

The use of medical cannabis in cancer patients

**Pearl Zaki¹, BSc(C), Alexia Blake², MSc,
Amiti Wolt², BA, Stephanie Chan¹, BSc(C),
Liyang Zhang¹, PhD, Angela Wan¹, MPhil,
Henry Lam¹, MLS,
Carlo DeAngelis¹, PharmD,
Marissa Slaven³, MD, Erynn Shaw³, MD,
Vithusha Ganesh¹, BSc(C),
Leila Malek¹, BSc(Hons),
Edward Chow¹, MBBS,
and Shannon O'Hearn^{2,*}, MSc**

¹Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada

²MedReleaf, Markham, Ontario, Canada

³Juravinski Cancer Centre, Hamilton Health Sciences, Hamilton, Ontario, Canada

Abstract

Therapeutic applications of medical cannabis within the cancer population, particularly for pain, treatment-related nausea and vomiting, and loss of appetite, have been investigated by few studies. The present study examined the efficacy of cannabis treatment for symptom relief among cancer patients receiving cannabis treatment from a single Canadian medical cannabis provider. Data was obtained from a voluntary online survey that consisted of questions related to demographic information, current medical conditions, presence and severity of symptoms, and quality of life (QOL). Follow-up (FU) surveys were completed at 4 and 10 months following initial use. 164 patients reported a current or previous diagnosis of cancer, of which the most common types of primary tumours were gastrointestinal (17.7%, n = 29), breast (13.4%, n = 22), leukemia and lymphoma (13.4%, n = 22), gynaecologic (9.2%, n = 15), prostate (7.3%, n = 12), and lung (7.3%, n = 12). While improvements were seen in commonly reported symptoms, including pain, depression, anxiety, exhaustion, and sleep problems, the observations were not statistically significant. Statistical significance was demonstrated in patients' ability to cope with pain at 4-month FU ($p < 0.0001$). QOL was stable from baseline to 4-month FU, where most reported good QOL (66.7%). Of associated QOL factors, only experience with sleep was found to be improved with statistical significance ($p = 0.02$). Side effects of cannabis use included dry mouth, psychoactive effects, decreased concentration and memory, and sleepiness. Further studies are needed to determine the efficacy of medical cannabis in comparison to conventional first-line therapies for management of symptoms in cancer patients in both short- and long-term treatment.

Keywords: Medical cannabis, cancer, quality of life, medical marijuana

Introduction

Cancer patients suffer from a range of disease- and treatment-related symptoms that negatively impact quality of life (QOL), the most common of which include pain, treatment-related nausea and vomiting, and loss of appetite. In particular, cancer-related pain

* Correspondence: Ms Shannon O'Hearn MSc, MedReleaf Corp, Markham Industrial Park, Markham ON, Canada.
E-mail: sohearn@medreleaf.com

can severely affect 70-90% of those with advanced cancers (1). The standard treatment for cancer pain is currently opioids; however, some patients continue to experience inadequate pain relief despite opioid therapy and the use of other common adjuvant analgesics (1-4). In the current literature, various studies have investigated clinical utility of cannabis as a potential treatment for a number of cancer-related symptoms including pain, nausea and vomiting, lack of appetite, and difficulty with sleep (2-4). However, confounding findings in the literature draw attention to the need for further investigation. To best guide clinical decision-making, it is important to determine potential benefits, adverse effects, drug interactions, and effective routes of administration and dosing of medical cannabis prior to implementation for therapeutic uses in the cancer setting.

Cannabinoids are the most well-known constituents of the *Cannabis sativa L* plant with over 60 unique compounds identified to date. Due to their potent biological activity, delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are the two most well-studied cannabinoids. While THC is known primarily for its psychoactive effects, it has also been shown to provide analgesic, anti-emetic, anti-inflammatory, muscle relaxant, and appetite stimulating properties (1, 2). In comparison, CBD provides anti-convulsive, muscle relaxant, anxiolytic, and anti-inflammatory properties (1, 2). Some studies have also suggested that CBD can counter-act the paranoia and anxiety sometimes induced by THC, possibly through modulatory effects (1, 2). This pharmacologic activity follows the activation of CB-1 and CB-2 receptors. These receptors are part of the endocannabinoid system, which has been shown to naturally influence and assist with the regulation of mood, sleep, memory, appetite, and emotions via activation by endogenous ligands (1-3).

The present study investigated the possible benefits and side effects of the use of medical cannabis for symptom management and relief among cancer patients.

Methods

Patients beginning cannabis treatment with a single Canadian medical cannabis provider completed a voluntary online survey at baseline, which is defined as the time of registration with the provider. Those who completed the survey at baseline were invited to complete a follow-up (FU) survey after four months. Similarly, those who completed the 4-month FU survey were prompted to complete a second FU survey at 10 months after baseline.

Survey design

The survey was designed by the medical cannabis provider using scientific literature as well as guidance from health care professionals with experience using medical cannabis for patient care. The questions were adapted from the literature to accommodate the wide range of patients surveyed. Pain was measured using the numeric rating scale. Additionally, an adaptation of the Pain Self-Efficacy Questionnaire was incorporated to determine perceived ability to cope with pain. QOL assessment was based on validated and commonly used screening tools.

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

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. For reported conditions, patients were asked FU questions specific to the condition to better characterize each patient's medical history. Patients who reported a diagnosis of cancer were asked to specify cancer type and stage.

Patients were also asked to report on any present symptoms related to medical conditions and classify the severity of symptoms as mild, moderate, or severe. If patients indicated the presence of pain, they were asked to rate their pain on a scale of 1 to 10, where 1 represented dull pain and 10 represented severe pain. In the absence of pain, patients reported 'no pain' and no further questions were asked. Ability to cope with pain was measured on a categorical scale using the following options: 'very easy,' 'somewhat easy,' 'somewhat difficult,' and 'very difficult.' Patients were also asked to report other current medications, specifying the name and dose, as well as any use of cannabis (previous or current) prior to beginning treatment with the cannabis supplied by the medical cannabis provider.

Patients were asked to rate their QOL using one of the following options: 'very good,' 'good,' 'fair,' 'bad,' or 'very bad,' as well as to indicate their perceived ability to perform activities of daily living (ADLs) with the options 'very capable,' 'somewhat capable,' 'somewhat incapable,' 'very incapable,' or 'unsure.' Additional questions assessed patients' current experiences with sleep, appetite, concentration, bowel activity, and sexual function based on difficulty, using the options 'severe difficulty,' 'moderate difficulty,' 'no difficulty,' 'good,' and 'very good.' Experiences with mobility and ability to dress and shower independently were also examined based on difficulty, with possible options ranging from severe, moderate, minimal, to no difficulty. General mood was assessed using the options 'very positive,' 'positive,' 'neutral,' 'negative,' and 'very negative.'

Follow-up

FU surveys were completed at 4 months and 10 months following the completion of the baseline survey. Patients were asked to report any changes in present medical conditions following cannabis use (from the options 'significant deterioration,' 'moderate deterioration,' 'slight deterioration,' 'no change,' 'slight improvement,' 'moderate improvement,' or 'significant improvement') as well as the time taken to achieve the change, if any. Information regarding medical cannabis use from the

cannabis provider, including strains used, frequency of consumption, and methods of consumption, was collected. If present, pain was measured on a scale of 1 to 10. Ability to cope with pain following use of medical cannabis was measured similarly to baseline, using the options: 'very easy,' 'somewhat easy,' 'somewhat difficult,' or 'very difficult.' Questions regarding QOL were also 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. Only patients reporting a diagnosis of cancer who completed the survey at baseline and FU at 4 or 10 months were included for analysis in this study.

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 responses from baseline to follow-up visits, between improvement status (improvement, no change, or deterioration), and the presence of most common medical conditions, symptoms, and QOL. 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

Of the 2573 patients who completed the survey at baseline, 164 patients reported a current or previous diagnosis of cancer. Among cancer patients, the majority were male (56.1%) and Caucasian (82.7%) with an average age of 54.9 years. The most commonly reported primary cancers included

gastrointestinal (17.7%, n = 29), breast (13.4%, n = 22), leukemia and lymphoma (13.4%, n = 22), gynaecologic (9.2%, n = 15), prostate (7.3%, n = 12), and lung (7.3%, n = 12). Additionally, the most common comorbidities included arthritis (20.4%, n = 29), depression (16.2%, n = 23), anxiety (13.4%, n = 12), PTSD (9.2%, n = 13), and sleep disorder (7.0%, n = 10). Most patients reported previous cannabis use (56.3%, n = 81) and current use of cannabis at baseline (73.8%, n = 62). All demographic information is presented in Table 1.

Table 1. Patient demographics

| Demographic | n (%) |
|----------------------------------------------|-------------|
| Gender (Total n = 164) | |
| Male | 92 (56.1%) |
| Female | 72 (43.9%) |
| Age (Total n = 164) in years | |
| ≤18 | 2 (1.2%) |
| 19-29 | 4 (2.4%) |
| 30-39 | 20 (12.2%) |
| 40-49 | 22 (13.4%) |
| 50-59 | 46 (28.0%) |
| 60-69 | 45 (27.4%) |
| ≥70 | 25 (15.2%) |
| Ethnicity (Total n = 162) | |
| Caucasian | 134 (82.7%) |
| Spanish/Hispanic/Latino | 2 (1.2%) |
| Native Canadian | 11 (6.8%) |
| Black/African American | 1 (0.6%) |
| Asian | 2 (1.2%) |
| Prefer not to answer | 6 (3.7%) |
| Other | 6 (3.7%) |
| Other conditions (Total n = 142) | |
| Arthritis | 29 (20.4%) |
| Depression | 23 (16.2%) |
| Anxiety | 19 (13.4%) |
| PTSD | 13 (9.2%) |
| Sleep disorder | 10 (7.0%) |
| Previous cannabis use (Total n = 144) | |
| Yes | 81 (56.3%) |
| No | 55 (38.2%) |
| Prefer not to answer | 8 (5.6%) |
| Current cannabis use (Total n = 62) | |
| Yes | 62 (73.8%) |
| No | 22 (26.2%) |
| Primary cancer (Total n = 164) | |
| Breast | 22 (13.4%) |
| Prostate | 12 (7.3%) |
| Lung | 12 (7.3%) |

| Demographic | n (%) |
|-------------------------------------|------------|
| Gastrointestinal | 29 (17.7%) |
| Gynecologic | 15 (9.2%) |
| Skin | 5 (3.1%) |
| Osteosarcoma | 3 (1.8%) |
| Urothelial | 5 (3.1%) |
| Brain | 7 (4.3%) |
| Leukemia and lymphoma | 22 (13.4%) |
| Hepatocellular | 3 (1.8%) |
| Male reproductive cancers | 2 (1.2%) |
| Thyroid | 5 (3.1%) |
| Other | 22 (13.4%) |
| Cancer stage (Total n = 159) | |
| Remission | 47 (29.6%) |
| 0 | 5 (3.1%) |
| 1 | 10 (6.3%) |
| 2 | 13 (8.2%) |
| 3 | 21 (13.2%) |
| 4 | 48 (30.2%) |
| Unknown | 15 (9.4%) |

PTSD: Post-traumatic stress disorder.

Pain and ability to cope with pain

Patients who reported experiencing pain ranked their pain on a scale of 1 to 10 at baseline and 4-month FU, where a score of 1-4 represented mild pain, 5-7 represented moderate pain, and 8-10 represented severe pain. At baseline, recurring pain was present in 75.0% (n = 140) of 160 cancer patients who responded to the question. Of the patients who reported on their pain at both baseline and 4-month FU (n = 24), the proportion of those experiencing severe pain was reduced from 45.8% (n = 11) to 16.7% (n = 4), however the differences were not statistically significant (p = 0.06). Since very few patients answered this question at baseline and 10-month FU, the results from 10-month FU were not included.

Twelve patients reported on ability to cope with pain at both baseline and 4-month FU. Seven patients reported 'very difficult' at baseline versus 0 patients at 4-month FU. These findings demonstrated statistically significant improvement in ability to cope with pain from baseline to 4-month FU (n = 12, p < 0.0001). Table 2 illustrates changes in pain scores and the ability to deal with pain in patients who responded at baseline and FU.

Table 2. Changes in pain severity and the ability to cope with pain at baseline and 4-month FU

| | Baseline n (%) | 4-month FU n (%) | P-value* |
|---------------------------------------|-------------------|---------------------|--------------------|
| Pain severity (Total n = 24) | | | |
| <i>Mild</i> | 6 (25.0%) | 13 (54.2%) | 0.06 |
| <i>Moderate</i> | 7 (29.2%) | 7 (29.2%) | |
| <i>Severe</i> | 11 (45.8%) | 4 (16.7%) | |
| Ability to cope (Total n = 12) | | | |
| <i>Very easy</i> | 1 (8.3%) | 5 (41.7%) | < 0.0001 |
| <i>Somewhat easy</i> | 2 (16.7%) | 4 (33.3%) | |
| <i>Somewhat difficult</i> | 2 (16.7%) | 3 (25.0%) | |
| <i>Very difficult</i> | 7 (58.3%) | 0 (0.0%) | |

*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 = 9) | 5 (55.6%) | 3 (33.3%) | 1 (11.1%) | 0.9 |
| Depression (Total n = 7) | 5 (71.4%) | 2 (28.6%) | 0 (0.0%) | 0.7 |
| Anxiety (Total n = 3) | 2 (66.7%) | 1 (33.3%) | 0 (0.0%) | 0.8 |
| PTSD (Total n = 5) | 5 (100.0%) | 0 (0.0%) | 0 (0.0%) | 0.07 |
| Sleep disorder (Total n = 7) | 4 (57.1%) | 2 (28.6%) | 1 (14.3%) | 0.9 |

Table 4. Symptom severity at baseline

| Symptom | Severity | | |
|--------------------------------|---------------|-------------------|-----------------|
| | Mild n (%) | Moderate n (%) | Severe n (%) |
| Anxiety (Total n = 116) | 36 (31.0%) | 70 (60.3%) | 10 (8.6%) |
| Depression (Total n = 91) | 43 (47.3%) | 33 (36.3%) | 15 (16.5%) |
| Exhaustion (Total n = 97) | 17 (17.5%) | 51 (52.6%) | 29 (29.9%) |
| Sleep problems (Total n = 108) | 22 (20.4%) | 58 (53.7%) | 28 (25.9%) |
| Weakness (Total n = 86) | 25 (29.1%) | 40 (46.5%) | 21 (24.4%) |

Table 5. Improvements in symptoms at four months

| Symptom | Improvement n (%) | No change n (%) | Deterioration n (%) | p-value |
|-------------------------------|----------------------|--------------------|------------------------|---------|
| Anxiety (Total n = 24) | 20 (83.3%) | 3 (12.5%) | 1 (4.2%) | 0.3 |
| Depression (Total n = 16) | 14 (58.3%) | 2 (8.3%) | 0 (0.0%) | 0.1 |
| Exhaustion (Total n = 15) | 6 (25.0%) | 5 (20.8%) | 4 (16.7%) | 0.05 |
| Sleep problems (Total n = 23) | 16 (66.7%) | 5 (20.8%) | 2 (8.3%) | 0.7 |
| Weakness (Total n = 15) | 10 (41.7%) | 3 (12.5%) | 2 (8.3%) | 0.9 |

Improvements in medical conditions

Table 3 presents improvements in medical conditions with responses grouped into improvement (significant, moderate, or slight), no change, and

deterioration (significant, moderate, or slight). Improvement was reported by 5 of 5 patients for PTSD (100.0%), 5 of 7 patients (71.4%) for depression, 2 of 3 patients (66.7%) for anxiety, 4 of 7 patients (57.1%) for sleep disorder, and 5 of 9 patients

(55.6%) for arthritis. However, the results did not demonstrate statistically significant change.

Improvements in symptoms

The most common symptoms reported by patients were anxiety, depression, exhaustion, sleep problems, and weakness, as illustrated in Table 4. Table 5 demonstrates changes in symptoms at 4-month FU with responses grouped into improvement

(signification, moderate, or slight), no change, and deterioration (signification, moderate, or slight). Patients reported changes in symptoms at 4-month FU and also rated the extent of change. Of the patients who responded at both baseline and 4-month FU, anxiety improved in 83.3% (n = 24), depression improved in 58.3% (n = 16), exhaustion improved in 25.0% (n = 15), sleep problems improved in 66.7% (n = 16), and weakness improved in 41.7% (n = 15). However, these findings were not statistically significant.

Table 6. Quality of life (QOL) and associated factors at baseline and follow-up

| Response | Time Point | | p-value* |
|-------------------------------------------------------------|-------------------|-------------------|-------------|
| | Baseline n (%) | 4 months n (%) | |
| Quality of life (Total n = 33) | | | |
| <i>Very good</i> | 3 (9.1%) | 3 (9.1%) | 0.9 |
| <i>Good</i> | 16 (48.5%) | 16 (16.5%) | |
| <i>Fair</i> | 11 (33.3%) | 12 (36.4%) | |
| <i>Bad</i> | 3 (9.1%) | 1 (3.0%) | |
| <i>Very bad</i> | 0 (0.0%) | 1 (3.0%) | |
| Mobility (Total n = 32) | | | |
| <i>No difficulty</i> | 9 (28.1%) | 11 (34.4%) | 0.9 |
| <i>Minimal difficulty</i> | 14 (43.8%) | 11 (34.4%) | |
| <i>Moderate difficulty</i> | 7 (21.9%) | 8 (25.0%) | |
| <i>Severe difficulty</i> | 2 (6.3%) | 2 (6.3%) | |
| Ability to dress/shower independently (Total n = 33) | | | |
| <i>No difficulty</i> | 22 (66.7%) | 23 (69.7%) | 0.2 |
| <i>Minimal difficulty</i> | 9 (27.3%) | 4 (12.1%) | |
| <i>Moderate difficulty</i> | 2 (6.1%) | 5 (15.2%) | |
| <i>Severe difficulty</i> | 0 (0.0%) | 1 (3.0%) | |
| Ability to perform ADL (Total n = 33) | | | |
| <i>Very capable</i> | 15 (45.5%) | 22 (66.7%) | 0.4 |
| <i>Somewhat capable</i> | 10 (30.3%) | 8 (24.2%) | |
| <i>Somewhat incapable</i> | 4 (12.1%) | 1 (3.0%) | |
| <i>Very incapable</i> | 3 (9.1%) | 1 (3.0%) | |
| <i>Don't know</i> | 1 (3.0%) | 1 (3.0%) | |
| General mood (Total n = 33) | | | |
| <i>Positive</i> | 19 (57.6%) | 7 (21.2%) | 0.02 |
| <i>Neutral</i> | 8 (24.2%) | 15 (45.5%) | |
| <i>Negative</i> | 5 (15.1%) | 9 (27.3%) | |
| <i>Very negative</i> | 1 (3.0%) | 2 (6.1%) | |

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

Table 7. Experience with quality of life factors

| Response | Time Point | | p-value* |
|--------------------------------------|-------------------|-------------------|-------------|
| | Baseline n (%) | 4 months n (%) | |
| Appetite (Total n = 24) | | | |
| <i>Very good</i> | 7 (29.2%) | 9 (37.5%) | 0.7 |
| <i>Good</i> | 4 (16.7%) | 6 (25.0%) | |
| <i>No difficulty</i> | 3 (12.5%) | 3 (12.5%) | |
| <i>Moderate difficulty</i> | 10 (41.7%) | 6 (25.0%) | |
| <i>Severe difficulty</i> | 0 (0.0%) | 0 (0.0%) | |
| Sleep (Total n = 22) | | | |
| <i>Very good</i> | 0 (0.0%) | 2 (9.1%) | 0.02 |
| <i>Good</i> | 2 (9.1%) | 6 (27.3%) | |
| <i>No difficulty</i> | 1 (4.6%) | 4 (18.2%) | |
| <i>Moderate difficulty</i> | 16 (72.7%) | 10 (45.5%) | |
| <i>Severe difficulty</i> | 3 (13.4%) | 0 (0.0%) | |
| Concentration (Total n = 24) | | | |
| <i>Very good</i> | 4 (16.7%) | 7 (29.2%) | 0.1 |
| <i>Good</i> | 7 (29.2%) | 5 (20.8%) | |
| <i>No difficulty</i> | 1 (4.2%) | 5 (20.8%) | |
| <i>Moderate difficulty</i> | 12 (50.0%) | 6 (25.0%) | |
| <i>Severe difficulty</i> | 0 (0.0%) | 1 (4.2%) | |
| Bowel activity (Total n = 23) | | | |
| <i>Very good</i> | 7 (30.4%) | 4 (17.4%) | 0.8 |
| <i>Good</i> | 7 (30.4%) | 7 (30.4%) | |
| <i>No difficulty</i> | 4 (17.4%) | 5 (21.7%) | |
| <i>Moderate difficulty</i> | 4 (17.4%) | 5 (21.7%) | |
| <i>Severe difficulty</i> | 1 (4.4%) | 2 (8.7%) | |
| Sexual function (N = 23) | | | |
| <i>Very good</i> | 1 (4.4%) | 2 (8.7%) | 0.01 |
| <i>Good</i> | 3 (13.0%) | 8 (34.8%) | |
| <i>No difficulty</i> | 3 (13.0%) | 4 (17.4%) | |
| <i>Moderate difficulty</i> | 8 (34.8%) | 9 (39.1%) | |
| <i>Severe difficulty</i> | 8 (34.8%) | 0 (0.0%) | |

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

Table 8. Side effects at follow-up

| Side effect | Time point | |
|-------------------------|---------------------------------|----------------------------------|
| | 4 months (Total n = 9) n (%) | 10 months (Total n = 3) n (%) |
| Dry mouth | 4 (44.4%) | 2 (66.7%) |
| Psychoactive effects | 4 (44.4%) | 1 (33.3%) |
| Decreased memory | 4 (44.4%) | 1 (33.3%) |
| Decreased concentration | 2 (22.2%) | 2 (66.7%) |
| Sleepiness | 3 (33.3%) | 1 (33.3%) |

Improvement in quality of life (QOL)

The survey measured overall QOL and associated QOL factors such as mobility, ability to dress and shower independently, ability to perform ADLs, and general mood; Table 6 illustrates responses from patients at both baseline and 4-month FU. From baseline to 4-month FU, QOL and associated QOL factors remained stable. Notably, however, there was an observed overall decline in general mood; of the 33 patients who responded at both baseline and 4-month FU, 19 (57.6%) reported having a 'positive' mood at baseline compared to only 7 (21.2%) at 4-month FU. Only changes in general mood were found to be significant ($p = 0.02$).

Patients also described their experiences with appetite, sleep, concentration, bowel activity, and sexual function based on difficulty. Table 7 shows the responses of patients who responded to this question at baseline and 4-month FU. Slight improvement in experiences with these factors was demonstrated between baseline and 4-month FU; however, the findings were only statistically significant for experiences with sleep ($p = 0.02$) and sexual function ($p = 0.01$).

Side effects

Nine patients reported the occurrence of side effects experienced due to cannabis use at 4-month FU, the most common of which were dry mouth, psychoactive effects, decreased memory, decreased concentration, and sleepiness; findings are demonstrated in table 8. Specifically, 4 of 9 reported dry mouth (44.4%), psychoactive effects (44.4%), and decreased memory (44.4%), 3 reported sleepiness (33.3%), and 2 reported decreased concentration (22.2%).

Discussion

The present study reviewed the results of a voluntary online survey administered by a Canadian medical cannabis provider to cancer patients. The efficacy of medical cannabis to treat cancer-related symptoms has been explored by few studies which have predominantly focused on nausea, appetite, and pain.

Cannabis has been previously evaluated for potential analgesic use in cancer-associated pain, which was the most commonly reported symptom among patients in the present study. A randomized control trial (RCT) conducted by Noyes et al. with 10 cancer patients of various diagnoses found that the analgesic effect of higher doses of THC (between 15 to 20 mg) was significantly superior to placebo, however with greater reports of sedation (5). The limitations of the study include a small sample size as well as the fact that the 10 patients in the study were also concurrently receiving their regular analgesics with either the THC or placebo, which may have confounded the findings of the study (5).

Portenoy et al. also conducted an RCT using 360 patients with advanced cancer and opioid-refractory pain to examine the efficacy of nabiximols, a new cannabinoid oromucosal spray containing a 1:1 THC and CBD combination (6). Low (1-4 sprays/day) and medium (6-10 sprays/day) doses of nabiximols demonstrated improved analgesia superior to placebo after 5 weeks, however higher (11-16 sprays/day) doses were not found to be more effective than lower doses (6). Another study by Johnson et al. assessed the effects of cannabis extract preparations containing THC and CBD in varying ratios in 177 advanced cancer patients with uncontrolled pain despite long-term use of opioids (1). The study consisted of 3 arms: THC:CBD extract ($n = 60$), THC extract ($n = 58$), and placebo ($n = 59$). Pain relief was greatest in the THC:CBD arm as double the number of patients reported a 30% reduction in pain compared to placebo. The THC arm and placebo arm were comparable. These studies suggest there is a potential role for THC and CBD combinations in the treatment of cancer-related opioid-refractory pain.

Loss of appetite is another common symptom among cancer patients that can impact QOL. In the present study, patients demonstrated slight improvement in experiences with appetite at 4-month FU; however, these results were not statistically significant, likely due to the small sample size. Few RCTs have investigated the effects of THC on appetite and weight loss; however, of those few, it has been found that oral THC can stimulate appetite and slow down chronic weight loss in advanced cancer patients (4, 7). Jatoi et al. also studied the effects of cannabis on appetite in 469 adults with advanced

cancer who had experienced weight loss of ≥ 2.3 kg or caloric intake of < 20 calories/kg/day (7). 159 patients were placed on oral megestrol, a steroid progestin, 152 patients were placed on oral THC, and 158 patients received a combination of the two. The study reported that megestrol alone stimulated appetite in 75% of patients and induced weight gain in 11%; whereas, oral THC alone stimulated appetite in 49% patients and induced weight gain in 3%. The combined treatment did not show any additional benefits. The differences observed were statistically significant. However, the study was criticized for using low doses of THC, which may have impacted the outcomes. These findings highlight the importance of investigating which doses are most effective for treating different symptoms, such as loss of appetite, prior to implementation of cannabis as a first-line or alternative treatment option for symptoms such as loss of appetite.

Cannabis is also known for its antiemetic properties. In the present study, while nausea and vomiting were not among the five most commonly reported symptoms, 35.1% ($n = 27$) of the 77 patients who reported nausea and 67.5% ($n = 25$) of the 40 patients who reported vomiting rated these symptoms as severe. The efficacy of cannabis on chemotherapy-induced nausea and vomiting (CINV) has been investigated in some studies. A meta-analysis by Amar lists 15 RCTs involving 600 total patients that compared nabilone, a synthetic cannabinoid-based medication, to placebo or other common anti-emetic drugs as a first-line agent (3). The findings demonstrated that nabilone is more effective compared to prochlorperazine, domperidone, and alizapride and preferred for continuous use by patients (3).

The present study demonstrated improvements in pain, QOL, and a variety of symptoms over the course of cannabis treatment, but only found statistically significant improvements in ability to cope with pain and experiences with sleep. Statistically significant changes were also found in general mood, where the change represented decline in mood; within the context of cancer, this finding is likely suggestive of disease-related changes among patients. The study at present has several limitations. The compliance rate was very low, especially at FU intervals. The small sample sizes of those responding at both baseline and

FU limited the power of the statistical analysis. It is also possible that there was a higher incidence of responses with patients experiencing more positive outcomes, resulting in a positive skew in the data. The survey also did not include validated questionnaires specific to cancer. FU surveys were not consistently completed at exactly 4 and 10 months from baseline by all patients. Invites were sent at each time point, and responses were received between 4 and 10 months, and any time after 10 months for the 4 and 10 month FU surveys, respectively. Moreover, at baseline, approximately 74% of patients reported current cannabis use; therefore, any changes observed at FU are likely to be more representative of the changes in cannabis treatment. Self-reported information on concurrent medications, including type and dose, was incomplete and therefore not available for analyses, limiting the ability to identify any further confounding factors. The study was also unable to account for any adverse events over the course of treatment. Additionally, while those invited to complete FU surveys had active prescriptions at baseline, it is not known whether they had continued to fill prescriptions to remain on cannabis treatment.

Conclusion

The present study demonstrated improvements in pain, QOL, and a variety of symptoms, but only found statistically significant improvements in ability to cope with pain and experiences with sleep. Further studies are required to investigate the potential uses and side effects of medical cannabis in comparison to current first-line therapies. Studies should also consider factors for both short- and long-term treatment to best guide future clinical practices.

Acknowledgments

We thank the generous support of Bratty Family Fund, Michael and Karyn Goldstein Cancer Research Fund, Joey and Mary Furfari Cancer Research Fund, Pulenzas Cancer Research Fund, Joseph and Silvana Melara Cancer Research Fund, and Ofelia Cancer Research Fund. This study was conducted in collaboration with MedReleaf.

References

- [1] Johnson JR, Burnell-Nugent M, Lossignol D, Ganae-Motan ED, Potts R, Fallon MT. Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of the efficacy, safety, and tolerability of THC:CBD extract and THC extract in patients with intractable cancer-related pain. *J Pain Symptom Manage* 2010;39(2):167–79.
- [2] Birdsall SM, Birdsall TC, Tims LA. The use of medical marijuana in cancer. *Curr Oncol Rep* 2016;18(7):40.
- [3] Amar BM. Cannabinoids in medicine: A review of their therapeutic potential. *J Ethnopharmacol* 2006;105(1-2):1–25.
- [4] Wilkie G, Sakr B, Rizack T. Medical marijuana use in oncology. *JAMA Oncol* 2016;2(5):670-5.
- [5] Noyes R, Brunk SF, Baram DA, Canter A. Analgesic effect of delta-9-tetrahydrocannabinol. *J Clin Pharmacol* 1975;15(2-3):139–43.
- [6] Portenoy RK, Ganae-Motan ED, Allende S, Yanagihara R, Shaiova L, Weinstein S, et al. Nabiximols for opioid-treated cancer patients with poorly-controlled chronic pain: A randomized, placebo-controlled, graded-dose trial. *J Pain* 2012;13(5):438–49.
- [7] Jatoi A, Windschitl HE, Loprinzi CL, Sloan JA, Dakhil SR, Mailliard JA, et al. Dronabinol versus megestrol acetate versus combination therapy for cancer-associated anorexia: a North Central Cancer Treatment Group study. *J Clin Oncol* 2002;20(2):567–73.

Submitted: January 19, 2017. *Revised:* February 07, 2017.
Accepted: February 17, 2017.