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Dispensary Cannabidiol (CBD): Nothing to Worry About!

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Abstract

Introduction: Despite US FDA approval of cannabidiol (CBD) liquid (Epidiolex®), patients with epilepsy still supplement prescription treatments with dispensary CBD. This study aimed to evaluate therapeutic effectiveness of dispensary CBD. **Methods:** We retrospectively collected dosage information, CBD serum levels, efficacy, and adverse effects from patient charts (children, adolescents, adults) (n = 18). **Results:** All 18 patients showed no clinical benefit from dispensary CBD as detectable serum levels never reached a therapeutic range of 150 ng/mL (6 patients had barely detectable levels that were below laboratory reporting thresholds). Minute levels of tetrahydrocannabinol (THC) were found in 3 patients, and moderate levels were found in 1 patient. **Conclusion:** Dispensary CBD failed to reach effective therapeutic levels in all of these patients. The presence of THC demonstrates the current lack of regulation of dispensary CBD. Anecdotal reports of clinical effectiveness should be considered an effect of concomitant prescription antiseizure medications and not dispensary CBD.

Keywords

antiseizure drugs, efficacy, epilepsy, seizures, treatment

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Introduction

The burden of epilepsy has been reduced by a vast array of new antiseizure medications, with more treatments in production or being trialed; nevertheless, generalized seizures continue to produce complicated cases for patients and physicians attempting to refine treatment regimens. Focal seizures are likewise similarly complex and comprise the most common form of epilepsy worldwide.[1] One possible treatment modality is cannabidiol (CBD), which is the second most common active ingredient found in the *Cannabis sativa* and *Cannabis indica* plants and has been utilized as a treatment for various diseases. CBD acts on multiple targets and increases adenosine uptake into neurons, which acts as an inhibitory signal and decreases the intracellular calcium release that precedes excitatory neuronal activity.[2] These unique modulations make it distinct from other antiseizure medications that primarily act on sodium and potassium currents. Likewise, its active metabolite—7-hydroxy-cannabidiol, produced from CYP2C19 metabolism of CBD—has been shown to have a mild anticonvulsant effect and can be affected by other antiseizure medications that inhibit CYP2C19.[3]

In 2018, the US Food and Drug Administration (FDA) provided initial approval for Epidiolex®, the prescription formulation of cannabidiol indicated for seizures associated with Lennox-Gastaut Syndrome and Dravet syndrome for patients aged 2 years and older. An indication for Tuberous Sclerosis Complex was added by the FDA in July 2020.[4] Prescription CBD is a purified plant-based CBD product that has proven efficacy as an anti-seizure medication, and lacks the psychoactive properties of tetrahydrocannabinol (THC).[5–7] Prior study has demonstrated its effectiveness in reducing seizures while also

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providing behavioral and sleep benefits.[8] Following prescription CBD's approval, patients have continued to use other cannabis products, which were studied to investigate their medicinal content.[9] However, dispensary and internet CBD products are not FDA approved and therefore regulated,[9] which results in uneven quality and unpredictable levels of CBD (and possibly THC) across products.[10–12] Ultimately, using these products could lead to unpredictable treatment responses.

Even before the FDA approved the prescription formulation of CBD, many epilepsy patients obtained internet-based dispensary CBD products to supplement their prescribed treatment regimen, and dispensary supplementation has occurred even with patients taking prescription CBD. We therefore sought to document and evaluate the pharmacology of internet dispensary CBD in a real-world clinical setting. We performed a retrospective chart review of patients from the epilepsy clinic at our institution with seizures who reported taking dispensary products purchased from various internet services. We examined serum levels of CBD in patients and evaluated the pharmacokinetic profile of dispensary products.

The purpose of this study is to demonstrate the pharmacokinetics of internet and store-bought dispensary CBD. We hypothesize that subtherapeutic levels of CBD will be found in patient serum levels with a concomitant lack of seizure suppression efficacy. We hope that awareness of assayed CBD serum levels (and the ability to perform these easily within the clinical setting) in patients on these non-prescription CBD products will better help inform patient care.

Methods

Institutional review board approval and approval to waive consent were obtained from The University of Tennessee Health Science Center, Memphis (22-08763-XP). We performed a retrospective chart review of all patients followed at the Comprehensive Pediatric Epilepsy Program clinic at Le Bonheur Children's Hospital in Memphis, TN who were reportedly taking a non-prescription internet or store-obtained cannabidiol product (ie, dispensary cannabidiol). We reviewed records for clinic patients from April 2015 to May 2022, which included patients from several age ranges: children (2-11 years of age), adolescents (12-17 years), and adults (≥18 years). Adult members present in the study were long-term patients who began epilepsy treatment in early childhood and continued seeking treatment at Le Bonheur Children's Hospital. Patients using a combination of prescription cannabidiol (ie, Epidiolex) and dispensary product were excluded from the study to ensure that only the dispensary product was responsible for serum levels.

Patients were not provided with, nor were they prescribed, dispensary cannabidiol; instead, they added it independently as an adjunct to their treatment regimen without prior consultation with their treating physician. When dispensary CBD use was discovered, patients were informed about the need to assay for serum levels, the questionable efficacy and risks involved with using a non-pharmaceutically regulated substance.

Data collected include patient demographics (age, sex, weight), epilepsy type and etiology, dispensary cannabidiol brand name, daily dosage, serum level, number of prior antiseizure medications, any reported clinical effects, duration on product, and reasons for discontinuation. At follow-up appointments, the treating physician ordered random levels of the cannabidiol product, and serum concentration was obtained through reports from NMS Labs (Horsham, PA) and Quest Diagnostics (New York City, NY), who currently use a reporting limit of 1 ng/mL. This limit was based on much higher doses of cannabidiol but is still applicable given the high variability of CBD levels. Both labs use High Performance Liquid Chromatography and Tandem Mass Spectrometry to determine serum levels.[13, 14] We set the lower limit of the therapeutic range for serum CBD at the 100–150 ng/mL range, as determined by previous studies.[15–17] Patients reported self-initiating treatment on dosages based on anecdotal evidence from dispensers, current users, and recommendations provided on the internet dispensary websites. Because of uneven dosages of dispensary CBD across patients, we reported only the stable dose that patients were on at the time serum levels were obtained.

Results

A total of 18 patients added dispensary CBD to their prescribed antiseizure regimen, consisting of 8 males and 10 females. The overall age range was 2-32 years; 50% (n = 9) were between the ages of 2-11 years (children), 33.3% (n = 6) were 13-15 years (adolescents), and 16.7% (n = 3) were 18 years or older (adults). All patients had a diagnosis of generalized seizures except for two who were diagnosed with focal seizures with secondary bilateral tonic-clonic activity. We found that 89% (n = 16) of patients had a seizure etiology with a genetic abnormality. Nine patients had significant cognitive delay associated with their seizure type (Table 1).

No new side effects were found in this study, nor were any side effects reported by patients. A total of 13 patients eventually discontinued dispensary cannabidiol either in favor of pursuing prescription cannabidiol (n = 7), after epilepsy surgery (n = 1), or due to a perceived lack of efficacy (n = 5).

Because each patient used a different product, there was little-to-no consistency in dosage and serum levels. Six patients had serum levels of CBD below the laboratory reporting level of 1 ng/mL (Table 2). Two patients modified their dosages of dispensary CBD but still maintained extremely low levels. Patients used cannabidiol from 12 different dispensaries: 6 from Charlotte's Web, 2 from Haleigh's Hope, 1 from Buffalo River, 1 from Phoenix Tears, 1 from Ancient Nutrition, 1 from Care by

Table 1. Patient Characteristics (n = 18).

Characteristics	Value
Gender, n (%)	
Male	8 (44.4%)
Female	10 (55.6%)
Age, median (range)	
Children (2-11 yrs)	9 (2-11)
Adolescents (12-17 yrs)	6 (13-15)
Adults (≥18 yrs)	3 (18-32)
Study Attributes, n (%)*	
Patients with generalized seizures	18 (100%)
Patients with focal seizures	2 (11%)
Patients with genetic abnormalities	16 (89%)
Patients taking concomitant EIAEDs	3 (17%)
Patients taking no concomitant EIAEDs	15 (83%)

EIAED: enzyme inducing antiepileptic drugs.

Table 2. Patient Cannabinoid Serum Levels from Each Dispensary Product.

Patient No.	Age (yrs)	Weight (kg)	Dispensary Product	Product Dose	Serum Level (CBD)	Serum Level (THC)
1	11	35.0	Charlotte's Web	1 mL/d	BRL	0
2	15	43.8	Buffalo River	2.4 mL/d	9.8 ng/mL	0
3	4	10.4	Charlotte's Web	2 mL/d	21 ng/mL	2 ng/mL
4	18	35.0	Phoenix Tears	2 mL/d	42 ng/mL	4 ng/mL
5	32	97.5	Ancient Nutrition	1 mL/d	BRL	0
6	15	39.6	Care by Design	10 mg/d	1.8 ng/mL	3 ng/mL
7	2	10.9	Haleigh's Hope	0.6 mL/d	1.3 ng/mL	0
8	24	152.9	PlusCBD	10 mg/d	BRL	0
9	14	29.2	Charlotte's Web	5.25 mL/d	BRL	0
				2.25 mL/d	BRL	
				2.52 mL/d	BRL	
				1.2 mL/d	31 ng/mL	
10	6	16.6	Charlotte's Web	0.6 mL/d	2.9 ng/mL	0
11	4	9.6	Charlotte's Web	2.4 mL/d	BRL	0
12	14	38.0	Palmetto Harmony	1.0 mL/d	31 ng/mL	0
13	15	50.6	Charlotte's Web	1.6 mL/d	BRL	0
14	5	11.4	TenneCBD	3 mL/d	48 ng/mL	0
15	11	21.9	Haleigh's Hope	1.4 mL/d	9.9 ng/mL	0
				1.0 mL/d	2.4 ng/mL	
16	13	42.2	Pure Cannaceuticals	100 mg/d	BRL	0
17	9	19.4	TreatWell CA	0.75 mg/d	4.9 ng/mL	0
18	6	20.3	Texas Original	4.5 mL/d	3.2 ng/mL	79 ng/mL

BRL: below reporting level (1 ng/mL); CBD: cannabidiol.

Design, 1 from PlusCBD, 1 from Palmetto Harmony, 1 from TenneCBD, 1 from Pure Cannaceuticals, 1 from TreatWell CA, and 1 from Texas Original. Of the 12 brands represented in the study, Charlotte's Web hemp oil was the most readily obtained and showed higher CBD levels in 2 patients (21 ng/mL and 31 ng/mL); however, even these were well below the lower limits of the therapeutic range (100-150 ng/mL). Three patients were taking enzyme-inducing medications at the time of initiation, and their average cannabidiol serum level was 1.52 μg/mL, barely above the detection limit. The remainder had an average cannabidiol serum level of 11.14 μg/mL. Children taking dispensary CBD had an average serum concentration of 9.4 μg/mL with adolescents and adults having 7.4 μg/mL and 14.2 μg/mL, respectively.

Discussion

This study demonstrated the inability of non-prescription cannabidiol to achieve minimally therapeutic serum levels, which is consistent with the low levels of cannabidiol contained in the various products. These subtherapeutic levels explain the lack of side-effects and also the perception of no significant improvement in seizure control. This information is especially pertinent to families who assume their family member with Dravet Syndrome, Lennox-Gastaut Syndrome, or Tuberous Sclerosis Complex may benefit from dispensary CBD; likewise, it is helpful for medical professionals to dissuade caregivers from purchasing these products. Other studies of dispensary CBD for seizures and epilepsy have noted a lack of data regarding safety, effectiveness, and dosing.[18–20] Not only were subtherapeutic and inconsistent levels of CBD found, but also the presence of THC, which were attributed to the lack of regulation of dispensary products.[19,20]

For those whose seizures would benefit from CBD, this study supports the usage of the prescription formulation cannabidiol over CBD obtained from the internet or local sources. Given the large presence that dispensaries such as Charlotte's Web and Haleigh's Hope have online and the patina of legitimacy online sources give to dispensary products, the lack of detectable or therapeutic CBD in dispensary products is vitally important for clinicians, patients, and families to know. All of our patients taking CBD from these and other sources showed serum levels that were undetectable or well below the therapeutic range, which only begins between 100 to 150 ng/mL[15–17]; therefore, this minimal concentration suggests that there is no benefit to adding these products to a treatment regimen. The lack of side effects in our patients additionally supports this claim because adverse effects would only be seen in concentrations around or above the therapeutic range. Sleepiness was reported in 1 patient, but their CBD level was below the reporting limit, and they had recently initiated an antiepileptic drug to their regimen that was known to cause somnolence. Interestingly, some patients showed extremely small levels of THC, which was expected because the product they chose reported a small concentration of THC, but 1 patient with Texas Original showed a much higher concentration of THC than expected. This finding suggests that Texas Original may actually contain more THC than reported on their bottle label and website and highlights the lack of regulation over the dispensary CBD industry.

Limitations of this study include its small sample size and reliance on patient reports for dosage and any clinical or

adverse effects. The true effect of these dispensary products may not be ideally represented in this study; therefore, larger studies should expand upon the relationship between serum level and seizure control. Additionally, a deeper investigation into the content of each product will be beneficial in identifying the risks involved and encouraging regulation of such dispensary products. Finally, there are many more dispensary products on the market than those reported here. We only had access to the products that our patients were taking. Obtaining serum levels of every dispensary CBD product is helpful to guide the clinical decision making as we suspect some products may produce a more significant CBD serum level, which would be important to know when converting to prescription cannabidiol.

Conclusion

This study supports the clinical practice of obtaining serum levels of cannabidiol (and THC) in all patients treated with internet-based dispensary products. We found that all 18 of our patients had no therapeutic level and would potentially benefit from switching to prescription cannabidiol. Even those with a recorded serum level above the reporting limit of 1 ng/mL never achieved therapeutic levels of 100-150 ng/mL. The presence of THC above advertised levels in 1 patient also demonstrates the current lack of regulation of dispensary CBD. Knowing serum levels in patients taking dispensary cannabidiol may help in determining the starting dose for prescription cannabidiol when physicians discuss switching to the prescription formulation. Given that serum levels obtained with internet-based dispensary cannabidiol are likely to be nontherapeutic, it is very unlikely that dispensary cannabidiol contributes any to seizure control. Anecdotal reports of clinical effectiveness should be considered an effect of prescription antiseizure medications and not dispensary CBD.

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Supplemental Material

Supplemental material for this article is available online.

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