Cannabis in the Treatment of Pediatric Epilepsy

By Bonni Goldstein, MD

The author documents the progress of more than 100 patients using CBD-rich cannabis oil to treat seizure disorders.

I have been a medical cannabis physician seeing adult patients in Los Angeles for the past six years. Occasionally, I would be approached by parents who knew of my background and asked me to monitor their children’s use of cannabis. (As a doctor who trained in pediatrics and practiced pediatrics and emergency medicine for 12 years, I have considerable experience taking care of children.)

In the summer of 2013 I evaluated a few adolescents for use of cannabis as a teen-age boy with cancer; a teen-age girl who went through a horrific trauma and was suffering with PTSD, anxiety and depression and had failed all conventional treatment; a teenage boy with Tourette Syndrome; and an 11-year-old girl with autism.

The nature of my practice changed dramatically after Dr. Sanjay Gupta’s documentary aired on CNN in August 2013. Parents of children with intractable epilepsy wanted to know about CBD and cannabis as a possible treatment. They learned about my background on the Internet and asked if I’d be willing to treat their children. Many of the parents were connected on a pediatric epilepsy Facebook page, through which most of my current patients found my practice.

Epilepsy is not a rare disorder. In the United States, according to the Centers for Disease Control, some 2.3 million adults and 468,000 children (under 17) have epilepsy. Epilepsy in children is often a genetic or congenital condition. Epilepsy can start at any time in life from head trauma, infections, or tumors.

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Many parents who get seizure relief from pharmaceutical anticonvulsants suffer intolerable side effects. About one-third of epilepsy cases are “intractable”—meaning available pharmaceutical drugs do not control the seizures.

Between August 2013 and April 2014, I became the medical cannabis consultant to 93 children with intractable epilepsy. Their parents had, in the past, authorized searching for stem-cell treatment. These are families that are desperately searching.

My first pediatric epilepsy patient was a 14-year-old girl with Lennox-Gastaut Syndrome. Her parents had learned about CBD and signed up to be on the waiting list of Realm of Caring, the Colorado non-profit run by Stanley Brothers, whose “Charlotte’s Web” strain was shown to be very effective in the case featured by Dr. Gupta.

Procedures

Prior to coming into my office, parents are required to fax over their child’s medical records for review. They fill out a questionnaire and sign an informed consent form. We talk about medical marijuana and they’re tried, what has helped and what has not helped. Is there a typical pattern to the child’s seizures? Do they occur more when the child is awake or asleep? What kinds of seizures does the child have? How do the medications and seizures affect their development? Have they tried cannabis medication yet?

After the evaluation, I decide if the patient qualifies for medical cannabis based on California law and if I think the child may benefit from medical cannabis. If the answers to these two questions are yes, the child is approved and receives a letter of recommendation to use medical cannabis. The parents receive caregiver letters.

I educate the parents about what we know so far about CBD and the endocannabinoid system. It’s important that they realize that although all of the studies are lacking, there’s a scientific basis for what we’re doing.

I explain that I have very high standards for the medical cannabis, that we’re still testing to see if they’re effective and are also dose dependent. We do not titrate up to the highest dose rapidly. Instead, we start with a very low dose and increase it gradually. For the children that respond well to CBD treatment, we usually start with a dose of 2 – 6 mg per pound per day for many of the children that respond well to CBD treatment.

Some patients do need higher doses to achieve good results. One little boy was still having about 20 seizures a month on three anti-epileptic drugs. With Charlotte’s Web oil he became seizure free for six months at a dose of 7.5 milligrams per pound per day, and he has been weaned off almost all of the seizure medications.

In Colorado one patient has gone as high as 8 milligrams per pound per day.

Diagnosing using GW Pharmaceuticals’ Epidiolex reportedly have gone as high as 24 milligrams per kilogram per day in an FDA-approved context.

About Epilepsy

Epilepsy is a condition of recurrent, unprovoked seizures. The seizures may result from a hereditary tendency or a brain injury, but often the cause is unknown. Many patients are diagnosed with “idiopathic epilepsy” because “epilepsy” seems more serious or stigmatized. However, almost all seizure disorders are epilepsy. A person with epilepsy has had two or more unprovoked seizures, regardless of seizure type.

An estimated 65 million people worldwide are afflicted with epilepsy —some 2.2 million in the U.S. When seizures cannot be controlled by medication, epilepsy is said to be “refractory” or “intractable” or “treatment-resistant” or “catastrophic.” Approximately one-third of all epilepsy cases are refractory.

Types of epilepsy have been defined in terms of age of onset, seizure types and where they arise in the brain. EEG findings, family history, and neurological history, among other factors.

Seizures are characterized as “generalized” or “partial.” Generalized seizures begin with a widespread, excessive electrical discharge involving most or all of the brain. Partial seizures involve a more localized electrical discharge restricted to one region of the brain.

Simple partial seizures: An episode of altered sensation, cognitive function, or motor activity during which the patient is fully alert. Patients usually call these seizures “aura” and symptoms vary depending on the brain region involved.

Complex partial seizures: An episode altered behavior, sensation or motor activity during which alertness and responsiveness are also compromised. The motor activity may consist of repetitive automatic movements of the face or limbs, or “automatisms.” Often patients are unaware of these seizures.

A partial seizure can develop into a tonic-clonic or “grand mal” seizure.

Types of Epilepsy

Temporal Lobe Epilepsy

Frontal Lobe Epilepsy

Parietal Lobe Epilepsy

Occipital Lobe Epilepsy

Primary Generalized Epilepsy

Idiopathic Partial Epilepsy

Symptomatic Generalized Epilepsy

Progressive Myoclonic Epilepsy

Reflex Epilepsy

Febrile Seizures

BenignRolandic Epilepsy

Juvenile Myoclonic Epilepsy

Infantile Spasms

Landau-Kleffner Syndrome

Childhood Absence Epilepsy

Benign Occipital Epilepsy

Mitochondrial Disorders

Landau-Kleffner Syndrome

Rasmussen Syndrome

Hypothalamic Hamartoma & Epilepsy

Source: NYU Langone Medical Center Comprehensive Epilepsy Center
Treatting Pediatric Epilepsy from previous page

THC free preparation

Converting oil to THC-free preparation easiest for the patient giving a dose. When you’re giving close to four mil- ligrams per pound per day to a 50-pound child, you’re giving up to 200 milligrams. If the oil has only 15 milligrams per milliliter, you are giving that child a lot of oil. When you lower quantities, even healthful olive oil or coconut oil can cause diarrhea.

Many people think that seizure reduction is the goal, but it’s only part of the goal.

Many people think that seizure reduction is the goal of treatment, but it’s only part of the goal. The effects of the conventional anti-epileptic drugs (AEDs) can be debilitating, especially during developmental delay, loss of language and more. The ultimate goal for pediatric epilepsy patients is freedom from seizures and the side effects of the AEDs. Interestingly, many parents whose children are having success with CBD oil to treat epilepsy are also reporting that their children have improved sleep, improved appetite, more alertness, and developmental progress. It is these other beneficial effects that make CBD a wonderful option for children suffering with seizures.

Drug Interactions

CBD has not been shown to be a pro-convulsant in 21 preclinical and laboratory studies (see below). If a parent using CBD has an increase in seizure activity, it is likely from an interaction with other AEDs that the patient is taking. Drug interactions are very complex. Each patient is on a different drug regimen and/or special diet. There are many variables in the patient’s metabolism, the other medications, the patient’s endocannabinoid system, and the profile of the particular cannabis product.

CBD is an inhibitor of the P450 enzyme system, and affects the rate at which other drugs are metabolized. Unfortunately, research is lacking on how CBD interacts with most of the other anti-epilepsy drugs in the liver but there are some studies that have started looking at these very important reactions.

A reassuring fact has been reported by G.W. Pharmaceu- tica, the British company that makes Epidiolex, and also makes Sativex, which is 50% CBD and has been ap- proved for use in 27 countries to treat pain and spasticity from Multiple Sclerosis. Sativex has been used for 30,000 patient-years by people taking concommitant drugs and there have been no confirmed adverse consequences due to drug-drug interactions.

A journal article from 1977 suggested that CBD potenti- ated the actions of an anti-convulsant (Dilantin) and phenytoin, but reduced the anticonvulsant potency of Leprom, Clom- azepam, Trihexphenidole, and Ethosuximide. Limited studies have shown that some but not all pa- tients on CBD oil can have decreased Depakote levels and decreased felbamate levels with CBD. It appears that CBD interacts to increase Onfi (clobazam) levels. Some have reported that Onfi decreased.

THCA

THCA is the raw, unheated, non-psychoactive phytocan- nabinoid that converts to THC when heated. THCA has been shown to be a significant anti-inflammatory. It has not been tested in clinical trials but the CBD preparations that have some but not all its cannabinoids that she was on, she had an increase in number of seizures. After about one week, she improved and seizures reduced again. Parents report that after the first week, she was much more alert and responsive. And now the hope is that seizure re- duction due to CBD will resume.

Preliminary Findings

In June 2014 I reported on what I had learned about can- nabis in the treatment of pediatric epilepsy at events put on by the Realm of Caring Foundation and the Epilepsy Foundation of Los Angeles. I reviewed the charts of the 93 patients that I approved to use CBD oil for epilepsy and who had been on the oil for at least three months. Two-thirds of the children benefited from CBD testing and the second half reduction in frequency of seizures, and some were in the process of weaning off other medications.

Ten children were on AC/DC oil and the success rate was very similar – 31 out of 41 reporting reduction in frequency of seizures. One child in this group was seizure free.

Ten children were using other CBD-rich oils, obtained from small collectives. Six experienced seizure reduction.

Twenty-two of the families had not started oil and were waiting for Charlotte’s Web to become available.

Eight patients had started taking CBD-rich oil from other sources but had stopped, six for financial reasons.

Some patients do not show up as seizure- reduction statistics because the frequency of seizures hasn’t gone down — but severity and recovery time have gone down.

On average, the patients had been on 10 anticonvul- sants over the course of their young lives. At present there were on between one and four AEDs. Only one out of every 93 patients had not taking pharmaceuticals at the time I collated my data.

In worth repeating: some patients do not show up as seizure-reduction statistics because the frequency of seizures hasn’t gone down — but severity and recovery time have gone down. Parents may report, “When he has a seizure he’s not wiped out for three hours.” Each case is so individual.

Report to the Society of Cannabis Clinicians

In September 2014 I described my work with pediatric epilepsy patients to colleagues in the Society of Cannabis Clinicians at a meeting in San Francisco. I had by then seen 200 children with almost every type of Epilepsy diagnosis.

My patients are concurrently being treated by a pediatric-ian and a neurologist and may be seeing other specialists such as a gastroenterologist or a brain surgeon. All of them almost been categorized as “refractory” or “intractable” cases, meaning anti-epileptic drugs have not eliminated their seizures. Almost all have been multiple medications with no improvement.

A study published in the New England Journal of Medi- cine in 2000 showed that the chances of achieving free- dom from seizures diminishes sharply with each drug tried. Where sewerant is a child who was not on any oil drug they were treated with, the response to a second drug — either substituted or added — went down to 13%. The third drug helped only 4% of patients.

The burdens of refractory epilepsy include poor quality of life, the debilitating side-effects of medications, cogni- tive decline, physical injuries from falling, psychosocial dysfunction, a restricted lifestyle — adults can’t drive, which makes living in our society very difficult — and in- creased mortality: the idea that you’re going to drop dead any day now.

One piece of advice I have is that if you have a seizure today and are feeling well afterward, you should get to a hospital for an EEG. If they find that a lack of endocannabinoids is associated with loss of alertness and responsiveness, which is very helpful to some parents of children suffering from intractable epilepsy.

The side effects of the anti-epilepsy drugs described by my patients and their families include lethargy and somno- lence, loss of focus, learning and memory problems, loss of appetite and weight loss, and motor skills, insomnia, anxiety, and failure to thrive. Felbamate can cause aplastic anemia and or liver failure. Vigabatrin can cause irreversible vision loss.

Parents have reported that their child seemed to be tol- erating the first one or two drugs, but then they’ll add an- other drug and they stop talking and walking, it just shuts them down.

Endocannabinoids and Epilepsy

Epilepsy — like any given medical problem — will re- main “treatment resistant” if the prescribed medications are not targeting the appropriate metabolic system(s). There is ample evidence that the endocannabinoid system plays an important role in modulating excitatory signals in the brain.

To cite a few examples, in 2008, Hungarian research- ers compared tissue from epileptic patients who had de- cided to undergo neurosurgery to tissue from patients who died naturally. Controlling for age and health status, they found that the level of endocannabinoids in the tissue from patients who died naturally was higher in brain tissue from the cadavers. The strong implication is that a lack of endocannabinoids is associated with loss of neurotransmitter control.

In 2010 Andrea Romigi and colleagues at the Univer- sity of Rome tested spinal fluid from patients with newly diagnosed temporal-lobe epilepsy and found lower-than- normal endocannabinol levels. These studies and others suggest that some types of epilepsy are associated with an “endocannabinoid deficiency syndrome.” (The concept of an endocannabinoid deficiency syndrome underling many disorders was first proposed by Ethan Russo, MD, him- self a pediatric neurologist). Because CBD can enhance endocannabinoid tone with- out inducing psychoactivity, it became a compound of interest to far-sighted medical researchers. In the 1970s and ’80s, in addition to animal studies, there were several small, promising studies in Brazil of CBD as a treatment for people with seizure disorders.

A 1978 paper co-authored by Raphael Mechoulam de- scribed the treatment of nine patients — four with CBD (200 milligrams/day) and five with placebo. Two of the four CBD patients were seizure free during the test period and suffered no toxic side effects. None on placebo report improvement.

In 1980 J.M. Cunha et al treated 16 refractory tonic- clonic seizure patients with 300 milligrams of CBD per day. Of these, three became seizure free, four had seizure reduction, and one was unchanged. In the pla- cebo group, one patient had seizure reduction, seven were unchanged.

“It seemed very promising,” said Mechoulam looking back decades later, “but unfortunately, nothing has been done ever since. To the best of my knowledge, nobody has done any work on cannabidiol in the clinic on epilepsy, and I just wonder why?”

At the 2005 meeting of the International Association for Cannabinoids in Medicine, Italian researchers led by A. Pel- liccia described an open study (“modulatin administrata- tion and titration schedules on a case-by-case basis, ac- cording to clinical symptoms”). In which 18 children with intractable epilepsy were treated with a low dose of CBD in corn oil.

The results were very promising. No patients continud- ing to use CBD had a new or increased seizure. Two of them had a decrease of 25% or more. And, according to Pelllicia: “in all CBD-

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SOURCES: Dr. Goldstein’s unpublished results were part of her presentation to the Epilepsy Foundation of Los Angeles and the Realm of Caring Foundation in June. Approximately two-thirds of the pediatric epilepsy patients whose cannabis use she has been monitoring have experi-enced seizure reduction.
CBD acts in ways similar to various anti-epilepsy drugs listed at left. In this chart developed by AJ Hill and colleagues, signs indicate the relative strength of the interactions (row at top) that have been observed in the laboratory. “This is a slide that parents find very useful,” according to Goldstein. “Instead of having to take all these different drugs, they can get many of the benefits with one medication.”

There are only a few suppliers of oil that seem to be consistent bottle to bottle. There have been instances of CBD oil products having similar CBD content but having different effects, as they are prepared from different CBD strains. Having a producer who makes oil from one specific strain increases the likelihood of obtaining consistent medication from month to month. Certain terpenes (essential oils in the cannabis plant) are known to have beneficial medicinal effects. Beta Caryophyllene, a terpene that binds to the CB2 receptor, is a potent anti-inflammatory that appears to work synergistically with CBD. Both Charlotte’s Web and AC/DC strains contain high amounts of this terpene. Anybody who is making oil should know that parents will get it tested at two or three different labs so they know what is in the oil that they are giving to their child.

Having a reliable supply, one that is available and won’t be “out of stock,” is also crucial. Patients who start CBD treatment because they could not afford the oil. These parents state that development is arrested when their very young child has frequent seizures. With reduction of seizures, better sleep and appetite. One parent reported “better sense of smell.” Half have been able to wean AEDs. There were no reports of negative side effects.

Of nine patients with other genetic syndromes, ages two to 17 years, one was seizure free. Four reported 75%-90% reduction in frequency. Three reported 50% reduction. One reported no change. Most reported improved alertness, better sleep and appetite. One parent reported “better sense of smell.” Half have been able to wean AEDs. There were no reports of negative side effects.

The database is currently limited to five CB2 patients, ages nine to 18 months. All five had 100% reduction. (Gedde notes that the CBD oil provider in Southern California at this time [September 2014].)

Of the 21 projects involving CBD or CBDB did researchers see a proconvulsant effect. In none of the 21 projects involving CBD or CBDB did researchers see a proconvulsant effect. In none of the 21 projects involving CBD or CBDB did researchers see a proconvulsant effect. In none of the 21 projects involving CBD or CBDB did researchers see a proconvulsant effect. In none of the 21 projects involving CBD or CBDB did researchers see a proconvulsant effect.