

Treatment of Crohn's Disease with Cannabis: An Observational Study

Timna Naftali MD¹, Lihi Bar Lev BA², Doron Yablekovitz MD¹, Elisabeth Half MD¹ and Fred M. Konikoff MD¹

¹Institute of Gastroenterology and Hepatology, Meir Medical Center, Kfar Saba affiliated with Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

²Department of Psychology, Faculty of Social Sciences, Tel Aviv University, Ramat Aviv, Israel

ABSTRACT: **Background:** The marijuana plant cannabis is known to have therapeutic effects, including improvement of inflammatory processes. However, no report of patients using cannabis for Crohn's disease (CD) was ever published.

Objectives: To describe the effects of cannabis use in patients suffering from CD.

Methods: In this retrospective observational study we examined disease activity, use of medication, need for surgery, and hospitalization before and after cannabis use in 30 patients (26 males) with CD. Disease activity was assessed by the Harvey Bradshaw index for Crohn's disease.

Results: Of the 30 patients 21 improved significantly after treatment with cannabis. The average Harvey Bradshaw index improved from 14 ± 6.7 to 7 ± 4.7 ($P < 0.001$). The need for other medication was significantly reduced. Fifteen of the patients had 19 surgeries during an average period of 9 years before cannabis use, but only 2 required surgery during an average period of 3 years of cannabis use.

Conclusions: This is the first report of cannabis use in Crohn's disease in humans. The results indicate that cannabis may have a positive effect on disease activity, as reflected by reduction in disease activity index and in the need for other drugs and surgery. Prospective placebo-controlled studies are warranted to fully evaluate the efficacy and side effects of cannabis in CD.

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KEY WORDS: Crohn's disease, inflammatory bowel disease, cannabis, marijuana

The marijuana plant, *Cannabis sativa*, has been used as a medicinal treatment for a variety of diseases [1]. Cannabinoids have been reported to alleviate neurological conditions including multiple sclerosis-related symptoms such as spasticity, pain, tremor and bladder dysfunction [2]. Other neurological conditions, such as chronic intractable pain, dystonic movement disorders, and Tourette's syndrome were also reported to be alleviated by cannabis use [3]. Cannabis has been used to treat anorexia in AIDS and cancer patients [2,3].

In gastroenterology, cannabis has been used to treat anorexia, emesis, abdominal pain, gastroenteritis, diarrhea, intestinal inflammation, and diabetic gastroparesis [4].

The cannabis plant contains over 60 different compounds, which are collectively referred to as cannabinoids [5]; of them Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD) seem to be the most active. Cannabinoids have a profound anti-inflammatory effect, mainly through the CB2 receptor [2]. Cell-mediated immunity was found to be impaired in chronic marijuana users [6]. A potent anti-inflammatory effect of cannabis was observed in rodents [7]. Studying the functional roles of the endocannabinoid system in immune modulation reveals that it is involved in almost all major immune events. Cannabinoids shift the balance of pro-inflammatory cytokines and anti-inflammatory cytokines towards the T helper cell type 2 profiles (Th2 phenotype) and suppress cell-mediated immunity, whereas humoral immunity may be enhanced [8]. Therefore, cannabinoids may be used to treat various inflammatory conditions including rheumatoid arthritis. In a mouse model of colitis, cannabinoids were found to ameliorate inflammation [9]. Consequently, the non-conventional medical community has recommended cannabis for patients with inflammatory bowel disease. However, there are no systematic reports of the effects of cannabis on IBD. The aim of this study was to describe the response of patients with Crohn's disease who have used cannabis to ameliorate their symptoms.

PATIENTS AND METHODS

This was a retrospective observational study. A voluntary organization that distributes cannabis for legally authorized medical use in Israel was contacted. We interviewed patients with CD who had permission from the Ministry of Health to receive cannabis for their symptoms. Patients were questioned about the details of their disease, previous medical and surgical treatments, and the reason for using cannabis. Disease activity before and after cannabis use was estimated by the Harvey Bradshaw index. All patients assessed their general

IBD = inflammatory bowel disease
CD = Crohn's disease

well-being before and after cannabis use on a Visual Analog Scale. The scale ranged from 0, which represented “very poor general well-being” to 10, indicating “excellent well-being.” Whenever possible, medical documents were reviewed for objective signs of disease severity, such as number of hospital admissions and use of other drugs, particularly steroids. The dose and form of administration of cannabis were documented. The study was approved by the institutional ethics committee of our hospital.

RESULTS

Thirty patients with CD who were using cannabis were interviewed. The average age was 36 years (range 21–65 years) and four were female. One patient with CD had a history of partial pancreatectomy for serous cystadenoma, one had asthma and two had hypertension. All other patients were generally healthy apart from their CD. Before the use of cannabis, five patients had undergone right hemicolectomy, three had resection of the terminal ileum, two had resection of a proximal section of the ileum, and three had drainage of a perianal fistula. One patient with severe colitis had a total proctocolectomy with ileoanal anastomosis. After the operation she developed perianal disease and the diagnosis was changed from ulcerative colitis to Crohn’s disease. Of the 15 patients who had an operation before using cannabis, 2 (13%) required another surgery during an average time of 2 years while on cannabis. The average duration of disease was 11.3 years (range 1–41 years). Twenty patients with CD had inflammation of the terminal ileum, 5 had inflammation of the more proximal ileum and 8 had Crohn’s disease of the colon. One patient had pouchitis. Crohn’s disease was fistulizing in 10 patients, fibrostenotic in 5, and luminal in 15. Before cannabis use, 27 patients had received 5-ASA (5-aminosalicylic acid), 26 received corticosteroids, 20 took thiopurines, 6 took methotrexate, and 12 took anti-tumor necrosis factor antibodies. Of 30 patients, 16 smoked tobacco regularly, 3 smoked tobacco before using cannabis but stopped when they started cannabis use, and 14 never smoked tobacco. Of the three patients who stopped tobacco smoking, one did not improve (Harvey Bradshaw score of 4 both before and after cannabis use), one improved significantly (from 11 to 2), and one improved slightly (from 9 to 7). Although tobacco smoking is known to have a negative effect on Crohn’s disease, these results do not indicate that smoking cessation in itself had any effect on disease severity in our patients.

The indication for cannabis use was lack of response to conventional treatment in 21 patients and chronic intractable pain in 6. Another four patients smoked cannabis for recreation and continued as they observed an improvement in their medical condition. Most patients smoked cannabis in the form of hand-rolled cigarettes (“joints”). Four patients inhaled the

smoke through water (“bong”), and one patient preferred to consume it orally. Most smoked between one and three “joints” a day, but one patient with chronic pain smoked seven joints a day. Since one cigarette contains about 0.5 mg of THC, patients were using 0.5–1.5 mg/day THC, with the exception of one patient who was using 3.5 mg. The average duration of cannabis use was 2.14 years (range 3 months to 9 years). In 14 patients the duration of cannabis use was less than a year.

All patients stated that consuming cannabis had a positive effect on their disease activity. This is also reflected in the Visual Analog Scale, which increased from 3.1 to 7.3. The Harvey Bradshaw index decreased from 14 ± 6.7 to 7 ± 4.7 ($P < 0.001$) [Figure 1]. The mean number of bowel movements decreased from eight to five a day and the need for other drugs was significantly reduced [Table 1]. Of particular interest is the observation that cannabis may have a steroid-sparing effect, since the number of patients requiring steroid treatment was reduced from 26 to 4. Fifteen of the patients had 19 surgeries during an average period of 9 years before cannabis use, but only 2 required surgery during an average period of 3 years of cannabis use. In nine patients cannabis treatment did not induce a significant improvement, as reflected by a change of less than 4 points in the Harvey Bradshaw index. Three of these patients did not respond to

THC = Δ^9 -tetrahydrocannabinol

Figure 1. Harvey Bradshaw index before and after cannabis use

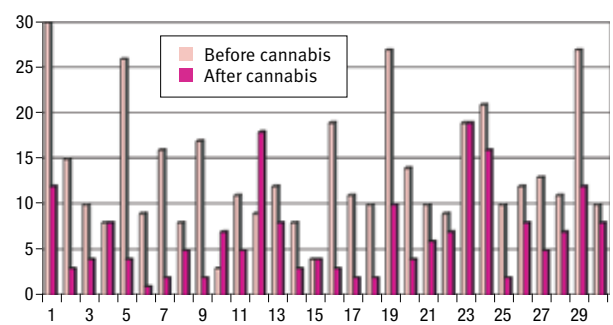


Table 1. Patient characteristics

	Average	Range
Age (yrs)	36	21–65
Male/Female	26/4	
Disease duration (yrs)	11.3	1–41
Disease phenotype	15 luminal, 10 fistulizing, 5 fibrostenotic	
Duration of cannabis consumption	2.1 yrs	3 mos–9 yrs
Amount consumed (“joints”/day)	2.4	0.5–7

Joint = cigarette

any other medical therapy, including TNF antagonists, and are now awaiting surgery.

DISCUSSION

In this study, we describe 30 patients with CD for whom the use of cannabis ameliorated disease activity and reduced the need for other conventional medications. This is the largest and, to the best of our knowledge, the first reported series of CD patients treated with cannabis. It is a retrospective observational study and as such is not a replacement for a prospective placebo-controlled study. There may be a population bias in the sense that some people may be more attracted to the possibility of smoking cannabis than others. This may explain the over-representation of young males in our study population. Also, there may be patients who tried cannabis and whose condition did not improve; they would be lost to follow-up and are not represented in our study. However, the benefit reported by most of the patients in our study suggests a possible significant therapeutic potential. Due to the retrospective nature of our study there may be a bias in recalling disease activity. However, several facts point to an objective benefit of cannabis use. The observed reduced use of steroids (from 26 to 4 patients) [Table 2] and other drugs may point to an objective beneficial effect of cannabis. Whereas 25% to 38% of operated Crohn’s disease patients are expected to require a second operation within 5 years of the first [11], only 2 of 15 patients (13%) who had surgery before cannabis consumption required surgery while consuming cannabis. Larger numbers and longer follow-up are needed to verify whether use of cannabis reduces the need for surgery.

The effects of cannabinoids on the immune system are diverse and include modulating proliferation of B cells, T cells, and natural killer cells, modulating production of antibodies and cytokines, and regulating functions of NK cells, macrophages, T helper cells, mast cells and dendritic cells [10]. Although anti-inflammatory effects of cannabis have been described previously, there are no systematic descriptions of

TNF = tumor necrosis factor
NK = natural killer

Table 2. Medical treatment before and after cannabis use (n=30)

Drug	Before	After
No treatment	None	9
5-ASA	27	5
Corticosteroids	26	4
Thiopurine	20	10
Methotrexate	6	0
TNF antagonist	12	4

5-ASA = 5-aminosalicylic acid

the efficacy of cannabis in Crohn’s disease. The restraint from the use of an illegal drug may have played a role.

The observed beneficial effect in this study may be due to the anti-inflammatory properties of cannabis, but additional effects of cannabinoids may also play a role. Cannabinoids influence gastrointestinal motility and, in particular, have an anti-diarrheal effect, as observed in mice injected with cholera toxin [12]. The central effect of cannabinoids may induce a sensation of general well-being, which could contribute to the feeling that cannabis use is beneficial. However, this general effect wears off with time as tolerance develops, while the positive effect of cannabis on disease activity in our patients was maintained for an average period of 3.1 years.

One of the reasons that cannabis is unappealing to many patients is that it is administered by smoking. Smoking in general is unacceptable to both medical professionals and many patients. The negative effect of tobacco smoking on Crohn’s disease is also well known. Several studies demonstrated a dose-related adverse effect of cannabis on large airway function, but not on small airway function, which is compromised by tobacco smoking [13,14]. Smoking cannabis is the preferred mode of consumption because upon smoking, blood levels of cannabinoids rise rapidly and a central effect is achieved quickly. However, an anti-inflammatory effect, especially in the gut, may be achieved equally well by consuming cannabis orally.

Although many side effects were connected with cannabis use, most of them were in people who consumed other drugs and alcohol together with cannabis. When consumed alone, the safety profile of cannabis is very good [15]. Wang et al. [16] reviewed 31 studies of medical cannabis use and found that 96% of 4779 adverse events were minor. The relative risk for serious adverse events was 1.04, which was not different between the placebo and study groups. Cannabinoids may therefore be a potential addition to the currently limited arsenal of medications used to treat IBD. On the other hand, because the use of medical cannabis may be exploited by drug abusers, extra caution is necessary before cannabis can be recommended to patients. A placebo-controlled study is needed to fully investigate the therapeutic value of cannabis for the treatment of Crohn’s disease.

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Corresponding author:

Dr. T. Naftali
Institute of Gastroenterology and Hepatology, Meir Medical Center, Kfar Saba 44281, Israel
Phone: (972-9) 747-1045
Fax: (972-9) 744-1731
email: naftali@post.tau.ac.il

References

1. Wingerchuk D. Cannabis for medical purposes: cultivating science, weeding out the fiction. *Lancet* 2004; 364: 315-16.
2. Baker D, Pryce G, Giovannoni G, et al. Therapeutic potential of cannabis. *Lancet Neurol* 2003; 2: 291-8.
3. Williamson EM, Evans FJ. Cannabinoids in clinical practice. *Drugs* 2000; 60 (6): 1303-14.
4. Izzo AA, Camilleri M. Gastrointestinal and liver diseases: basic and clinical aspects: emerging role of cannabinoids. *Gut* 2008; 57: 1140-55.
5. Hall W, Solowij N. Adverse effects of cannabis. *Lancet* 1998; 352: 1611-16.
6. Nahas G, Succi-Foca N, Armand JP. Decrease of cellular immunity in hashish (marihuana) smokers. *C R Acad Sci Hebd Seances Acad Sci D* 1973; 277: 979-80.
7. Sofia RD, Knobloch LC, Vassar HB. The anti-edema activity of various naturally occurring cannabinoids. *Res Commun Chem Pathol Pharmacol* 1973; 6: 909-18.
8. Pacifici R, Zuccaro P, Pichini S, et al. Modulation of the immune system in cannabis users. *JAMA* 2003; 289: 1929-31.
9. Storr MA, Keenan CM, Zhang H, et al. Activation of the cannabinoid 2 receptor (CB(2)) protects against experimental colitis. *Inflamm Bowel Dis* 2009; 11: 1678-85.
10. Dai Lu V, Kiran V, Richard I, et al. The cannabinergic system as a target for anti-inflammatory therapies. *Curr Topics Med Chem* 2006; 6: 1401-26.
11. Whelan G, Farmer RG, Fazio VW, et al. Recurrence after surgery in Crohn's disease. Relationship to location of disease (clinical pattern) and surgical indication. *Gastroenterology* 1985; 88: 1826-33.
12. Izzo AA, Capasso F, Costagliola A, et al. An endogenous cannabinoid tone attenuates cholera toxin-induced fluid accumulation in mice. *Gastroenterology* 2003; 125: 765-74.
13. Aldington S, Williams M, Nowitz M, et al. Effects of cannabis on pulmonary structure, function and symptoms. *Thorax* 2007; 62 (12): 1058-63.
14. Hancox RJ, Poulton R, Ely M, et al. Effects of cannabis on lung function: a population-based cohort study. *Eur Respir J* 2010; 35 (1): 42-7.
15. Kumar RN, Chambers WA, Pertwee RG. Pharmacological actions and therapeutic uses of cannabis and cannabinoids. *Anaesthesia* 2001; 56: 1059-68.
16. Wang T, Collet JP, Shapiro S, et al. Adverse effects of medical cannabinoids: a systematic review. *CMAJ* 2008; 178 (13): 1669-78.