CASE REPORT

Cannabidiol: A case presentation on the shortcomings in clinical application

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ABSTRACT

Nearly four percent of the global population consumes cannabis with the highest prevalence among young people. Proponents of its use boast a myriad of benefits, including relief of pain, depression, anxiety, and insomnia. Pharmacologic research on cannabidiol (CBD) first occurred in the late 1970s, and more recently has garnered expanded focus due to mounting consumption despite a dearth of evidence in health efficacies. Tetrahydrocannabinol (THC) is deemed to be the intoxicating component of the flowering plant, lending to psychoactive outcomes, including euphoria and psychosis. Conversely, CBD is not thought to be psychotropic in nature. While there are a number of considerations regarding the utilization of CBD, emphasis is placed on the fact that medical-use indication is limited to its anti-seizure effects. In addition, high-grade evidence-based research data regarding the use of CBD for other medical diseases is deficient. Negative health consequences for consumers who may be unaware that inaccurate labeling and dose variability across the product backdrop is problematic. All things considered, counsel against the use of CBD products may be a judicious clinical approach.

Key Words: Cannabidiol, CBD, Tetrahydrocannabinol, THC, Indications, Side effects, Adverse outcomes

1. INTRODUCTION

Nearly four percent of the global population consumes cannabis, with the highest prevalence of use being 13.9% among young people aged 15 to 34 years.[1] Usage of cannabis for the treatment of pain dates to 2900 BCE.[2] However, proponents of its use have claimed a multitude of other benefits, including but not limited to, reducing symptoms of depression and anxiety, providing anti-inflammatory effects, and enhancing sleep.[3] Regardless of these assertions, the Controlled Substances Act has listed cannabis as a Schedule I drug at the federal level since 1970. This designation is largely due to the high abuse potential of the tetrahydrocannabinol (THC) component, along with a lack of medically recognized use indications. Consequently, it has historically been illegal for clinical providers to prescribe and pharmacies to dispense cannabis.[4] In recent years, however, nearly two-thirds of U.S. states have disregarded this federal designation and approved cannabis for a variety of medical and complementary health purposes. Such state sanctions have included broad marketing strategies for the use of cannabidiol (CBD) products, assuming them safe for use given that CBD lacks the euphoric and psychoactive properties of THC.[5]

Pharmacologic research on CBD first occurred in the late

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1970s and recently gained expanded focus due to mounting use despite a lack of evidence in its health efficacies.[3] Retail efforts have only inflated since the 2018 Farm Bill removed hemp from the U.S. scheduled drug designation, so long as THC levels were less than 0.3%. Since this legislative passage, annual U.S. sales of CBD products exceed an estimated $200 million. This is principally the case because CBD can be readily extracted from both cannabis and hemp. Complicating matters are recent position statements of the Food and Drug Administration (FDA) denoting that CBD products cannot legally be sold in edible forms due to already having been approved as a drug.[6] Further, the FDA maintains its authority to regulate CBD products through the Food, Drug, and Cosmetic Act because the categories of CBD use fall under its jurisdictional umbrella. Nonetheless, FDA strategies for regulating CBD products have not been clear.[4] While manufacturers along with state and local officials continue to ignore federal designations, FDA enforcement has been limited to removing CBD products, making unsubstantiated claims for disease management, in the process, leaving many CBD products widely marketable for consumer use.[6] As such, laws regarding CBD products are being developed and implemented on a state-by-state basis, further muddying the uncertain medical, legal, and ethical issues consumers face.[4] Though the FDA has expressed concerns over CBD's long-term safety,[6] consumers are increasingly seeking guidance on the consumption of these products.[4] With a deficiency in high-grade evidence-based research for application of CBD outside of medical-use indications including healthy athletes, case reports offer the ability to provide an early clinical practice framework which addresses both effectiveness and adverse events.

2. Case presentation

Maria Jones is an 18-year-old student-athlete entering her senior year of high school. She presents to clinic with her father for an annual sports and wellness exam. She is a dual-sport athlete, participating in soccer and basketball with aspirations to play collegially. She is ranked academically in the top ten percent of her class. Her health history is negative for pre-existing medical conditions, use of prescription medications, and significant sports injuries. In addition, she denies use of substances, including alcohol, nicotine, and illicit substances. She does report use of over-the-counter (OTC) CBD products including oil, gummies, and topical preparations since the end of her last competition season. Her use of these products is largely based on information she found on the Internet asserting CBD utilization will help reduce her anxiety and fears associated with sports performance while also easing inflammation and pain related to training and game play. She reports intermittent diarrhea and headaches over the summer months. Her parents express concerns of increasing distrust and even paranoia in her belief that teammates and coaches are trying to sabotage her chances at a sports scholarship.

Maria's physical exam was unremarkable. Her mood is anxious, particularly as she voices negative statements without evidence that teammates and coaches are trying to hurt her scholarship chances. Her laboratory workup was ordinary except for a positive THC result on a urine drug screen. Maria and her parents were advised that the diarrhea, headache, and paranoia symptoms, along with positive urine drug screen, were likely attributable to use of CBD products with poor quality control measures lending to the presence of THC contamination.[3,7] The World Anti-doping Agency (WADA) does not currently have CBD on its list of banned substances, though THC remains on this list. As such, WADA and organizations at most sports levels, including high school and college, can penalize participants by revoking their eligibility to play. With this in mind, Maria and her parents were advised to discontinue CBD products, as this is the most appropriate risk-mitigation strategy.[8] Moreover, the symptoms of diarrhea, headache, and paranoia should subside over time with CBD cessation.

3. Implications for clinical practice

3.1 THC and CBD

More than 500 different chemical composites comprise the flowering cannabis plant.[1] While there are more than 80 active compounds in cannabis-generated therapeutic products,[6] both THC and CBD are closely enough linked pharmacologically that they belong to the same drug class.[9] THC works as a partial-agonist binding to the CB1 and CB2 cannabinoid receptors which are responsible for psychoactive effects.[1] THC is considered the intoxicating component of the plant, lending to psychoactive outcomes, including euphoria and psychosis.[10] Conversely, CBD is not thought to be psychoactive in nature[9] due to not binding to the same CB1 and CBD receptors as THC.[1] Both THC and CBD have contrasting mechanisms of action, therapeutic indications,[10] and side-effect profiles. The foundation of these differences is thought to be related to variations in THC and CBD binding to cannabinoid receptors.[9] Cannabis products containing THC have demonstrated three therapeutic uses in the research literature: 1) treatment of chemotherapy-induced nausea and vomiting; 2) spasticity in multiple sclerosis; and 3) chronic pain in adults. Even though CBD is promoted by users to hold a wide range of therapeutic uses, the sole FDA-approved indication is the treatment of intractable seizures in persons with Lennox-Gastaut or Dravet syndrome.[4]

3.2 Associated risks

While prolonged use of THC lends to euphoria and increased risk of developing psychotic disorders such as schizophrenia, evidence is lacking with CBD emoting euphoria, psychosis, and cognitive impairments.[11] In fact, CBD has been shown to negate some of the adverse reactions of THC, such as memory impairment and paranoia.[10] Mindful of this, CBD proponents frequently dismiss FDA concerns related to adverse drug events (ADEs) and potential drug-drug interactions (DDIs). These are resultant of CBD pharmacokinetics and pharmacodynamics as it relates to Cytochrome P450 and other enzyme systems being inhibited or induced. Almost half of CBD users can experience ADEs, and the risk of DDIs is high with routine everyday medications.[5] Common ADEs include diarrhea, nausea and vomiting, headache, liver injury, fatigue, and somnolence with an increased incidence of diarrhea and headache.[3,7] Animal studies have demonstrated an array of ADEs: developmental toxicity, embryo-fetal mortality, alterations in central nervous system function, elevated liver enzymes, reduction in sperm count, organ weight changes, male reproductive alterations, and low blood pressure.[3] In light of this, the FDA has expressed safety concerns including pregnancy-related risks.[6] A final consideration is that a number of these ADEs appear to be dose-dependent, with higher doses increasing risks.[5,7,9]

4. Additional considerations

While there are myriad considerations regarding the utilization of CBD, emphasis is placed on the fact that medical-use indication is limited to its anti-seizure effects. In addition, high-grade evidence-based research regarding the use of CBD for other medical diseases is limited.[3] Current evidence limitations underscore the dearth of information on the full reporting of outcomes, consistency of products across the landscape, dosing regimens, and dose-response ADEs and DDIs.[10] Compounding this problem is the fact that CBD products continue to be sold without meticulous standardization of CBD potency.[3] In fact, labeling of CBD products often does not correctly display accurate CBD and THC levels.[4] At times, these inaccuracies and inconsistencies in CBD preparations lead to THC quantities exceeding legal specifications.[10]

5. Discussion

Patient education must include notation that CBD products should not be treated similar to traditional medications in the sense that there is so much variability in products sold across the retail landscape.[10] Furthermore, the lack of compliance with quality control production standards amplifies the risk of THC contamination, posing greater risks for positive drug tests.[8] Products include many formulations involving administration through inhalation, oral, buccal, and topical routes. As such, CBD is being commonly marketed and sold through items such as dietary supplements, food products, e-liquids for vaping, and cosmetics.[4] This results in a marketplace replete with CBD products available for purchase by varied consumers, including athletes.[8] All of this imparts grave concern that ADEs and DDIs propagate negative health consequences for consumers who may be unaware that inaccurate labeling and dose variability across the product backdrop is present. Consequences can be both profound and exponential when considering today's consumers are markedly more proactive in self-medicating through OTC purchases.[3] Advisement against the use of OTC CBD products may very well be a reasonable or even preferable clinical strategy[8] based on the augmented risks for ADEs, DDIs, and positive drug screen for THC.

Conflicts of Interest Disclosure

The authors declares that there is no conflict of interest.

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