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Brief Report

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Relief in Gastrointestinal Symptoms with Medical Marijuana Over 1 Year

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Adverse effects · Cannabis · Gastrointestinal symptoms · Integrative medicine · Medical cannabis

Abstract
Introduction: Subjective improvement in gastrointestinal (GI) symptoms was assessed among patients using medical marijuana (MMJ). ***Methods:*** Participants completed surveys at 0 days, 30 days, 6 months, and 12 months with questions about the severity of their GI symptoms on a scale from 1 (mild) to 3 (severe). ***Results:*** In each survey, participants reported a significant decrease in GI symptom severity when using MMJ versus when not using MMJ ($p < 0.05$). The most common self-reported side effects from using MMJ were increased appetite (12–21.4%), fatigue (6–16.7%), anxiety (4–11.9%), cough (4–11.9%), headache (6–7.9%), and dry mouth (4–7.1%). ***Conclusion:*** In patients with chronic GI symptoms, MMJ may provide persistent symptom severity improvement. Limited product availability and mild to moderate side effects are factors to consider before trialing MMJ.

Introduction

In the USA, gastrointestinal (GI) symptoms affect over 60% of adults and are associated with a significantly lower quality of life [1, 2]. In a national survey, GI symptoms such as heartburn, abdominal pain, bloating, diarrhea, and constipation were most common. Optimal treatment involves a biopsychosocial model approach [3]. However, treatments are not always effective, and some first-line medications like proton pump inhibitors may introduce new symptoms like nausea or bloating [4]. Increasingly, some patients are trialing medical marijuana (MMJ) for GI symptoms, but the literature is conflicted regarding the potential benefits of its use [5–7] and whether symptom relief endures long-term. This observational study seeks to describe patterns of MMJ use in patients with self-reported GI symptoms and to evaluate if changes in GI symptom severity occurred at each time point over 1 year.

Methods

This was a 12-month retrospective, survey-based study of patients who self-described as suffering from refractory GI and non-GI symptoms despite previous medical management and who were

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Table 1. Demographic data at 0 days from the baseline survey

	Total sample (n = 55)	Persistent (n = 36)	Variable (n = 19)
Age, years	39.0 (12.9)	39.1 (13.6)	38.6 (11.8)
Male sex, n (%)	21 (38.2)	16 (44.4)	5 (26.3)
Ethnicity, n (%)			
Hispanic or Latino/a	4 (7.3)	2 (5.6)	2 (10.5)
Non-Hispanic or Latino/a	49 (89.1)	32 (88.9)	17 (89.5)
Prefer not to answer	2 (3.6)	2 (5.6)	0
Race, n (%)			
Black	6 (10.9)	5 (13.9)	1 (5.3)
Latino/a	4 (7.3)	2 (5.6)	2 (10.5)
Other	4 (7.3)	3 (8.3)	1 (5.3)
White	41 (74.5)	26 (72.2)	15 (78.9)
Medical conditions	4.0 (2.7)	3.6 (2.5)	4.7 (3.0)
Medications	4.2 (3.0)	4.0 (3.0)	4.5 (3.0)
Certifying conditions[a] for MMJ use, n (%)			
Anxiety	25 (45.5)	15 (41.7)	10 (52.6)
Chronic pain	17 (30.9)	11 (30.6)	6 (31.6)
PTSD	6 (10.9)	5 (13.9)	1 (5.3)
IBD	4 (7.2)	3 (8.4)	1 (5.3)
HIV	2 (3.6)	2 (5.6)	0 (0)
Neuropathy	2 (3.6)	0 (0)	2 (10.5)
Opioid use disorder	2 (3.6)	1 (2.8)	1 (5.3)
Cancer	1 (1.8)	1 (2.8)	0 (0)
Epilepsy	1 (1.8)	1 (2.8)	0 (0)
Irritable bowel syndrome	1 (1.8)	1 (2.8)	0 (0)
Other pain syndrome	1 (1.8)	0 (0)	1 (5.3)
Participants with GI symptoms at, n (%)			
all 4 time points	36 (65.5)		
3 time points	8 (14.5)		
2 time points	6 (10.9)		
1 time point	5 (9.1)		
Participants with GI symptoms that are present at day 0, stop, and then return, n (%)	2 (3.6)		
Participants with GI symptoms that are present at day 0 and then stop by a future survey, n (%)	17 (30.9)		

Data are presented as n (%) or mean (SD). ADHD, attention-deficit/hyperactivity disorder; HIV, human immunodeficiency virus; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; PTSD, post-traumatic stress disorder. [a]Certified reasons for MMJ use are those approved in Pennsylvania. Notably, 87.3% of participants reported their correct certifying condition. The certified and self-reported reasons were in 55.8% agreement. Participants could have multiple certifying conditions or self-reported reasons for MMJ use.

certified to use MMJ. The inclusion criterion was at least one GI symptom reported at the first survey such as anorexia, nausea, vomiting, constipation, diarrhea, stomach bloating, stomach pain, and heartburn. Exclusion criteria were pregnancy, lactation, active substance abuse, and GI symptoms appearing after the first survey. Recruitment occurred between May and October 2020 through public advertisements and an MMJ dispensary in Pennsylvania, USA. Participants completed phone surveys at 0 days, 1 month, 6 months, and 12 months after study initiation. The baseline survey queried the participant's demographics, qualifying medical conditions for MMJ use (later confirmed by Pennsylvania's Office of MMJ database), additional medical conditions, medications, and patterns of MMJ use. Participants self-reported their current symptoms and rated each symptom severity "while not using medical marijuana," abbreviated as SnoMMJ, and "while using medical marijuana," abbreviated as SyesMMJ, on a scale from 1 (mild) to 3 (severe). The difference in symptom severity when using and when not using MMJ, SyesMMJ minus SnoMMJ, is denoted as ΔS. Follow-up surveys documented self-reported side effects of MMJ use and changes in MMJ use behavior (for the complete baseline and follow-

Table 2. GI symptoms and their severity change with and without MMJ (persistent and variable groups combined)

	0 days (n = 55)	30 days (n = 50)	6 months (n = 42)	1 year (n = 38)
Total sample statistics				
Self-reported GI symptoms, *n* (%)				
Anorexia	21 (38.9)	19 (38.0)	14 (34.1)	12 (31.6)
Nausea/vomiting	20 (37.0)	17 (34.0)	15 (36.6)	14 (36.8)
Other[a]	24 (44.4)	24 (48.0)	21 (51.2)	19 (50.0)
Number of GI symptoms	1.4 (0.7)	1.4 (0.8)	1.4 (0.8)	1.3 (0.7)
Mean GI symptom severity				
SnoMMJ	2.6 (0.6)	2.4 (0.7)	2.2 (0.7)	2.3 (0.7)
SyesMMJ	1.3 (0.5)	1.2 (0.5)	1.2 (0.5)	1.2 (0.4)
ΔS	−1.3 (0.6)[b]	−1.2 (0.7)[b]	−1.0 (0.7)[b]	−1.1 (0.6)[b]
GI symptom severity by symptom category				
Anorexia				
SnoMMJ	2.6 (0.5)	2.4 (0.7)	2.2 (0.8)	2.4 (0.7)
SyesMMJ	1.3 (0.6)	1.1 (0.3)	1.1 (0.5)	1.2 (0.4)
ΔS	−1.3 (0.6)[b]	−1.3 (0.7)[b]	−1.1 (0.8)[b]	−1.2 (0.6)[b]
Nausea/vomiting				
SnoMMJ	2.4 (0.7)	2.3 (0.8)	2.0 (0.8)	2.0 (0.8)
SyesMMJ	1.1 (0.2)	1.1 (0.3)	1.1 (0.3)	1.0 (0.0)
ΔS	−1.3 (0.5)[b]	−1.2 (0.8)[b]	−0.9 (0.8)[b]	−1.0 (0.8)[b]
Other[a]				
SnoMMJ	2.8 (0.4)	2.2 (0.7)	2.3 (0.6)	2.5 (0.5)
SyesMMJ	1.4 (0.5)	1.3 (0.6)	1.3 (0.5)	1.3 (0.6)
ΔS	−1.4 (0.5)[b]	−0.9 (0.6)[b]	−1.0 (0.6)[b]	−1.2 (0.7)[b]

There were no statistically significant differences in ΔS overall and by symptom category between the persistent and variable sub-groups at baseline (independent *t* tests, $p > 0.05$). There were no consistent differences in the number of GI symptoms, mean GI symptom severity, and GI symptom severity by category for males versus females (independent *t* test, $p > 0.05$). In addition, age was not consistently correlated with these variables ($p > 0.05$). Data are presented as *n* (%) or mean (SD). ΔS, SyesMMJ – SnoMMJ. [a]Other includes stomach pain, stomach cramps, gas, bloating, heartburn, constipation, and diarrhea. [b]Paired *t* test performed at each time point, *p* value <0.05.

up surveys, see online suppl. Digital Content 1; for all online suppl. material, see https://doi.org/10.1159/000538694). Statistical analyses were conducted with SPSS 28 (IBM Corp. Armonk, NY, USA). The Thomas Jefferson University Institutional Review Board approved this study.

Results

Of the 216 participants who consented to participate in the first survey, 55 participants met the inclusion criteria based on their reported GI symptoms shown in Table 1. The sample was further divided into participants who had at least one GI symptom across all four surveys ("persistent" group) and those who had GI symptoms that either stopped before the last survey or stopped and then resumed at a later survey ("variable" group). At 1 month, 6 months, and 12 months, 50, 42, and 38 participants had persistent symptoms, respectively. Of the 162 not included, 9 had GI symptoms that started after the first survey. Respondents were majority female, non-Hispanic, and White. The female participants were significantly older than the male participants (years, mean [SD]: 42.1 [3.5] vs. 33.8 [10.2] at baseline, $p < 0.05$ at each time point). The three most common certified conditions for MMJ use were chronic pain (30.9%), anxiety (45.5%), and PTSD (10.9%). The combined representation of inflammatory bowel disease (IBD) and irritable bowel syndrome as self-reported reasons for using MMJ was 14.4% at baseline.

Table 3. Participant experience with MMJ at 30 days, 6 months, and 1 year

	0 days (*n* = 55)	30 days (*n* = 50)	6 months (*n* = 42)	1 year (*n* = 38)
People using each MMJ form, *n* (%)				
Flower or leaf	39 (70.9)	25 (50.0)	6 (14.3)	18 (47.4)
Vaporization cartridge	38 (69.1)	25 (50.0)	18 (42.9)	21 (55.3)
Extract[a]	14 (25.5)	8 (16.0)	1 (2.4)	7 (18.4)
RSO or edible oil	12 (21.8)	9 (18.0)	4 (9.5)	7 (18.4)
Liquid	11 (20.0)	5 (10.0)	2 (4.8)	7 (18.4)
Topical	8 (14.5)	7 (14.0)	6 (14.3)	5 (13.2)
Pills	5 (9.1)	33 (66.0)	33 (78.6)	29 (76.3)
Other	1 (1.8)	1 (2.0)	1 (2.4)	1 (2.6)
MMJ forms used	3.7 (1.6)	3.5 (1.5)	3.2 (1.3)	4.7 (2.3)
People using each route combination, *n* (%)				
Oral	1 (1.8)	1 (2.0)	1 (2.1)	1 (2.6)
Inhaled	31 (56.4)	25 (50.0)	25 (52.1)	21 (55.3)
Topical	0 (0)	0 (0)	0 (0)	0 (0)
Oral and inhaled	16 (29.1)	15 (30.0)	10 (20.8)	10 (26.3)
Oral and topical	1 (1.8)	1 (2.0)	2 (4.2)	1 (2.6)
Inhaled and topical	3 (5.5)	4 (8.0)	2 (4.2)	2 (5.3)
Oral, inhaled, and topical	3 (5.5)	4 (8.0)	2 (4.2)	3 (7.9)
MMJ Routes used	1.5 (0.6)	1.6 (0.7)	1.4 (0.6)	1.5 (0.6)
MMJ products used	3.7 (1.6)	2.8 (1.5)	2.7 (1.6)	3.21 (2.7)
Average MMJ uses per day	5.6 (5.8)	3.5 (3.1)	2.7 (2.4)	2.1 (1.8)
Total product changes		2.7 (2.2)	3.9 (3.2)	3.13 (3.1)
Discontinued products		1.8 (1.4)	2.4 (1.9)	1.7 (1.5)
New products		0.9 (1.2)	1.5 (1.5)	1.4 (2.4)
Reason for discontinuing MMJ, *n* (%)				
Availability		31 (58.5)	35 (66.0)	21 (50.0)
Experimenting		5 (9.4)	0 (0)	3 (7.1)
Not effective		3 (5.7)	9 (17.0)	2 (4.8)
Prefer other meds		3 (5.7)	0 (0)	9 (21.4)
Dislike form		2 (3.8)	1 (1.9)	1 (2.4)
Finished course		2 (3.8)	0 (0)	0 (0)
Too expensive		1 (1.9)	3 (5.7)	0 (0)
Side effects		1 (1.9)	0 (0)	3 (7.1)
Dispensary too far		0 (0)	0 (0)	0 (0)
Unknown reason		5 (9.4)	6 (11.4)	5 (11.9)
Self-reported side effects, *n* (%)				
Anhedonia		0 (0)	1 (2.4)	2 (5.3)
Anxiety		2 (4.0)	4 (9.5)	5 (11.9)
Chest pain		0 (0)	0 (0)	1 (2.6)
Congestion		0 (0)	0 (0)	0 (0)
Cough		2 (4.0)	2 (4.8)	5 (11.9)
Dizziness		2 (4.0)	2 (4.8)	3 (7.1)
Drowsiness/fatigue		3 (6.0)	7 (16.7)	4 (9.5)
Dry mouth		2 (4.0)	3 (7.1)	3 (7.1)
Headaches/migraines		3 (6.0)	3 (7.1)	3 (7.9)
Impaired mentation		2 (4.0)	4 (9.5)	1 (2.6)
Increased appetite		6 (12.0)	9 (21.4)	6 (14.3)
Itchy		1 (2.0)	1 (2.4)	1 (2.6)
Lung/breathing problem		1 (2.0)	2 (4.8)	2 (4.8)
No side effect		1 (2.0)	3 (7.1)	0 (0)
Other		0 (0)	0 (0)	1 (2.6)
Sleep disturbance		1 (2.0)	0 (0)	0 (0)
Sweating		1 (2.0)	1 (2.4)	1 (2.6)

Table 3 (continued)

	0 days (n = 55)	30 days (n = 50)	6 months (n = 42)	1 year (n = 38)
Side effects		1.1 (0.3)	1.1 (0.8)	1.4 (1.2)
Mean side effect severity[b]		1.4 (0.6)	1.5 (0.5)	1.7 (0.6)
Side effects no longer present		1.1 (0.3)	1.7 (0.8)	

There were no consistent statistically significant differences in the number of MMJ forms, number of MMJ routes, number of MMJ products, and average MMJ uses per day between the persistent and variable sub-groups, males and females, and white and non-white participants (independent t tests, $p > 0.05$). In addition, age did not consistently correlate with these variables ($p > 0.05$). Data are presented as n (%) or mean (SD). RSO, Rick Simpson Oil. [a]Extract includes forms such as shatter, wax, oil, resin, sugar, and budder. [b]Mean side effect severity ratings of 1, 2, and 3 correspond to low, medium, and severe.

Reported GI symptoms fell into three categories: anorexia, nausea, or vomiting, and "other" symptoms, which included dyspepsia, stomach pain, flatulence, bloating, acid reflux, constipation, and diarrhea. Specifically, the anorexia category included responses such as "decreased appetite," "loss of appetite," and "couldn't eat." The nausea or vomiting category included responses such as "nausea," "nausea (IBD)," and "vomiting." The "other" category included the following responses: "stomach pain," "chronic stomach pain," "abdominal pain," "abdominal pain (IBD)," "stomach cramps," "intestinal spam," "bloating," "gas," "GI discomfort (nervous stomach)," "upset stomach," "upset GI tracts," "bowel issues," "heartburn," "eating and digestion," "bloody stools," "diarrhea," and "constipated."

Across all surveys shown in Table 2, ΔS was significant ($p < 0.05$; Cohen's d ranging from 0.6 [baseline] to 0.7 [6 months]). Age, number of medications, number of medical conditions, average doses of MMJ used per day, and sex were either not consistently correlated with or did not show consistent differences (independent t tests) in ΔS across time points ($p > 0.05$). Across follow-up surveys, most participants reported that their symptoms had improved "a little" (31.4–47.4%) or "a lot" (36.8–52.0%) since their last visit to the dispensary, and most reported using MMJ "regularly" (84.2–95.2%) as opposed to "occasionally" (4.4–11.6%) or "never" (0–2.3%) in the prior week.

Across follow-up surveys, participants used between a mean (SD) of 2.7 (1.6) to 3.7 (1.6) different MMJ products (see Table 3). Vaporization cartridges (42.9–69.1%), flower (14.3–70.9%), pills (9.1–78.6%), and liquid (4.8–20.0%) were the most popular MMJ forms. Inhalation only (50.0–56.4%) or a combination of inhalation and oral (20.8–30.0%) were the most popular routes of administration. The mean (SD) number of MMJ product changes ranged from 2.7 (2.2) to 3.9 (3.2) across time points. About 80% of participants reported starting a new product at follow-up. The three most common reasons for discontinuing an MMJ product were "availability" (50.0–66.0%), "not effective" (4.8–17.0%), and "prefer other meds" (0–21.4%).

The most common self-reported side effects from using MMJ were increased appetite (12.0–21.4%), fatigue (6.0–16.7%), anxiety (4.0–11.9%), cough (4.0–11.9%), headache (6.0–7.9%), and dry mouth (4.0–7.1%). The average side effect severity was low to moderate.

Discussion

This is the first study to examine MMJ's longitudinal effects on GI symptoms in patients with refractory GI and non-GI MMJ-certified conditions. Overall, participants reported significant, enduring moderate GI symptom relief when using MMJ. Importantly, there were no differences in GI symptom relief based on age, sex, the number of medical conditions, and the number of patient medications. Notably, age-associated differences in MMJ efficacy have been reported in patients with GI and pelvic pain symptoms secondary to endometriosis [8].

Inhalation was the most popular administration method, followed by oral administration, consistent with other studies [8]. The bioavailability of drugs is generally higher with inhalation than with ingestion, increasing both the speed of onset and the drug effect size [9]. Differences in symptom severity improvement based on the route of administration (e.g., inhalation vs. oral) were not assessed due to sample size constraints.

Availability was the most common reason for discontinuing an MMJ product, and it is notable that data collection occurred during the COVID-19 pandemic when product shortages were a frequent occurrence. No participants discontinued taking MMJ products entirely. Instead, participants either continued existing MMJ

products or tried a new MMJ product. Most participants continued to report reductions in GI symptom severity after trying new products. This is a surprising result. Either most MMJ products share similarly effective compounds or there is a profound placebo effect.

Strengths of the study include the longitudinal follow-up over 1 year and information regarding patterns of MMJ use. Limitations of the study include reliance on self-report and lack of controls and formal GI diagnoses (e.g., functional dyspepsia based on the ROME IV criteria).

Overall, this study suggests there may be a role for MMJ to treat GI symptoms. Importantly, MMJ use is associated with adverse effects, including dry mouth, diarrhea, nausea, and vomiting [7]. Also, inhaling MMJ products increases the risk of cardiovascular events [10]. Therefore, patients considering MMJ for GI symptoms off-label should be counseled accordingly. Additional studies are required to confirm the association between MMJ use and GI symptom relief. Specifically, studies should assess the effects of different CBD/THC ratios, dosing, and methods of administration on GI symptom relief.

Statement of Ethics

The study was approved by the Thomas Jefferson University Institutional Review Board (IRB# 17C.478; board# 2405). Due to COVID-19 restrictions and concerns over participant internet access, verbal consent with documentation was obtained from all participants with approval from the IRB. Written consent was not obtained from participants.

Conflict of Interest Statement

Dan Hanna has worked for a MMJ dispensary in PA, USA Brooke Worster is an advisory board member for PAX Therapeutics.

Funding Sources

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Author Contributions

The overall study was designed, planned, and supervised by E.L.K. and B.W. This subsample study was developed by M.P.W. Data curation was done by E.L.K., A.H., B.W., and E.H. The data were analyzed by E.L.K. and M.P.W. The manuscript was drafted by M.P.W and D.H. The manuscript was reviewed and edited by all authors. All authors approved the final manuscript.

Data Availability Statement

The datasets generated during the current study are not publicly available but will be available from the corresponding author upon reasonable request.

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