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The use of medical cannabis in common medical conditions excluding cancer

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Abstract

The potential clinical utility of medical cannabis in the management of a wide variety of symptoms and conditions is gaining increasing attention. The present study investigated possible benefits and side effects associated with the use of cannabis in patients diagnosed with non-cancer-related conditions. All patients received cannabis from a single Canadian medical cannabis provider. 2,588 patients completed a voluntary online survey prior to the initiation of cannabis use, defined as baseline. Follow-up (FU) surveys were completed at 4 and 10 months after baseline. The survey collected information pertaining to patient demographics, medical conditions, presence and severity of symptoms, and quality of life (QOL). The most commonly reported medical conditions other than cancer were anxiety disorder (32.9%, n = 713), depression (32.6%, n = 706), sleep disorders (26.7%, n = 579), post-traumatic stress disorder (PTSD) (22.6%, n = 489), and arthritis (22.5%, n = 488). At 4-month FU, a majority of patients demonstrated improvement in all conditions: arthritis (70.0%, n = 98), anxiety (77.5%, n = 162), depression (71.6%, n = 211), sleep disorders (79.2%, n = 154) and PTSD (76.9%, n = 160), with significant improvements seen in anxiety ($p = 0.0006$), PTSD ($p = 0.006$), and sleep disorders ($p = 0.0006$). Reductions in symptoms and symptom severity, as well as improvement in QOL were also demonstrated at 4-month FU and remained stable from 4-month to 10-month FU. Pain severity was significantly reduced from baseline to 10-month FU ($p < 0.0001$). To achieve optimal patient outcomes, future studies should investigate the efficacy of medical cannabis including effects of different cannabis varieties, doses, and methods of consumption when used for various medical conditions.

Keywords: Medical cannabis, quality of life, medical marijuana

Introduction

Medical cannabis has been investigated for the potential to provide a variety of therapeutic benefits. Current literature and anecdotal accounts suggest that

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cannabis is most commonly used to reduce nausea and vomiting, stimulate appetite, assist with sleep, and relieve pain (1, 2). However, thorough clinical investigation is required to fully understand the intricacies of using medical cannabis in a clinical setting, with a focus on safety and efficacy. This information will be valuable to both patients and physicians, and help guide clinical decision-making.

The pharmacological properties of cannabis make it well-suited for potential uses in the treatment of various conditions and symptoms. Cannabis contains over 60 cannabinoids, with delta-9-tetrehydrocannabinol (THC) and cannabidiol (CBD) being the two most well-known examples. THC is the major psychoactive component of cannabis and is known to possess analgesic, anti-emetic, appetite stimulating, and muscle relaxant properties (1, 2). Cannabidiol (CBD) is another well-studied cannabinoid that has demonstrated anti-convulsant, anxiolytic, and anti-inflammatory effects (1, 2). The present study examined possible benefits and adverse effects associated with the use of medical cannabis for therapeutic applications in common medical conditions, with the exception of cancer, through a voluntary online survey.

Methods

Patients receiving cannabis treatment completed a voluntary online survey designed by a Canadian medical cannabis supplier. Participating patients completed the survey at baseline (i.e., the time of registration with the cannabis provider). Those who completed the survey at baseline were invited to complete a follow-up (FU) survey at four months from baseline and similarly, those who completed the survey at four months were prompted to complete a second FU survey at 10 months from baseline.

Survey design

The survey consisted of over 100 questions presented in a dynamic format customized to individual responses, where responses determined the subsequent questions asked (e.g., if a patient was not experiencing pain, no further pain-related questions were asked). Patients were also given the choice to skip questions. As such, each patient completing the survey answered a unique set of questions and each question received different numbers of responses.

The survey was developed using scientific literature and in collaboration with health care professionals with experience using medical cannabis for patient care. The questions were modified from the literature to accommodate a wide range of patients. Pain was measured using the numeric rating scale. An adaptation of the Pain Self-Efficacy Questionnaire was included in the survey to determine perceived ability to cope with pain. Assessments of quality of life (QOL) were adapted from validated and commonly used screening tools.

Baseline

Demographic information, including age, sex, ethnicity, and employment status was collected at baseline. Patients were asked to identify any present medical conditions, including duration and severity of the conditions, as well as to report on the presence and severity of any symptoms related to medical conditions. If patients indicated the presence of recurring pain, they were subsequently asked to rate their pain on a scale of 1 to 10, where 1 represented dull pain and 10 represented severe pain. Ability to cope with pain was measured using the options: 'very easy,' 'somewhat easy,' 'somewhat difficult,' and 'very difficult.' Patients were also asked to report any other current medications as well as previous experience with cannabis, including the frequency of use and method of consumption, if any.

Patients were asked to rate their overall QOL using the options 'very good,' 'good,' 'fair,' 'bad,' and 'very bad' and indicate their perceived ability to perform activities of daily living (ADLs) from the options 'very capable,' 'somewhat capable,' 'somewhat incapable,' 'very incapable,' or 'unsure.' Mobility and ability to dress/shower independently were measured based on difficulty ranging from no, minimal, moderate, to severe difficulty. General mood was assessed using the options 'very positive,' 'positive,' 'neutral,' 'negative,' or 'very negative.' Additional questions assessed patients' current experiences with sleep, appetite, concentration, bowel

activity, and sexual function, where patients were able to select from the options 'severe difficulty,' 'moderate difficulty,' 'no difficulty,' 'good,' or 'very good' to represent their experience.

Follow-up

FU surveys were completed at 4 months and 10 months from baseline. To assess the response to medical cannabis, patients were asked to rate the effect of cannabis on present medical conditions, by categorizing the status of their conditions as one of the following: 'significant deterioration,' 'moderate deterioration,' 'slight deterioration,' 'no change,' 'slight improvement,' 'moderate improvement,' and 'significant improvement,' as well as the time taken to achieve the change, if any. Questions regarding medical cannabis use including frequency of and methods of consumption were repeated from baseline. Patients were also asked to report which cannabis strains they had used. If present, pain was measured on a scale of 1 to 10 and ability to cope was categorized using the same options as presented at baseline. Questions regarding QOL were repeated from baseline. Additionally, patients were asked to report any side effects experienced as a result of cannabis use, including type of side effect, frequency, duration, and severity.

Patient population

Baseline and FU surveys were completed between January 2015 and October 2016. Patients reporting non-cancer conditions who completed surveys at minimum at baseline and 4 month FU were included.

Statistical analysis

Descriptive analysis was conducted using proportions for categorical variables. The Fisher test or Chi-squared test was used as appropriate to determine significant association between pain severity and ability to cope with pain responses from baseline to FU, and between improvement status (improvement, no change, or deterioration) and the presence of the most common medical conditions, QOL, and symptoms. Changes in pain scores between baseline and FU were compared using paired t-tests. Two-sided p-value < 0.05 was considered statistically significant. All analyses were conducted using Statistical Analysis Software (SAS version 9.4, Cary, NC).

Results

2,588 of the 2,752 patients who completed the survey at baseline reported medical conditions other than cancer. The majority of patients were Caucasian (79.2%) and male (69.2%) with an average age of 42.7 years. The most commonly reported medical conditions included anxiety disorder (32.9%, n = 713), depression (32.6%, n = 706), sleep disorders (26.7%, n = 579), post-traumatic stress disorder (PTSD) (22.6%, n = 489), and arthritis (22.5%, n = 488). 1772 patients (76.8%) reported previous cannabis use, while 366 patients (15.9%) reported no previous cannabis use and 170 patients (7.37%) preferred not to answer. Current cannabis use at the time of baseline was reported by 86.2% of patients (n = 1492). Table 1 illustrates all patient demographics.

Pain and ability to cope with pain

Patients reported pain severity on a scale of 1 to 10, from which scores were categorized into mild (1-4), moderate (5-7), and severe (8-10). 30.2% of patients (n = 633) reported pain at baseline with the majority rating their pain as severe (n = 68, 61.3%). Notably, severe pain was reduced from 61.3% (n = 68) of patients at baseline to 10.8% (n = 12) at 4-month FU and 6.31% (n = 7) at 10-month FU. Changes in pain severity were found to be statistically significant ($p < 0.0001$) at all-time points.

Sixty-seven patients reported their ability to cope with pain at all-time points (baseline, 4-month FU, and 10-month FU). From baseline, the proportion of those who reported ability to cope as 'very easy' increased from 0% of patients to 20.8% (n = 14) at 4-month FU and 25.4% (n = 17) at 10-month FU. Similarly, those who reported ability to cope as 'very

difficult' decreased from 64.2% of patients (n = 43) at baseline to 1.49% (n = 1) at 4-month FU and remained stable at 10-month FU. Changes in ability to cope with pain were statistically significant ($p < 0.0001$) between baseline and 4-month and 10-month FUs. Table 2 demonstrates changes in pain severity and ability to cope with pain at all-time points.

Table 1. Patient demographics

Demographic	n (%)
Gender (Total n = 2753)	
Male	1790 (69.2%)
Female	798 (30.8%)
Age in Years (Total n = 2753)	
≤18	22 (1.7%)
19-29	403 (15.6%)
30-39	713 (27.6%)
40-49	563 (21.6%)
50-59	571 (22.1%)
60-69	237 (9.2%)
≥70	57 (2.2%)
Ethnicity (Total n=2601)	
Caucasian	2060 (79.2%)
Spanish/Hispanic/Latino	20 (0.8%)
Native Canadian	123 (4.7%)
Black/African American	41 (1.6%)
Asian	45 (1.7%)
Other	312 (12.0%)
Other Conditions (Total n = 2165)	
Anxiety	713 (32.9%)
Depression	706 (32.6%)
Sleep disorder	579 (26.7%)
PTSD	489 (22.6%)
Arthritis	488 (22.5%)
Previous Cannabis Use (Total n = 2821)	
Yes	1772 (76.8%)
No	366 (15.9%)
Prefer not to answer	170 (7.4%)
Current Cannabis Use (Total n = 1730)	
Yes	1492 (86.2%)
No	238 (13.8%)

PTSD: Post-traumatic stress disorder.

Improvements in medical conditions

Responses for changes in medical conditions were more broadly categorized into improvement (comprising slight, moderate, and significant), no change, and deterioration (comprising slight, moderate, and medium). These results are presented in Table 3. Improvements were observed in all major conditions including sleep disorder (79.2%, n = 122), anxiety (77.5%, n = 162), PTSD (76.9%, n = 122), depression (71.6%, n = 151), and arthritis (70.0%, n = 98). Statistical significance was demonstrated for anxiety ($p = 0.0006$), PTSD ($p = 0.006$), and sleep disorder (n = 0.0006).

Improvements in symptoms

Patients reported on frequently experienced symptoms and their severity at baseline, the most common of which were pain, anxiety, depression, exhaustion, and sleep problems. At baseline, patients predominantly reported severe pain (50.3%, n = 950), moderate anxiety (49.0%, n = 923), moderate depression (45.8%, n = 706), moderate exhaustion (47.4%, n = 832), and moderate sleep problems (45.9%, n = 832). Symptom severity at baseline is illustrated in Table 4.

Changes in experiences of symptoms and symptom severity were measured at 4-month and 10-month FU using the following options: deterioration, no change, improvement, or resolved, as demonstrated in Table 5. Improvement was reported in 79.5% of patients (n = 346) for pain, 74.8% (n = 323) for anxiety, 68.7% (n = 250) for depression, 59.3% (n = 181) for exhaustion, 74.5% (n = 315) for sleep problems, and 48.6% (n = 89) for weakness. Between 1-7% of patients reported complete resolution of symptoms at 4-month FU, including anxiety (1.9%, n = 8), depression (2.5%, n = 9), exhaustion (2.6%, n = 8), sleep problems (3.6%), and weakness (6.6%, n = 12). Changes in pain ($p = 0.002$) and sleeping problems ($p = 0.01$) were found to be statistically significant. At 10-month FU, improvement in symptoms ranged from approximately 51% to 79%, however, none were found to be statistically significant.

Table 2. Changes in pain severity and the ability to cope with pain at baseline and FU

	Baseline n (%)	**4-month FU n (%)**	**10-month FU n (%)**	**p-value***
Pain Severity (Total n = 111)				
Mild	9 (8.1%)	53 (47.8%)	71 (64.0%)	**<0.0001**
Moderate	34 (30.6%)	46 (41.4%)	33 (29.7%)	
Severe	68 (61.3%)	12 (10.8%)	7 (6.3%)	
Ability to Cope (Total n = 67)				
Very easy	0 (0%)	14 (20.8%)	17 (25.4%)	**<0.0001**
Somewhat easy	2 (3.0%)	40 (59.7%)	38 (56.7%)	
Somewhat difficult	22 (32.8%)	12 (17.9%)	11 (16.4%)	
Very difficult	43 (64.2%)	1 (1.5%)	1 (1.5%)	

*****Bolded values represent statistical significance ($p < 0.05$).

Table 3. Improvement in medical conditions at 4-month FU

Medical Condition	**Improvement n (%)**	**No Change n (%)**	**Deterioration n (%)**	**p-value***
Arthritis (Total n = 140)	98 (70.0%)	23 (16.4%)	19 (13.6%)	0.6
Depression (Total n = 211)	151 (71.6%)	34 (16.1%)	26 (12.3%)	0.2
Anxiety (Total n = 209)	162 (77.5%)	17 (8.1%)	30 (14.4%)	**0.0006**
PTSD (Total n = 160)	123 (76.9%)	17 (10.6%)	20 (12.5%)	**0.007**
Sleep disorder (Total n = 154)	122 (79.2%)	17 (11.0%)	15 (9.7%)	**0.0006**

*****Bolded values represent statistical significance ($p < 0.05$).

PTSD: Post-traumatic stress disorder.

Table 4. Symptom severity at baseline

Symptom	**Severity**		
	Mild n (%)	**Moderate n (%)**	**Severe n (%)**
Pain (Total n = 1887)	172 (9.1%)	765 (40.5%)	950 (50.3%)
Anxiety (Total n = 1882)	495 (26.3%)	923 (49.0%)	464 (26.7%)
Depression (Total n = 1541)	493 (32.0%)	706 (45.8%)	342 (22.2%)
Exhaustion (Total n = 1289)	354 (27.4%)	611 (47.4%)	324 (25.1%)
Sleep problems (Total n = 1814)	360 (19.8%)	832 (45.9%)	622 (34.3%)
Weakness (Total n = 870)	383 (44.0%)	384 (44.1%)	103 (11.8%)

Improvement in quality of life (QOL)

Patients reported changes in QOL and associated QOL indicators, which included mobility, ability to dress/shower independently, ability to perform activities of daily living (ADLs), and general mood from baseline to 4-month and 10-month FU, as shown in Table 6. Reports of 'very good' QOL were increased from 4.8% of patients (n = 6) at baseline to 14.5% (n = 18) at 4-month FU and 13.7% (n = 17) at 10-month FU. From baseline to 4-month FU, a greater proportion of patients reported 'good' QOL (increased

from 22.6% to 33.9%) and a smaller proportion reported 'Fair' (decreased from 45.2% to 41.1%), 'Bad' (decreased from 22.6% to 8.9%), or 'Very Bad' (decreased from 4.8% to 1.6%) QOL; however there was little difference in QOL between 4-month and 10-month FU. Changes reported in QOL from baseline to 4-month and 10-month FU were statistically significant ($p = 0.001$). Of the associated QOL indicators, only changes in general mood were found to be statistically significant. Compared to 5.0% of patients (n = 6) at baseline, 'very positive' general mood was reported by 12.4% (n = 15) at 4-month FU and 14.9% (n = 18) at 10-month FU.

Patients were also asked about changes in experiences with other QOL indicators including appetite, sleep, concentration, bowel activity, and sexual function, the findings of which are illustrated in Table 7. Improved experiences were observed with each of the QOL indicators. From baseline to 4-month FU, reports of 'very good' experiences increased from 20% to 26.4% of patients for appetite, 2.8% to 19.3% for sleep, 8.2% to 19.1% for concentration, 10.8% to 27.0% for bowel activity, and 16.3% to 26.0% for sexual function. 'Very good' experiences were notably reduced for concentration at 10-month FU (10.9%), however 'good' experiences improved from 20.9% of patients to 35.5% of patients from 4-month to 10-month FU. Otherwise, most experiences with QOL factors remained stable between 4-month and 10-month FU. Only findings for experiences with sleep and concentration were found to be statistically significant ($p < 0.001$ and $p = 0.002$ respectively).

Table 5. Improvements in symptoms at FU

Symptom	**Deterioration n (%)**	**No Change n (%)**	**Improvement n (%)**	**Resolved n (%)**	**p-value***
4-month FU					
Pain (Total n = 435)	33 (7.6%)	49 (11.3%)	346 (79.5%)	7 (1.6%)	**0.002**
Anxiety (Total n = 432)	38 (8.8%)	63 (14.5%)	323 (74.8%)	8 (1.9%)	0.06
Depression (Total n = 364)	40 (11.0%)	65 (17.9%)	250 (68.7%)	9 (2.5%)	0.9
Exhaustion (Total n = 305)	21 (6.9%)	95 (31.1%)	181 (59.3%)	8 (2.6%)	0.1
Sleep problems (Total n = 423)	33 (7.8%)	60 (14.2%)	315 (74.5%)	15 (3.6%)	**0.01**
Weakness (Total n = 183)	22 (12.0%)	60 (32.8%)	89 (48.6%)	12 (6.6%)	0.06
10-month FU					
Pain (Total n = 113)	6 (5.3%)	17 (15.0%)	84 (74.3%)	6 (5.3%)	0.5
Anxiety (Total n = 103)	10 (9.7%)	12 (11.7%)	77 (74.8%)	4 (3.9%)	0.4
Depression (Total n = 85)	5 (5.9%)	7 (8.2%)	66 (77.6%)	7 (8.2%)	0.6
Exhaustion (Total n = 70)	5 (7.1%)	19 (27.1%)	44 (62.9%)	2 (2.9%)	0.7
Sleep problems (Total n = 105)	7 (6.7%)	7 (6.7%)	83 (79.0%)	8 (7.6%)	0.8
Weakness (Total n = 47)	3 (6.4%)	18 (38.3%)	24 (51.1%)	2 (4.6%)	0.7

*****Bolded values represent statistical significance ($p < 0.05$).

Table 6. Quality of life and associated factors at baseline and FU

Response	Time Point			p-value*
	Baseline n (%)	**4-month FU n (%)**	**10-month FU n (%)**	
Quality of Life (Total n = 124)				
Very good	6 (4.8%)	18 (14.5%)	17 (13.7%)	**0.001**
Good	28 (22.6%)	42 (33.9%)	44 (35.5%)	
Fair	56 (45.2%)	51 (41.1%)	46 (37.1%)	
Bad	28 (22.6%)	11 (8.9%)	16 (12.9%)	
Very bad	6 (4.8%)	2 (1.6%)	1 (0.8%)	
Mobility (Total n = 119)				
No difficulty	34 (28.6%)	39 (32.8%)	45 (37.8%)	0.1
Minimal difficulty	32 (26.9%)	41 (34.5%)	25 (21.0%)	
Moderate difficulty	43 (36.1%)	33 (27.7%)	43 (36.1%)	
Severe difficulty	10 (8.4%)	6 (5.0%)	6 (5.0%)	
Ability to Dress/Shower Independently (Total n = 121)				
No difficulty	65 (53.7%)	71 (58.7%)	69 (57.0%)	0.9
Minimal difficulty	37 (30.6%)	36 (29.8%)	35 (28.9%)	
Moderate difficulty	18 (14.9%)	13 (10.7%)	17 (14.0%)	
Severe difficulty	1 (0.8%)	1 (0.8%)	0 (0.0%)	
Ability to Perform ADL (Total n = 124)				
Very capable	50 (40.3%)	47 (37.9%)	47 (37.9%)	0.4
Somewhat capable	39 (31.5%)	52 (41.9%)	49 (39.5%)	
Somewhat incapable	25 (20.2%)	20 (16.1%)	16 (12.9%)	
Very incapable	9 (7.26%)	5 (4.0%)	11 (8.9%)	
Don’t know	1 (0.8%)	0 (0.0%)	1 (0.8%)	
General Mood (Total n = 121)				
Very positive	6 (5.0%)	15 (12.4%)	18 (14.9%)	**<0.001**
Positive	43 (35.5%)	55 (45.5%)	53 (43.8%)	
Neutral	41 (33.9%)	47 (38.8%)	34 (28.1%)	
Negative	27 (22.3%)	2 (1.7%)	15 (12.4%)	
Very negative	4 (3.3%)	2 (1.7%)	1 (0.8%)	

*****Bolded values represent statistical significance ($p<0.05$). ADL: Activities of daily living.

Side effects

The most commonly reported side effects included dry mouth, psychoactive effects, decreased memory, decreased concentration, and sleepiness. 23 patients reported side effects at both 4-month and 10-month FU, as illustrated in Table 8. At 4-month FU, 16 (69.6%) reported dry mouth, 15 (65.2%) reported psychoactive effects, 12 (35.3%) reported decreased memory and concentration, and 11 (32.4%) reported sleepiness. At 10-month FU, reports of side effects were decreased for dry mouth (63.9%), psychoactive effects (50.0%), and decreased concentration (33.3%), but increased for decreased memory (36.1%) and sleepiness (44.4%). Patients also reported on severity of side effects at FU; the results at 4-month FU are displayed in Table 9. A majority of patients reported mild dry mouth (45.9%, n = 39), mild psychoactive effects (45.5%, n = 30,), mild decreased memory (56.7%, n = 17), mild decreased concentration (60.0%, n = 21), and moderate sleepiness (46.8%, n = 22).

Table 7. Experience with quality of life factors at baseline and FU

Response	Time Point			p-value* 4-month FU n (%)
	Baseline n (%)	4-month FU n (%)	Baseline n (%)	
Appetite (Total n = 110)				
Very good	22 (20.0%)	29 (26.4%)	31 (28.2%)	0.4
Good	32 (29.1%)	40 (36.4%)	36 (32.7%)	
No difficulty	21 (19.1%)	17 (15.5%)	22 (20.0%)	
Moderate difficulty	27 (24.5%)	19 (17.3%)	18 (16.4%)	
Severe difficulty	8 (7.3%)	5 (4.5%)	3 (2.7%)	
Sleep (Total n = 109)				
Very good	3 (2.8%)	21 (19.3%)	14 (12.8%)	**<0.001**
Good	3 (2.8%)	21 (19.3%)	32 (29.4%)	
No difficulty	3 (2.8%)	10 (9.2%)	8 (7.3%)	
Moderate difficulty	59 (54.1%)	43 (39.4%)	40 (36.7%)	
Severe difficulty	41 (37.6%)	14 (12.8%)	15 (13.8%)	
Concentration (Total n = 110)				
Very good	9 (8.2%)	21 (19.1%)	12 (10.9%)	**0.002**
Good	22 (20.0%)	23 (20.9%)	39 (35.5%)	
No difficulty	17 (15.5%)	21 (19.1%)	17 (15.5%)	
Moderate difficulty	43 (39.1%)	38 (34.5%)	37 (33.6%)	
Severe difficulty	19 (17.3%)	7 (6.4%)	5 (4.5%)	
Bowel Activity (Total n = 23)				
Very good	22 (10.8%)	30 (27.0%)	24 (21.6%)	0.6
Good	31 (27.9%)	23 (20.7%)	30 (27.0%)	
No difficulty	26 (23.4%)	22 (19.8%)	25 (22.5%)	
Moderate difficulty	20 (18.0%)	29 (26.1%)	22 (19.8%)	
Severe difficulty	12 (19.8%)	7 (6.3%)	10 (9.0%)	
Sexual Function (Total n = 23)				
Very good	17 (16.3%)	27 (26.0%)	32 (30.8%)	0.1
Good	18 (17.3%)	24 (23.1%)	22 (21.2%)	
No difficulty	20 (19.2%)	22 (21.2%)	21 (20.2%)	
Moderate difficulty	29 (27.9%)	18 (17.3%)	18 (17.3%)	
Severe difficulty	20 (19.2%)	13 (12.5%)	11 (10.6%)	

*****Bolded values represent statistical significance ($p < 0.05$).

Table 8. Side effects at 4-month and 10-month FU

Side Effect	Time Point	
	4-month FU (Total n = 34) n (%)	**10-month FU (Total n = 36) n (%)**
Dry mouth	24 (70.6%)	23 (63.9%)
Psychoactive effects	21 (61.8%)	18 (50.0%)
Decreased memory	12 (35.3%)	13 (36.1%)
Decreased concentration	12 (35.3%)	12 (33.3%)
Sleepiness	11 (32.4%)	16 (44.4%)

Table 9. Severity of side effects at 4-month FU

Side effect	Severity		
	Mild n (%)	**Moderate n (%)**	**Severe n (%)**
Dry mouth (Total n = 85)	39 (45.9%)	35 (41.2%)	11 (12.9%)
Psychoactive effects (Total n = 66)	30 (45.5%)	29 (43.9%)	7 (10.6%)
Decreased memory (Total n = 30)	17 (56.7%)	10 (33.3%)	3 (10.0%)
Decreased concentration (Total n = 35)	21 (60.0%)	11 (31.4%)	3 (8.6%)
Sleepiness (Total n = 47)	20 (42.3%)	22 (46.8%)	5 (10.6%)

Discussion

The present study investigated the results of a voluntary online survey administered by a Canadian medical cannabis supplier, with the focus on the responses to cannabis use in patients with medical conditions excluding cancer. The goal of the study was to assess the effects of cannabis treatment for symptom management and relief in various medical conditions, of which the most common were anxiety, depression, sleep disorder, PTSD, and arthritis.

From the survey data collected, there was a statistically significant ($p < 0.0001$) reduction in pain severity between baseline and 4-month and 10-month FU. Similarly, patients reported an increase in their ability to cope with pain following cannabis use from baseline to 4-month and 10-month FU ($p < 0.0001$).

These findings are consistent with results of other studies found in the literature which examined the analgesic properties of cannabis. A thorough literature review conducted by Amar (1) identified nine controlled studies which have examined pain in patients with a variety of medical conditions excluding cancer (1). One of the identified studies was a randomized control trial (RCT) by Notcutt et al. (3) that examined the analgesic effects of THC and CBD in 34 patients with chronic pain (3). Patients were randomized to receive one of three varieties of cannabis-based extracts: THC, CBD, or 1:1 THC:CBD administered by a sublingual spray over a 12-week period. Two patients dropped out of the study, one was unable to cope with study requirements and the other was unable to tolerate the treatment. In the remaining 32 patients, extracts containing THC (THC alone and THC:CBD combination) demonstrated effective pain relief as well as improvement of sleep quality, while CBD alone was ineffective. Some minor side effects were observed, including dry mouth, drowsiness, euphoria/dysphoria, and dizziness.

Similar findings were reported by Berman et al. (4) in their RCT involving 48 patients with central neuropathic pain treated with either THC or THC:CBD sublingual spray for three periods of two weeks (4). Three patients withdrew prior to study completion, of which two experienced adverse effects of THC. The results of the 45 patients completing the study demonstrated a statistically significant decrease

in pain and improvement in sleep quality with both the THC alone and the THC:CBD combination with only mild to moderate side effects.

However, another RCT by Buggy et al. (5) examined the analgesic effect of oral THC in 40 women undergoing hysterectomies with post-operative pain and found no significant differences between treatment and placebo groups in mean summed pain intensity difference (SPID, primary outcome) 6 hours after intake (5). No significant adverse outcomes were observed with the dosage used in this study, thus future studies may consider the use of higher doses, while being cognizant that previous studies have indicated a higher incidence of adverse events with higher doses (1,5).

Notcutt et al. (3) and Berman et al. (4) demonstrated significant improvements in pain and sleep with mild to moderate side effects in patients suffering from chronic pain while Buggy et al. (5) did not find significant improvements among patients with post-operative or acute pain. This may suggest differences exist in the treatment of chronic and acute pain. In the present study, significant changes were found in the presence and severity recurrent or chronic pain, however acute pain was not considered. Patients of this study also reported similar side effects as those found by Noctcutt et al. (3) and Berman et al. (4), including dry mouth and psychoactive effects or euphoria/dysphoria. Further investigations should explore appropriate dosing, combinations of cannabinoids, and methods of consumption to assess the efficacy of cannabis as an analgesic for both chronic and acute pain.

Medical cannabis has also been indicated for appetite stimulation, particularly cancer- or AIDS-related anorexia-cachexia; however, present evidence is limited and further research is required to understand its potential role in the treatment of these conditions (1). Struwe et al. (6) studied the efficacy of cannabis for appetite stimulation in 12 men with symptomatic HIV and weight loss of >2.3 kg using 5 mg oral THC (6). Of the 12 patients, 2 experienced sedation and mood disorders and withdrew prior to completion. Out of the remaining 10 patients, THC was found to stimulate appetite but there was no statistically significant difference in weight variations between patients receiving THC or placebo. A larger study by Beal et al. (7) examined the use of oral THC in 139 patients with AIDS and weight loss of >2.3 kg and found a statistically significant stimulation of appetite and stabilization of weight in those using THC compared to those using the placebo (7). Only minor side effects were reported, including euphoria, dizziness, confusion, and drowsiness. In the present study, those with HIV/AIDS accounted for < 1% (n = 7) of all patients surveyed. While overall experiences with appetite for all patients (excluding cancer patients) demonstrated improvement from baseline to 10-month FU (20.0% reported 'very good' at baseline, 28.2% at 10-month FU), the changes were not statistically significant (p = 0.4). This may have been due to the characteristics of the study population, many of which did not report loss or trouble with appetite; in fact, only 7.3% (n = 8) reported severe difficulty with appetite at baseline. Further studies should investigate the efficacy of cannabis for appetite stimulation in particular study samples where appetite stimulation is an appropriate indication, for example cancer or HIV patients.

Cannabis has also demonstrated anti-spastic properties, which present potential therapeutic uses in the treatment of multiple sclerosis (MS) (1). Approximately 2% of the patients surveyed in the present study reported having MS. Zajicek et al. (8) studied the effects of oral THC on spasticity in 630 MS patients and found a small treatment effect on muscle spasticity as well as improvements in mobility, pain, sleep quality, and general condition (8). Wade et al. conducted a study in 160 MS patients using a 1:1 combination of THC:CBD administered via sublingual spray (9). They reported statistically significant reductions in spasticity with the THC:CBD combination compared to placebo as well as significant improvements in sleep quality but insignificant improvement in mobility.

Some anecdotal reports have also suggested that cannabis may function as an anti-convulsant, particularly in epilepsy and generalized tonic-clonic seizures (1). In this study, epilepsy was also observed in approximately 2% of patients surveyed. Cunha et al. (10) examined the efficacy of CBD in treating seizures in 15 patients with generalized epilepsy inadequately controlled by conventional medications (10). Of the eight patients randomized to receive CBD, 50% (n = 4) remained convulsion-free over the duration of the study and 38% (n = 3) demonstrated

improvement. Drowsiness was reported by 50% of the patients on CBD. Overall, the evidence to support anti-spastic and anti-convulsant properties of cannabis remains low. Further investigation is required before cannabis may be implemented as effective treatment for conditions such as MS and epilepsy.

CBD is also known to provide anxiolytic effects, and therefore may be used in the treatment of anxiety disorders, insomnia, and epilepsy. Both sleep problems and anxiety were amongst the most commonly reported symptoms in this study. Carlini and Cunha (11) assessed the effects of 3 doses of CBD (40, 80, and 160 mg) in 15 insomniac patients and found a significant increase in the duration of sleep in those receiving 160 mg CBD (11). Findings in the present study also reported significant improvement in experiences with sleep from baseline to 10-month FU ($p < 0.0001$). However, dose and variants of cannabis taken were not specified.

Another study by Fabre and McLendon (12) investigated the effects of nabilone, a synthetic cannabinoid mimicking THC, in 20 patients diagnosed with anxiety (12). Nabilone was found to be significantly more effective than placebo in relieving anxiety ($p < 0.0001$). While this study demonstrated improvements in anxiety at 4-month and 10-month FU (74.8% improved at both 4-month FU and 10-month FU), the changes were not statistically significant ($p = 0.07$ at 4-month FU, $p = 0.4$ at 10-month FU).

The results of the present study indicate that cannabis may be used in the treatment of pain, anxiety, sleep disorders, as well as a number of other symptoms in patients suffering from a variety of medical conditions, excluding cancer. These findings are in general agreement with those reported in the literature. However, there are significant limitations in the present study that should be considered. Since the survey was completed on a voluntary basis, the compliance rate was very low. As such, despite having an initially large sample size at baseline, the results returned low numbers of responses for many of the parameters, especially at later FU intervals. The smaller sample sizes may have limited the power of the statistical analysis. It is also possible that there was a higher incidence of responses from patients experiencing more positive outcomes, resulting in a positive skew. Also, the time at which FU surveys were completed was not consistent between subjects, since patients may have completed FU surveys at any time after receiving a survey invitation. Moreover, at baseline, approximately 86% of patients reported current cannabis use; therefore, any changes observed at FU are likely due to a change in cannabis treatment. Furthermore, since the data on concurrent medications, including type and dose, was self-reported, much of the information was incomplete and therefore not available for analysis. The study was also unable to account for any adverse events that occurred over the course of cannabis use. Finally, it is not known if those who were invited to complete FU surveys had continued to fill prescriptions from baseline to 10-month FU, although patients had active prescriptions at the time of invite.

Conclusion

Further clinical investigation is required to determine the utility of medical cannabis and support its use as an alternative or first-line treatment for a variety of common conditions and symptoms. Future studies should focus on the effects of different cannabis varieties, dosing, and methods of consumption as they pertain to different medical conditions in order to optimize patient outcomes.

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