal. In the study[14], 188 children with a mean age of 13 years old were evaluated, with a follow-up of six months. A cannabis oil-based product was used, containing high levels of cannabidiol, 30% CBD and 1.5% THC, that is, a ratio of 20 CBD: 1 THC, in addition to other cannabinoids in low concentrations, terpenes and flavonoids. An improvement of 80% in global and quality of life was found, few side effects, the most common being drowsiness, and good compliance, since 60% of patients chose to continue treatment even after the study was over.

Similarly, a double-blind, randomized study[15] with the use of cannabis extract in ASD observed improvement in disruptive behavior, good tolerability, and few side effects, such as drowsiness, nausea, and eating disorders.

CONCLUSION

In pharmacoresistant epilepsy, cannabidiol is already FDA approved for Dravet, Lennox- Gastaut syndromes and in tuberous sclerosis complex. Epilepsy patients taking clobazam and valproate should receive special attention when taking cannabinoid derivatives concomitantly due to pharmacological interactions.

In ASD, cannabinoid derivatives have demonstrated efficacy in controlling disruptive behavior and irritability. However, to date, there is no FDA-approved product for their regular use.

Although more scientific evidence is needed, the use of CNB, both for epilepsy and ASD, has been shown to be generally safe and effective and an alternative option for those patients with poor response to traditional treatment modalities.

AUTHORS' CONTRIBUTIONS

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Project Management, Methodology, Writing - Preparation of the original, Writing - Review and Editing, Supervision, Visualization

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