Case Study Report – Subject 3

Cannabidiol Oil trial in Adult Female with Complex Post Traumatic Stress Disorder and Pain

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).

Post-traumatic stress disorder (PTSD) is a psychological condition caused by witnessing or being involved in traumatic events e.g. physical/sexual assault, military combat, natural disasters (www.nhs.uk 2015; Bailey et al., 2013).

It is typified by symptoms which last for over a month after the event (Bailey et al., 2013), with reliving of traumatic memories through flashbacks or nightmares, sometimes with feelings of isolation, guilt and irritability, insomnia, and concentration problems (www.nhs.uk) avoidance and numbing, alteration in physical and emotional reactions and hypervigilance (Mayo Clinic 2018) (Nebraska Department of Veterans Affairs, 2007).

Complex PTSD is more likely to be diagnosed in adults and children who had traumatic experiences in early childhood e.g. violence, abuse or neglect; whose trauma went on over a period of time; whose abuse was caused by a parent or carer; who still have contact with their abuser/s; who were isolated during the trauma (www.nhs.uk). In adults it can occur as a result of prolonged trauma e.g. kidnap or torture scenarios. It can take years for the symptoms of complex PTSD to be recognised, and a child’s development can be altered. The earlier the age, the worse the trauma. (Royal College of Psychiatry 2015).

PTSD is prevalent in the US population, at approximately 8-14% (Davison et al., 1991. Kessler et al., 1995. Breslau et al., 1998), with twice as many cases in females compared with males (Breslau et al., 1998. Resnick et al., 1993). This author was unable to find comparative data for the UK.

Pharmacological treatment is based on selective serotonin reuptake inhibitors (SSRIs) or selective noradrenaline (norepinephrine) combined with cognitive behavioural therapy, (Benedek 2009) but response rates are low, with only 20-30% clinical remission, and poor comparison to placebo in trials Davidson 2006. Friedman et al., 2007).

Medication in PTSD has been largely based on observation of drugs approved for other conditions, (no drug has been developed specifically for treatment of PTSD) and there are limited effective treatment options in chronic PTSD (Papini et al., 2015).

The cannabinoid receptor system, along with other receptors, has been shown to play a crucial role in fear patterns (Ruehle et al., 2012). A study where PTSD symptoms were induced in mice by scaring them with a cat showed a reduction in histological changes at the hippocampus and frontal cortex following use of CBD (Campos AC et al., 2012). A gender difference has also been shown in animals (Reich et al., 2009. Suarez et al., 2009)
supporting the figures for higher incidence of PTSD in human females (Galovski et al., 2013, McGregor et al., 2017).

Papini et al., 2015 stated that a review of current research done in humans with PTSD using CBD showed inconsistent results. Shannon et al., (2016) cite a case of successful outcomes with cannabidiol oil for a child with PTSD.

Blessing et al., 2015 state that the evidence from preclinical and human experimental trials reviewed by them ‘strongly supports CBD as a treatment for generalized anxiety disorder, panic disorder, social anxiety disorder, obsessive-compulsive disorder, and post-traumatic stress disorder when administered acutely; however, few studies have investigated chronic CBD dosing.’ They suggest the need for more study, particularly of chronic PTSD cases.

**Pain** is described as an "unpleasant feeling that is conveyed to the brain by nerves in the body" (Health of Children 2018) which can arise from multiple causes such as injury, illness, or as a co-symptom with a psychological condition, or from no known cause.

Pain sensation is used to signal potential or actual damage to the body, by triggering protective responses, but it may cease to be simply a warning system and become chronic and debilitating instead (Julius and Basbaum 2008).

According to McCaffrey (1999), quoted in Pasero, 2009, “Pain is what the experiencing person says it is, existing whenever he says it does”. A web article aimed at medical students (Symptoms and Descriptions of Pain, 2018) states that the commonest descriptors of pain level are mild, bad, severe, violent and excruciating. These are then given other descriptors to explain the sensation for example stabbing, cutting, stinging, burning, boring, splitting, colicky, crushing, gnawing, nagging, gripping, scalding, shooting, throbbing, cramping, radiating, dull, sharp, localized, general, persistent, recurrent, chronic. Patients may complain of insomnia, dizziness, nausea, anorexia or heartburn, restlessness and fatigue (Symptoms and Descriptions of Pain, 2018).

Russo (2004) suggested that endocannabinoid deficiency may be a factor in some treatment-resistant pain subjects and conditions, supported by research by Sarchielli et al. (2006) which found a decrease in anandamide levels in patients with migraine.

Cannabinoid receptors CB1 (Howlett et al. 1988)and CB2 (Munro et al., 1993) are distributed widely throughout the body, but the CB1 receptor is present in more areas, especially in the nociceptive areas in the central (Herkenham et al., 1990; Hohmann et al. 1999) and peripheral nervous systems (Fox et al. 2001; Dogrul et al., 2003). There is a direct link between the action of the CNS and peripheral nervous system receptors (Dogrul et al., 2003).

Cannabinoids are 10-fold more efficient in thalamic pain mediation than morphine receptors (Martin et al., 1996). Experiments in mice suggest that peripheral CB1 nociceptors are more important in pain perception than central ones (Agarwal et al., 2007) and stimulation of CB1 receptors decreases pain, hyperalgesia and inflammation.

CBD also promotes signalling of the A2A adenosine receptor which may additionally explain its inflammatory and analgesic effects (Carrier et al. 2006). Malfait et al. (2000) demonstrated inhibition of the TNF-α tumour necrosis factor in rodent models of rheumatoid arthritis by CBD.
CBD Blocks hyperalgesia in substance P mechanisms (Li et al., 1999), and by inhibiting calcitonin gene-related peptide (Richardson et al., 1998). It also has a higher anti-oxidant function than vitamins C and E (Hampson et al., 1998). CBD has been recognised as the first clinically available endocannabinoid modulator (Russo and Guy 2006).

Trials done in Canada with Sativex® (GW Pharmaceuticals), a whole cannabis spray for oromucosal use (Russo and Guy 2006) have shown that this product, compared with placebo and THC extract, gives significant improvements in opiate non-responsive pain in cancer subjects. The suggestion is that it is therefore the CBD component of Sativex®, rather than the THC component that is necessary for pain relief (Johnson and Potts 2005). Sleep patterns in chronic pain subjects have also improved with this product in nearly all random controlled trials (Russo et al., 2007). Treatment effects ceased after 7-10 days when medication with Sativex® was stopped, but symptom control was easy to re-establish by taking the medication again (Wade et al., 2006).

**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 gastro-intestinal 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).

Research for PTSD and pain, as cited above, has been done mostly with THC containing compounds, so it was felt that case study research with CBD oil may add to the existing knowledge base.

**History**

This case involves a 56-year old adult female who was diagnosed with complex PTSD in 2000, and has ongoing pain following a car crash in 2010.

The PTSD symptoms started after recovery of memories of childhood abuse. She was diagnosed with complex Post Traumatic Stress Disorder (PTSD) and subsequently with
Disassociative Identity Disorder (DID) in 2016 and has been under the continuing care of her GP for medication. She has had multiple interactions with counselling services since initial diagnosis of PTSD in 2000.

Unremitting pain began following a car accident, where the car rolled over several times following a skid in ice/snow. Because of her history of PTSD, she has poor self-care strategies, and failed to seek appropriate treatment until 2017, when she began a weekly course of physiotherapy because the pain was increasing, spreading to other structures and limiting her capacities. She reports a decrease in pain of about 25% of previous following this treatment, which stopped a few weeks prior to the CBD trial. She has problems with her left foot, including ‘giving way, suddenly, pain in certain prolonged positions ie high heels, and reduced balance. She has right pelvic pain, right thoracic pain with nerve involvement, almost constant head and neck pain, low back pain and bilateral leg pain with regular cramp.

Medication consists of venlafaxine 50mg x 1 daily for the PTSD and regular self-medication with ibuprofen and paracetamol PRN for pain.

She is in the middle of divorce proceedings from her marriage in 2013 and has been living with her current partner for a year. She runs two businesses and travels abroad extensively for work.

It is postulated that increasing cannabinoids in this subject’s system may help in controlling PTSD symptoms and reducing pain.

**Tests And Measurements**

The McGill Pain Questionnaire (Melzack 1975) was administered to establish pre-trial pain levels.

Self-reported pain in multiple areas: left foot, constant head, cervical, thoracic and leg pain with cramp, and regular low back pain.

A PTSD test (Weathers et al., 1994) was administered to establish pre-trial PTSD levels. Self-reported pain in multiple areas: left foot, constant head, cervical, thoracic and leg pain with cramp, and regular low back pain.

Self-reported PTSD symptoms were ‘moderate’.

**Table 1 Pre-trial scores**

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<td>PPI</td>
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<td>NWC</td>
<td>15.00</td>
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Pain Perception Index (PPI) at 3, discomforting, on the McGill Pain Questionnaire. This is the patient’s perception of their pain level, with a choice of six options, ranging from 0 – none to 6 – excruciating (Melzack 1975).

Number word count (NWC) 15.
This is the number of descriptive words chosen for pain, from a possible maximum total of 78. The descriptive words are also in categories for sensory perception of pain, affective, emotional and miscellaneous. Higher numbers here indicate more perceived pain (Melzack 1975).

Pain score 32.54 on the McGill Pain Questionnaire. This is the total score for all categories, from a possible maximum total of 214 with each word being multiplied by a ranking for each section. An example for this subject would be the word ‘tiring’ which has a ranking of 1 and a multiplier of 1.74, or ‘hurting’, which has a ranking of 3 and a multiplier of 0.72 (Melzack 1975).

PTSD score of 66 on the PTSD Checklist (Weathers et al., 1994).

**Treatment**

The subject was supplied with an EVR 22% 10 ml airless metered pen and instructed to use it once daily for 6-8 weeks, and a jar of EVR Premium Hemp Oil CBD Salve to use topically at pain sites.

Subjective reporting was an admission to only using the pen when the pain was bad enough to remind her to do something, rather than taking it daily as instructed. She used the topical salve and reported that it gave good relief of pain when applied.

**Results**

PPI remained the same, at 3, ‘discomforting’, on the McGill Pain Questionnaire possibly because of bilateral shoulder pain, which had not been present at the beginning of the trial. This is the patient’s perception of their pain level, with a choice of six options, ranging from 0 – none to 6 – excruciating (Melzack 1975).

Number word count (NWC) had decreased from 15-13 possibly due to an alteration in the number and types of pain site.
This is the number of descriptive words chosen for pain, from a possible maximum total of 78. The descriptive words are also in categories for sensory perception of pain, affective, emotional and miscellaneous. Higher numbers here indicate more perceived pain (Melzack 1975).

Pain levels had reduced by 15.77% (non-significant) on the McGill Pain Questionnaire.
This is the total score for all categories, from a possible maximum total of 214 with each word being multiplied by a ranking for each section. An example for this subject would be the word ‘tiring’ which has a ranking of 1 and a multiplier of 1.74, or ‘hurting’, which has a ranking of 3 and a multiplier of 0.72 (Melzack 1975).

PTSD score (Weathers et al., 1994) had dropped to 44 from 66.

Score still indicative of PTSD presence, but there was a slight improvement in all areas, and improvement to non-symptomatic in the areas of “loss of interest in previously enjoyed activities” and “feeling distant or cut off from other people”.

Subject reported that nightmares were episodic during the trial, rather than every night but increased when stress levels were higher. “Loss of interest in previously enjoyed activities” stopped being an issue during the trial and had not returned by 3 weeks post trial, which had improved perceived quality of life.

Previous head pain had gone completely, previous right cervical pain was now occasional instead of continuous, low back pain was rare, leg pain had gone.

Regular cramp still present, thoracic pain unaltered and developed bilateral shoulder pain which hadn’t been present previously. This was attributed to a huge increase in driving. The salve was effective in reducing this “by about 75%” when applied.

The subject reports that she felt that the products supplied to her for the trial had been partially effective, and she would use them again, and more regularly now that she had been reminded to use them daily, to see if all of her symptoms could be further improved.

A preference for an oral CBD product in tablet form was expressed due to disliking the taste of the oil.

Table 2 Post-trial scores

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<th>Pre</th>
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<tbody>
<tr>
<td>PPI</td>
<td>3.00</td>
<td>3.00</td>
</tr>
<tr>
<td>NWC</td>
<td>15.00</td>
<td>13.00</td>
</tr>
<tr>
<td>PRI</td>
<td>32.54</td>
<td>27.41</td>
</tr>
<tr>
<td>Anxiety Screening</td>
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<td>n/a</td>
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<tr>
<td>PTSD Screening</td>
<td>66.00</td>
<td>44.00</td>
</tr>
<tr>
<td>Change in Pain Levels</td>
<td></td>
<td>15.77%</td>
</tr>
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Discussion
This subject was non-compliant with the case study protocol in that she failed to take the CBD product supplied daily for the course of the trial period. This may be a continuing example of her poor self-care strategies, which cannot be examined in this study.

There was a statistically insignificant reduction in pain scores, although the latter may have been skewed by development of severe shoulder pain which had not been present previously and be affected by intermittent use of the product.

The study protocol was flawed in respect of the CBD topical product. There is no way to separate its potential effects from those of the oral product, and any results that may have been suggested can only be taken as anecdotal. Further double-blinded, controlled trials with large participant numbers are suggested to judge the efficacy of the topical product in isolation from the oral product.

Use of the products was intermittent throughout the trial however there was still a good reduction in the PTSD score, which is potentially very encouraging for other adults with this condition.

Further research is therefore suggested especially in the use of CBD products for PTSD.

**Author Notes**

Jane S. Campbell BSc (Hons) qualified as an acupuncturist in 1985, added cranio-sacral therapy training to advanced level and subsequently did a BSc Professional Studies in Healthcare at Teesside University in 1992. She has private practices in Guisborough, North Yorkshire, UK, and in Rhodes, Greece.

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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