

# USE OF CANNABIDIOL IN EPILEPSY TREATMENT: LITERATURE REVIEW

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## ABSTRACT

Cannabidiol (CBD) represents a promising alternative for epileptic patients who do not respond to the available treatments, since it can prevent the occurrence of brain damage and consequently modify the natural history of the disease. Several clinical studies have demonstrated the beneficial effects of Cannabidiol against seizures, with total or partial improvement in most of the patients analyzed, especially in refractory cases to traditional medications. However, further studies are needed to support its use.

**KEYWORDS:** Cannabidiol, Epilepsy, Neurology.

## 1. INTRODUCTION

Epilepsy is one of the major neurological diseases affecting young adults in the world. It is characterized by perturbation of the cerebral physiological function, being able to generate brief or prolonged episodes of excessive neuronal activity, due to a state of neuronal hyperexcitability. It is diagnosed by the history of at least two unprovoked seizures (or reflexes) occurring more than 24 hours apart <sup>1</sup>. This pathology may have genetic, metabolic or structural etiology, as well as neurobiological, cognitive, psychological and social consequences, which affect the life quality of the affected individual. Patients with epilepsy whose seizures do not respond successfully to therapy with three anticonvulsant drugs are considered to be epilepsy patients refractory to drug therapy.

Recent studies for the refractory treatment of epilepsy have demonstrated a new therapeutic alternative: Cannabidiol (CBD). The CBD is one of the cannabinoid assets of *Cannabis sativa*, popularly known as marijuana, and constitutes about 40% of the active substances of this plant. Although it is considered an isomer of -9-tetrahydrocannabinol (THC - the main active component of marijuana and responsible for its psychoactive actions), the pharmacological effects of Cannabidiol are different and often opposed to THC effects<sup>2</sup>. Standardized extracts with high Cannabidiol content have been shown to be effective in reducing the frequency and severity of seizures, particularly in children with rare types of epilepsy who are refractory to conventional drugs<sup>3</sup>.

## 2. MATERIALS AND METHODS

To structure this study, we carried out a literature review of scientific literature, available in SciELO databases, Lilacs, MedPub and Medline.

For the article development literary sources that defined the use of Cannabidiol in the treatment of epilepsy were used.

Inclusion criteria were free full text, human-based texts, review and clinical trial articles and articles published over the past 10 years. Exclusion criteria were articles that did not focus on the treatment of epilepsy with cannabidiol use and articles that were published in non-indexed journals.

The terms used for the research were: Cannabidiol, epilepsy, neurology, treatment of epilepsy.

## 3. LITERATURE REVIEW

Despite the existence of a broad therapeutic armamentarium for epilepsy, there has been no major advance in therapeutic efficacy for traditional refractory patients in the last couple of years<sup>4</sup>. Considering this fact, there is a clear demand for the development of new anticonvulsant drugs that are both more effective for refractory cases and have a favorable safety profile. In this scenario, cannabinoid derivatives are gaining ground, since their action mechanism is distinct from the one of conventional anticonvulsant drugs and appear to have well tolerated side effects by patients<sup>5,6</sup>.

A study authored by the Food and Drug Administration (FDA), which is still underway, involves 23 patients diagnosed with epilepsy who were refractory to conventional treatment (average age 10) and obtained preliminary results in which 39% of patients had a reduction of 50% in their seizures. The 23 patients were divided into a group with a diagnosis of Dravet Syndrome (a severe type of myoclonic epilepsy characterized by convulsive seizures of difficult drug control, promoting a decline in neuropsychomotor development, language delay, ataxia in 80% of cases and hyperreflexia) and in a second group encompassing the other forms of epilepsy. From the 9 patients with Dravet's Syndrome, 5 had total control of seizures. In the group with other forms of

epilepsy, only 1 patient out of the 14 evaluated patients achieved the same result. The most common side effects of Cannabidiol were: drowsiness, fatigue, loss or weight gain, diarrhea and increased or decreased appetite, mild effects compared to traditional medications's<sup>7</sup>.

Another study carried out in Brazil also demonstrated the therapeutic potential of the use of Cannabidiol for epilepsy. The double-blind study was performed with 15 patients who experienced at least one generalized seizure per week, even receiving some other anticonvulsant (Phenytoin, Primidone, Clonazepam, Carbamazepine, Trimetadione and / or Etosuximide). The treated group consisted of 8 patients who received between 200-300mg / day pure oral CBD for 8 weeks. Of these patients, only 1 did not achieve any clinical improvement. Among the others, 4 had the seizures totally abolished during the period when they took CBD and 3 had a significant reduction in the frequency of seizures. In the group of patients who received placebo along with their other anticonvulsant, only 1 showed improvement. However, there is no evaluation of the effect of CBD in the absence of any other anticonvulsant, suggesting that CBD could be an adjuvant in the treatment of epilepsy<sup>8</sup>.

The first drug derived from Cannabis available for clinical use since 2005 was Nabiximols (Sativex®). This medicinal product consists of an alcoholic extract of Cannabis containing almost equimolar proportions of THC and CBD, available as an oral spray, used to treat spasticity in patients with multiple sclerosis and in the relief of neuropathic and oncological pain in some countries. In addition, there already are allopathic drugs containing synthetic cannabinoid agonists such as Dronabinol and Nabilone, available for clinical use in some countries. These drugs appear as a thriving alternative for the treatment of intractable epilepsy and very difficult to control epilepsy<sup>9</sup>.

#### 4. CONCLUSION

Taking into account the recent bibliographic research carried out within the scope of this study, it is concluded that Cannabidiol has a wide therapeutic potential capable of significantly reducing seizures in a patient with epilepsy refractory to traditional medicines. However, further studies are still needed for doctors to be allowed to freely prescribe the use of Cannabidiol in Brazil. For various reasons, including the limited number of patients in each of the clinical trials, its efficacy alone cannot be concluded with certainty, once it is not clear if it would only have the possibility to potentialize the effect of other drugs<sup>10</sup>.

According to the Brazilian Academy of Neurology, the data currently available in the literature are not sufficient to support the use of Cannabidiol as a routine treatment in epilepsy, but it claims to be quite effective in difficult-to-treat refractory cases<sup>11</sup>.

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