Case Study Report 4

Cannabidiol Oil Trial in Adult Male with Anylosing Spondylitis 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, musculo-skeletal 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).

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, 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 CB_1 (Howlett et al 1988)and CB_2 (Munro et al 1993) are distributed widely throughout the body, but the CB_1 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 CB_1 nociceptors are more important in pain perception than central ones (Agarwal et al 2007) and stimulation of CB_1 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 1998a). 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).

Ankylosing Spondylitis is an inflammatory disease which affects the skeleton. It is more prevalent in men than women (Mouyis and Keate, 2012) and onset is usually in young adults.

It is typified by low back pain and morning stiffness, which improves with movement or exercise. In most cases, symptoms gradually spread to the cervical and thoracic spine, and other joints may be involved eg hips and knees. Some cases develop a severe disease process with unremitting pain (McKenna 2010).

There is a genetic association with the HLA B27 antigen, though many people who have the antigen do not go on to develop the disease (McKenna 2010).

CBD research in ankylosing spondylitis per se is rare, but studies have shown beneficial anti-inflammatory effects of CBD and THC at cellular level via modulation of cytokenes (Nagarkatti et al., 2009).

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 in pain, as cited above, has been done mostly with THC containing compounds, so there is a case for more study with CBD oil only. There is no meaningful research for the use of CBD in ankylosing spondylitis.

History

This case involves a 32-year-old adult male with ankylosing spondylitis. He has daily low back, thoracic and cervical pain and intermittent hip and knee pain. Morning stiffness.

Medication consists of Simponi injection once monthly, and ibuprofen PRN.

He has been married for 5 years, with two young sons. He is a primary school deputy headmaster with an active social life based around his family and local church.

It is postulated that increasing cannabinoids in this subject's system may help in reducing ankylosing spondylitis-related pain.

Pre-trial

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

Self-reported moderate pain levels.

Table 1 Pre-trial scores

PPI	3.00
NWC	20.00
PRI	44.71
PR1 S	31.06
PR1 A	5.22
PR1 E	6.06
PR1 M	2.37
Anxiety Screening	n/a
Change in Pain Levels	

Subject reported pain in jis thoracic and lumbar spine, and pelvic region.

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) 20 on the McGill Pain Questionnaire.
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 44.71 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 different ranking applicable to each section. An example 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. Higher numbers indicate more severe levels of perceived pain (Melzack 1975).

Trial

The subject was supplied with a bottle of 10% (1000 ml) Cherry CBD oil, with instructions to take it daily and a jar of EVR Premium Hemp Oil CBD Salve to use topically at pain sites.

No reporting during trial from this subject.

Post-Trial

Pain Perception Index (PPI) at 2, 'mild', on the McGill Pain Questionnaire, a drop from the previous 3, discomforting. This is the patient's perception of their pain level, with a choice of six options, ranging from 0 – none to 6 – excruciating

Number word count (NWC) 12, lower than the previous 20 . 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.

Pain score 22.15 on the McGill Pain Questionnaire, a significant decrease of 50.46% from the previous overall score of 162.35. This is the total score for all categories, from a possible maximum total of 214 with each word being multiplied by a different ranking applicable to each section. An example 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. Higher numbers indicate more severe levels of perceived pain.

Subject reported that he didn't feel that the CBD product used had been helpful, either topically applied or orally administered. His wife had applied the salve to the whole of his back on several occasions without a noticeable decrease in his pain levels. (His wife however reported using it for her own persistent thumb and low back pain with excellent results, although she wasn't part of this trial.)

The subject attributes his improved pain scores to a new programme of gym exercises for four days every week beginning 3 weeks into the trial. He reported that gym days were good days and continue to be so after the end of the trial. Based on his experience, he would not buy the products as supplied for the trial in future.

Table 2 Post-trial scores

NWC	20.00	12.00

PRI	44.71	22.15
PR1 S	31.06	17.43
PR1 A	5.22	1.74
PR1 E	6.06	1.01
PR1 M	2.37	1.97
Anxiety Screening	n/a	n/a
Change in Pain Levels		50.46%

Discussion

This subject had a significant reduction in pain but it he attributed this to his new exercise regime. This is entirely possible, as exercise is known to improve the function and pain levels in patients with ankylosing spondylitis. There is a possibility that the combination with CBD enhanced this effect, but it cannot be proven by this study.

The effects of oral CBD products in this trial can be neither proved or disproved.

No beneficial affects were shown for the topical CBD products, and in any case, 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.

Further study on the effects of oral CBD products in ankylosing spondylitis are suggested, at a higher dose, and with no other changing parameters in eg lifestyle to obfuscate the results.

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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Ends …