CASE REPORT

Whole Plant Cannabinoid Nonpharmaceutical Treatment Protocols for a Young Male With Dravet Syndrome

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ABSTRACT

Objective: This case report describes the outcomes of a novel, conservative approach for a young male patient with Dravet syndrome, which is a genetic epileptic encephalopathy resulting in frequent and recalcitrant seizures and developmental delays.

Clinical Features: A male infant began to experience seizures before 7 months of age, and genetic testing revealed an SCN1A mutation, confirming the diagnosis of Dravet syndrome. At age 7, despite standard polypharmacy consisting of antibiotics, steroids, and antiepileptic drugs, he continued to suffer from approximately 25 to 28 daily tonic-clonic refractory seizures.

Intervention and Outcome: The clinical objective was to restore the function of the endocannabinoid system by integrating very low-dose, whole-plant extracted, naturally chiral, hemp-derived phytocannabinoid formulations, and broad environmental and dietary modifications. Within the first week of treatment, the patient had only 1 to 2 mild seizures per day. Four years later, all pharmaceuticals were discontinued, and by age 12, the patient's daily hemp formulation was reduced to as-needed status. At the time of this writing, the patient was 16 years of age and had an average of 7 to 10 very mild petit mal seizures per month. The whole plant hemp formulations generated no observable side effects.

Conclusion: This case study demonstrates conservative comanagement of a patient with a catastrophic seizure disorder using novel nonpharmaceutical comanagement strategies. (J Chiropr Med 2025;00;1-6)

Key Indexing Terms: *Cannabidiol; Epilepsies; Myoclonic; Cannabinoids*

INTRODUCTION

Dravet syndrome, Severe Myoclonic Epilepsy of Infancy, is a rare genetic pediatric encephalopathy that results from a mutated apha-1 subunit of voltage-gated calcium channel (SCN1A). The incidence of Dravet syndrome is estimated to be 1/15 000 to 40 000.[1]

The disease course typically begins with seizures in the first 15 months of life, eventually progressing to frequent and recalcitrant seizure activity, and worsening motor, behavioral, cognitive decline, and disability. There is increased mortality in up to 20% of patients with Dravet syndrome, resulting from sudden death seizures.[2] The side effects of antiepilepsy drugs (AEDs) are severe and can lead to significant morbidity or death. The positive treatment effects of are limited in some patients; a clinical trial in 2016 found a 36.5% reduction in motor seizure frequency for Epidiolex.[3]

The objective of this case report is to describe 10 years of treatment effects of whole plant hemp cannabidiol (CBD) extracts in a young male patient with Dravet syndrome, who was responding poorly to the standard polypharmacy approach.

CASE REPORT

A male infant had confirmed SCN1A mutation and his first seizure at 7 months of age, which is when he began management with a neuropediatrician (MD, PhD); the patient was diagnosed with Dravet syndrome by this clinician, and currently remains under their care. Throughout the management of the patient, he was examined by said

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neuropediatrician to monitor for treatment outcomes and assure no adverse side effects. His seizures were initially mild and febrile, but worsened in intensity and frequency, in parallel with increased use of prescribed antiepileptics, steroids, and antibiotics. His clinical status continued to deteriorate from onset at 7 months until 6 years of age. Seizure frequency was monitored throughout the care plan in written logs from the caregivers and managing clinicians. At 6 years of age, he was suffering from up to 28 daily grand mal tonic clonic cluster seizures, while simultaneously taking varying combinations of six different AEDs, prophylactic steroids, and antibiotics.

The AEDs prescribed included CBD, phenobarbital, sodium valproate, felbamate, Keppra, Diastat (diazepam), Onfi, clonazepam, zonisamide, Topamax, Tegretol. The pharmaceutical protocol included hospital visits every 5 days for phenobarbital loading to manage cluster seizures. At this time, due to the uncontrollable nature of the cluster seizures and nonresponse to the standard treatment protocol, the patient was at a heightened risk for a sudden death seizure.

At age 7, because of Missouri state law allowing whole plant extracted CBD supplements for the treatment of epilepsy disorders, the patient's neuropediatrician incorporated CBD therapy through the nonprofit organization BeLeaf, which held one of the two Missouri CBD licenses. One of the authors, a chiropractor with 10 years of experience with CBD formulations, provided the plant genetics, formulations, and consultations to the neuropediatrician for whole plant hemp-derived CBD treatments, and a new treatment protocol including whole plant extract was initiated, dosed as a botanical extract at 1 mg/kg/d of whole plant CBD.

The hemp-derived, whole plant botanical extracts were purposely formulated to deliver an entourage of specific, very low-dose cannabinoids, terpenes, polyphenols, flavonoids, essential fatty acids (omega-3 and oleic acid), amino acids, vitamins, minerals, and more (Fig 1).

The patient also had pro re nata manual chiropractic manipulations and exercise recommendations throughout the case study (~10 years). Whole plant extracted CBD formulations were selected over CBD isolate formulations because of empirical patient outcomes, combined with growing support in the literature for the "Entourage Effect" (Fig 1).[4-6]

Key dietary restrictions and environmental triggers were also identified and removed from the patient. Specific dietary recommendations were given, including the removal of environmental, xenobiotic, and chemical triggers. Some examples included the removal of processed foods and beverages with proinflammatory drivers like monosodium glutamate, aspartame, and trans fats. The patient also added

Test: Terpenoid/Cannabinoid Profile	Type: Flower	Customer's ID: -	Sample ID: FL-1739-R01
Submitted: -	Tested: 10/20/2014	Reported: 10/20/2014	Sample Mass: 573.9 mg

Cannabinoid Profile

Compound	% mass	≈ mg/g
CBGA	0.22	2.2
CBG	ND	ND
THCA	0.32	3.2
THCAC4	ND	ND
THCVA	ND	ND
D9THC	ND	ND
D8THC	ND	ND
THCV	ND	ND
CBNA	ND	ND
CBN	0.14	1.4
CBDA	9.1	91
CBDVA	ND	ND
CBD	ND	ND
CBDV	ND	ND
CBCA	0.075	0.75
CBC	ND	ND
CBLA	ND	ND

Fractions of Measured Cannabinoids

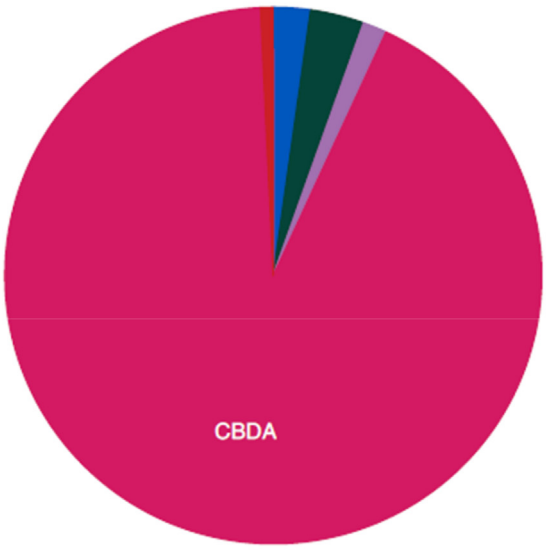

Fig 1. *The cannabinoid composition of the whole plant hemp formulation used in the case report is derived from unique plant genetics.*

daily dosages of multivitamin and mineral, probiotics, Vitamin D3/K2, and omega-3 fatty acids throughout the treatment protocol. The patient's seizures reduced in frequency by 90% within the first 2 weeks of treatment onset. The seizure intensity also reduced from severe grand mal seizures to mild petit mal seizures.

During this time, the patient's sleep patterns improved significantly, and he began to experience dreaming. The parents noted that the onset of dreaming included smiling and laughing while sleeping. The treatment outcomes were multifaceted, improving the patient's growth rates and muscle mass, his ability to achieve deep sleep, his social skills, and his vocabulary/sentence structuring. Examples of improved physical activities of daily living included throwing and catching a ball, riding an all-terrain vehicle, and fishing.

By age 11, the patient's seizure activity was sufficiently reduced to discontinue all prescription prophylactic antibiotics and corticosteroids, and all six AEDs. The patient was experiencing 5 to 10 low-intensity seizures per month at this point in the treatment protocol.

By age 12, he reduced his CBD supplement use to as-needed/pro re nata only, taking the whole plant botanical only when ill from the common cold or the flu; the dosage was maintained at 1 mg/kg/d as before, and throughout the treatment protocol. The patient was experiencing 4 to 6 very low-intensity seizures per month at this point in the treatment protocol.

The patient is currently 16 years old and remains on the same nonpharmaceutical treatment protocol, supported by the same nutritional and lifestyle modifications. All pharmaceutical interventions remain discontinued. No adverse effects were reported throughout the case study. Throughout the trial, the patient's height and weight normalized, beginning below the 50th percentile, and now approaching the 75th percentile. The patient has some persistent reduced mental function. The patient's mother provided consent for this case to be published.

Discussion

The diagnosis of Dravet syndrome is made by the managing neuropediatrician following genetic testing in young patients with recurrent or prolonged seizures, especially those occurring in the setting of vaccination or fever. All of these patients have diffuse, severe, chronic inflammatory patterns throughout the central and peripheral neuroimmune and organ biome systems. The central nervous system microglial cells are especially adversely hyperactive.[7-10] It is believed that the endocannabinoid system (ECS), the microbiota-gut-brain-axis (MGBA), and the neuroimmune central and peripheral nervous systems are codependent, and when fully functional, successfully manage the body and brain without the presence of chronic inflammatory patterns. Thus, a healthy functioning neuroimmune system is dependent upon a normally functioning ECS and MGBA.[6,11-14] Based on this understanding, it is plausible that patients with Dravet syndrome are born genetically predisposed to catastrophic seizure syndromes, and when a "perfect storm" of multifactorial biological and environmental factors are introduced, the symptoms appear.

Some patients diagnosed with Dravet syndrome and other epileptic disorders may have worse symptoms after adding the pharmaceutical treatments, presumably related to gut dysbiosis.[12-21] In this case, the constant ingestion of xenobiotic categories, namely 6 different AEDs, antibiotics, and steroids, disequilibrated the patient's ECS and MGBA. This demanded a lengthy rehabilitation of the two critical systems through the removal of the pharmaceutical, environmental, and dietary xenobiotics, and the addition of the whole plant botanicals.[15-17]

The treatment goals of Dravet syndrome are to control seizure activity. When patients fail to respond to the typical recommended care, it is advised to add additional therapies.[1] Our treatment protocol addressed the dysfunctional ECS and MGBA, with the goal of minimizing chronic inflammatory patterns and restoring long-term homeostasis. Proper management in this regard can only be accomplished with the constant supervision of in-house parents or caretakers, making small dietary and environmental adjustments day to day, as the evolving MGBA repairs and reduces proinflammatory metabolites. As the MGBA function improved, the patient's need for the whole plant hemp formulations reduced. There is growing evidence that the gut biome contributes to the anti-inflammatory effects of cannabinoids through the growth of key organisms.[18,19] No adverse side effects were reported throughout this patient's nonpharmaceutical whole plant CBD treatment.

Per Zhang et al,[22] CBD is effective at micromolecular dosages, acting on numerous membrane-bound proteins of the ECS (see supplementary file for glossary). Its most potent effect is the inhibition of endocannabinoid modulation; this is mediated by a negative allosteric effect on CB1 receptors, shifting the voltage dependence of activation in the hyperpolarizing direction, with significant subthreshold activation. Activation of neuronal M-current may exert an antiepileptic action. Clinical Endocannabinoid Deficiency is the process of ECS exhaustion by chronic demand from hyperinflammatory states, directly altering the MGBA. The complex interplay of these systems is relevant to the pathophysiology of catastrophic seizure syndromes.

Patients respond differently to cannabinoid-based formulations due to myriad factors such as dosage, concentrations, delivery route, treatment duration, fed vs nonfed states, drug-to-drug interactions, isolated vs whole plant formulations, molecular chirality, patient genetics and epigenetics, and far more (and dietary xenobiotics). Cannabinoid use demonstrates the biphasic state of hormesis,

which in toxicology refers to a dose-response to an environmental agent, with a low-dose stimulation or beneficial effect, and a high dose inhibitory or toxic effect. Per the individuality response review of Kitdumrongthum and Trachootham,[14] the cannabinoid dosage recommendation is to begin "low and slow". The ideal cannabinoid formulations and dosages are unique for each patient and for each condition.[23,24] It is likely that dietary and lifestyle modifications increased the stability of the ECS and MGBA during the management of this patient. Dietary and lifestyle modifications likely also contributed in part to patient's outcomes; further studies would be needed to isolate the contribution of each treatment.

Thus, we believe the diversity of low concentration "food ingredients" (sometimes referred to as the "entourage effect") found in the whole plant, hemp-derived formulations were critical to the outcomes of this patient. The phytocannabinoid ligands (CBDA, CBD, THCA, D9-THC, CBCA, CBC, CBGA, CBG, CBN, CBDV. See supplementary file for glossary) derived from the formulations positively affected the microglial cells, the ECS, and the MGBA by acting on CB1, CB2, TRPV1-TRPV4, TRPVA1, and TRPM8 receptors[20,21] and altering other unknown pathways. For example, CBD is known to modulate about 15 different key receptor sites (CB-1, CB-2, GPAR-55, serotonin, GABA, glutamate, etc.) without directly binding to any of them. This creates positive outcomes through yet to be discovered "quantum biological" activities.[25-27] The authors have strategically chosen an "Entourage" of natural, whole plant cofactors such as terpenes, flavonoids, polyphenols, omega-3s, chlorophylls, amino acids, vitamins, minerals, and many other macro- and micronutrients. These significantly improve receptor site responses and bolster the bioavailability of each molecule within the formulation's Entourage. Collectively, this contributes to significant reductions in the required effective dosages and lends support to the safe and successful management of these patients.

The outcomes of the "Entourage Effect," as first reported by Ben-Shabat and Mechoulam,[4] and further expanded by Russo,[5] were verified by the outcomes of this patient. Regarding catastrophic seizures, whole plant extracted cannabinoids were more efficacious with far fewer adverse side effects than isolated cannabinoid formulations. In the management of catastrophic seizure syndromes, isolated cannabinoid preparations require much higher daily doses of total CBD when compared to the whole plant cannabinoid extractions utilized in this case report. The patient was dosed at only 1 mg/kg/d, while the BMJ whole plant extraction case series dosed 8.55 mg/kg/d.[6] By comparison, the original Epidiolex recommended dosage was 20 mg/kg/d, and recommendations are now increasing above 20 mg/kg/d to sustain only a 38% reduction in catastrophic seizures.

Georgieva's 2023 "real world" review of Epidiolex's safety, toxicology and outcomes details important clinical issues that may be due to the use of isolated cannabinoids instead of whole plant formulations.[13] They reported 108 young adult patients who began Epidiolex with mean initial and maintenance doses of 5.3 mg/kg/d (1.3) and 15.3 mg/kg/d (5.8), respectively. At the final evaluation of the study, 75% of patients remained on Epidiolex; the 25th percentile for discontinuation was 19 months. Patients most often discontinued therapy after 1 to 4 months due to side effects, and after 12 to 15 months due to lack of efficacy. Overall, 46.3% of patients experienced at least one treatment-emergent adverse effect, with 14.5% d/c Epidiolex. The most common reasons for discontinuation were lack of efficacy (37%), increased seizure activity (22%), worsened behavior (22%), and sedation (22%). One out of 27 discontinuations was due to liver function test elevations (3.7%). At initiation, 47.2% were concurrently taking clobazam, and 39.2% of those patients had an initial clobazam dose decrease. Overall, 53% of patients were able to either discontinue or lower the dose of at least one other antiseizure medication.[13,28]

The United States Food and Drug Administration has approved only one cannabis derived drug, Epidiolex, for the treatment of Dravet syndrome. This drug isolate has a 50:1 CBD to THC ratio. The Food and Drug Administration approved dosage of Epidiolex is 20 mg/kg/d of CBD, which may yield up to a 39% seizure rate reduction.[10] Off-label dosage of Epidiolex may reach up to 50 mg/kg/d.

Lowering the total daily CBD dosage is important for the prevention of key adverse side effects found in daily doses exceeding 200 to 800 mg of CBD per day, especially when considering the liver function test and the p450 pathways of the patients consuming AEDs.[12] CBD's interactions with other drugs are largely based on its inhibition of CYP2C19, CYP2D6, and CYP2C9. CBD may inhibit some CYP3 isoenzymes, but this is not well established. CBD is metabolized in the liver by CYP3A4 and CYP2C19.[28] Devinsky further detailed that CBD interacts with the benzodiazepine anticonvulsant clobazam (and its active metabolite, *N*-desmethylclobazam [N-CLB]).[3] In pediatric epilepsy cases, CBD increases the steady-state concentrations of clobazam by 60% and N-CLB by 100% to 400%. This finding has led some to believe that part of CBD's efficacy in isolate formulations is due to higher clobazam and N-CLB levels.[3] At 1 mg/kg/d of CBD dosage, drug-to-drug interactions and related adverse side effects were not a concern in this case.

Since chirality determines receptor site activity, reviewing the chirality of key active ingredients in whole plant extracted hemp formulations is integral to reduce the required daily dosage of CBD ingested by each patient.[29] The delivery of specific, naturally occurring, negative-negative isomers can be achieved by carefully selecting specific hemp plant genetics, cultivation methods, extraction methods, and carrier oils that deliver a

whole plant chemical entourage.[30] Thus, nonsynthetic, naturally chiral formulations were intentionally made for this patient to deliver a very low daily dose of hemp-derived cannabinoids that were supported by a full spectrum of whole plant derived molecules that fulfilled the Entourage Effect.[4,6,11,31,32] All of these factors played a tremendous role in targeted, specific receptor site activities that minimized seizure activities and adverse side effects (like THC-derived psychoactivity and adverse p450 pathway/drug-to-drug interactions), while simultaneously encouraging patient homeostasis via improvements in neural function, cognitive development, sleep patterns, the ECS and MGBA.

Limitations

Definitive conclusions based on the result of a single patient cannot be generalized to other patients. The noncontrolled environment in which the patient lives makes it impossible to make firm conclusions about the effectiveness of the treatment provided. Future studies may be strengthened by incorporating pre-, during, and post-treatment EEGs, blood inflammatory marker assays, gut biome assays, and specific blood serum levels for Vitamin D3 and endogenous endocannabinoids. These findings could supplement treatment and outcome data for catastrophic seizures, especially in first-line therapy decisions to use low-dose whole plant CBD formulations.

Conclusion

Chronic seizure activity in a young male patient was reduced after the introduction of whole plant extracted hemp and diet modifications.

Funding Sources and Conflicts of Interest

No funding was received for this study. The authors declare no conflicts of interest.

Contributorship Information

Concept development (provided idea for the research): T.J. Design (planned the methods to generate the results): T.J. Supervision (oversight, organization, and implementation): T.J. Data collection/processing (experiments, organization, or reporting data): T.J., J.H., N.K. Analysis/interpretation (analysis, evaluation, presentation of results): T.J., J.H., N.K. Literature search (performed the literature search): T.J., J.H., N.K. Writing (responsible for writing a substantive part of the manuscript): T.J., J.H., N.K. Critical review (revised manuscript for intellectual content): T.J., J.H., N.K. Other (list other specific novel contributions).

Practical Applications

- A young male patient with Dravet syndrome had improved outcomes using whole plant CBD formulations.
- He was eventually able to discontinue all prescribed pharmaceuticals.
- He currently has only occasional mild seizure activity.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jcm.2025.09.014.

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