

Cannabis Improves Clinical Outcomes and Quality of Life in Patients With Chronic Pouchitis

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ABSTRACT

Many patients with ulcerative colitis after ileoanal pouch anastomosis report improvement of pouchitis with the use of cannabis. Nine patients with chronic pouchitis used 1 g/d of cannabis: 7 patients were male with average age 51 ± 16 years. Average partial pouchitis disease activity index were 11 (range 8–17), 6 (range 5–8), and 5 (range 4–8); endoscopic subscores were 7.3 ± 2.3 , 6 ± 1.1 , and 4.4 ± 0.9 ; average bowel movements per day were 14 (range 8–20), 8 (range 2–13), and 10 (range 13–8); and quality of life increased from 72 ± 1 to 90 ± 16 and 97 ± 10 ($P = 0.001$) before cannabis treatment and after 8–12 and 52 weeks, respectively. No adverse events were reported.

KEYWORDS: ulcerative colitis; pouchitis; ileoanal pouch anastomosis; cannabis; quality of life

INTRODUCTION

The 10-year colectomy rate of patients with ulcerative colitis (UC) is 10%–30% in Western countries.¹ The most common procedure is total proctocolectomy with ileoanal pouch anastomosis (IPAA). However, up to 70% of patients with IPAA may develop acute pouchitis,^{2–4} and 10%–15% of them will deteriorate to chronic pouchitis,³ in which case, the same treatment modalities used in UC are implemented.⁵ In animal and in vitro models of UC, cannabinoids improved inflammation,⁶ and in patients with UC, cannabis as adjuvant therapy improved symptoms and quality of life.^{7,8} However, to date, cannabis as a treatment of chronic pouchitis has not been studied. In this case series, we investigated the outcome of adding cannabis to the treatment regimen of patients with refractory chronic pouchitis.

CASE REPORTS

Nine patients after IPAA referred to the gastroenterology clinic at the Meir Medical Center in Kfar Saba, Israel, were recruited during 2013–2018. Indication for total proctocolectomy with IPAA was intractable UC in all 9 patients, and none had colon cancer. Chronic pouchitis was defined according to the pouchitis disease activity index (PDAI), including clinical, endoscopic, and histologic assessments⁹ with active continuous symptoms for more than 4 weeks despite antibiotic or anti-inflammatory therapy¹⁰ (Table 1).

Cannabis use was licensed by the Ministry of Health. Treatment included smoking 1 g/d of dried cannabis flowers of genetically identical plants of *Cannabis sativa* var. Indica “Erez” (courtesy of Tikun-Olam, Tel Aviv, Israel). The cannabis contained 16% (80 mg) Δ -9-tetrahydrocannabinol, 0.5% cannabigerol, and 0.1% cannabidiol. Cannabis was added to the patient’s current treatment (Table 1).

Data were captured before cannabis consumption and 8–12 and 52 weeks after starting cannabis. Data included patients’ symptoms, physical examination, complete blood count, liver enzymes and kidney function test, C-reactive protein, and fecal calprotectin, as

Table 1. Patients' demographic data

Patient	Age (yr)	Sex	Time since UC diagnosis (yr)	Time since IPAA (yr)	Treatment at baseline
1	51	M	24	12	None
2	70	M	16	6	Antibiotics and thiopurine
3	48	M	29	26	None
4	72	M	22	5	Antibiotics and vedolizumab
5	24	M	13	7	5-ASA
6	38	F	4	3	VSL-3
7	51	M	30	23	None
8	70	F	29	11	Steroids (prednisone)
9	38	M	11	4	Metronidazole and ciprofloxacin
Mean	51.33		19.7	10.7	
Range	24–70		4–30	3–26	

5-ASA, 5-aminosalicylic acid; IPAA, ileoanal pouch anastomosis; UC, ulcerative colitis.

well as pouch endoscopy. Patients completed quality-of-life (36-Item Short Form Survey Quality of Life) and side-effect questionnaires at the same time points. SPSS for Windows, version 25 (IBM, Armonk, NY), was used for statistical analysis.

Clinical and endoscopic activity index (PDAI), before and after cannabis, is presented in Table 2. Laboratory parameters

including complete blood count, liver enzymes and kidney function tests, and C-reactive protein did not change throughout the study period. However, average fecal calprotectin increased between visits 1 and 2, from 115 ± 80 to 200 ± 83 ($P = 0.043$). All 9 patients reported anal incontinence at visit 1, but only 2 patients suffered from anal incontinence at visits 2 and 3. Symptom improvement was reported by 8 of 9 patients, including improvements in abdominal pain and swelling, nausea, appetite, and general well-being. Mood, memory, concentration, sleep, alertness, and daily function were also improved. Patients reported no events of hallucinations, negative behavioral effects, restlessness, or confusion. None reported IBD exacerbation (Figure 1).

DISCUSSION

To the best of our knowledge, this is the first report on the effect of cannabis consumption among patients with chronic pouchitis. All patients reported significant symptomatic improvement, including improved PDAI, fewer bowel movements and nocturnal diarrhea, reduced fecal incontinence, and consequently, improved quality of life. This positive effect was maintained after 1 year.

Pouchitis treatment fails in as many as two-thirds of patients, and in 6%–10% of patients, pouch failure leads to ileostomy.^{3,5,11–13} Despite the importance of endoscopic remission as a main treatment goal,¹⁴ symptom reduction is the first priority of the patient.¹⁵ Symptomatic improvement is the cardinal factor that enables normal daily function in all dimensions, including work, social life, and family connections. Therefore, improvement in

Table 2. Disease activity data before, after 8–12 weeks, and after 52 weeks of cannabis treatment

Patient	PDAI			Bowel movements/24 h			Nocturnal bowel movements		
	V1	V2	V3	V1	V2	V3	V1	V2	V3
1	12	6	4	16	6	8	5	0	0
2	13	8	8	14	12	12	4	2	0
3	11	5	6	20	10	10	3	0	1
4	8	5	4	8	2	8	4	2	0
5	12	7	5	15	8	8	2	0	0
6	11	5	6	20	13	13	3	0	0
7	10	8	6	12	5	12	3	0	0
8	17	5	4	20	12	12	3	0	6
9	11	5	4	8	5	8	1	0	0
Mean	11.6	6	5.3	14.7	8.11	10.3	3.11	0.44	0.25
SD	8.4	1.3	1.4	4.7	3.8	2	1.1	0.8	0.4
<i>P</i> (V1-V2)		0.007			0.007			0.007	
<i>P</i> (V1-V3)		0.11			0.29			0.07	

PDAI, including clinical, endoscopic, and histologic assessments, has been described in detail in Methods. V1-visit 1 before treatment, V2-after 8–12 weeks, V3-after 52 weeks. PDAI, Pemphigus Disease Area Index.

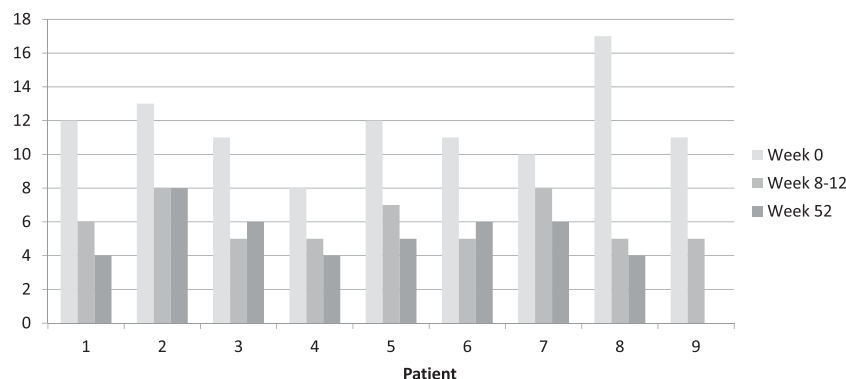


Figure 1. Mean pouchitis disease activity index before and after cannabis. * P value for all patients between V1 and V2 = 0.007.

symptoms is as important as decreases in inflammatory markers or endoscopy scores, especially in patients with refractory pouchitis in whom other treatment options have failed.

Activation of the endocannabinoid system delays colonic transit, increases pain thresholds, and reduces fluid secretions. Cannabis improves colitis in experimental rodent models of UC and in human patients.^{7,8,14,15} The patients in our study received cannabis with a well-known composition, containing 16% Δ -9-tetrahydrocannabinol and only traces of cannabidiol. Endoscopic scores improved in 5 of the 8 patients who underwent a second (week 12) and third (week 52) endoscopy. Fecal calprotectin increased between visits 1 and 2, but it should be noted that while objective, fecal calprotectin has not been validated or well-studied in pouchitis to date. Further investigation of various cannabis components is warranted to identify those with maximal anti-inflammatory effects.

Despite the open design and small number of patients, the strength of our study is in the prospective design, precise profile of the cannabis used, and long-term follow-up of 12 months.

In conclusion, cannabis use led to significant symptomatic improvement and better quality of life in this group of patients with refractory pouchitis. Larger, controlled studies are needed to further evaluate the role of cannabis in the treatment of chronic pouchitis.

DISCLOSURES

Author contributions: T. Naftali performed the literature review and wrote the manuscript, and is the article guarantor. L. Bar-Lev Schleider and H. Kayless assisted with gathering objective data and performing chart review. Z. Bromberg, I. Dotan, and E. Broide reviewed and edited the manuscript.

Financial disclosure: L. Bar-Lev Schleider is an employee of Tikun Olam Canbit who supplied the cannabis for the study.

Informed consent was obtained for this case report.

Ethical considerations: The study was approved by the Israeli Ministry of Health Cannabis Authority Ethics Committee and the Meir Medical Center Ethics Committee (MMC 0308-13 on October 2013). All participants provided written informed consent before any study-related procedure was carried out. All methods were carried out in accordance with relevant guidelines and regulations.

Received May 15, 2023; Accepted July 20, 2023

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