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Original Research Paper

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EFFICACY OF CANNABIDIOL IN DRUG RESISTANT EPILEPSY IN A PRIVATE THIRD-LEVEL HOSPITAL

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ABSTRACT **Introduction:** In 2016, the first results of phase III clinical trials showed beneficial effects of CBD in treatment-resistant seizure disorders, **Objective:** To evaluate the efficacy of cannabidiol in patients with drug resistant epilepsy in a private third-level hospital. **Methods:** Descriptive, retrospective, observational and cross-sectional study. Inclusion criteria were patients under treatment with cannabidiol and drug resistant epilepsy from January 2017 to March 2022. Study variables were age, gender, evolution of epilepsy (years), epileptic syndromes, numbers of antiseizure drugs, reduction of seizures (more tan 50%), cannabidiol dose (mg/kg/day), treatment time (months) and adverse effects. Information was captured in Excel and analyzed in SPSS. **Results:** 31 patients. The epileptic syndromes found were Lennox Gastaut 32%, West 12.9%, Dravet 3.2%, Doose 3.2% and no syndromic 48.3%. Reduction of seizures more than 50% was shown in 25 patients (80.6%). Seizure free in 5 patients (16%). Cannabidiol dose was: <1 mg/kg/day (9.6%), 1-5 mg/kg/day (77.4%), >5 mg/kg/day (12.9%). Association was found between a decrease in the number of seizures and a higher dose of cannabidiol with statistical significance ($p<0.05$). **Conclusion:** Our study suggests that cannabidiol reduces seizures with few adverse effects in drug resistant epilepsy.

KEYWORDS : cannabidiol, drug resistant epilepsy.

INTRODUCTION:

Cannabis sativa L. is an ancient medicinal plant wherefrom over 100 cannabinoids are extracted[1]. Among them, the most studied are Δ^9–tetrahydrocannabinol (3^9–THC), a psychoactive compound, and the cannabidiol (CBD), a non-psychotropic phytocannabinoid.[2]

CBD has been investigated for its anticonvulsant effects.[3] One of the most important ion channel targets towards which the CBD shows a high affinity is the Transient Receptor Potential Vanilloid (TRPV).

Specifically, TRPV1 is a non-selective channel that shows a high calcium (Ca^{2+}) permeability and is involved in the modulation of seizures and in epilepsy. The interaction of the CBD with the T-type Ca^{2+} channels causes a blockage of these channels, this mechanism could be responsible for the antiepileptic action.[4]

Serotonin receptors (5-HT_{1A} e 5-HT_{2A} subtypes) may represent a valid therapeutic target through which CBD can perform its anti-epileptic action.

The CBD also shows a good affinity towards the orphan G-protein-coupled receptor (GPR55), a class of receptors involved in the modulation of the synaptic transmission.

CBD inhibits CYP450, but this mechanism does not seem to be directly involved in the antiepileptic mechanism. It seems to be responsible for the hepatic metabolism of a variety of antiepileptics drugs, as shown by the combined administration of CBD and clobazam.

Several studies confirmed its efficacy in the treatment of epileptic seizures, especially in pediatric age.[5,6] In 2016, the first results of phase III clinical trials showed beneficial effects of CBD in treatment-resistant seizure disorders, including Lennox-Gastaut Syndrome and Dravet Syndrome.[7]

Purpose:

To evaluate the efficacy of cannabidiol in patients with drug resistant epilepsy in a private third-level hospital.

METHOD:

This was a descriptive, retrospective, observational, cross-sectional study. Inclusion criteria were patients under treatment with cannabidiol and drug resistant epilepsy from January 2017 to March 2022.

Exclusion criteria were files with incomplete data.

Data were obtained from clinical records. Study variables were age, gender, evolution of epilepsy (years), epileptic syndromes, numbers of antiseizure drugs, reduction of seizures (more tan 50%), cannabidiol dose (mg/kg/day), treatment time (months) and adverse effects.

Cannabidiol presentation used was 5000 mg purified 100% oil. Information was captured in Excel.

Tests (measures of central tendency, graphs, chi squared test, T student test) were applied in the SPSS program.

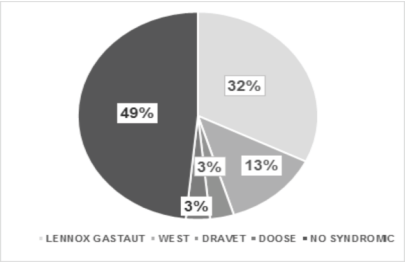
RESULTS:

31 patients were included.

The mean age of the studied population is 10.23 years old, DE+_7.21 (3-26 years old). The female gender is predominant with 54.8%.

The evolution of epilepsy was: <1 year (9.7%), 1-5 years (38.7%), 6-10 years (38.7%) and >10 years (12.9%).

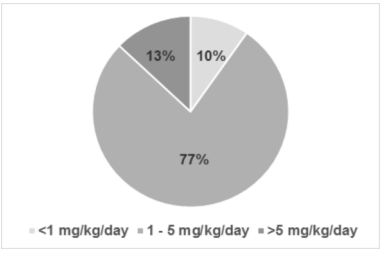
The epileptic syndromes found were Lennox Gastaut 32%, West 12.9%, Dravet 3.2%, Doose 3.2% and no syndromic 48.3% (Gráfica 1).



Graph 1. Epileptic syndromes

The number of antiseizure drugs was: 2 (6.4%), 3 (32.2%), 4 (25.8%) and 5 or more (35.4%).

Reduction of seizures more than 50% was shown in 25 patients (80.6%). Seizure free in 5 patients (16%). Cannabidiol dose was: <1 mg/kg/day (9.6%), 1-5 mg/kg/day (77.4%), >5 mg/kg/day (12.9%) (Gráfica 2).



Graph 2. Cannabidiol dose

Treatment time (months) was: <1 (3.2%), 1-3 (19.3%), 4-6 (58%), 7-12 (12.9%), >12 (6.4%). Adverse effects were: none (70.9%), increased appetite (12.9%), drowsiness (9.6%), diarrhea (3.2%), constipation (3.2%).

Association was found between a decrease in the number of seizures and a higher dose of cannabidiol with statistical significance ($p<0.05$).

DISCUSSION:

Epilepsy is a chronic neurological disorder, 30% patients have drug resistant epilepsy or treatment failure with 2 antiseizure drugs. The probability that a third drug achieves control is less than 4%.[8]

With cannabidiol, a response greater than 4% was achieved, compared to the use of a third antiepileptic drug.

Reductions in the frequency of seizures of over 50% have been reported by Devinsky et al. (67%) and Porter and Jacobson[9] (42%) compared to the 80.6% reduction of our study.

Devinsky et al. and Porter and Jacobson reported freedom from seizure in 14.5% and 11% of cases, respectively, compared to 16% of cases in our study.

Most of the patients had a prolonged evolution time with epilepsy of more than 5 years and were in polypharmacy.

An epileptic syndrome was diagnosed in 51.7% of the patients and no syndromic was determined in 48.3% of the patients.

The 58% obtained a response to cannabidiol treatment after 4-6 months of use, compared with 12 weeks reported in literature.

The 77% obtained a response to cannabidiol treatment with a dose of 1-5 mg/kg/day, compared with 4 mg/kg/day reported in literature.

Most patients had no adverse effects in 70.9%, compared with 79% reported in literature.

CONCLUSION:

Our study suggests that cannabidiol reduces seizures with few adverse effects in drug resistant epilepsy. Randomized clinical trials are necessary to determine efficacy, safety and its true role in epilepsy and other pathologies.

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