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Medical Cannabis for Adult Attention Deficit Hyperactivity Disorder: Sociological Patient Case Report of Cannabinoid Therapeutics in Finland

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Keywords

Cannabinoid therapy · Attention deficit hyperactivity disorder · Case report · Finland · Qualitative research

Abstract

This paper presents a detailed patient case report of a male patient who was diagnosed in adulthood (aged 33) with attention deficit hyperactivity disorder (ADHD) and treated initially with immediate-release methylphenidate (Ritalin® 10 mg twice daily). After experiencing adverse effects from prolonged use of this medication and afterwards other medications that were prescribed as alternatives, the patient discovered that cannabinoid therapeutics (CT) had been experimented inside the EU area to treat patients with ADHD. Subsequently, he was evaluated by a physician in Germany (June 2010) who prescribed CT (Bedrocan®, Bediol®). A Finnish neurologist later confirmed the two prescribed medicines (Bedrocan®, October 2010; Bediol®, May 2011) in the patient's own country of permanent residence (Finland). During a 5-year period of access, Bedrocan®, which mainly contains Δ9-tetrahydrocannabinol (Δ9-THC), was found to be helpful in alleviating the patient's ADHD symptoms, in particular poor tolerance to frustration, outbursts of anger, boredom, and problems related to concentration. The second CT medication, Bediol®, which contains both Δ9-THC and the phytocannabinoid cannabidiol, was found to neutralize the excessive dronabinol effects of Bedrocan® as well as zo offer other medical benefits (e.g., improved sleep). In addition to the case report, this paper also offers a brief review of the literature surrounding the medical benefits of CT for AD(H)D, which includes observational studies, clinical case reports, and one randomized clinical experiment. This paper also briefly discusses the endocannabinoid system in relation to ADHD, although more preclinical and clinical research is warranted to establish the optimal levels of cannabinoids, terpenes, and dosing regimens, which vary between different ADHD patients.

Introduction

There are numerous qualitative and quantitative studies as well as a recent online study [1] reporting an association between attention deficit hyperactivity disorder (ADHD) and cannabis use [2–4]. Many studies, however, often interpret cannabis use as nonmedical, "recreational," and/or drug abuse, not as a potential, albeit often illegal, form of (self-)medication. As with all medicines, the potential harms – and the risk of developing a substance abuse disorder – should be considered, especially for this patient group [5]. Nonetheless, it has been demonstrated that use of (non)medical cannabis can also help to keep

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adult individuals with ADHD away from other more harmful substances, like cocaine [6]. Observational studies have shown that medical cannabis patients in general use cannabinoids as a substitution for alcohol, illicit drugs, and/or commonly used prescription drugs for better symptom management, as well as to experience fewer side effects [7, 8].

This paper offers a medical sociological case study of a Finnish resident adult male diagnosed with combined-type ADHD. He was treated with standardized cannabinoids in botanical (whole-plant) form between 2010 and 2016, after experiencing adverse effects from immediate-release methylphenidate. The patient was prescribed cannabinoid therapeutics (CT) initially by a physician practicing in Germany, and the prescriptions were later confirmed by a Finnish neurologist. In December 2010 and in May 2011 the Finnish Medicines Agency (Fimea) authorized the patient's access to Bedrocan® and Bediol®, respectively, which he used on a daily basis until 2016.

A single detailed case study, although not generalizable to wider patient populations, brings important insights to further develop clinical practice and research around CT for adult ADHD patients. For a comprehensive review of cannabinoids in other neurological and mental health conditions see Fattore [9]. Before presenting the case report, this paper offers a brief review of the literature surrounding the medical benefits of CT for ADHD, which include observational research, clinical case reports, and one randomized clinical trial. This paper also briefly discusses the endocannabinoid system (ECS) in relation to ADHD. For a more comprehensive review of the ECS and impulsive behavior, see Wiskerke and Pattij [10].

Surveys and Qualitative Studies

In the author's previous study, an online survey with a convenience sample of university students in Amsterdam (n = 113), the following qualitative answer was given by a respondent who identified himself as having ADHD in an open-ended question [11]:

> Ritalin made me very slow and unable to concentrate. Cannabis on the other hand creates a state of hyperconcentration (which is more common amongst ADHDers). So it helps me sit still and read and helps me when writing essays. When in a state of hyperconcentration I write 2,000 words in an afternoon easily.

In *Marihuana, the Forbidden Medicine*, Grinspoon and Bakalar [12] offer a similar type of report from a California State University student using cannabis for his attention deficit disorder. Also, in a demographic survey of 4,117 cannabis users in California who applied to access medical cannabis between 2001 and 2007, the researchers state that "a significant percentage of male applicants under 30 had been treated or evaluated for treatment with Ritalin or other stimulants for attention deficit hyperactivity disorder (ADHD) as children and their histories of a preference for morning use of minimal amounts *(of cannabis)* strongly suggest that inhaled cannabis enhances their ability to concentrate" (italics added by the author for clarity) [13].

In a six-country survey of (illegal) cannabis cultivators, ADHD was the fifth (15.3%, n = 2,070) most commonly reported medical reason to grow and use cannabis, the most common ones being depression/anxiety and chronic pain [14]. According to the study, "Scandinavian growers seem to use cannabis for the treatment of ADHD more often than growers in other countries" [14, p. 253]. In a qualitative interview study of 100 (illegal) cannabis users in Norway, alleviating ADHD symptoms was the most common medical motive reported by the users [15].

Clinical Studies and Case Reports

In Germany, there was a detailed clinical case report in 2008 that depicted the medical benefits of cannabinoids, especially Δ9-tetrahydrocannabinol (Δ9-THC), for an adult male ADHD patient who had previously been unsuccessfully treated with methylphenidate [16]. In a larger series of clinical cases, also done in Germany with 30 treatment-resistant adults with ADHD, it was found that medical cannabis was helpful for a variety of symptoms, including improved concentration and sleep as well as reduced impulsivity [17]. Seventy-three percent (n = 22) preferred to use only cannabinoids after the study, while 27% (n = 8) continued to combine cannabinoids with other stimulant medications. The researchers also noted that "Many patients were diagnosed before with cannabis use disorders by psychiatrists in hospitals or medical practices due to misinterpretation of effective illegal self-medication. Patients reported that their therapeutic experiences were not taken seriously by most physicians and that they were not listening to them due to strong prejudices." The researchers conclude that "for adult patients with ADHD, who experience side effects or do not profit from standard medication, cannabis may be an effective and well-tolerated alternative."

So far, there is only one controlled study on cannabis-based medication in ADHD [18]. A formal clinical trial in the UK treating adult ADHD patients with the Sativex Oromucosal Spray®, a cannabinoid medication containing a 1:1 ratio of Δ9-THC to cannabidiol (CBD), found

that despite there being no statistically significant difference in the primary outcome of cognitive performance and activity level (measured by QbTest), the overall trend was that the active group (n = 15) achieved better results than the placebo group (n = 15) and reported reduced hyperactivity/impulsivity symptoms as well as improved emotional lability [18]. Further studies with other CT are warranted, as at least in Finland, the price of Sativex Oromucosal Spray® is a barrier for many patients.

The ECS and ADHD

ADHD is a multifaceted disorder involving multiple genes as well as neurobiological and environmental factors [19] in its age-related development and treatment. Recently increased attention has been given to the role of the ECS in ADHD. For instance, children with ADHD have been suggested to have impaired anandamide degradation compared to healthy control subjects [20]. In addition, genetic studies have found a correlation between the cannabinoid receptor gene and ADHD [21]. However, the link between endocannabinoids and ADHD comes often from preclinical models [22–25], which require further translation into clinical practice. This section does not seek to offer a complete picture of the ECS and the complex neurobiological and metabolic interactions involved, but rather seeks to offer some potential research directions and mechanisms of action for exogenous cannabinoids research as a potential pharmacological treatment for some of the main symptoms of ADHD.

The ECS, which includes the cannabinoid receptors (e.g., CB1, CB2) and the endocannabinoids anandamide and 2-arachidonoylglycerol, has also been found to interact with the central nervous system and the neuroimmune system [26, 27]. Traditionally, ADHD pathology has been associated with the dopaminergic system [19]. Cannabinoid 1 (CB1) receptors, which interact with the dopaminergic system [24, 28, 29], have been suggested as possible pharmacological targets to reduce hyperimpulsivity [10, 25, 30] and distractibility [16, 31, 32]. Therefore, exocannabinoids, such as Δ9-THC, hold potential as a pharmacological therapy, as they have been demonstrated to induce dopamine release in the human striatum [33]. It has been suggested that the brain regions where the modulation of endocannabinoids might lead to action restraint and to the regulation of impulsive action are the medial prefrontal cortex and the ventral tegmental area [10].

In addition to dopamine, the role of for instance glutamate, GABA, and other neurotransmitter systems need consideration, as well as *N*-methyl-D-aspartate and cannabinoid 2 (CB2) receptors, which have been suggested to modulate, for instance, impulsivity in interaction with endocannabinoids [10, 22, 23, 34, 35]. Therefore, further preclinical and clinical studies are warranted to map the complex interactions involved with the ECS in various pathophysiologies [35]. The case report presented below offers potential directions for future research and clinical practice. As the studies above and the following case study show, CT seem to provide a valuable treatment option for a treatment-resistant adult ADHD patient [31].

Case Report

The patient was contacted via the Finnish Medical Cannabis User Organization (Lääkekannabiksen käyttäjien yhdistys ry). The case report is based on a combination of interviews with the patient at his home, doctors' statements, medical records, and other documents relevant to the case provided by the patient and analyzed by the author since early 2016 with the full consent of the patient.

Results

The patient is an EU citizen, educated to Master's Degree level, and who has been permanently resident in Finland since 1995. In September 2003, at the age of 33 years, he was diagnosed with combined-type ADHD by a Finnish psychiatrist and prescribed immediate-release methylphenidate (Ritalin®, 10 mg twice daily). In particular, the patient's low frustration tolerance required pharmacological intervention to manage demanding work tasks that required sustained concentration and higher cognitive functioning, to reduce chronic distractibility, and to remain concentrated on tasks until completion.

From 2003 up until 2009, the patient consumed immediate-release methylphenidate on a regular basis, taking breaks from time to time to ease the negative impact of the medication upon his digestive system. During that 6-year period of use, methylphenidate clearly demonstrated efficacy, helping the patient to remain concentrated on work matters, particularly during work situations when he must remain seated for extended periods of time. Additionally, the patient received psychotherapy and guidance on alcohol dependency and on the management of the anger and violent outbursts that resulted from his low tolerance to frustration.

In 2009, however, under increasing work stress, the patient began noticing a lack of efficacy and an increase in the severity of the adverse effects (stomach problems, sweating, irritability, insomnia) from the immediate-release methylphenidate. These adverse effects forced him to make major changes to his diet to manage the worsening adverse effects of this stimulant medication, the most severe effects typically being stomach and lower bowel convulsions and pains. Upon further investigation, varicose veins were detected in the patient's left testicle, which became progressively more aggravated by the orally ingested methylphenidate. The patient's worsening stomach condition meant that he used methylphenidate less frequently, and he was offered a number of substitute prescriptions (e.g., Pramipexole®, Bupropion®, Buspirone®, Lorazepam®, Temazepam®, Alprazolam®) between January 2009 and August 2010. These medications, however, offered poor efficacy for the primary indication and only further exacerbated the

adverse effects suffered by the patient. The substitute prescribed to the patient that gave the worst adverse effects was the Pramipexole®/Bupropion® combination prescribed in July 2010, which rendered him unable to sleep for 4 whole days and nights, gave suicidal thoughts, pounding head pains, and excessive heart palpitations. Later, in October 2014, examination finally revealed a 2-cm hernia on the left side of the patient's lower bowel region.

Earlier in 2010, the patient became aware that there was a small European study where standardized medicinal cannabis products (manufactured by Bedrocan B.V. of the Netherlands), Bedrocan® and Bediol®, were prescribed to 2 European ADHD patients in Germany. The patient also became aware of recent amendments made to the Finnish Medicines Act, formally allowing the prescription of medicinal cannabis by Finnish doctors under special authorization by Fimea. The patient contacted the former Director of Fimea seeking clarification over the prescription of Bedrocan®. The Director informed the patient in a personal e-mail that Fimea has "no requirement regarding the prescriber which would not allow a psychiatrist to prescribe this product. Our criteria (coming from the Medicines Act) for the decision are that (1) other available treatments of the patient's condition have not given a favorable result or have been poorly tolerated and that (2) the indication applied for is medically justified."

After receiving this confirmation that the legal framework supported his right to access cannabinoids, the patient began to formally seek Bedrocan® as a substitute medication for methylphenidate. It was hoped that cannabinoids would offer equivalent or better efficacy with more tolerable adverse effects. After failing to find a Finnish psychiatrist or neurologist with sufficient medical knowledge of CT, the patient exercised his right to patient self-determination and finally, in June 2010, visited the prescribing physician behind the small European ADHD study in Germany. Afterwards, the patient returned to Finland with prescriptions for standardized Bedrocan® and Bediol® medicinal cannabis products.

Upon arrival to Finland, the next challenge for the patient was to find a suitable Finnish physician to validate the prescriptions for the cannabinoid treatment model. It took him until October 2010 – a period of almost 4 months – to find a suitably qualified neurologist who was prepared to endorse the treatment model. At that time, the patient presented the prescribing neurologist with a challenge: no Finnish neurologist or psychiatrist had previously substituted Bedrocan® for short-acting methylphenidate as a pharmacological intervention for a neuropsychiatric medical condition. Clinical guidelines for adult ADHD were only introduced in Finland in 2017, updating pediatric treatment guidelines published in 2007, which were updated for adolescents in 2013 [36]. These guidelines mention no possibility of CT for either adult, adolescent, or pediatric ADHD. However, the Bedrocan® application was submitted to Fimea in late November 2010 and approved by the end of December 2010.

As described in the statement made to Fimea by the prescribing physician, the use of Bedrocan® had a positive impact on the patient's ADHD symptoms, reducing hyperactivity, improving focus and impulse control, and giving better tolerance to frustration. However, during a period of increased stress due to the sudden and unexpected termination of the patient's full-time employment, in spring 2011, the use of Bedrocan® began to induce sleeping problems and agitation. The patient who participated in the small European study had highlighted Bediol®, the medicinal cannabis preparation rich in CBD, as being of value to reduce the potential adverse dronabinol effects of Bedrocan®, such as sleeplessness and anxiety [31]. After an urgent consultation with his neurologist, the patient's second cannabinoid medication, Bediol®, was prescribed as an evening medication to address these adverse dronabinol symptoms. The authorization to access Bediol® was processed by Fimea in May 2011. Bediol® did indeed give the desired anxiety-reducing effects, and the patient's sleeping pattern improved significantly; he was now able to fall asleep quickly and sleep through the night with only the need to get up to urinate one or two times. To our knowledge, no single patient in Finland prior to that time had ever been prescribed two separate medicinal cannabis preparations concomitantly.

It was at this time in May 2011 that the patient also noticed the beneficial effects of Bediol® for secondary medical indications. Inflammation, resulting from an anterior cruciate ligament knee injury in November 2010, was reduced, as well as the patient's chronic pain in his left ankle and lower back. In addition to the pharmacological intervention, the patient also practiced supplementary physical therapies to build up the supporting muscles around the knee, including water therapy, hyperthermia treatments, cycling, walking, and gardening. The rehabilitation of the patient's knee was accomplished without the need for surgery or the consumption of any other pain or muscle relaxant medication. Since 2010, on two occasions only, has there been any knee instability. While further studies are warranted to confirm these secondary therapeutic benefits, the synergy between the two primary cannabinoid components, THC and CBD, has been reported earlier [37, 38].

The average daily dosage for the patient ranged between 1 and 2 g, usually with a 2:1 ratio of Bedrocan® to Bediol®. For fast absorption and convenient titration, the cannabinoids were administered via a Volcano vaporizer. The patient reported that when vaporizing, this method of administration delivered the full therapeutic effects rapidly (within 10–15 min). The botanical form gave the patient the ability to control dosage more flexibly, including the possibility to produce his own cost-effective extracts and tinctures. According to the patient, Bediol® was ideal for evening use, but also during activities that required prolonged sitting. In the patient's view, this was the key therapeutic value of Bediol® in combination with the Bedrocan® stimulant. Bedrocan® aided concentration and reduced distractibility; Bediol®, on the other hand, reduced feelings of anxiety and restlessness and the need to be on the go all the time, as well as reducing the patient's chronic pain indications.

Despite these therapeutic benefits, there remain barriers to successful CT in Finland. As seen above, finding a physician willing to prescribe medical cannabis, despite being legally able to do so, is one of the barriers. The high price of the medication as well as inconsistencies with regards to reimbursement of cannabinoid medications remain other key barriers for a successful cannabinoid therapy. These topics, however, will be explored in more detail in another publication.

Discussion and Conclusions

The current study provides the first detailed investigation of CT for a male combined-type adult ADHD patient in Finland who accessed Bedrocan® and Bediol® for

more than 5 years. The patient found relief for his ADHD symptoms, the cannabinoids offering reduced hyperactivity as well as improved focus, impulse control, and better frustration tolerance. This is in line with clinical studies on medical cannabis for ADHD [16–18]. In addition, the patient experienced other medical benefits that contributed to his overall wellbeing, especially with the combination of the high-dronabinol product Bedrocan® and the moderate-dronabinol/high-CBD product Bediol® [31]. Russo and Guy [37, p. 242] have also concluded that "the data herein presented strongly support the therapeutic rationale for combining THC and CBD for therapeutic usage."

Endocannabinoid signaling modulation through the dopaminergic system offers a promising target for pharmacological interventions, not only for ADHD [31] as shown above, but also for other neuropsychiatric disorders [9, 39], such as Tourette syndrome tics [40], fears [41, 42], anxiety [43, 44], as well as improving synaptic plasticity for emotional learning [45]. Although many questions remain, this paper argues that there is a plethora of supporting evidence that, for individuals who obtain no relief for their ADHD symptoms from prescription stimulants like methylphenidate and/or experience adverse effects from other pharmacological therapies, CT can offer a safe and efficient mode of treatment, potentially in conjunction with other forms of psychotherapy [31]. This was noted already 15 years ago by Ethan Russo [46, pp. 170–171], who "in his practice of child and adult neurology, has heard dozens of unsolicited testimonials to the benefits of cannabis in attention-deficit hyperactivity disorder (ADHD)," and also stated that "although the idea of using cannabis-based medicines for this indication may seem surprising to most experts, controlled trials of cannabis medicines for children *(and adults)* with ADHD seem clearly indicated, particularly in view of the controversies and side effects of existing psychotropic medications" (italics added by the author for clarity).

However, further longitudinal studies are needed to quantify the quality of life changes of ADHD patients who use CT. Also, what are the most efficient modes of administration and dosages [47] and what kind of (phyto)cannabinoid and terpenoid combinations [38] are effective for different ADHD patient profiles [3, 10] remain open research questions. For instance, Loflin et al. [3, p. 428] hypothesized that "cannabis might compensate for low frontal alpha relative and absolute power, which potentially underlies hyperactive symptoms." Thus, therapeutic uses of cannabinoids could be more effective among hyperactive-impulsive subtypes compared to the inattentive type of ADHD [3].

Before well-designed clinical trials have established the detailed mechanisms of action and potential positive patient outcomes for using CT, especially for individuals with ADHD, but also for other patient groups, clinical practice should take seriously the experiences of patients who find relief from cannabinoids. The amount of medical conditions reported to be alleviated with CT is vast [12, 48], and while the "evidence" is not always based on the golden standard of double-blind randomized placebo-controlled clinical trials, the well-established historical use of cannabinoids across the globe to treat human ailments [49, 50] gives reason to patients and medical professional alike to consider this treatment option. More medical sociological investigation of the general attitudes and knowledge of policymakers, patients, and treating physicians is warranted to identify possible barriers for CT, as lack of training for medical professionals, the high cost of the medication, and lack of government reimbursement remain the main barriers to continued therapeutic use of cannabinoids in Finland.

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Statement of Ethics

The author has no ethical conflicts to disclose. This case report was conducted in accordance with the ethical guidelines provided by the University of Tampere and the National Advisory Board on Research Ethics [51] with the fully informed consent and cooperation of the patient.

Disclosure Statement

The author has no conflicts of interest to declare.

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