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Relationship of Cannabis Use to Patient-Reported Symptoms in Cancer Patients Seeking Supportive/Palliative Care

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Abstract

Background: The use of cannabis by cancer patients has become increasingly common. With expanding access to medical cannabis, unsanctioned cannabis use is likely to increase. Despite this, the extent to which patients seeking specialized palliative or supportive care for cancer-related symptoms are actively using cannabis has not been well established.
Objective: We sought to determine the extent to which patients seeking specialized symptom management were using cannabis and to compare the severity of cancer-related symptoms between users and nonusers.
Methods: We conducted a retrospective review of objectively measured tetrahydrocannabinol (THC) and subjectively reported cannabis use, its demographic and clinical correlates, and patient-reported symptoms in 816 cancer patients in active treatment referred to a supportive/palliative care outpatient clinic for specialized symptom management between January 2014 and May 2017.
Results: Nearly one-fifth (19.12%) tested positive for THC on urine drug testing. Users were younger, more likely to be men, single, and to have a history of cigarette smoking. Users also were likely to be more recently diagnosed and to have received radiotherapy. Certain moderate-to-severe symptoms, such as lack of appetite, shortness of breath, tiredness, difficulty sleeping, anxiety, and depression, were associated with use after accounting for sociodemographic and clinical differences between cannabis users and nonusers.
Conclusions: Findings suggest patients seeking specialized symptom management are self-treating with cannabis, despite the lack of high-quality evidence for its use in palliative care. Unsanctioned use is likely to increase in cancer patients. Accurate information is urgently needed to help manage patient expectations for its use and increase understanding of risks and benefits.

Keywords: cancer; cannabis; oncology; symptom management

Introduction

The use of cannabis by persons with a diagnosis of cancer has become increasingly common. Although empirical data on use in cancer patients are limited, an analysis of U.S. population-based datasets suggests upward of 40% of patients use cannabis.[1] Recent descriptive studies indicate patients are using cannabis for the treatment of a wide array of cancer-related symptoms, including nausea, anorexia, pain, weakness, depressed mood, and anxiety.[2–4] However, the effectiveness of cannabis for treatment of these symptoms has not been established and evidence of its clinical utility is needed. Of note, recent reviews report that the most bothersome symptoms for patients receiving palliative or supportive care are nausea, poor appetite, weight loss, pain, and anxiety.[4–6] Despite the increasing use of cannabis among cancer patients, the extent to which patients seeking specialized palliative or supportive care for these symptoms are actively using cannabis is not well known.

To date, more than 30 states and the District of Columbia have passed laws permitting the use of cannabis and cannabinoid-based drugs to treat medical conditions. To the best of our knowledge, there are few published studies of cancer patients' use of cannabis either in the period before legalization or after in these states. Furthermore, there are no published studies describing objectively assessed cannabis use in cancer patients and its relationship to symptoms in a palliative care population. In the context of rapidly expanding access to medical cannabis, prevalence data are sorely lacking. This is especially significant given the likelihood that

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unsanctioned cannabis use is likely to increase as the use of medical cannabis becomes more acceptable. Prevalence data and clinically relevant data are urgently needed to establish the clinical utility of cannabis, establish benchmarks for use, and facilitate research examining changes over time in cannabis use.

This study sought to determine the extent to which patients seeking specialized symptom management were using cannabis and to compare the severity of cancer-related symptoms between patients actively using and not using cannabis. Ultimately, we sought to identify the symptoms and characteristics uniquely associated with cannabis use for patients seeking specialized symptom management.

Methods

Participants

Participants included in the current analyses were cancer patients in active treatment at a large comprehensive cancer center who were referred to the Supportive Care Medicine (SCM) outpatient clinic for specialized symptom management between January 2014 and May 2017. Data were derived from their initial clinic visit.

Procedures

We conducted a retrospective review of objectively measured tetrahydrocannabinol (THC) and subjectively reported cannabis use and its demographic and clinical correlates, and patient-reported symptoms. Patient-level data were derived from a secure clinical database, the electronic health record (EHR), and the cancer center's health research informatics platform.

Data sources

Cannabis use was identified through urine drug testing (UDT). UDT is ordered at the initial SCM visit of every new clinic patient. Individual results were entered into a secure clinical database and scanned into the patient's EHR. For this study, results specific to cannabinoids were extracted from the clinical database.

Demographic and disease-related clinical data were obtained through the center's health research informatics platform. Demographic characteristics included sex, age, race, ethnicity, and relationship status. Clinical characteristics included cancer type, stage of disease at diagnosis, date of diagnosis, types of treatment received, and performance status approximate to the date of UDT. Data on tobacco status were also extracted.

Symptoms were assessed through the patients' self-report on an expanded Edmonton Symptom Assessment Scale-Revised (ESAS-r-css),[7–9] a well-validated, brief measure of common symptoms in patients with cancer. Item level scores were documented in the EHR at the initial SCM clinic visit.

Statistical analyses

Descriptive statistics, including frequencies and percentages, were computed to identify the prevalence of cannabis use and to describe the study sample. Descriptive statistics were also computed for item-level scores on the ESAS-r-css. Sporadic missing data on the ESAS for 28 patients (3.4%) were estimated using multiple imputation techniques.[10] As recommended, a score of four or greater on the ESAS-r-css item was considered a clinically significant symptom.[11] To identify clinical and demographic correlates of use, univariate relationships between the objective UDT result for cannabinoids and patient demographics and clinical characteristics were examined using analysis of variance for continuous variables and logistic regression for categorical variables. Fisher's exact test was then used to examine the relationship of cannabis use to moderate-to-severe symptomatology. Finally, significant univariate predictors were subjected to multiple logistic regression analysis to explore the relationship of cannabis use to each symptom and to identify those characteristics uniquely associated with use. For the logistic regression, results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). A value of $p < 0.05$ (two-tailed) was used in all analyses to evaluate statistical significance. Analyses were conducted using SAS statistical software (SAS Institute, Cary, NC).

Results

For the period under review, 1243 patients underwent UDT at their initial clinic visit. Due to staggered initiation of the use of ESAS-r-css within the clinic during the study period not all patients completed the ESAS-r-css at their initial visit. Patients identified as being prescribed a synthetic cannabinoid (e.g., dronabinol) were excluded. Thus, data from 816 patients were included in this study.

Nearly one-fifth (19.12%) of patients tested positive for THC on UDT. Among those who tested positive and self-disclosed their use of cannabis, no patients reported using medical cannabis or having a state-issued registration card for medical cannabis. As shown in Table 1, patients who were currently using cannabis were significantly younger in age, a mean of 49.2 years versus 56.2 years ($p < 0.0001$). They were nearly twice as likely to be men (OR = 1.88, 95% CI = 1.32–2.67) versus women and to be single (OR = 1.96 95% CI = 1.32–2.92) versus married or partnered. Patients using cannabis also were twice as likely to be ''ever'' smokers (OR = 2.28, 95% CI = 1.49–3.49) compared to ''never'' smokers. With respect to clinical characteristics, the length of time since diagnosis for patients using cannabis was shorter than for those not using cannabis (2.0 years vs. 2.6; $p = 0.05$). Cannabis users also were more likely to have received radiotherapy (OR = 1.43, 95% CI = 1.01–2.04) than not.

Results of the Fisher's exact tests examining the univariate association between cannabis use and moderate-to-severe symptomatology as evidenced by symptom scores on the ESAS-r-css are given in Table 2. Cannabis use was significantly associated with higher rates of moderate-to-severe symptoms specific to tiredness, lack of appetite, anxiety, depression, and difficulty sleeping ($p < 0.05$). Cannabis use was not significantly associated with higher rates of moderate-to-severe pain, drowsiness, nausea, shortness of breath, constipation, and poorer spiritual well-being and overall well-being ($p > 0.05$).

In separate multiple unadjusted logistic regression analyses, the following moderate-to-severe symptoms were predictive of cannabis use: tiredness (OR = 1.69, 95% CI = 1.03–2.77), lack of appetite (OR = 2.25, 95% CI = 1.54–3.29), shortness of breath (OR = 1.55, 95% CI = 1.04–2.31),

Table 1. Demographic and Clinical Characteristics of Sample

	Total sample N = *816*	*THC positive* n = *156*	*THC negative* n = *660*	*Univariate statistic*[a]	p *Value*
Mean age	55.0 (13.4)	49.2 (12.6)	56.2 (13.4)	30.79	<0.0001
Male sex	466 (57.1)	87 (55.5)	263 (39.9)	12.53	0.0004
White race	676 (82.9)	132 (84.5)	545 (82.5)	0.24	0.55
Non-Hispanic ethnicity	716 (87.7)	141 (90.3)	575 (87.1)	1.26	0.28
Married or partnered	634 (77.70	107 (68.4)	527 (79.9)	9.9	0.002
Cancer[b]				18.21	0.90
Breast	91 (11.1)	12 (8.0)	78 (11.8)		
Head and neck	34 (4.2)	5 (3.3)	29 (4.4)		
Colorectal	50 (6.1)	15 (9.3)	35 (5.3)		
Lung	125 (15.3)	24 (15.2)	100 (15.1)		
Leukemia	70 (8.6)	11 (7.3)	59 (8.9)		
Melanoma	36 (4.4)	8 (5.3)	28 (4.2)		
Gynecologic	113 (13.8)	17 (10.6)	96 (14.5)		
Sarcoma	40 (4.9)	5 (3.3)	35 (5.3)		
Lymphoma	39 (4.8)	10 (6.6)	29 (4.4)		
Pancreatic	29 (3.6)	6 (3.9)	23 (3.5)		
Multiple myeloma	29 (3.6)	7 (4.5)	23 (3.3)		
Disease type[c]				0.59	0.46
Solid tumor	645 (80.6)	120 (78.4)	525 (81.1)		
Hematologic	155 (19.4)	33 (21.6)	122 (18.9)		
Stage[d]				0.10	0.99
I	99 (15.6)	19 (15.0)	80 (15.8)		
II	97 (15.3)	19 (15.0)	77 (15.2)		
III	171 (27.0)	34 (26.8)	137 (27.0)		
IV	268 (42.2)	55 (43.3)	213 (42.0)		
Surgery	438 (53.7)	78 (50.0)	360 (54.6)	.85	0.31
Chemotherapy	580 (71.1)	118 (75.5)	463 (70.1)	2.36	0.18
Radiation	308 (37.7)	69 (44.2)	235 (35.6)	3.99	0.045
Performance status[e]					
10–30	11 (1.5)	0 (0.0)	11 (1.9)	2.36	0.31
40–60	85 (11.6)	23 (15.7)	63 (10.6)		
70–100	633 (86.9)	119 (84.3)	514 (87.5)		
Time since diagnosis	2.5 (12.2)	2.0 (3.0)	2.6 (3.7)	4.54	0.05
Smoking status				15.01	0.0001
Ever	538 (65.9)	124 (79.5)	414 (62.7)		
Never	278 (34.1)	32 (20.5)	246 (37.3)		

[a]Analysis of variance for continuous variables, logistic regression for categorical variables.
[b]Diagnoses are listed separately if 3% or greater of total.
[c]Sixteen missing: 3 in THC-positive group, 13 in THC-negative group.
[d]One hundred eighty one missing: 29 in THC-positive group, 152 in THC-negative group.
[e]Eighty-nine missing: 14 in THC-positive group, 72 in THC-negative group.
THC, tetrahydrocannabinol.

anxiety (OR = 1.57, 95% CI = 1.08–2.27), depression (OR = 1.56, 95% CI = 1.08–2.25), and difficulty sleeping (OR = 2.07, 95% CI = 1.35–3.15). For each of these six symptoms, and without exception, younger age, being men, being an ''ever'' smoker, and not receiving radiation remained significant, independent predictors of cannabis use ($p < 0.05$).

Discussion

We sought to determine the extent to which patients seeking specialized symptom management at a large comprehensive cancer center were using cannabis and to examine the relationship of cannabis use to patients' cancer-related symptomatology. In this study, 19% of patients tested positive for cannabis on routine UDT. Data on cannabis use, whether medically authorized or not, in cancer patients are limited, although our findings are consistent with results from a recent study from the state of Washington where medicinal and recreational cannabis use was legalized in 1998 and 2012, respectively,[3] and from a study from the province of Alberta in Canada, where possession of cannabis for medical use is legal.[12] Although our finding is most similar to those reported by Pergam et al.,[3] direct comparisons with existing studies are difficult to make. This is because existing studies are marked by a number of methodological differences and because published data are from states and countries where the legal status of cannabis differed over time.[3,12–15] Whereas Pergam et al.[3] attempted to validate patients' report of cannabis use with anonymous UDT, ours is the only self-report study that did not rely solely on patient self-disclosure and used routine UDT to objectively assess each patient's cannabis use.

Table 2. Rates of Moderate-to-Severe Symptoms

	THC positive (%) n = *156*	*THC negative (%)* n = *660*	*Univariate statistic*	p *Value**
Pain			3.13	0.08
0	1.9	7.5		
1–3	18.1	19.5		
≥4	80.0	73.0		
Tiredness			4.60	0.03
0	1.3	4.5		
1–3	14.2	17.7		
≥4	84.5	77.9		
Drowsiness			0.26	0.66
0	17.1	18.9		
1–3	29.0	30.5		
≥4	54.0	50.5		
Nausea			2.74	0.10
0	45.2	52.8		
1–3	28.4	27.2		
≥4	26.5	20.0		
Lack of appetite			10.71	0.001
0	18.7	31.9		
1–3	22.6	24.5		
≥4	58.7	43.7		
Shortness of breath			2.60	0.11
0	40.7	46.7		
1–3	26.5	27.0		
≥4	32.9	26.3		
Anxiety			4.76	0.04
0	24.5	31.8		
1–3	27.8	31.2		
≥4	47.7	37.1		
Depression			4.97	0.03
0	21.4	25.8		
1–3	24.0	29.8		
≥4	54.6	44.4		
Overall well-being			0.61	.49
0	4.5	5.4		
1–3	16.8	20.9		
≥4	78.7	79.7		
Constipation			1.80	0.18
0	19.5	22.0		
1–3	24.2	28.4		
≥4	56.4	49.6		
Spiritual well-being			0.03	0.91
0	40.0	36.6		
1–3	24.5	27.5		
≥4	35.5	35.9		
Difficulty sleeping			10.83	0.0009
0	14.8	16.0		
1–3	7.1	23.7		
≥4	78.1	60.4		

*p Values calculated using Fisher's exact test for relationship of cannabis use to presence of clinically significant symptoms.

Certain sociodemographic characteristics associated with cannabis use in this study merit attention. Although only significant at the univariate level, that younger patient age (although still late middle-aged) was associated with cannabis use in our sample is largely consistent with findings to date.[16] Our finding that male sex was associated with use at the univariate and multivariable level is also noteworthy. Existing findings with respect to sex differences in cannabis use in cancer are limited and results are mixed.[2,3,17] In this study, use of cannabis was highly likely to be unsanctioned and so findings may be more analogous to a recent analysis of data from the National Survey on Drug Use and Health that demonstrated increasing use of cannabis among men relative to women from 2002 to 2014.[18] In our sample, using tobacco was associated with cannabis use at the univariate and multivariable level. Although we do not know the specific formulations of cannabis in use, given the timeframe, it is likely that inhalable forms predominated. Thus, patients using cannabis would likely be more comfortable with smoking in general. The relationship between cannabis and tobacco use is not well understood; there is much to be gained by elucidating whether medical cannabis use promotes tobacco use (and vice versa). To the best of our knowledge, ours is one of the few studies to examine smoking status and its association with cannabis use in cancer patients. In general, current findings suggest select sociodemographic characteristics are associated with higher likelihood of cannabis use although any definitive conclusions are premature.

In our sample, certain moderate-to-severe symptoms—namely, lack of appetite, shortness of breath, tiredness, difficulty sleeping, anxiety, and depression—were associated with cannabis use after controlling for sociodemographic differences between cannabis users and nonusers. With the exception of lack of appetite and anxiety, these symptoms are not typical indications for cannabis use. Previous studies have found patients using cannabis for a variety of symptoms, however. In one study, whereas 75% of active users used cannabis for pain, nausea, and/or appetite, 63% used it because it improved their mood, helped them ''deal with stress,'' and/or to cope with their illness, symptoms for which the evidence base is especially lacking.[3] In another study, patients using medical cannabis reported significant improvement in ''all'' the cancer- and treatment-related symptoms assessed, including fatigue, sexual function, itching, and mood disorders.[17]

Patients in our sample may have been self-treating in an effort to control their cancer-related symptoms. Our cross-sectional design precludes us from inferring precisely which symptoms and how effective these efforts might be. In addition, we cannot know whether patients' symptoms predated their use of cannabis. Similarly, we cannot infer that those symptoms not associated with cannabis use in our sample would not be responsive to cannabis treatment. Rates of moderate-to-severe pain were not only comparable between users and nonusers, but quite high. This high rate of uncontrolled pain across the entire sample likely accounts for why cannabis use did not differentiate between the groups. To suggest this means cannabis use is not effective for treatment of pain belies the existing evidence base.[19] Regardless, our findings strongly suggest patients seeking specialized symptom management are self-treating with cannabis in an attempt to relieve a wide array of troublesome symptoms and to manage certain poorly controlled symptoms. Our findings also suggest cannabis users tend to rate their cancer-related symptoms as more severe than nonusers. Findings clearly support the need for patient education about the potential therapeutic benefits and adverse effects of cannabis use in cancer.

Limitations of the study should be noted. First, as previously noted, our cross-sectional design precludes us from knowing whether patients were using cannabis before the onset of cancer-related symptoms. Second, because of the exploratory and retrospective nature of our study, we elected to conduct our analyses without adjusting for multiple comparisons. Third, because we used existing clinical data, we were unable to assess patients' patterns and methods of use or to assess which symptoms patients perceived as most responsive to cannabis, information that would have enabled us to more fully characterize patients' use. Although there are few prospective, observational studies,[17] recent studies have described patients' methods of inhalation and use of edibles, and expounded on patients' reasons for use.[3,12,15] Fourth, it is possible that patients who knew UDT was a part of their initial visit avoided the clinic because they were concerned about how their use of cannabis or other substances would be perceived, thus biasing our results. Fifth, this study examined only a limited number of variables as potential correlates. There is evidence in the general population that other variables, including additional sociodemographic characteristics like income and education, are likely to influence cannabis use.[16,18] Future studies, in addition to working to confirm our results, should examine a broader range of potential predictors over time in samples sufficiently large to identify whether there may be distinct trajectories of patterns of cannabis use in cancer patients and to measure its health effects and the associated risks and benefits.

To our knowledge, ours is the first large-scale study of objectively assessed cannabis use in cancer patients seeking specialized symptom management. Findings indicate that approximately one in five patients was using cannabis at the time of their initial clinical appointment. Cannabis users were more likely to have a range of moderate-to-severe symptomatology compared with nonusers. These findings suggest patients were self-treating with cannabis, despite the lack of high-quality evidence for its use in palliative care.[4] In the current climate of expanding access to medical cannabis, unsanctioned cannabis use is likely to increase in cancer patients. Thus, accurate information about cannabis is urgently needed to help providers manage patient expectations for its use and to assist patients in anticipating and coping with potential side effects.

Author Disclosure Statement

No competing financial interests exist.

References

1. Tringale KR, Shi Y, Hattangadi JA: Marijuana utilization in cancer patients: A comprehensive analysis of National Health and Nutrition Examination Survey Data from 2005–2014. Int J Radiat Oncol Biol Phys 2017;99:S11.
2. Waissengrin B, Urban D, Leshem Y, et al.: Patterns of use of medical cannabis among Israeli cancer patients: A single institution experience. J Pain Symptom Manag 2015;49: 223–230.
3. Pergam SA, Woodfield MD, Lee CM, et al.: Cannabis use among patients at a comprehensive cancer center in a state with legalized medicinal and recreational use. Cancer 2017; 123:4488–4497.
4. Mücke M, Weier M, Carter C, et al.: Systematic review and meta-analysis of cannabinoids in palliative medicine. J Cachexia Sarcopenia Muscle 2018;9:220–234.
5. Van Lancker A, Veighe A, Van Hecke A, et al.: Prevalence of symptoms in older cancer patients receiving palliative care: A systematic review and meta-analysis. J Pain Symptom Manage 2014;47:90–104.
6. Sigurdardottir KR, Kaasa S, Rosland JH, et al.: The European Association for palliative care basic dataset to describe a palliative care cancer population: Results from an international Delphi process. Palliat Med 2014;28:463–473.
7. Watanabe SM, Nekolaichuk C, Beaumont C, et al.: A multi-centre comparison of two numerical versions of the Edmonton Symptom Assessment System in palliative care patients. J Pain Symptom Manage 2011;41:456–468.
8. Bruera E, Kuehn N, Miller MJ, et al.: The Edmonton Symptom Assessment System (ESAS): A simple method for the assessment of palliative care patients. J Palliat Care 1991;7:6–9.
9. Johnstone PA, Lee J, Zhou JM, et al.: A modified Edmonton Symptom Assessment Scale for symptom clusters in radiation oncology patients. Cancer Med 2017;6:2034.
10. Schafer JL: *Analysis of Incomplete Multivariate Data*. New York: Chapman and Hall, 1997.
11. Selby D, Cascella A, Gardiner K, et al.: A single set of numerical cutpoints to define moderate and severe symptoms for the Edmonton Symptom Assessment System. J Pain Symptom Manage 2010;39:241–249.
12. Martell K, Fairchild A, LeGerrier B, et al.: Rates of canabis use in patients with cancer. Curr Oncol 2018;25:219–225.
13. Hazekamp A, Heerkink ER: The prevalence and incidence of medical cannabis on prescription in the Netherlands. Eur J Clin Pharmacol 2013;69:1575–1580.
14. Ryan-Ibarra S, Induni M, Ewing D: Prevalence of medical marijuana use in California, 2012. Drug Alcohol Rev 2015; 34:141–146.
15. Luckett T, Phillips J, Lintzeris N, et al.: Clinical trials of medicinal cannabis for appetite-related symptoms from advanced cancer: A survey of preferences, attitudes and beliefs among patients willing to consider participation. Int Med J 2016;46:1269–1275.
16. Carliner H, Mauro PM, Brown QL, et al.: The widening gender gap in marijuiana use prevalence in the U.S. during a period of economic change, 2002–2014. Drug Alcohol Depend 2017;1:51–58.
17. Bar-Sela G, Vorobeichik M, Drawsheh S, et al.: The medical necessity for medicinal cannabis: Prospective, observational study evaluating the treatment in cancer patients on supportive or palliative care. Evid Based Complement Alternat Med 2013;2013:1–8.
18. Hasin DS, Saha TD, Kerridge BT, et al.: Prevalence of marijuana use disorders in the United States between 2001–2002 and 2012–2013. JAMA Psychiatry 2015;72:1235–1242.
19. Abrams DI: The therapeutic effects of cannabis and cannabinoids: An update from the National Academies of Sciences, Engineering, and Medicine report. European J Int Med 2018;49:7–11.

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