The Role of Cannabidiol in the Treatment of Refractory Epilepsy in Pediatric Patients

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Background

- Epilepsy is the most frequently diagnosed chronic neurological condition in children and affects between 0.5% and 1% of children[1]
- Behavioral disorders are disproportionately high in children with epilepsy and include increased anxiety, depression, irritability, hyperactivity, and aggression.[2] Psychiatric disorders have been identified in up to 34% of children with seizures, compared to 6.6% in the general population.[2]
- Seizures are traditionally treated with antiepileptic drugs (AEDs). First-line agents most commonly used for generalized tonic-clonic seizures include valproic acid, lamotrigine, and topiramate.[3]
- Common adverse effects associated with these drugs are slowed psychomotor speed, poorer attention, and mild memory impairment.[4]
- In recent years, marijuana, and more specifically the compound CBD, has emerged as a potential treatment for intractable epilepsy in children

Purpose

This study posed the following question:

- In pediatric patients with drug-resistant epilepsy, is cannabidiol (CBD) more effective in reducing seizure activity than traditional anti-epileptic drugs (AEDs) alone?

Methods

A systematic review was utilized to produce this evidence-based review article. Literature searches were performed using the PubMed database, Arcadia's Landman Library EBSCO database, and Google scholar. Key words such as "refractory epilepsy", "children", "CBD", and "cannabis" were included in the search terms. Exclusion criteria were non-human subjects and meta-analysis or systematic reviews. Seven of the most relevant articles were selected for critical analysis.

Results

There is hopeful evidence that CBD oil has the potential to increase quality of life and decrease seizure activity in this specific population. One study, Tzadok et al., demonstrated a reduction in seizure activity in 89% of the participants (2016). In a separate study, nineteen patients (41%) partially or completely tapered 1–3 AEDs during the follow-up period due to their improvement in seizure activity (Hausman-Kedem et al., 2018). The results of Mitelpunkt et al. were particularly promising: 56% of patients reported a ≥50% reduction in their seizures and two patients became fully seizure-free. At the end of the study, 73% of caregivers reported an improved/very much improved condition, and 82% reported reduced/very much reduced seizure severity (2019).

Study	Design	Total N	Age Range (years)	Duration of Treatment	CBD Treatment Formulation	Outcome Measurements
Mitelpunkt et al (2019)	Prospective Cohort	16	2-15	12 weeks	PTL-101	CGI-I, CGI-S, seizure frequency
Devinsky et al (2017)	RCT	120	2-18	14 weeks	GW Pharmaceuticals	CGI-C, CGI-S, QOLCE, seizure frequency
Tzadok et al (2016)	Retrospective Cohort	74	1-18	3-12 months	20:1 CBD: THC	Seizure frequency
Hausman-Kedem et al (2018)	Prospective Cohort	57	1-20	3-33 months	20:1 CBD: THC	Seizure frequency
Neubauer & Benedik (2018)	Retrospective Cohort	70	5-23	8-12 months	Bionorica	Seizure frequency
Porcari et al (2018)	Retrospective Cohort	108	1-18	12-36 months	Artisanal preparations	Seizure frequency
Rosenberg et al (2017)	Prospective Cohort	60	3-27	12 weeks	GW Pharmaceuticals	QOLCE, seizure frequency

Key: RCT = Randomized Control Trial; CGI-I = Caregiver Global Impression of Improvement; CGI-S = Caregiver Global Impression of Seizure Severity; CGI-C = Caregiver Global Impression of Change; QOLCE = Quality of Life in Childhood Epilepsy

Discussion

- There was a statistically significant change in participant seizure frequency in five of the seven studies included, and CBD was not found to cause serious or life-threatening adverse effects
- A major issue with this systematic review is that only one of the relevant studies is an RCT. This makes it difficult to assess the efficacy of CBD, as only RCTs can adequately control for bias and produce the strongest evidence
- Selection bias, small sample sizes, and lack of comprehensive outcome measurements are the issues most affecting the validity and generalizability of these studies

Conclusions

- The seven studies chosen for this evidence-based review article demonstrate promising results for the use of cannabidiol oil in treating intractable pediatric epilepsy
- Future research should focus on randomized control trials with rigorous study designs
- Due to the lack of availability and access, no change in standard treatment practices can be recommended at this time, but these studies demonstrate positive findings and indicate that CBD can reduce seizure frequency in some pediatric patients