

Case Study Report 1

Cannabidiol Oil trial in Adult Female with Uncontrolled Epilepsy

Introduction

Cannabidiol/CBD has recently come to prominence in the media as a treatment for a variety of ailments, ranging from reduction of simple mechanical pain e.g. knocks and bruises, to a cure for cancer. It is a derivative of the hemp/cannabis plant, without the active ingredient (tetrahydrocannabinol/THC) that induces the cannabis "high" (Wray et al., 2017). There is a plethora of anecdotal "evidence" to be found on the internet, with the suggestion that it can help almost any condition, including epilepsy, musculoskeletal pain, and Post Traumatic Stress Disorder (PTSD). It is available in a wide range of strengths and qualities, from back street herbalists to medical grade suppliers (Halperin, 2018).

Epilepsy is a condition typified by so called electrical storms or seizures in the brain. Causality varies. There may be a genetic cause in some people, but genetic testing isn't yet available for many types of epilepsy. About 30% of epilepsy is caused by a change in the structure of the brain. Brain infections can leave scarring on the brain that can cause epilepsy onset at a later stage. Head injuries can also lead to epilepsy, and later in life, strokes and tumours may be the cause, as can Alzheimer's disease and other neurological conditions (Schacter et al., 2013)

The research done and published to date with cannabinoids documents some positive outcomes in research and treatment of mostly childhood epilepsy, central nervous system problems and psychotic disorders, although much of it is based on self-reporting by users/parents of children with epilepsy (Devinsky et al., 2016; Porter and Jacobsen, 2013; Palmieri et al., 2017).

Latterly, as interest has risen in self-reported improvements and anecdotal evidence, research has progressed to more robust controlled trials (Devinsky, Patel et al., 2018). There continue to be interesting studies in animals *for example* research on CBD in mice relating to Huntington's Disease (Consroe et al., 1991; Valdeolivas et al., 2015) but these cannot yet be extrapolated to the human population.

It is known, following extensive research into the properties of cannabis and related products, which includes CBD oil, that the body has 2 types of cannabinoid receptors which are distributed throughout the central nervous system (CNS) (Rosenberg et al., 2015). These receptors have an important role in the control of transmission across synapses and the regulation of neural firing (Mechoulam and Parker).

A study found that anandamide, an endogenous substance which interacts with cannabinoid receptors (Di Marzo et al., 2002), was reduced in adults with recently diagnosed temporal lobe epilepsy (Romigi et al., 2010). CBD has been shown to stop electrically induced seizures in mice (Consroe et al., 1991).

A 2017 trial with cannabinoids in childhood epilepsy which was randomised, controlled and double blinded, showed a reduction in seizures with a significance of +-50 (Devinsky et al., 2017) but a critic of the trial (Peruca 2017), says that this may be more due to CBD and drug interaction with clobazam which the patients were already taking.

In epilepsy, there is some evidence that CBD administration can interact with clobazam, causing drowsiness, therefore adding a caution to patients already taking this drug for their epilepsy. However, the increased drowsiness experienced was eliminated by reducing the

clobazam dosage (Geffrey et al., 2015). The only other adverse effects of CBD have been elevation in liver enzymes, much more frequently with those taking sodium valproate, but these levels returned to normal after a few weeks of using CBD products (Devinsky et al., 2016; Devinsky et al., 2017; Thiele et al., 2018).

General CBD information

CBD has an initial half-life of 6 hours, as it is digested, and then an additional 24-hour half-life as it is slowly distributed into tissues (Welty et al., 2014).

There is some evidence that CBD becomes more bio-available if ingested at the same time as food, but this was research done with a nasal spray also containing THC (Sativex®), approved in some countries for the reduction of spasticity in Multiple Sclerosis (Stott et al., 2013) so may not be relevant to oral administration (Peruca 2017).

Trial dosages have been from 10 mg per kilo to 20 mg CBD per kilo body weight, with adverse effects in the higher dosage groups, mostly somnolence and decreased appetite (Devinsky et al., 2017)

There is no evidence of withdrawal symptoms after medication with CBD (Devinsky et al., 2017). Treatment with NSAIDs for pain has been shown to increase likelihood of gastrointestinal ulcers and bleeding, myocardial infarction and strokes (Fitzgerald 2004; Topol 2004), but none of these increased risk factors has been found with CBD (Stott et al 2005).

Cannabinoids may offer significant “side benefits” beyond analgesia. These include anti-emetic effects, well established with THC, but additionally demonstrated for CBD (Pertwee 2005), the ability of THC and CBD to produce apoptosis in malignant cells and inhibit cancer-induced angiogenesis (Kogan 2005; Ligresti et al 2006), as well as the neuroprotective antioxidant properties of the two substances (Hampson et al 1998), and improvements in symptomatic insomnia (Russo et al 2007).

There are some concerns about quality control and variability of products available to the general public, as most adult patients self-medicate with CBD products (Peruca, 2017).

This author has been unable to find any published research available in adults for uncontrolled epilepsy. It was felt that case study research in CBD for adult uncontrolled epilepsy would add to the existing research base, whilst potentially helping this subject to get symptomatic relief.

History

This case involves a 34-year old adult female who has had uncontrolled epilepsy since 2004. Her diagnoses varied for a few years, from epileptic to non-epileptic seizures and back again, with various differing medication regimes. She was finally diagnosed with “comorbid” epilepsy, a combination of frontal lobe, complex parietal lobe and non-epileptic seizures, in 2015.

Her epilepsy has resulted in at least 10 episodes of hospitalization in the past 12 months. Her seizures are of three different types, which she describes as: 1) complex, big/massive, usually falls to the floor and moves around a lot, with drooling and /or tongue bite. Followed by sleep for 20 minutes to 2 hours, with a big headache and aches in the right side of her body afterwards 2) Focal partial, not so big, less intense/shorter (sometimes) but otherwise similar to type 1). Sleeps for about 20 minutes afterwards 3) non-epileptic, absence, feels

disconnected. Followed by confusion, sometimes tiredness and slight headache, with some memory loss from seconds/minutes pre-seizure.

Medication consists of Keppra/levetiracetam 1500 mg twice daily, Lamotigrine 200mg twice daily, Lacosamide 150mg twice daily, fluoxetine 40mg once daily

She has been married for 10 years and has a four-year-old daughter.

It is postulated that increasing cannabinoids in this subject's system may help in reducing epileptic seizure activity.

Tests And Measurements

Prior to the start of the trial, the subject was asked to keep a seizure diary, as supplied by the UK epilepsy society (Epilepsy Society 2016 and smartphone app) to provide a baseline number of seizure episodes over a four-week period prior to the commencement of the trial. This showed fits from 1-6 times per week (mean average 3.5), with no warning that they were coming on. She was hospitalised 3 times in the 4 weeks prior to the trial.

Table 1 Pre-trial scores

	Pre
Fit Frequency (per week)	1 to 6
Fit Frequency Change %	

Treatment

The subject was supplied with an EVR 25% 10 ml airless metered pen and instructed to use it once daily for 6-8 weeks, and to take an additional dose if she knew that she was about to have a fit; or get another adult to administer it during fits.

Subjective reporting was that during the trial, there was a gradual decrease in fit frequency and episodes of hospitalisation. She was now able to tell when a lot of her fits were about to start and was able to self-medicate with an additional dose of CBD oil and prevent or curtail them. Her husband had been unable to administer doses during fits.

Results

There had been a mean average 100% decrease in fit frequency (from mean average 3.5 to mean average 0 seizures per week). She was hospitalised only once in the final four weeks of the trial.

Subject reported she was unwilling to stop using CBD products as she felt so much improved, so kept the remains of the contents of the metered pen to use in case she could feel a seizure coming on and bought some low percentage (un-stated) CBD oil from a local shop to take twice daily. Four weeks post trial, she has had only one seizure, but it was a severe one and she was hospitalised. She puts this down to over-heating whilst on holiday.

Table 2 Post-trial scores

	Pre	Post
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Fit Frequency (per week)	1 to 6	0
Fit Frequency Change %		100.00%

Discussion

There can be no doubt that the CBD product used by this subject was exceptionally effective in decreasing epileptic and non-epileptic seizure activity, as she had a 100% reduction in seizure activity.

There would appear to be a benefit in taking a higher percentage CBD product for several weeks, and then moving to a lower 'maintenance dose'.

The exact dosages required to terminate seizure activity will probably differ from subject to subject, but this study shows potentially very encouraging results for adults with uncontrolled epilepsy. Further research with double blinded and controlled trials and large patient numbers is suggested.

Author Notes

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These Case Studies are a result of being asked to provide CBD products for sale in the practices. This was not possible without knowing the possible benefits or side effects. Since there was little evidence other than anecdotal, or in children, or using products containing THC, the case studies were the only way to provide the information necessary to consider offering the products for eventual sale.

The samples used were provided free on request from EVR, with no expectation of reward, sales or endorsement.

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