Patients' perspectives on marijuana use for inflammatory bowel disease: a multicenter survey

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Abstract	**Background** As marijuana use is rising among patients with inflammatory bowel disease (IBD), so is interest in its potential use as a therapeutic agent. We sought to survey IBD patients regarding marijuana use, self-reported impact on IBD symptoms, and perceptions of safety. **Methods** A multicenter anonymous survey was administered to patients with IBD between October 2020 and June 2021. The 70-question survey collected demographic variables, clinical variables, attitudes about marijuana, and perceptions of its safety and efficacy in IBD. Participants were classified by their marijuana use: "rarely/never," "current," and "former". Percentage and chi-square tests were used to compare categorical variables between the 3 groups, and means and 2-group ANOVA were used for continuous variables. **Results** Of 181 patients surveyed, 166 were eligible for the study. Of these, 70 (42.2%) participants were rare/never marijuana users, 44 (26.5%) were current users, and 52 (31.3%) were former users. Fifty-three percent thought marijuana would help with IBD inflammation and 80% thought it would help with IBD pain. Over 70% of patients from all groups thought marijuana had a low-to-moderate risk of harm, and 69.6% of the participants who never or rarely used marijuana thought marijuana was addictive, compared to 20.5% of the current users and 44% of the former marijuana users. **Conclusions** While many patients thought marijuana use helps with IBD-related pain and inflammation, many expressed concerns about addiction to marijuana and a possible risk of harm. Further studies are needed to examine the benefit and harm of marijuana in IBD. **Keywords** Inflammatory bowel disease, marijuana, patient perspectives *Ann Gastroenterol 2023; 36 (6): 624-629*

Introduction

With the spreading legalization of marijuana, there has been growing interest among researchers and patients in its use for a variety of medical conditions. Use among patients with inflammatory bowel disease (IBD) in the United States (US) is higher than the national average, and prevalence studies in the US and beyond suggest that 10-16.4% of IBD patients are active cannabis users [1-3].

Given the intense interest in its potential effects, the IBD community has started investigating marijuana's role in inflammation and symptom control. Research has shown that marijuana acts on the cannabinoid CB1 and CB2 receptors in the enteric nervous and immune systems of the gastrointestinal tract [4]. Its effects reduce gut motility, intestinal secretion and epithelial permeability, and induce inflammatory leukocyte

recruitment and immune modulation [5]. However, there are very few clinical trials examining the effect of marijuana use on disease management in IBD [6-8]. Among the available studies, there is no clear evidence of disease remission, or improvement in severity or biochemical scores, and some studies have shown worse outcomes and greater need for surgery in patients with Crohn's disease (CD) [9]. Importantly, however, patients do report symptomatic improvement and better quality of life (QoL) when they have a poor or incomplete response to standard therapy.

While there is currently no strong evidence indicating a role for marijuana in the biochemical improvement of disease, its positive effect on symptom burden has been demonstrated in a number of studies. Research by Lal and Allegretti showed significant IBD-related symptom improvement among marijuana users, with alleviation of abdominal pain and diarrhea in both ulcerative colitis (UC) and CD patients [10,11]. Apart from symptom control, IBD patients have reported improved QoL in other areas, including general health perception, social functioning, ability to work and depression symptoms [3].

Additionally, there has been increasing international investigation into marijuana's use more broadly in autoimmune disease. One systematic review demonstrated that, among 2900 self-reported marijuana users with various autoimmune disorders, average pain levels dropped from 8.2 to 5.6 of 10 with marijuana use [12]. In a small study of 58 patients with rheumatoid arthritis, there was a significant decrease in pain levels among those treated with cannabinoids for 5 weeks [12]. Cannabinoids have had positive effects on patients with multiple sclerosis and autoimmune encephalitis, with patients showing a reduction in spasticity and pain [13]. Various mechanisms, including decreased expression of various inflammatory interleukins and tumor necrosis factor-α, as well as a reduction in oxidative species, have been proposed [12-14]. Hence, it is reasonable to hypothesize a potential translation of this effect to patients with IBD. Accordingly, with results suggesting that marijuana has a positive effect on symptom control and QoL, we sought to survey IBD patients regarding marijuana use, self-reported impact on IBD symptoms and perceptions of safety.

Patients and methods

Study design

This was a multicenter survey study conducted at 2 IBD centers: Beth Israel Deaconess Medical Center (BIDMC) and

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Lahey Medical Center (LMC). Patients with IBD scheduled for clinic visits were identified via billing information and contacted via phone in order to obtain their consent to participate in the study. Those who consented to the study received emails containing survey instructions, a concise overview of the study, and a link to an anonymous questionnaire on an online platform (REDCap), between October 2020 and June 2021. To ensure anonymity, all responses were kept confidential. A total of 181 patients answered the survey, 151 from BIDMC and 30 from LMC. Patients younger than 18 years and those who were non-English speakers were excluded. The Institutional Review Boards at BIDMC and LMC approved the study.

Questionnaire development

The questionnaire was designed to assess the patients' use of marijuana, cigarettes, e-cigarettes, alcohol and other substances, as well as their effects on IBD symptoms from the patients' standpoint. It contained 70 questions, including demographic information (age, sex, race), type of medical insurance (public, private, other), gastrointestinal diagnoses and symptoms, prescribed medications, history and frequency of use of marijuana, cigarettes, e-cigarettes, alcohol and other substances. Patients were asked about their concerns that marijuana would be harmful or addictive, or trigger an IBD flare, as well as whether it could treat pain or inflammation.

Based on their marijuana use, patients were classified as: a) "never or rarely used", if the participants reported never using marijuana, or using it once or twice; b) "current users", if they were occasional or regular users; or c) "former users", if they had consumed marijuana either regularly or occasionally in the past.

Statistical analysis

We compared the groups in term of demographics (age, sex, race), health insurance, employment status, IBD type, IBD symptoms, IBD medications, alcohol use, other substance use, tobacco use and e-cigarette use. Percentage and chi-square test were used to compare categorical variables between the 3 groups, and means and 2-group ANOVA were used for continuous variables. R version 4.04 (R foundation for statistical computing, Vienna, Austria) was used to analyze the data and the ggplot2 library was used to create illustrated bar-charts to compare the groups' answers to the questionnaire [15].

Our investigation conformed with the principles outlined in the Declaration of Helsinki.

Results

Of the 181 participants who answered the questionnaire, 166 were eligible to be included in the study. We excluded 7 participants who reported no history of IBD, while 8 did

not answer whether they were current, former, or never users of marijuana. The average age for all the participants was 63.73±15.4 years, 92 (56.1%) were female, 158 (95.2%) were white, and 136 (84%) had private insurance. Among the eligible patients, 45.8% had UC and 51.8% had CD; the most common IBD symptom (50%) was abnormal or bloody bowel movement, and 54.8% of the patients were on biologic medication for IBD. Seventy (42.2%) participants were rare or never marijuana users, 44 (26.5%) were current users, and 52 (31.3%) were former users of marijuana. Comparison of the 3 groups revealed that the former marijuana users were older, while 68% of those who never or rarely used marijuana were women (Table 1).

Regarding IBD characteristics, there were no statistical differences between the 3 groups in terms of reported IBD symptoms or IBD medication use; however, participants with current marijuana use had a trend to report more nausea and vomiting: 15.9%, compared to 8.6% in those who never or rarely used marijuana and 11.5% in former marijuana users. In addition, current marijuana users reported a trend towards less steroid use compared to the other 2 groups, but it was not statistically significant (Table 1).

Fifty-three percent of the patients thought that marijuana would help with IBD inflammation, and 80% thought it would help with IBD pain, more prominently in those with current or former marijuana use compared to never users (Fig. 1A,B). The majority of patients thought that marijuana would not increase the frequency of IBD flare compared to tobacco, and that it is less harmful than opioids, regardless of their history of marijuana use (Fig. 1C,D). 69.6% of the participants who never or rarely used marijuana thought that marijuana was addictive, compared to 20.5% of current users and 44% of former marijuana users (Fig. 1E). Other questions regarding the harmful risk of marijuana from the patients' perspectives are summarized in Fig. 1F,G.

Table 1 Demographic and clinical characteristics of patients by degree of marijuana use

Patient characteristics	Marijuana use			
	Never or rarely	Current	Former	P-value
Number of patients	70	44	52	
Age (mean±SD)	48.77±15.84	47.5±16.56	55.68±15.65	0.035
Female sex (%)	47 (68.1)	19 (44.2)	26 (50)	0.026
White race (%)	63 (90)	44 (100)	51 (98.1)	0.026
Private insurance (%)	60 (89.6)	37 (84.1)	39 (76.5)	0.159
Employment (%)				0.237
Yes	45 (64.3)	35 (79.5)	34 (65.4)	
No	19 (27.1)	6 (13.6)	10 (19.2)	
Other	6 (8.6)	3 (6.8)	8 (15.4)	
IBD (%)				0.393
Ulcerative colitis	29 (41.4)	19 (43.2)	28 (53.8)	
Crohn's disease	38 (54.3)	25 (56.8)	23 (44.2)	
Other	3 (4.3)	0 (0)	1 (1.9)	
IBD symptoms				
Number of IBD symptoms (mean±SD)	1.29±1.08	1.50±1.30	1.52±1.20	0.479
Any IBD symptom (%)	43 (61.4)	26 (59.1)	32 (61.5)	0.962
Nausea or vomiting (%)	6 (8.6)	7 (15.9)	6 (11.5)	0.488
Abdominal pain (%)	19 (27.1)	14 (31.8)	17 (32.7)	0.772
Abnormal or bloody bowel movement (%)	34 (48.6)	22 (50)	26 (50)	0.984
Other symptoms (%)	17 (24.3)	7 (15.9)	13 (25)	0.493
IBD meds (%)				
Steroids	8 (11.4)	2 (4.5)	5 (9.6)	0.452
Antibiotics	2 (2.9)	0 (0)	0 (0)	0.250
Aminosalicylates	13 (18.6)	9 (20.5)	13 (25)	0.685
Immunomodulators	12 (17.1)	4 (9.1)	6 (11.5)	0.424
Biologic medications	32 (45.7)	27 (61.4)	32 (61.5)	0.132
Alcohol use (%)	38 (54.3)	29 (65.9)	39 (75)	0.059
History of substance abuse	0 (0)	0 (0)	7 (13.5)	<0.001
Current or former user of electronic cigarettes (%)	4 (6.1)	4 (9.1)	7 (13.7)	0.367
Tobacco use (%)				
Never or rarely	46 (66.7)	20 (45.5)	23 (44.2)	0.095
Current or former	23 (33.3)	14 (54.6)	29 (55.8)	

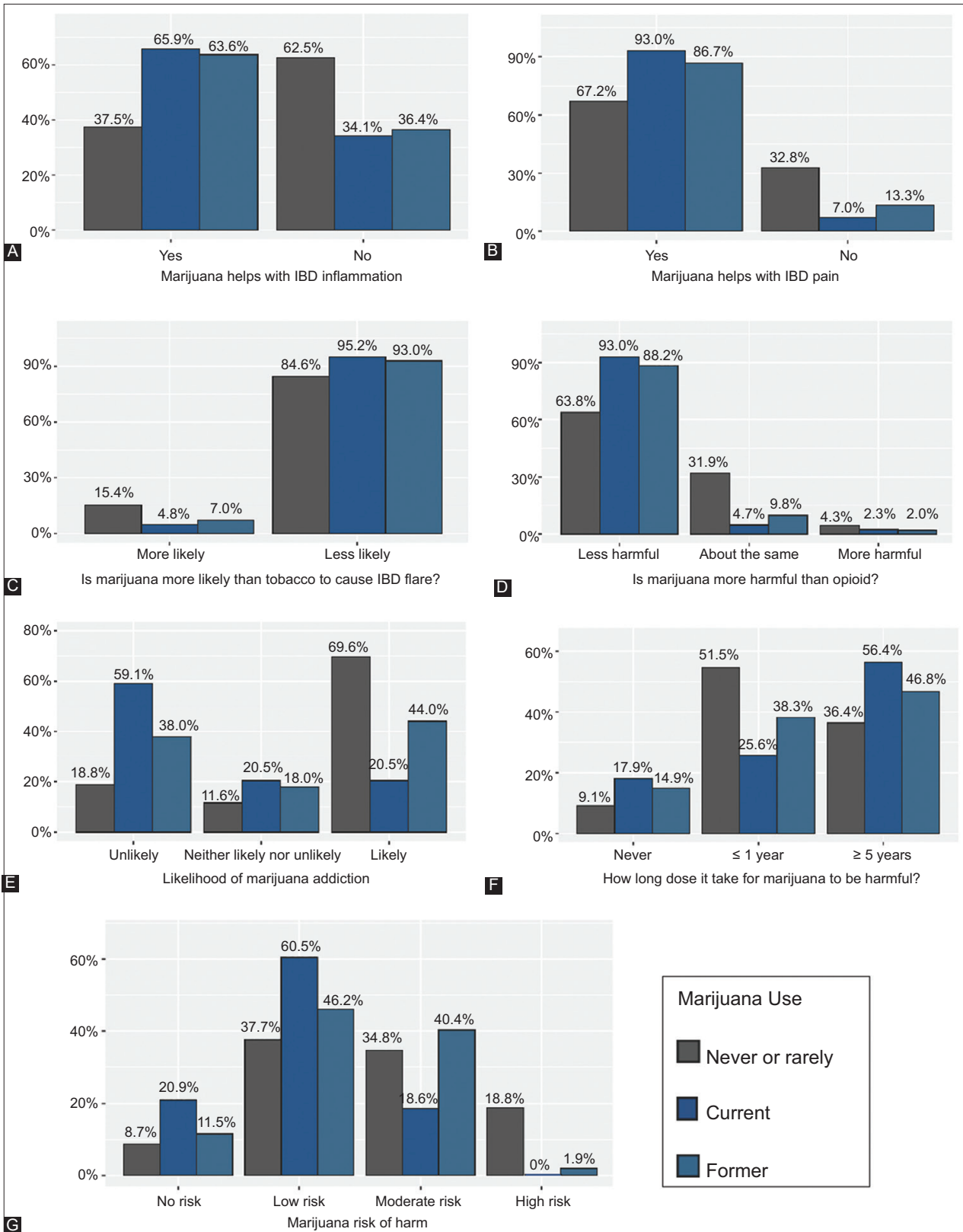*SD, standard deviation; IBD, inflammatory bowel disease*

Figure 1 (A-G) Survey responses of patients' perspectives on marijuana use for inflammatory bowel disease (IBD)

Discussion

With increasing patterns of legalization across the US, interest has emerged in marijuana as a potential new therapy for IBD; however, given the many ongoing barriers to research in the field, there is limited evidence concerning its efficacy and safety in improving outcomes in patients with IBD. While objective endpoints have shown no evidence of disease improvement, there has been a trend in the literature towards improved subjective IBD symptom management with marijuana use, but with little understanding of the patient's perspectives on its use. Therefore, in the current study we report on IBD patients' views regarding marijuana use patterns, self-reported impact on IBD symptoms, and perceptions of safety. While several studies have investigated the effect of marijuana on symptom burden, our study is unique in its investigation of patient perspectives and attitudes towards marijuana use [1,9,16].

Exploring patient perspectives on an emerging therapeutic modality is important for several reasons. It allows investigators to confirm that there is sufficient patient interest to warrant further investigation into the therapy, understand its current effect, and elicit patient concerns and barriers to use so that they can be addressed.

Overall, in this survey of 166 eligible IBD patients, we demonstrated that the majority thought that marijuana use would help with IBD pain and inflammation, regardless of whether they had ever used marijuana. IBD patients largely thought marijuana was safer than tobacco in terms of flare risk, and less harmful than opioids for pain reduction. This opinion was more prevalent among current/former marijuana users. The majority of all patients surveyed, however, expressed concern that marijuana use was associated with a low-to-moderate risk of harm, while almost 20% of never users were concerned about a high risk of harm, indicating a need to address concerns about marijuana use. The average age of our population may appear higher than that of some clinic populations, and reflects the clinic patients at our medical centers; however, when the standard deviation is included our population age spans approximately 32-64 years, which captures the majority of the adult population.

Our survey revealed that the majority of patients are concerned about harms associated with marijuana; this represents a major potential barrier to use that requires further exploration. Interestingly, perceptions of the amount of time using marijuana required to cause harm varied widely among the 3 patient groups. This is likely reflected by the dearth of longitudinal data investigating the long-term effects of marijuana use. In their 2017 randomized control trial, Naftali *et al* investigated the safety and efficacy of ingested cannabidiol (CBD) and saw a low side-effect profile over the study period [7]. Importantly, however, the study had an 8-week duration of therapy with an additional 2-week follow up, much shorter than the typical months to years of use seen in practice, and therefore does not fully investigate the ongoing risk of harm. Additionally, their study acknowledges the use of a low dose of CBD, which may explain the minimal

observed benefit and low risk profile. Storr *et al* went so far as to demonstrate significant harm associated with marijuana, with use greater than 6 months being a predictor of surgery in CD [9]. The spectrum of results varies significantly, and further investigation is necessary to demonstrate safety and address patient concerns.

Patient-centered studies are necessary to identify common misconceptions of a therapy that require further investigation or education. In our study, approximately two thirds of current and former smokers believed that marijuana use helped with inflammation; however, our current body of literature suggests no impact on inflammation or disease remission [1,4,6-8]. When discussing the benefits and risks of marijuana use with patients, it would therefore be important to emphasize that we do not expect disease regression, but rather focus on potential symptom relief. Additionally, concern about marijuana addiction was high among non-users, with over 70% expressing the opinion that addiction was likely. This may represent a significant barrier to use among current non-users. While investigation is ongoing, marijuana does appear to mimic the addictive properties of other substances, but to a lesser extent [17]. Additional counseling on these topics will be helpful for patients considering marijuana therapy.

The prevalence of marijuana use varies greatly internationally. Reported rates of use among adolescents and young adults have been shown to be higher in the US (2.5-11.7%) than in other European countries (0.0-2.6%) [18]. Differences in reported rates likely reflect cultural and legal differences in marijuana use. If the effects of marijuana are largely driven by perceived symptom relief, rather than objective signs of reduced inflammation, it is possible that the effect of marijuana on IBD symptoms may be lower in countries where marijuana is less liberally used.

The greatest challenge to counseling patients on marijuana use is the lack of literature addressing its true risk-benefit profile and effect on symptoms. Currently, there are 3 studies that investigated marijuana compared to placebo/standard of care and evaluated the response to therapy and/or induction of remission, as described in the meta-analysis by Desmarias *et al* [6-8,19]. Irving *et al* [8] investigated marijuana use in UC patients, finding no evidence of treatment remission, while additionally all 29 patients in the treatment group had adverse events. In the 2 CD trials by Naftali *et al* [6,7] there was no evidence of remission, while adverse events were not reported on a per-patient basis and therefore could not be determined. Overall, the quality of evidence was graded as low and very low for UC and CD, respectively, owing to factors including small sample sizes and high variability in the formulations of marijuana used. The Crohn's and Colitis Foundation commissioned a review that also reports the need for further safety information, and attributes the difficulty in evaluating the effect of use to the large heterogeneity in study design [3]. Further systematic research protocols with discrete formulations and larger sample sizes will be needed to advance our body of knowledge.

While our study has many strengths, it is limited by a patient population that was primarily white and privately insured, representing a relatively higher socioeconomic status (SES) than the average population. It will be important in

future studies to engage patients of lower SES, who may have a more challenging social and political history associated with marijuana, and whose perceptions of use may differ from our population. Because of our sample size, we were not able to perform a subgroup analysis comparing UC and CD, or those who are on biologics vs. other treatment. Marijuana doses were not registered, and patients were not surveyed on their type of marijuana use (e.g., tetrahydrocannabinol vs. CBD); however, there is currently no literature delineating any known differences between these formulations in IBD. Additionally, our cohort had a high rate of comorbid tobacco use. Marijuana may appear less harmful to those using a substance that is known to cause harm and worsen IBD.

Overall, our multicenter study is unique in its investigation of patient perceptions of the safety and efficacy of marijuana use in IBD. We demonstrated that, while many patients have reported a reduction in symptom burden, there is concern about the harms and addictive potential associated with marijuana use that will need to be addressed with ongoing research and counseling by physicians. Based on the results of this study, we argue that continued investigation into marijuana as a potential therapy is warranted, given patients' acceptance of its use in IBD.

Acknowledgment

Summary Box

What is already known:

- The spreading legalization of marijuana has led to increased interest in its application to medical therapeutics
- Marijuana use among patients with inflammatory bowel disease (IBD) is higher than the national average among the United States population
- While the current literature suggests that marijuana does not improve inflammation due to IBD, its impact on symptom burden is unknown

What the new findings are:

- Patients (both marijuana users and non-users) largely thought that marijuana would improve pain and symptom burden
- Patients were concerned about the addictive potential of marijuana
- Patients perceived marijuana as safer than tobacco and opioids

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