SAFETY AND EFFICACY OF CANNABIDIOL VERSUS FIRST-LINE ANTI-EPILEPTIC DRUGS (AEDS) FOR THE TREATMENT OF DRAVET SYNDROME:SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction

- Epilepsy is a frequent neurological disorder with a prevalence of 0–1% and a lifetime incidence of up to 5%. According to the International League Against Epilepsy, it's a complicated disorder with a variety of origins and seizure types and syndromes.
- Dravet syndrome (DS) is an early-onset treatment-resistant epilepsy syndrome that typically presents during the first year of life.It typically causes epileptic encephalopathy.
- Seizures in patients with DS are particularly difficult to manage since they are usually resistant to therapy (requiring the combination of two or more correctly chosen ASMs) and patients frequently fail to achieve total seizure control.
- SCN1A mutations, are usually found in 70 to 80% of patients with Dravet syndrome.
- Furthermore, medication with specific mechanisms of action may be required for seizure types, and individual responses to these drugs can be unpredictable
- Therapy for DS typically involves a trial-and-error approach with first-line AEDs such as clobazam, valproic acid and topiramate. A newer agent, cannabidiol was approved by FDA in 2018 as adjunctive therapy for DS.

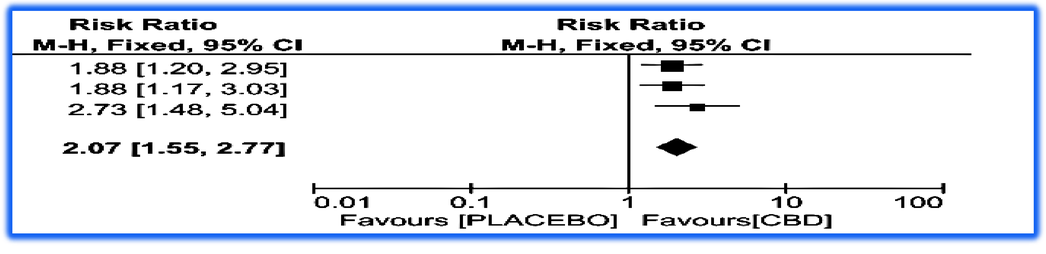
Methodology

- The study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines (PRISMA Checklist).
- This systematic review included all randomized control trials representing the following, criteria: patients with medical history to support the clinical diagnosis of DS, aged 2-60 years (infants, children, and adolescents).
- Participants on first-line antiepileptic agents or cannabidiol as monotherapy for a minimum 4-week period, and subjects with a minimum of a one-month drug-free period before initiating the drug therapy under study.
- The literature search, data extraction, and data input into spreadsheets for analysis were performed simultaneously and independently by two authors
- To organize the data and perform analyses using the standard Cochrane Collaboration approach, we utilized Review Manager 5.4.1 and R-package(meta) version 4.1.0. For dichotomous data, we estimated risk ratios (RR)

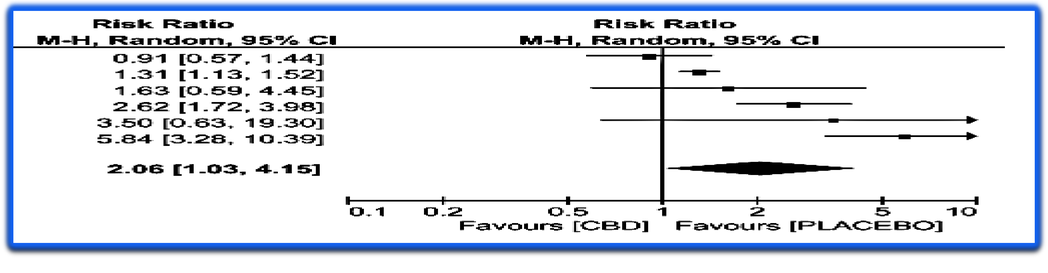
Results

- Six studies were finalized from the retrieved 1845 after systematic search and screening. It included a total of 501 patients. CBD showed more efficacy when compared to placebo.
- Throughout the trial, there was a higher incidence of treatment-emergent adverse events in the CBD group when compared to the placebo and they demonstrated that CBD along with first line antiepileptics was better in reducing seizure frequency, with an overall risk ratio (RR=2.07) at 95% confidence interval of 1.55-2.77.

EFFICACY OUTCOME



SAFETY OUTCOME



Conclusion

Add-on cannabidiol (CBD) with conventional treatment for DS showed a greater reduction in all types of seizure frequencies from baseline when compared to placebo. Overall, CBD had a greater efficacy as an adjuvant and was well tolerated by the subjects with no death reports.

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