Cannabidiol (CBD) Use in Type 2 Diabetes: A Case Report

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Cannabidiol (CBD) oil has been gaining popularity as a natural alternative for numerous disease states. CBD is a phytocannabinoid obtained from the *Cannabis sativa* plant. Unlike its relative tetrahydrocannabinol (THC), CBD does not activate CB_1 receptors in the brain and therefore lacks psychotropic effects (1). Instead, this substance is thought to work on the G-protein coupled receptor, endothelial cannabinoid receptor, and serotonin-1A receptors, among others.

Diabetes is the seventh leading cause of death and affects >30 million people in the United States (2). CBD has been investigated, mostly in animal models, for its ability to help treat diabetes. It is theorized that cannabis has desirable effects on hyperglycemia through its anti-inflammatory and antioxidant properties (3). The endocannabinoid system modulates food intake and energy homeostasis by activating cannabinoid receptors. Modulation of these receptors with CBD has the possibility to reduce body weight and A1C in people with diabetes.

In one study using mouse models, CBD was shown to significantly reduce the incidence of diabetes in these mice (4). This was shown by a significant decrease in pancreatic islets production of destructive insulitis and inflammatory cytokine production.

The potential to use CBD as a method to treat diabetes reveals the need for studies and case reports. The following case illustrates the initiation of CBD in a patient with type 2 diabetes.

Case Presentation

A 62-year-old Hispanic obese man (weight 113 kg, BMI 39 kg/m^2) with a history of type 2 diabetes for 11 years began taking CBD oil to control his blood glucose in place of insulin degludec. Initiation of this product was independent of his clinician's recommendation and based on the patient's personal review of information that suggested CBD was beneficial for people with type 2 diabetes.

As shown in Table 1, the week before the patient's initiation of CBD, his A1C was 7.6%, and he was taking his currently prescribed medications: insulin degludec 32 units subcutaneously daily, metformin 1,000 mg orally twice daily, and empagliflozin 25 mg orally once daily. The patient reported adherence to his medications 6 days out of the week. Insulin degludec had been supplied as a sample, but his refill history suggested exceptional adherence to metformin and empagliflozin. His self-monitoring of blood glucose (SMBG) readings ranged from 124 to 176 mg/dL, with an average of 144 mg/dL. Because he was not meeting his goal A1C of <7.0%, he was prescribed saxagliptin 5 mg to be taken once daily. The patient had no macrovascular complications of diabetes and had normal liver and renal function but did have albuminuria.

One week later, the patient contacted his provider to report that he had self-discontinued insulin degludec after an episode of hypoglycemia and replaced his insulin therapy with 20 mg of oral CBD daily (SA Botanicals, San Antonio, TX). Given his history of side effects to glucagon-like peptide 1 receptor agonists and refusal to use insulin again because of concerns about hypoglycemia, the clinician agreed with his decision to discontinue insulin and suggested evaluating the patient's A1C on triple oral therapy plus CBD at his next visit.

At the next clinic visit 6 weeks after his CBD initiation, the patient's SMBG readings ranged from 122 to 158 mg/dL, with an average of 142 mg/dL. Based on his refill history and self-report, he had been adherent to his regimen of metformin, empagliflozin, saxagliptin, and CBD oil, and he reported no changes in diet or lifestyle. His weight remained stable at 112 kg.

Because his SMBG readings had not drastically changed with the discontinuation of insulin degludec, no medication

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TABLE 1 Patient's Blood Glucose Control and Medications During Case Timeline

	A1C, %	Preprandial Blood Glucose Range, mg/dL	Medications
Routine clinic visit	7.6	124–176	• Insulin degludec 32 units SQ daily • Metformin 1,000 mg PO twice daily • Empagliflozin 25 mg PO daily • Started saxagliptin 5 mg PO daily
1 week later: patient self-discontinued insulin degludec and started CBD 20 mg PO daily			
Week 6	NC	122–158	• Metformin 1,000 mg PO twice daily • Empagliflozin 25 mg PO daily • Saxagliptin 5 mg PO daily • CBD 20 mg PO daily
Week 11	7.6	130–177	• Metformin 1,000 mg PO twice daily • Empagliflozin 25 mg PO daily • Saxagliptin 5 mg PO daily • CBD 20 mg PO daily
Week 23	7.6	157–183	• Metformin 1,000 mg PO twice daily • Empagliflozin 25 mg PO daily • Saxagliptin 5 mg PO daily • CBD 18 mg PO twice daily
Week 56	7.7	127–184	• Metformin 1,000 mg PO twice daily • Empagliflozin 25 mg PO daily • Saxagliptin 5 mg PO daily • CBD 18 mg PO twice daily

NC, not collected; PO, orally; SQ, subcutaneously.

changes were made. After 4 months of using CBD oil, the patient increased his CBD dose to 18 mg twice daily and self-reported benefits for joint pain management. After 13 months of the patient's same medication regimen, his A1C remained stable at 7.7%, and his weight was 113 kg.

Discussion

CBD has become a popular substance since the Farm Bill was passed in 2018, removing hemp and cannabis from the Controlled Substance Act if they contain ≤0.3% THC (5). The U.S. Food and Drug Administration (FDA) has approved Epidiolex, a pharmaceutical-grade CBD, for treatment of seizures from Lennox-Gastaut syndrome; however, no other CBD products have been identified as safe and effective by the FDA. Despite this, several CBD products have been marketed for medical uses.

The literature regarding the use of CBD products as a medical treatment remains sparse. A meta-analysis published in 2015 in the *Journal of the American Medical Association* reviewed 79 studies that used CBD to treat various disease states (6). To date, promising results have only been demonstrated for the use of CBD as a treatment for severe forms of epilepsy, leading to the FDA's approval of Epidiolex (7,8).

With a deficit of studies on the use of CBD as a diabetes treatment, its effects in this regard have yet to be elucidated. One study of 62 patients with noninsulin-treated type 2 diabetes examined the effects of CBD 100 mg twice daily and tetrahydrocannabivarin (THCV) 5 mg twice daily for glycemic control (3). This study found a statistically significant reduction in resistin and an increase in glucose-dependent insulinotropic peptide compared with baseline but not compared with placebo, as well as surrogate outcomes suggesting a possible improvement in glycemic control. Beneficial effects on fasting plasma glucose levels and pancreatic β-cell function were only observed with THCV and not with CBD. The outcomes from this small study provide little confidence with regard to a benefit of CBD for people with type 2 diabetes.

In the case presented, several factors may have confounded the results in terms of efficacy, but useful conclusions may be drawn about the safety of CBD in people taking diabetes therapies. First, the nearly concurrent discontinuation of insulin degludec and initiation of both CBD oil and saxagliptin raises interest as to whether the CBD oil used had an appreciable effect on blood glucose and A1C. Saxagliptin has been proven in major clinical trials to reduce A1C for patients already on metformin therapy (9). Because the patient's A1C and SMBG remained stable when insulin

degludec was replaced with CBD and saxagliptin was initiated, the saxagliptin may have masked a possible benefit from CBD. However, dipeptidyl peptidase-4 inhibitors such as saxagliptin reduce A1C by 0.7–0.8%, and it is unlikely that it had an equivalent A1C lowering to the dose of insulin degludec the patient had been taking previously. In addition, the patient used 20 mg of CBD oil daily, which may not have been a sufficient dose to receive the benefits mentioned in the aforementioned trial (3). Finally, the endocannabinoid system may vary among individuals, and CBD may be more effective in some patients.

The stable nature of the patient's A1C and SMBG readings and his general tolerability to this regimen does suggest that his use of CBD was safe, despite having questionable efficacy in this scenario. Additionally, his relatively stable A1C may have been attributable to the CBD. Most patients would have a significant increase in A1C after discontinuing insulin degludec at the dose the patient was taking. However, the insulinotropic effects of CBD may have maintained the patient's glycemic control by decreasing resistin. Increased resistin has been linked to insulin resistance and obesity, and because this patient was obese, it is reasonable to consider this as a possible mechanism for his stable A1C. In addition to its possible effects in improving glucose control, CBD may potentially have both macrovascular and microvascular benefits related to its anti-inflammatory effects (10–12).

No side effects were noted, including hypoglycemia or suspected CBD-induced hyperglycemia. The FDA and a meta-analysis have raised concerns that CBD products could cause liver injury, diarrhea, decreased appetite, male reproductive toxicity, irritability, agitation, and drowsiness (6,13). The potential for drug-drug interactions with CBD also exists. CBD is a strong cytochrome P450 inhibitor, as well as an inhibitor of UGT, and medications that are substrates of these enzymes may have decreased efficacy and safety when used in conjunction with CBD (14–16).

It should be reiterated that the risk of adverse effects may be heightened with the use of CBD products because of misbranding and adulteration (5). Risks may also be associated with patient nonadherence to guideline-recommended therapy in favor of CBD, as in this case. Widespread availability of CBD products and misleading marketing raise concern for unmoderated self-care of disease states that require professional intervention.

Summary

This case does not provide evidence for the use of CBD as an alternative treatment for uncontrolled type 2 diabetes. However, it does show that use of CBD did not cause harm or worsening of diabetes control. Regardless, health care providers should advocate for the continued use of proven therapies and monitor for harmful outcomes that may be associated with CBD should patients choose to use such therapy. Health care providers should be ready to discuss CBD and educate patients about the risks of CBD products and the potential for adulteration and misbranding in an effort to deliver the best care they can for their patients.

DUALITY OF INTEREST

No potential conflicts of interest relevant to this article were reported.

AUTHOR CONTRIBUTIONS

R.G.M. researched data and wrote and reviewed/edited the manuscript. M.L.E. and S.S.O. wrote the manuscript. E.M.A. researched data and wrote the manuscript. E.M.U. obtained case report data, contributed to discussion, and reviewed/edited the manuscript. E.M.U. is the guarantor of this work and, as such, takes responsibility for the integrity of the data presented and the accuracy of the data analysis.

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