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In an effort to give a voice to emerging talent, AJEM *created a column publishing the work of students who are pursuing a graduate degree in medical cannabis.*

Medical Cannabis for Ulcerative Colitis and Inflammatory Bowel Disease: A Patient's Insight

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Ulcerative colitis (UC), a type of inflammatory bowel disease (IBD) that extends from the rectum to varying lengths of the colon, is characterized by alternating cycles of relapse and remission. The etiology of UC is unknown; it is a complex, chronic systemic disease with potential extraintestinal manifestations. In the United States, it is currently estimated that 1 to 1.3 million individuals have IBD.[1] Unfortunately, according to a 2019 review by Danese et al., there are several critical unmet medical needs of patients with UC, particularly the effects of UC on the ability of patients to lead a "normal" life (ie, reduced quality of life [QoL], reduced ability to work, and drawbacks related to current therapeutic strategies).[2]

The goal of treatment for UC is endoscopic and histologic remission, not necessarily relief of symptoms. Currently, many treatment options exist for UC, including aminosalicylates, corticosteroids, immunomodulatory agents, and monoclonal antibodies.[3] More recently, Janus kinase inhibitors are used to treat refractory UC, and surgical options are indicated for severe cases.[4] Despite these myriad therapeu-

tic options, only surgery has been considered a definitive curative option for UC. Moreover, drugs to treat UC can be costly, have side effects, and do not completely manage symptoms that decrease patient QoL.

Preclinical data suggest that alterations in the endocannabinoid system are associated with UC-related symptoms. For example, some studies demonstrated elevated anandamide and cannabinoid receptor-1 (CB_1) expression in mouse models of inflammation and increased susceptibility to colonic inflammation in CB_1 knockout mouse models.[5,6] However, although numerous studies in cell lines and animal models show positive effects of cannabinoids, including reversal of inflammation relevant to the gastrointestinal (GI) tract, few human studies have evaluated the therapeutic effects of cannabinoids.[7] Overall, only a small number of clinical studies have probed cannabinoid-based treatments for UC, and interpretation is limited by poorly designed trials, suboptimal administration strategies, and limited pharmacodynamic and pharmacokinetic data.[8] In observational studies, moderate delta-9-tetrahydrocannabinol (THC) administration reduced corticosteroid use in patients with IBD.[9] A randomized controlled clinical trial on cannabidiol (CBD) vs placebo in 20 patients with IBD demonstrated a nonstatistically signifi-

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cant improvement in the CBD group. This was a short study conducted on a small sample of patients using low-dose CBD; therefore, the results may be difficult to interpret.[10] It is of note, however, that no serious adverse events were reported in this study.

Other cannabinoids do not appear to have been systematically investigated for UC/IBD. Anecdotally, it is known that patients commonly self-medicate with cannabis for symptomatic relief (eg, to improve appetite, reduce pain and nausea, or to provide a general sense of well-being).[11]

One Patient's Perspective

An otherwise healthy 33-year-old woman with IBD (hereafter referred to as Katherine), who receives treatment at an alternative medicine clinic in Philadelphia, Pennsylvania, described her experience with medical cannabis. Katherine was diagnosed with IBD by her family physician when she was 18 years old. Although she has met with multiple GI specialists since her diagnosis, prescribed inflammatory drugs and nutritional support alone have failed to completely control her symptoms. Over the course of her treatment, Katherine has taken prescription omeprazole for related discomfort, low-dose mirtazapine for anxiety, and nonprescription analgesics for pain. None of these treatment options has completely controlled her symptoms or greatly improved her QoL. Katherine pursued medical cannabis as a supplemental intervention based on its associated anti-inflammatory, analgesic, anxiolytic, and hunger-stimulating effects. Since taking medical cannabis, Katherine said she has "gained the ability to eat without severe discomfort" and has experienced "relief from the cramping and pain without having to take pain medication." She currently takes a daily 6:1 THC:CBD full-spectrum capsule, manufactured and distrubuted by Vireo Health, and vaporizes various hybrid strains for flare-ups and anxiety. This combination has allowed her to discontinue her other prescribed medications for IBD and anxiety. The patient noted that she has had no negative side effects from the THC:CBD and that it has not affected her productivity. Based on the improvements in her QoL due to symptom relief and the lack of negative side effects noted with this supplemental treatment, Katherine intends to incorporate medical cannabis permanently into her IBD management strategy.

Discussion

Although this patient's case illustrates the potential therapeutic utility of medical cannabis for IBD, pharmacodynamic, pharmacokinetic, and safety data are limited, and the long-term effects of cannabinoids on UC are unknown. The limited available data on CBD use in patients with UC show no significant adverse events and anecdotal reports indicate that cannabis use is relatively safe with respect to toxicity and adverse side effects relative to other drugs. CBD in particular has been shown to be safe at relatively high doses following long-term use, as evidenced by the approval of Epidiolex by the FDA in 2018 and continued clinical investigations of safety and efficacy end points.[12] Importantly, given the variety of drugs that are commonly prescribed for UC, coupled with the known potential for cannabinoids to interact with the metabolism of other drugs, continued clinical research is necessary to determine potential drug–drug interactions that may take place with coadministration of cannabinoids.

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