Knowledge, Perception, and Use of Cannabis Therapy in Patients with Inflammatory Bowel Disease

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Objective: In 2017, the government of Puerto Rico legalized medical cannabis for several conditions including Crohn's disease (CD). There is little information about cannabis use in this population. This study aimed to develop a demographic characterization and evaluate patient perception on cannabis use for Inflammatory Bowel Disease (IBD) at the University of Puerto Rico Center for Inflammatory Bowel Diseases.

Methods: One hundred patients of ages 21 or older with a confirmed diagnosis of IBD were recruited to complete a voluntary anonymous questionnaire.

Results: 27% of the surveyed participants reported use of cannabis. Of these, 39% reported moderate knowledge and 53% reported little to no knowledge of medical cannabis. The majority did not discuss cannabis use with their physician (78%), and most saw improvement of their symptoms (68%).

Conclusion: Cannabis is frequently considered by patients as a treatment option for IBD but most have limited knowledge about its use. The low number of patients that discuss cannabis use with their physician suggests the need for physician awareness of unreported use. It should also lead to the development of strategies for patient orientation regarding the uses, properties, and expectations of cannabis as a therapy.
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Key words: Cannabis, Inflammatory Bowel Disease, Puerto Rico, Medical Marihuana

Inflammatory Bowel Diseases (IBD) are chronic inflammatory conditions of unknown etiology comprised mainly of ulcerative colitis (UC) and Crohn's disease (CD). The gastrointestinal symptoms of IBD include nausea, abdominal pain, diarrhea, and hematochezia and extraintestinal manifestations include arthritis and fatigue (1). A "treat to target" management strategy is recommended with the aim of symptomatic improvement along with endoscopic and histologic remission (2). A significant proportion of patients, particularly those with severe disease not responding to therapy, seek complementary and alternative medications to improve symptoms of pain, nausea, appetite, and overall mood, and between 10 and 18% have been reported to use cannabis as part of the treatment for their IBD (3, 4). Previous abdominal surgery, chronic analgesic use, chronic abdominal pain and low quality of life have been associated to cannabis use (3, 4). There is little scientific data and no current accepted medical indication for the use of cannabis as treatment for IBD (5).

The basis for the use of cannabis as an alternative medication lies in the components of the Cannabis sativa plant, THC and cannabidiol, which can act via the endocannabinoid system similar to the endogenous cannabinoids. The gastrointestinal tract is lined with multiple receptors of the endocannabinoid system, including the main receptors: Cannabinoid Receptor 1 and 2 (CB1 and CB2). CB1 receptors are mainly expressed in the enteric nervous system, the epithelial lining, plasma cells, and smooth muscle cells lining blood vessels in the gastrointestinal tract. Cannabinoids can reduce gastric acid secretion by activating CB1 receptors and slow or increase gut motility via activation or inhibition, respectively, of the CB1 receptors present in enteric neurons (4, 6). Activation of CB1 receptors may therefore reduce hypermotility associated symptoms such as diarrhea and nausea reported by patients (7). On the other hand, CB2 receptors are mostly found in immune cells, myenteric plexus neurons, and in epithelial cells during UC (5, 6). CB2 receptor activation has been found to attenuate the immune response by inducing apoptosis and decrease proliferation of T cells, and by reducing the recruitment of neutrophils, T cells, and macrophages to the inflamed colon (7).

The endocannabinoid system signaling appears to be altered during inflammation of the intestine. Increased expression of CB1 and CB2 receptors, endogenous cannabinoids, and

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reduced expression of cannabinoid degrading enzymes have been observed in the early phases of colitis (6). However, endoscopic biopsies in patients with CD and UC, which were taken from small bowel (CD) and colon, were evaluated for endocannabinoid levels, expression of receptors, and activity of enzymes involved in endocannabinoid synthesis and degradation found that CB1 levels were increased in areas of inflammation whereas CB2 expression was unaltered (4). Another study found increased CB2 expression in endoscopic biopsies taken from the colon of UC patients with mild to moderate pancolitis (4). Although research is still underway to determine exactly how gastrointestinal inflammation affects the endocannabinoid system, pharmacologic strategies to amplify cannabinoid levels have been found to ameliorate inflammation in experimental colitis models (6). These studies are suggestive of how cannabinoids could act to reduce symptoms and provide relief in patients suffering from IBD.

In 2017, the government of the Commonwealth of Puerto Rio legalized medicinal cannabis for several specific indications, including CD. The process does not require the recommendation of a gastroenterologist and prescription privileges are limited to specifically certified physicians. Patients with IBD and their relatives inquire about the benefits of the drug and an undetermined number are using medicinal cannabis, with or without their physicians' knowledge and/or approval. Current expert reviews do not recommend the use of cannabis for the treatment of IBD in view of the lack of literature supporting its benefits (5).

Understanding the use of cannabis in patients with IBD can be helpful for the treating physicians. Knowing the prevalence of cannabis use in these patients and the purpose and pattern of use could be useful in improving physician-patient communication, designing treatment strategies, and addressing patient needs. To attempt to answer some of these questions, we designed a research to determine the prevalence of cannabis use in patients with IBD in the UPR Center for Inflammatory Bowel Diseases, describe the demographics of cannabis users, and evaluate patient perception on the benefits of cannabis use.

Materials and Methods

The Center for Inflammatory Bowel Diseases of the University of Puerto Rico is an integrated interdisciplinary academic healthcare service for patients with IBD from all the island composed of adult and pediatric gastroenterologists, health psychologists, IBD surgeons, an enterostomal nurse and pharmacists. This cross-sectional study was carried out in the weekly IBD clinics. The study consisting of a self-administered anonymous survey was introduced by the investigators to patients attending the clinic. Anonymity was selected as an incentive to foster participation and honesty. Exclusion criteria included the following: unwillingness to participate, inability to fill out the questionnaire, being a minor under Puerto Rico law, and not having a confirmed diagnosis of IBD. Participants who did not meet exclusion criteria and were interested in participating were taken to a private room to receive more information about the study and given the survey. After completing the questionnaire, patients placed it in a plain envelope and deposited it in a box (urn) in the same room. The questionnaires did not include any identifiable information or date of completion and were not collected by the research staff until the end of the clinic. This was an additional precaution for assuring anonymity. Treating physicians were not involved in the recruitment nor notified of any patient participation. Envelopes were collected by a research assistant and maintained under lock at the research unit.

One hundred patients of ages 21 or older with a confirmed diagnosis of IBD were recruited and completed the questionnaire. The questionnaire, shown in Figure 1, consisted of 19 questions including demographics (only age group and sex), clinical diagnosis (CD or UC), and use of cannabis. For patients who indicated that they were using or had used cannabis, specific questions followed regarding mode (smoked or ingested), frequency, purpose (recreational or medicinal), source, and the cost of cannabis. Patients were specifically asked if they had used cannabis to alleviate IBD-related symptoms and if it had relieved their symptoms.

The survey was designed by the investigators and tested for clarity with relatives and peers. The content was developed based on the literature of the subject and common concerns and questions raised by patients and physicians. The study characteristics were described using frequency distributions for categorical variables and summary measures for quantitative variables. Estimated prevalence of cannabis use among patients with IBD was calculated. Statistical analyses were performed using STATA v14. To determine whether the probability of wanting physician approval of medical cannabis for IBD was associated with its use or perceived knowledge, a logistic regression analysis was performed for both variables independently. The protocol was approved by the MSC IRB.

Results

One hundred subjects completed the survey. The distribution of subjects into age groups was as follows: thirty-nine were between 21 and 30, twenty-four were between 31 and 40, sixteen were between 41 to 50, fourteen were between 51 and 60 and seven were older than 60. The majority were diagnosed with Crohn's disease (78%). Male to female ratio was 1:1. Self-reported classification of IBD severity among responders was in remission (42%), followed by moderate (30%), severe (15%), and mild (10%). Only 3% of respondents classified their severity as other. As seen in Table 1, although the largest group (39%) reported moderate knowledge about medical cannabis, 37% reported lack of knowledge about possible therapeutic properties in IBD. Of the 63% that considered cannabis use, only 21% had consulted with their physician. Table 2 shows aspects related to the use of cannabis. Of those who reported use of cannabis (27%), only 40% were licensed for medical cannabis

Figure 1. Survey

A survey of cannabis use among patients with Inflammatory Bowel Disease (IBD)
Un cuestionario sabre el uso de cannabis entre los pacientes de Enfermedades Inflamatorias del Intestino (EII)

Cuestionario

1. Edad:
   a. 21-30 años
   b. 31-40 años
   c. 41-50 años
   d. 51-60 años
   e. >60 años
2. Sexo:
   a. Masculino
   b. Femenino
3. ¿Cuál Enfermedad Inflamatoria de Intestino (EII) padece?
   a. Crohn
   b. Colitis Ulcerosa
   c. Indeterminada
   d. Otros: _____
4. ¿Cómo clasificaría su enfermedad inflamatoria del intestino actualmente?
   a. En remisión - No activa (controlada)
   b. Leve
   c. Moderada
   d. Severa
   e. Otra:_____
5. ¿Cuánto conoce usted sobre el cannabis medicinal?
   a. Nada
   b. Poco
   c. Regular
   d. Mucho
6. ¿Cuánto conoce usted sobre el uso del cannabis como tratamiento para enfermedades inflamatorias del intestino?
   a. Nada
   b. Poco
   c. Regular
   d. Mucho
7. ¿Ha considerado utilizar cannabis para EII?
   a. Sí
   b. No
   c. Tal vez
8. ¿Ha consultado con su médico sobre el uso del cannabis?
   a. Sí
   b. No
9. ¿Utiliza o ha utilizado usted el cannabis? Si su contestación es NO, continúe en la pregunta #19
   a. Sí
   b. No
10. Si lo utiliza, ¿Cuál es el propósito?
    a. Medicinal para EII
    b. Medicinal para otra condición médica
    c. Recreacional
    d. Otro: _____
11. Si lo ultiliza, ¿Cómo obtiene el cannabis que se administra?
    a. Recetado
    b. No Recetado
    c. Otro: _____
12. ¿Qué método ha utilizado para administrarse el cannabis?
    a. Inhalación (fumado)
    b. Ingerido (e.g. *Brownies*, bebidas, pastillas, etc.)
    c. Vaporización
    d. Aceite
    e. Otros: _____
13. ¿Con que frecuencia utiliza el cannabis a la semana?
    _____
14. ¿Cuánto diría que gasta mensualmente en cannabis?
    _____
15. ¿Para qué síntomas utiliza o ha utilizado el cannabis? Elija todas las que aplique.
    a. Dolor abdominal
    b. Dolor en articulaciones
    c. Dolor de espalda baja
    d. Diarrea
    e. Pérdida de apetito
    f. Malestar general
    g. Otros: _____
16. ¿Ha notado alguna mejoría en sus síntomas luego de la utilización del cannabis?
    a. Sí
    b. No
    c. Tal vez
17. ¿Ha notado alguna mejoría en su calidad de vida con la utilización del cannabis?
    a. Sí
    b. No
    c. Tal vez
18. ¿Recomendaría el uso del cannabis para enfermedades inflamatorias del intestino?
    a. Sí
    b. No
    c. Tal vez
19. ¿Cree usted que deberían aprobar el uso del cannabis como posible tratamiento complementario para EII?
    a. Sí
    b. No
    c. Tal vez

use, 36% (8/22) reported daily use, and 56% used cannabis to relieve IBD-related symptoms. The largest group (42%, n=19) spent between $25-50 monthly and the most frequent formulations were vaporized (59%) and smoked (56%). Table 3 shows symptoms leading to the use of cannabis. The majority (68%) reported an improvement of symptoms and 72% an improvement in quality of life; 85% (n=26) of users would recommend cannabis use for IBD and 79% of all respondents believed it should be approved as a potential complementary treatment for IBD. The probability of wanting physician approval of medical cannabis for IBD was related with its use (P=0.03) but not related to perceived knowledge (P=0.36).

Discussion

This study provides a demographic characterization of a cohort of patients attending the IBD clinics and the estimated prevalence, purpose of use, knowledge, and perception about cannabis in the group. The surveyed population was composed mostly of patients in their third decade of life, with an equal distribution between males and females. Nearly 80% of the participants were diagnosed with Crohn's disease and most perceived their IBD to be in remission. Most of the other studies that surveyed IBD patients regarding cannabis use were composed of a predominantly female population with a mean age of participants older than 30 years of age, and most had a diagnosis of CD (1, 3, 8, 9). One study which only surveyed patients between ages 18-21 years old found predominantly males; the majority were also diagnosed with CD (10). Compared to these studies, the cohort evaluated in our study is predominantly composed of younger patients with an equal representation of males and females. Most of the participants were diagnosed with CD, as seen in all the other studies.

The prevalence of current or past use of cannabis in this cohort was 27%. There is limited data regarding the prevalence of cannabis use in the general population of Puerto Rico, but an estimated annual 4.88% of those between 15 and 64 years

Table 1. Knowledge about cannabis

Patient Understanding (n=100)			
Knowledge About Medical Cannabis	**Knowledge About Cannabis for IBD**	**Considered Cannabis for IBD**	**Consulted Physician About Cannabis Use**
None 15%	None 37%	Yes 63%	Yes 21%
Low 38%	Low 26%	No 10%	No 78%
Moderate 39%	Moderate 31%	Maybe 27%	n/a 1%
High 8%	High 6%		

Table 2. Cannabis use

Cannabis Users		
Purpose of Cannabis Use (n=27)	**Method of Administration (n=27)**	**Method of Acquiring Cannabis (n=25)**
IBD 56%	Inhaled 56%	Prescription 40%
Other Condition 11%	Ingested 37%	No Prescription 48%
Recreational 41%	Vaporized 59%	Other 12%
Other 4%	Oil 41%	
	Other 4%	

Table 3. Symptoms leading to cannabis use and outcomes

Cannabis Users		
Symptoms Provoking Use of Cannabis (n=27)	**Improvement of Symptoms (n=25)**	**Quality of Life Improvement (n=25)**
Abdominal Pain 56%	Yes 68%	Yes 72%
Joint Pain 44%	No 8%	No 8%
Lower Back Pain 41%	Maybe 24%	Maybe 20%
Diarrhea 30%		
Poor Appetite 41%		
General Malaise 52%		
Other 26%		

of age had used cannabis in 2005 according to the United Nations World Drug Report (11). Our study reveals a much higher prevalence of patients in the UPR-IBD population who use or have used cannabis as an alternative or complementary medication. A survey of 302 patients attending an IBD center in Massachusetts in 2017 reported 22.8% of the participants were users of marijuana (recreational or medicinal) (3). Similarly, a survey of 319 patients in the Gastroenterology outpatient department at the University of Calgary found that 17.6% of participants reported current or past use of cannabis, which is lower than the prevalence in the cohort presented in our study (1). On the other hand, several surveys reported a higher prevalence of cannabis use. These included a survey of 291 IBD patients at the Mount Sinai Hospital Centre (Toronto), which found a prevalence of 48.9% of current or previous cannabis use (8), and a survey of 292 IBD patients at the Brigham and Women's Hospital Crohn's and Colitis Center, which found a prevalence of 51.3% of current or previous use (9). In addition, another survey of IBD patients from Yale New Haven Children's Hospital between the ages of 18-21 found a prevalence of 70% of current or past use of cannabis (10). Although our study has a much smaller number of participants, the prevalence of use of cannabis was slightly higher than of that reported in Massachusetts and the University of Calgary but much lower than the other reports.

The majority (56%) of cannabis users in our study stated IBD as the main reason for use. Furthermore, cannabis users reported an improvement of their overall symptoms (68%) and their quality of life (72%). Among the symptoms reported to have improved with the use of cannabis, abdominal pain was the most prevalent, similar to several other studies reported (1, 8, 9). These results could suggest that cannabis may be an effective alternative for the symptomatic management of abdominal pain in IBD. However, most of the patients in the present study reported having their disease in remission, which may also account for a better outcome due to a milder disease process. Similar to abdominal pain, symptoms such as general malaise, joint pain, lower back pain, and poor appetite were reported as being improved with the use of cannabis. Further studies are warranted in order to objectively assess if there is an actual improvement of these symptoms and measurable disease activity and whether the alleviating effects of cannabis are due to its potential anti-inflammatory or psychotropic effects.

The mode of administration of cannabis was also evaluated. The main method of cannabis administration found in this study was vaporized cannabis products, with smoking following closely. This finding differs from results in past and recent literature, where smoking joints or cigarettes were the predominant mode of cannabis consumption (1, 8, 9, 10). One study reports that vaporized cannabis consumption may have increased in recent times due to the emerging popularity and availability of assorted vaporizers (12). Other findings reported in this study include stronger drug effects and an association with less toxicant exposure with vaporized cannabis use when compared to smoking. The rising popularity of vaporizers, increased cannabis effects, and reduced exposure to toxic substances may be reasons as to why the participants in this study preferred vaporizers over smoking.

The results obtained show that more than half of responders have considered the use of cannabis as an alternative medicine. However, the vast majority also reported moderate to no knowledge of its therapeutic properties. Within the group of patients that reported cannabis use, most (78%) had not discussed cannabis use with their physician. Other studies also reported 70% and 87.2% of their patients respectively did not discuss use with their gastroenterologist. (10, 13) This high percentage may be due to the taboos or misconceptions

associated with the use of cannabis in general or the belief that their physicians would disapprove. This reinforces the need for physicians to inquire about cannabis use when seeing IBD patients and the development of strategies that help with both physician awareness and patient orientation on the uses, properties, and expectations of cannabis as a treatment for IBD symptoms. Of note, of those who reported using cannabis, only a small portion had a medical license for its use. This may suggest a lack of information among patients about how to access medical cannabis legally and the need for a better understanding as to why respondents choose the specific method of acquiring cannabis. Physical and/or monetary access to medical cannabis also warrants investigation.

There are several limitations in this study. The study population is small, and there may be a bias towards more severe cases given that we are a specialized IBD center, which may impact the prevalence of medical cannabis use. No objective measures were used and therefore, the data is limited to the participant's perception about their disease severity and the improvement of symptoms with the use of cannabis. Because we designed the study to guarantee anonymity, no data was collected on the use of other medications for IBD or pain management to assess alternate causes for symptom improvement that may have been inadvertently attributed to cannabis use. Additionally, data regarding the type of cannabis used by the participant, the dosage, or any adverse effects associated with the use of cannabis was not collected. Lastly, further studies are also needed to determine whether cannabis use has a clinically relevant effect on IBD inflammatory activity. Until all these important questions are answered, the addition of medical cannabis to the management of IBD lacks conclusive evidence to warrant a recommendation.

Resumen

Objetivo: En el 2017 el gobierno de Puerto Rico legalizó el cannabis medicinal para varias condiciones, incluyendo la enfermedad de Crohn. Existe muy poca información sobre el uso de cannabis en esta población. Este estudio tuvo como meta desarrollar una caracterización demográfica y evaluar la percepción de los pacientes del Centro para Enfermedades Inflamatorias del Intestino de la Universidad de Puerto Rico en cuanto al uso de cannabis para enfermedad inflamatoria intestinal (EII). Métodos: Cien pacientes de 21 años o mayor con diagnóstico confirmado de EII fueron reclutados para llenar un cuestionario anónimo y voluntario. Resultados: El 27% de los pacientes reportaron uso de cannabis. De estos, 39% reportó conocimiento moderado y 53% reportó conocimiento pobre o ninguno sobre cannabis medicinal. La mayoría (78%) no discutió el uso de cannabis con su médico y la mayoría (68%) reportó una mejoría en sus síntomas. Conclusión: El uso de cannabis medicinal como una opción para tratar su EII es considerado frecuentemente por los pacientes, aunque la mayoría tiene un conocimiento limitado sobre su uso. Son pocos los que discuten el uso de cannabis con su médico, lo cual sugiere la necesidad de crear conciencia en los médicos sobre el uso no reportado de cannabis. Sugerimos desarrollar estrategias para orientar a los pacientes sobre el uso, las propiedades y expectativas que podrían tener en cuanto al cannabis medicinal para tratar EII.

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References

1. Storr M, Devlin S, Kaplan GG, Panaccione R, Andrews CN. Cannabis use provides symptom relief in patients with inflammatory bowel disease but is associated with worse disease prognosis in patients with Crohn's disease. Inflamm Bowel Dis 2014; 20:472-480.
2. Darr U, Khan N. Treat to Target in Inflammatory Bowel Disease: An Updated Review of Literature. Curr Treat Options Gastroenterol. 2017 Mar;15(1):116-125. doi: 10.1007/s11938-017-0130-6. PMID: 28161818.
3. Merker AM, Riaz M, Friedman S, Allegretti JR, Korzenik J. Legalization of Medicinal Marijuana Has Minimal Impact on Use Patterns in Patients With Inflammatory Bowel Disease. Inflamm Bowel Dis 2018; 24:2309-2314.
4. Ahmed W, Katz S. Therapeutic Use of Cannabis in Inflammatory Bowel Disease. Gastroenterol Hepatol 2016; 12:668-679.
5. Kafil TS, Nguyen TM, MacDonald JK, Chande N. Cannabis for the Treatment of Crohn's Disease and Ulcerative Colitis: Evidence from Cochrane Reviews Inflamm Bowel Dis 2019; 20:1-8.
6. Hasenoerhl C, Taschler U, Storr M, Schicho R. The gastrointestinal tract – a central organ of cannabinoid signaling in health and disease. Neurogastroenterol Motil 2016; 28:1765-1780.
7. Weiss A, Friedenberg F. Patterns of cannabis use in patients with Inflammatory Bowel Disease: A population-based analysis. Drug Alcohol Depend 2015; 156:84-89.
8. Lal S, Prasad N, Ryan M, Tangri S, et al. Cannabis use amongst patients with inflammatory bowel disease. Eur J Gastroenterol Hepatol 2011; 23:891-896.
9. Ravikoff Allegretti J, Courtwright A, Lucci M, Korzenik JR, Levine J. Marijuana use patterns among patients with inflammatory bowel disease. Inflamm Bowel Dis 2013; 19:2809-2814.
10. Phatak UP, Rojas-Velasquez D, Porto A, Pashankar DS. Prevalence and Patterns of Marijuana Use in Young Adults with Inflammatory Bowel Disease. J Pediatr Gastroenterol Nutr 2017; 64:261-264.
11. World Drug Report 2019. United Nations : World Drug Report 2019. https://wdr.unodc.org/wdr2019/. Published 2019. Accessed April 18, 2021.
12. Spinle TR, Cone EJ, Schlienz NJ, Mitchell JM, et al. Acute Effects of Smoked and Vaporized Cannabis in Healthy Adults Who Infrequently Use Cannabis: A Crossover Trial. JAMA Netw Open 2018; 1:e184841.
13. Kerlin AM, Long M, Kappelman M, Martin C, Sandler RS. Profiles of Patients Who Use Marijuana for Inflammatory Bowel Disease. Dig Dis Sci 2018; 63:1600-1604.