

Short Communication

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Patient Reported Outcomes after Cannabis Use to Control Symptoms

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The study was deemed exempt by the Investigational Review Board of City of Hope (study #19027).

ABSTRACT

In order to determine the frequency of cannabis product (marijuana, THC or CBD) use and determine the patient reported outcomes to control symptoms, an anonymous survey of cannabis product use was conducted in patients who had cancer, non-malignant hematologic disorders or other diseases. Patients reported the degree of control of symptoms using a Likert scale. The use of cannabis products was 23.3% (36 users in 154 patients). This did not vary by age, gender, or disease. Use was predominately CBD in patients over 65, but was either marijuana, THC or CBD in younger patients. Patients reported some degree of control of at least one symptom in 91.9%, and high degree of control in 51.7% of patients. Most patients relied on recommendations of family or friends to try cannabis, but only 4% relied on clinician advice. 53% of patients said they were willing to consider participating in a prospective clinical trial of cannabis products to control symptoms. We conclude that cannabis product use is frequent in cancer patients. Physicians should obtain a detailed history of cannabis product use in patients, and could consider a therapeutic trial of cannabis products in selected patients with symptoms not controlled by usual treatments. Clinicians may need additional education to provide the highest level of evidence-based support for cannabis product use in patients in need of symptom control.

Background

Cannabis use has been described for 5000 years¹ and its medicinal use has been scientifically documented since 400 A.D.². Recent studies have shown increased use of cannabis products and variation by age groups. A 2018 survey of Americans over 25 years of age indicated that 13.3% had used marijuana in the past year, with 8.6% having used it in the past month³. A Gallup poll in July 2019 reported that 12% of adults have used cannabis in the prior 12 months⁴, but only 3% of adults 65 or over had used it in that period.

Recent surveys have studied use of cannabis products in cancer patients^{5,6}. A 2018 report of marijuana use in a community oncology office reported 18.3 % users⁵. Another study of patients in a comprehensive cancer center in 2015-2016 documented that 24% of patients used cannabis⁶.

The use of cannabis products may be increasing due to legal and social factors in the United States. In 2020, cannabidiol (CBD) was legalized for any use in 50 states. 33 states had legalized marijuana use for medicinal purposes, and of those 15 states had legalized marijuana use for medicinal or recreational purposes. Cannabis use has been promoted in the media and on the internet. Still, many patients have not disclosed use of cannabis products to their doctors. It is unclear whether there has been an increase in usage of cannabis products in cancer patients. The authors initiated this study to

determine cannabis product use and patient reported outcomes in a mixed ambulatory outpatient population of patients being cared for in a comprehensive cancer center-affiliated community hematology/oncology clinical office. To maximize accurate responses, the study was conducted anonymously.

Methods

This observational study was conducted at the City of Hope Medical Foundation at the community network cancer center in West Covina, CA. The site cares for oncology patients, malignant and benign hematology patients, and patients with other conditions (osteoporosis, neurological and rheumatologic diseases). The racial and ethnic makeup of the patients is diverse, with large numbers of Hispanic, Asian-Pacific Islander, Caucasian and African-American individuals. The catchment area for this center includes 1,156,000 people in separate communities with average household incomes ranging from \$72,000 to \$128,000 in the various cities.

The primary objectives of the study were to determine the frequency of cannabis product use, reasons for cannabis product use, and patient reported outcomes of cannabis product use in a diverse ambulatory patient population in a community cancer center. Secondary objectives were to describe the patterns of use of cannabis products and compare use among patient subgroups according to diagnosis, gender, age, and patient reported outcomes of cannabis product use. We also determined who had recommended cannabis use and whether patients were interested in participating in future cannabis product trials.

Consecutive patients without regard to diagnosis who were being seen at the ambulatory cancer center were given the consent information and research survey by medical staff. They were asked if they were willing to complete the Cannabis Use Survey. After obtaining consent to participate, the patient completed the anonymous survey. The survey was then deposited anonymously into a designated drop tray. Results were kept confidential and were not entered into an electronic medical record.

The survey was designed to obtain information about gender, age, diagnosis, symptom burden, use of cannabis product, type of cannabis product used, who recommended cannabis use, and response of symptoms to cannabis product use according to a Likert 5 point scale. The exact wording describing cannabis product use in the survey instrument was "cannabis (marijuana, CBD or THC)" so as to include all possible cannabis products. In order to comply with Investigational Review Board requirement for anonymity, we did not collect individual data on race, ethnicity, organ specificity of cancer, or socioeconomic status. Results were entered into the database and evaluated.

Evaluations for patient reported outcomes were grouped from the 5 point Likert scale. The scale asked for a response of either full control of the symptom, a lot of control of the symptom, some control of the symptom, a little control of the symptom, or no control of the symptom. Patients who indicated full or a lot of control of symptoms were considered a "good response". Patients who indicated full control, a lot of control, some control, or a little control were considered "any response".

The data were accumulated in RedCap for analytics using chi squared and Fisher exact statistics from SAS. Statistical analysis was reviewed by the Research Informatics Core of the City of Hope Comprehensive Cancer Center at the Biostatistical Department of City of Hope.

The study was deemed exempt by the Investigational Review Board of City of Hope (study #19027). The study was supported in part by NIH Grant P30 CA033572.

Results

The total number of patients invited to participate was 261. Of those, 85 patients declined or were duplicated (had completed the study previously). 176 patients returned the questionnaire, but 22 patients had missing data. Of the 154 evaluable patients with completed questionnaires, median age was 65 or over, with slightly more females (Table 1). Most patients 72.7% had solid tumors or hematologic malignancies. Older patients more often had malignancy compared to younger patients ($p=0.0012$). 37.5% of patients under the age of 45 had malignancy, compared to 71.2% of patients aged between 45 and 64, and 81.5% of patients 65 or older.

Cannabis product use was reported in 36 of the 154 evaluable patients (23.3%). Cannabis product use did not vary significantly by age ($p=0.48$), by disease ($p=0.61$), or by gender ($p=0.51$).

The reasons given by patients for use of cannabis products were most frequently pain (73.7%) as seen in Table 2. Many patients used cannabis products for several different reasons, representing 87 uses among the 38 patients using cannabis. Some patients reported using cannabis products for "control of my disease" which might have implied either controlling some symptoms or reducing the extent of disease.

There was an association of type of cannabis product use by age. There was slightly higher use of marijuana or THC (63.6%) versus CBD (35.4%) in patients age 21 to 64, whereas most patients age 65 or older used CBD (87.5%) versus marijuana or THC (12.5%) ($p=0.00001$).

Patients reported a remarkably high degree of control of symptoms by use of cannabis products (Table 3). Of 87 uses of cannabis products for any reason or symptom, 51.7% had a high degree of control of symptoms (full or lots

of control) and 91.9% reported any degree of improvement (full, lots, some, or a little control of symptoms) by use of any type of cannabis product. High degrees of control (50% or more) were reported for pain, nausea, vomiting, appetite loss, fatigue and/or weight loss, but not for other symptoms.

There was a trend, which was not significant, between type of cannabis product use and response ($p=0.17$). Patients reported a high degree of response (full or a lot of control of symptoms) in at least 1 symptom in 10 out of 14 uses of marijuana or THC (71.4%), compared to 8 out of 17 uses of CBD (47.1%).

The source of the recommendation for use of cannabis (when patients reported the source) was family or friends in 22 patients (75.9%), clinician in only 4 patients (13.8%), and internet/television/newspaper in only 2 patients (6.9%). Of those patients, family or friends recommended marijuana or tetrahydrocannabinol (THC) in 9 (40.9%) similar to recommendation to use cannabidiol (CBD) in 12 (54.5%). Of the 4 clinician recommendations, 3 recommended CBD and only 1 recommended marijuana or CBD. Both recommendations from the internet, television or newspaper were for use of CBD.

Patients were asked if they would be interested in participating in a clinical trial of cannabis products. 53% of patients said they would be interested, 42% were not, and 5% declined to answer.

Discussion

Use of cannabis products in patients with cancer or non-malignant diseases is common. Our results indicated at least 23.3% use. The population which we studied was a small sample and community-based and not at an academic or tertiary care center. It is thus a snapshot of cannabis product use at one clinic. Both cancer patients and patients with non-malignant diseases were studied. Because this study was anonymous, the authors believe it is not biased, and the results are likely generalizable to community based ambulatory cancer centers. The frequency of use was similar to prior reports from community and academic sites from 2015 to 2018 (5,6) and had not increased despite legalization efforts and advertising.

85 of the 261 patients (32.6%) were not evaluable. It is possible that many of these patients who were unwilling to be surveyed might have been cannabis product users uncomfortable with reporting their use. That would result in our 23.3% usage rate being an under-estimate.

This study was conducted in a state that had legalized medicinal marijuana in 1996 and both medicinal and recreational marijuana in 2020. Therefore, the results may have been influenced by the legal and social settings of California.

Despite extensive media and internet promotion of cannabis product use, these results suggest a rate of cannabis product use similar to prior publications in 2015-2018. We presume that among predominately older patients (the median age in our study was over 65), only a quarter of patients used cannabis products, and usually did so when recommended by family or friends. The remainder of the patients may either have had no symptoms or symptoms controlled by current medications, or may have been reluctant to use cannabis products as a consequence of prior prohibitions and fear of addiction.

Although use of cannabis products did not statistically vary by age (although this was a small study), the use of cannabis products in older patients in this study was predominately CBD, compared to the use of either marijuana, THC or CBD in younger patients. This has implications for future clinical trials to be certain older participants in future trials have an option of using predominately CBD to avoid potential toxicity of marijuana or THC. It also indicates the clinicians who might want to recommend a therapeutic trial of cannabis products to control symptoms should consider preferentially using CBD in older patients.

Importantly, many patients are participating in clinical trials, the results of which might be confounded by cannabis product usage. Since so many patients are using cannabis products, it is important to interpret improvement in symptoms or occurrence of side effects in patients on clinical trials in light of cannabis product usage. It is theoretically possible that improvements in symptoms in trial patients might be due to cannabis products rather than an investigational drug or treatment. Alternatively observed toxicity might be due to cannabis products rather than an experimental agent or treatment. Theoretically, actual disease response might be due to cannabis product use (as suggested by anti-tumor effects in preclinical studies⁷⁻¹⁰), or a favorable interaction between cannabis products and an investigational drug¹⁰ (or lack of response due to deleterious effect of cannabis product on action of the investigational drug as suggested in a study of cannabis plus nivolumab¹¹). We propose that patient participation in clinical trials in the future should be stratified by cannabis product use.

Importantly, over 90% of patients felt that cannabis products helped their symptoms, and over 50% had a high degree of response. This suggests that randomized prospective trials of cannabis products to control symptoms are urgently needed. Since so many patients stated they were willing to consider participation in a cannabis product clinical trial, such studies of cannabis-induced palliation would be feasible. Because this study suggests that preference for type of cannabis product use depends on age, future trials should target appropriate age populations

and test appropriate products. Recent legalization of marijuana in many states should facilitate performance of randomized studies. The data for cannabis products in treatment of neoplasm-associated pain and chemotherapy-induced nausea and vomiting is evolving¹²⁻¹⁴. With frequent use of cannabis products as noted in our study, regulatory barriers needs to be reduced so that more specific studies in cancer patients can be performed.

The most common symptoms in patients had very favorable patient reported outcomes. Fatigue was reported by patients to have high control in 50% of our patients and any relief in 78.5%. Pain had high control in 60.7% of patients and any relief in 96.4%. This suggests that a therapeutic trial of cannabis products might be considered if patients are not responding well to usual medications. It also suggests that if patients are at risk of non-compliance with an antineoplastic treatment plan due to side effects, use of cannabis products may alleviate side effects and result in higher compliance and improved therapeutic outcomes of their cancer or other condition.

However, only 4% of patients used cannabis products because of advice of clinicians. This demonstrates an urgent need for clinicians to be more knowledgeable about evidence-based cannabis product use for symptom control so patients can make an informed choice to try or not to try cannabis products. Clinicians should also recognize that cannabis product use can be associated with drug interactions and side effects, and should be prepared to discuss this with patients. It also implies that many clinicians and their staffs, including physicians, nurses, advanced practice nurses, and pharmacists, may need additional education or training to optimally provide evidence-based recommendations to help patients and their families make appropriate decisions to improve symptom control. Recent evidence suggests that many physicians lack a sufficient knowledge base to feel proficient in cannabis issues¹⁵.

Limitations of this study include that the study was observational and neither prospective nor randomized. Also, the study was anonymous, which precluded detailed information about age, type of malignancy, stage of cancer, and other medications being used. Cannabis product route, dose duration and side effects were not available and only a limited number of patients were enrolled.

Conclusions

In this study, cannabis product use in patients with symptoms was common and patients reported a high degree of improvement in a variety of symptoms with cannabis product use. Our findings can help in planning future clinical trials, which are urgently needed to help alleviate severe symptoms not responding to conventional therapies.

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