Cannabis Oil Use by Adolescents and Young Adults With Inflammatory Bowel Disease

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ABSTRACT

Objectives: The aim of the study was to describe use of oral or sublingual cannabis oil (CO) by adolescent and young adult patients with inflammatory bowel disease (IBD).

Methods: A descriptive study of IBD patients 13 to 23 years of age seen between January 2015 through December 2017 at Children's Hospital Colorado. Information obtained included chart abstraction, electronic and interview self-report, and serum cannabinoid levels. We compared CO users and cannabis non-users for clinical characteristics and perceptions of risk. Users of CO provided information on routes, patterns, motivations, and perceived benefits and problems with use.

Results: The 15 users and 67 non-users were similar for clinical characteristics and pain and appetite scores. 9 of 15 (60%) CO users had used in the past 30 days, an average of 22 ± 9 times; and 4 used daily. A variety of strengths and CBD:THC ratios were reported. Most common perceived effect of use was on sleep quality, nausea, and increase in appetite. Of the 15 users, 6 used only CO and no additional forms of cannabis. Of these 6 CO only users, 5 reported a medical reason for use, most commonly to relieve pain.

Conclusions: Adolescent and young adults with IBD used oral CO and many used other cannabis products as well. Users perceived some medical benefit. Care teams should strive for open communication about use until further information on safety and efficacy becomes available.

Key Words: cannabidiol, Crohn disease, marijuana, ulcerative colitis

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What Is Known

- Patients with inflammatory bowel disease frequently use complementary and alternative therapies, including cannabis enriched in cannabidiol.
- A single small clinical trial of cannabidiol-enriched botanical product suggested a possible benefit for adults with ulcerative colitis.

What Is New

- Adolescents and young adults with inflammatory bowel disease used cannabis oil, with a variety of delivery methods, concentrations and ratios of cannabidiol to delta-9 tetrahydrocannabinol.
- CO use frequency was about 1 time a day.
- Although scores for pain, appetite, and disease activity were similar to non-users, cannabis oil users perceived a positive impact in sleep quality, nausea, and appetite.

In states with legal cannabis (marijuana [MJ]), multiple formulations are now available. Among these, edible products are popular (1). One type of edible cannabis product, cannabis oil (CO), may be manufactured with specific concentrations and ratios of cannabidiol (CBD) and delta-9 tetrahydrocannabinol (THC). In contrast to THC, CBD is thought to have little to no psychoactive effect (2). Extensive media coverage highlighting the purported medical benefits of cannabis motivated desperate families to move to states such as Colorado that provide access to legal medical MJ (3). In Colorado, families have enrolled their children in clinical studies evaluating the medical benefits of CO for conditions such as pediatric epilepsy (4) and Dravet syndrome (5) for which an oral CBD product has recently received Food and Drug Administration approval (6). Patient and family testimonials endorse high CBD CO as safe and effective for treatment of other conditions including pediatric IBD (7). Since alternative, ''natural,'' and diet treatments are commonly tried by patients with IBD (8), it is not surprising that cannabis, and CO, attracts interest as a therapy for IBD (9).

CO may contain varying amounts and ratios of THC and CBD, the most well-known cannabinoids, and may be administered multiple ways including oral, smoke, vape, and dab as well as in ointments and patches for topical use. These chemicals act through the mammalian endocannabinoid system via receptors throughout the body including the cell membrane G protein-coupled CB1 (present in central and peripheral neurons) receptors and CB2 (present in immune cells) receptors as well as other receptors including TRPV1 and GPR55 (10). The endocannabinoid system may impact many biologic processes including epithelial growth and regeneration, immune function, motor function, appetite control, and secretion. The benefits of CO for patients with IBD may include modulation of visceral pain perception, gastrointestinal

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motility, nausea and vomiting, appetite and the inflammatory response (10–12). These benefits need to be balanced against the risks of the psychoactive component THC as well as the respiratory side effects from smoking or inhaling cannabis (13). Recognizing the therapeutic potential of cannabinoids, the Crohn's and Colitis Foundation supports ''clinical research and the potential development of cannabinoid-based medications'' (14) and the National Academy of Sciences Engineering and Medicine recommends prioritizing research on the health effects of cannabis use in children and youth as well as on assessing the benefits and harms associated with cannabis products such as edibles (2).

At our center, patients and families have asked about the possible benefit of ingested CBD-enriched CO for IBD and have shared their individual experiences (12,15). In a prospective observational study, about 30% of our adolescents and young adults with IBD reported use of cannabis of any type and of these, about 30% (10% overall) have used CO (15). Here we report on 15 pediatric IBD patients who have completed 6-month follow-up in our ongoing study and endorsed use of ingested CO. The CO users are compared to those who have never used cannabis (15).

METHODS

All patients 13 to 23 years of age, followed at Children's Hospital Colorado for IBD, and enrolled in ImproveCareNow (16) with standardized clinical information obtained, were eligible. Participants were identified through enrollment in a larger prospective study evaluating cannabis exposure in patients with IBD in which 70% of approached subjects enrolled (15). Participants had been recruited, independent of cannabis use, by a research coordinator during their outpatient clinic visit, inpatient admission, or during a medication infusion visit (Fig. 1) with the aim of following them for 6 to 12 months. This report includes the subset of patients who reported by their 6-month assessment that they had either never used any form of cannabis (non-user) or that they had taken oral or sublingual CO (user) even if they also used other forms of cannabis; those cannabis users who have never used CO were excluded from this portion of the study.

Study information was provided and assent/consent obtained in a private setting. Information obtained from the electronic medical record included demographic and clinical characteristics such as age, race, gender as well as clinical data such as type of IBD and physician global assessment of disease activity (17). Self-report data on appetite, pain, and CO use were collected and managed using REDCAP electronic data capture tools (18). Appetite and pain scores were assessed by a visual analog scale from 0 to 100 (19).

Questions on use were developed from studies on cannabis and alcohol use (20). Motivation for use was assessed using exploratory questions adapted from studies of cannabis use, non-medical opiate prescription use, and alcohol drinking motives, or created for this study (20–22). Questions of how cannabis use has impacted health were assessed by 3 possible selections: better, no change, or worse. Serum cannabinoid levels were measured by a liquid chromatography/mass spectrometry technique (23).

Statistical Analysis

Data were examined for accuracy and the distributional properties of each variable. Many of the results are descriptive, consisting of self-reports of MJ perceptions, and use in adolescents with IBD. We compared the CO user and non-user groups on demographics; IBD disease characteristics; detectable levels in plasma of CBD or THC or their metabolites; and perceptions of risk with regular MJ use. Groups were compared with independent *t* tests, χ^2 tests, and Fishers exact tests using 2-tailed probability tests with 0.05 significance level. This study was approved by the Colorado Multiple Institution Review Board.

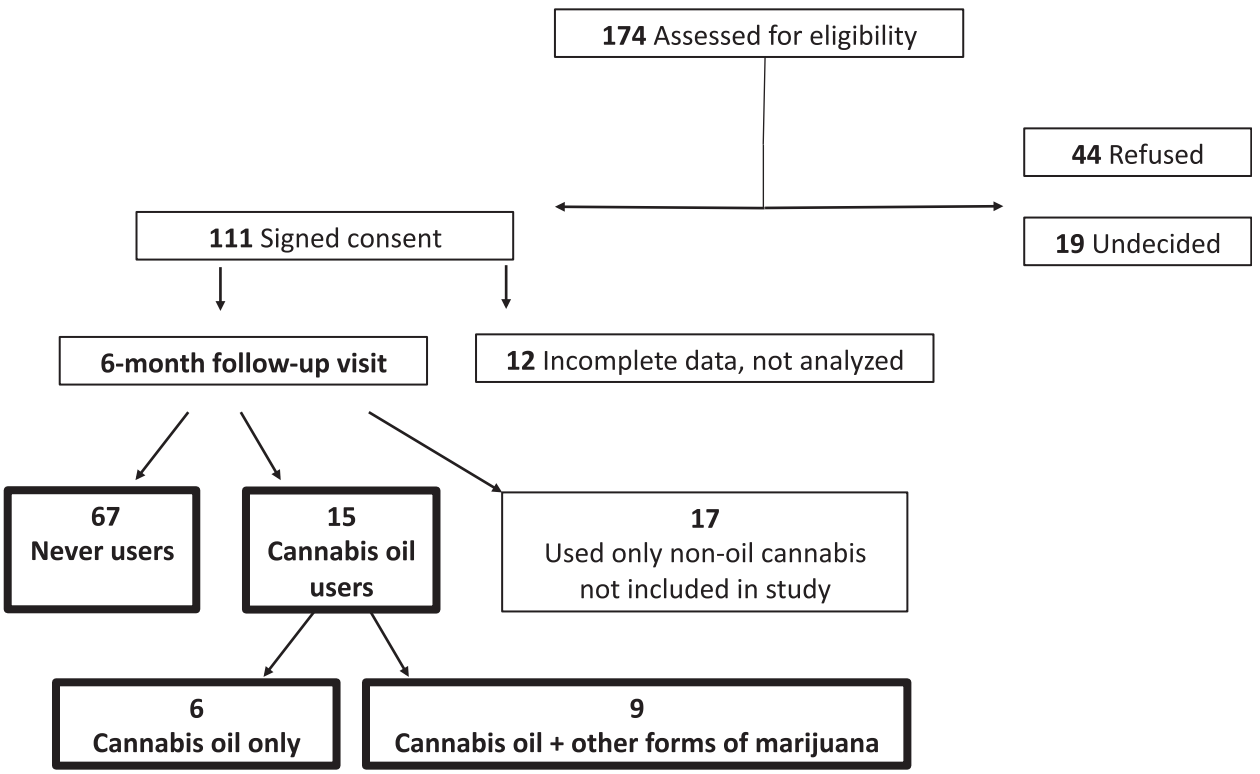

FIGURE 1. Flow diagram of patient enrollment.

TABLE 1. Demographic and Clinical Characteristics for Inflammatory Bowel Disease Patients Who Self-report no Cannabis Use or Cannabis Oil Use

	Cannabis Non-user, N = 67	CO User, N = 15	P
Demographic data			
Age, y			
Mean, SD	16.8, 2.2	17.2, 2.0	NS
Median, range	16.8, 13–22	16.6, 14–20	
Male n (%)	34 (51)	8 (53)	NS
Caucasian n (%)	56 (84)	13 (87)	NS
Disease type, n (%)			
Crohn disease	37 (55)	11 (73)	NS
Ulcerative colitis	23 (34)	2 (13)	
IBD-undifferentiated	7 (10)	2 (13)	
Physician global assessment, n (%)			
Quiescent/mild	42 (63)	10 (67)	NS
Moderate/severe	6 (9)	1 (7)	
Unknown	19 (28)	4 (27)	
Have a medical MJ card, n (%) (n = 14)	0 (0)	7 (50)	χ^2 (1) = 36.7, $P < 0.0005$
Detectable cannabinoid level, n (%) (n = 56 cannabis non-users and 12 CO users)	0 (0)	9 (75)	Fisher's exact test $P < 0.0005$
Perceived low to no risk of harm with regular smoking of MJ, n (%)	29 (43)	10 (67)	NS
Scores for self-reported analog scales 0–100, mean ± SD			
Pain	26.7 ± 24.4	22.0 ± 21.2	NS
Appetite	62.1 ± 28.8	66.7 ± 18.9	NS

CO = cannabis oil; IBD = inflammatory bowel disease; MJ = marijuana.

RESULTS

We identified 15 participants who used CO products and compared them to 67 who never used CO or any other cannabis products. The 2 groups were similar for age, gender, race, disease type, physician global assessment, pain and appetite scores (Table 1). Seven of the CO users reported having a medical MJ card (1 did not answer), 10 of 15 (67%) perceived low to no risk of harm with regular smoking of MJ.

Nine of 15 (60%) reported using CO in the past 30 days and 9 of 12 (75%) who provided a blood sample had a detectable cannabinoid level. Median number of days used in the past 30 days was 25 days, range 10 to 30 days (average 22 ± 9 days). The frequency of use was a little higher, with a median of 30 times per month, range 10 to 120 times per month (Table 2). Daily use (30 times in 30 days) was reported by 4.

A variety of ways to consume the CO was reported as well (Table 2). Although 7 reported consuming oil that contained both CBD and THC, there was a wide range of doses and CBD:THC ratios; 7 knew the content in the oil but only 5 knew the plant strain.

Nine users reported on the impact of CO use. Most commonly reported was improved sleep quality, nausea, and appetite (Table 2). None reported a change in weight. No effect from CO use was reported by 3.

Six patients reported that the only form of cannabis they had used was CO (Table 3). Five reported medical motivations for use (pain, abdominal cramping, and nausea) and 3 reported psychological or recreational motivations for use including to improve attention and to not get sick.

DISCUSSION

This is the first study to describe CO use by pediatric IBD patients in a state with pathways to legal recreational and medical MJ. Our data show that CO was used by 15 (15%) of the 99 adolescent and young adult IBD patients who participated in our larger study. Therefore, it is important to understand the implications of CO use.

A medicinal motivation for use of CO was more commonly reported than for psychological or recreational purposes. This seems consistent with the use of high CBD and low THC products that may have an immunomodulatory effect while minimizing the risks of the psychoactive component (24). Nevertheless, this study identified a perception of both benefit and safety with chronic use. Consumers of cannabis products, especially from online stores, should be cautious as the content of the CO may be significantly different from that on the label (25). As in our study, a trial of CBD oil in adults with ulcerative colitis also showed a perception of improvement in quality of life and in global impression of feeling better (26). The CBD treated group, however, had more adverse events compared to placebo, most notably dizziness. A small placebo controlled trial of 10 mg CBD in olive oil for Crohn disease in adults showed no benefit but tolerability was excellent (27). High-quality data are lacking on the clinical efficacy of CBD for treatment of IBD.

Psychosocial health and mental health are important determinants of IBD outcomes (28), yet little is known about CO users. The tools used to screen for substance use (29) and guides to counseling teens about MJ use (30) focus on recreational use of THC-containing cannabis and may not apply to primarily CBD-based use for medicinal purposes. Therefore, there is a need for open communication between patients and providers about this non-traditional approach. Our experience has been that many patients and families are open to reporting their use (15,31). There are, however, potential issues for routinely inquiring about cannabis use in the clinical setting, including potential legal responsibility to report use by minors (12), need for screening for conditions such as anxiety or depression for which patients may be self-medicating with cannabis, and the perception of validation of unrealistic patient/family expectation that cannabis (or CO) is an effective treatment for IBD. In this study, we did not identify differences in

TABLE 2. Characteristics for 9 Inflammatory Bowel Disease Patients Who Used Cannabis Oil in the Past 30 Days

Past 30-day use, mean (SD), median, range		
Number of days	22.3 (8.7), 25, 10–30	
Number of days n (%)		
10	2 (22.2)	
15	1 (11.1)	
21	1 (11.1)	
25	1 (11.1)	
30	4 (44.4)	
Number of times	46.7 (42.8), 30, 10–120	
Route of use: n, (%) (may report more than 1 route)		
By Mouth (not specified further)	3 (33.3)	
Under the tongue	3 (33.3)	
By Pill	2 (22.2)	
Tincture	2 (22.2)	
Drink	1 (11.1)	
Content of CO		
Dose range, mg	CBD: 1.2–500	
	THC: 1–50	
CBD + THC n, (%)	1:1	3 (33.3)
	19:1	2 (22.2)
	10:1	1 (11.1)
	100:0.1	1 (11.1)
	Unknown	2 (22.2)

Has the use of CBD oil impacted the following?...n (%)	Better	No Change	Worse
Sleep quality	4 (44.4)	5 (55.6)	0 (0)
Nausea	4 (44.4)	5 (55.6)	0 (0)
Appetite increase	4 (44.4)	4 (44.4)	1 (11.1)
Mood	2 (22.2)	7 (77.8)	0 (0)
Ability to focus	2 (22.2)	7 (77.8)	0 (0)
Dizziness	2 (22.2)	7 (77.8)	0 (0)
Anxiety	2 (22.2)	7 (77.8)	0 (0)
Vomiting	1 (11.1)	8 (88.9)	0 (0)
Better relationships	1 (11.1)	8 (88.9)	0 (0)
Appetite decrease	1 (11.1)	8 (88.9)	0 (0)
Fatigue	1 (11.1)	8 (88.9)	0 (0)
Irritability	1 (11.1)	8 (88.9)	0 (0)
Rash	0 (0)	9 (100)	0 (0)
Weight gain	0 (0)	9 (100)	0 (0)
Weight loss	0 (0)	9 (100)	0 (0)

CBD = cannabidiol; CO = cannabis oil; THC = tetrahydrocannabinol.

scores between CO users and non-users for appetite, pain, or disease severity, despite their self-reported perceived benefits.

The American Academy of Pediatrics (AAP) recognizes that cannabinoid medications may be an option for life-limiting or severely debilitating conditions in which approved therapies are inadequate and that the impact of legalizing medical MJ requires further study (32). Research is needed on the effects of different delivery systems (smoked, ingested oil, vape) of cannabis and how cannabis may interact with other medications (33). Prospective studies are needed to determine the trajectory of use of CBD-rich products with possible transition to THC-rich ones or other drugs of use among teens and young adults, as well as to understand the public health implications of the rapidly growing cannabis industry (34,35). Strategies for screening and intervening will need to consider these myriad novel issues.

Dosing frequency and duration of use by IBD patients seems quite variable. It is unknown why 6 of the 15 CO users in our study did not consume CO in the past 30 days. In a retrospective study of pediatric epilepsy patients in Colorado, with similar issues of chronic illness and keen lay interest, the mean duration of cannabis use was 11.7 months with range of 0.3 to 57 months. The majority who discontinued use did not report adverse events, suggesting ''sociological factors'' influencing decision about use (36). In a 14-week trial of cannabis oral solution for Dravet syndrome, only about 50% of those completing the study enrolled in a long-term extension study (5). In contrast, a European registry of adults using a nasal THC:CBD spray for spasticity related to multiple sclerosis found that 68% continued long-term use, and, after mean duration of 1 year, found no evidence for addiction (24). Factors leading to discontinuation of use remain unclear. Possible explanations for discontinuation include that CO may not have provided expected benefits over time, or patients may have shifted to other established therapies or to other alternative therapies.

In conclusion, use of cannabis products is common, and new products such as CO are increasingly used. Some use CO daily or almost daily, perceive a medicinal benefit as well as low risk.

TABLE 3. Motivations for Use and Problems With Use for 6 IBD Patients Who Reported Using Cannabis Oil and No Other Forms of Cannabis

Survey Question: Do You Think You Use Marijuana ... (Check All That Apply)		
Medical reasons, n = 5/6	To relieve physical pain	4
	To relieve abdominal cramping	3
	To relieve nausea	2
Non-medical reasons	Attention: So that I can function: study, work, concentrate	2
Recreational and psychological, n = 3/6	Helps me not to get sick	2
	To feel good	1
	To feel normal	1
	It helps when I feel depressed or anxious	1
Recreational and psychological, n = 3/6	To relax and relieve tension	1
	To help me get to sleep	1

Prospective studies are needed to assess the effect of CO on pediatric IBD outcomes. Care teams should strive for open communication about use until further information on safety and efficacy becomes available.

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