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Medical marijuana utilization in gynecologic cancer patients

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ABSTRACT

Background: Medical marijuana (MM) use is common among cancer patients, but relatively little is known about the usage patterns and efficacy of MM used by gynecologic cancer patients.
Methods: Demographic and clinical data were collected for gynecologic cancer patients prescribed MM between May 2016 and February 2019. The electronic medical record was used to query formulation prescribed, usage patterns, length of use, symptom relief, and side effect profile. Descriptive statistics were calculated.
Results: Of 45 gynecologic cancer patients prescribed MM, 89% were receiving chemotherapy; 56% were undergoing primary treatment. MM was used for a median of 5.2 months (range 0.6–25.4). Over 70% of patients reported improvement in nausea/vomiting, compared to 36% of patients using MM for pain relief ($p = 0.02$). Of 41 patients with follow-up information, 71% found MM improved at least one symptom.
Conclusions: Among a small sample of gynecologic cancer patients prescribed MM for symptom management, self-reported follow-up indicated symptom relief for the majority of patients and minimal therapy-related side effects. This data can prove useful for counseling gynecologic cancer patients on the efficacy and side effects of MM.

1. Introduction

Medical marijuana (MM) has attracted a great deal of attention as an adjunct to conventional pharmacologic approaches to symptom management for patients with cancer. Gynecologic cancer patients commonly experience nausea, vomiting, pain, anorexia, and fatigue related to cancer-directed therapy or to their cancer itself, that may be treated with MM or synthetic cannabinoids.

A meta-analysis by Whiting et al found a trend towards benefit for cannabinoids compared to either placebo or anti-emetics for nausea and vomiting due to chemotherapy, but no statistically significant improvement across studies (Whiting et al., 2015). In the United States, both dronabinol and nabilone are FDA-approved for the treatment of chemotherapy-induced nausea/vomiting that has not responded to conventional antiemetics. Several small randomized trials have compared dronabinol or nabilone in combination with or versus standard anti-emetics in preventing chemotherapy-induced nausea/vomiting (Lane et al., 1991; Meiri et al., 2007; Crawford and Buckman, 1986; Herman et al., 1979). Dronabinol was found to be equivalent to ondansetron with no benefit for combined therapy (Meiri et al., 2007). The National Comprehensive Cancer Network includes dronabinol and nabilone as therapeutic options for breakthrough nausea/vomiting (NCCN, 2019). The American Society of Clinical Oncology considers the evidence insufficient to recommend marijuana for prevention of nausea/vomiting or as an alternative to dronabinol and nabilone for chemotherapy-induced nausea/vomiting (Hesketh et al., 2017).

There is limited evidence regarding the effectiveness of MM or synthetic cannabinoids for pain management compared to multimodality symptom management with conventional medications. In cancer patients with inadequately controlled pain on opioids, the addition of THC:CBD containing compounds and nabiximols improves pain scores compared to placebo in some, but not all studies (Johnson et al., 2010; Portenoy et al., 2012; Lichtman et al., 2018; Fallon et al., 2017). In preclinical and pilot studies investigating the modulation of the cannabinoid pathway for the treatment of cancer-associated neuropathic pain, preliminary data suggest a benefit (O'Hearn et al., 2017; Lynch et al., 2014).

Improved pain control, however, may come at the cost of side effects

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associated with cannabinoids, including somnolence, dizziness, confusion, and nausea (Johnson et al., 2010; Lichtman et al., 2018).

Medical marijuana use is common among patients with cancer. Among respondents to the U.S. National Health and Nutrition Examination Survey between 2005 and 2014 with cancer, 40% had used marijuana within the past year and the likelihood of marijuana use increased over time (Tringale et al., 2019). Among 290 gynecologic cancer patients in California and Colorado surveyed by Blake et al, 27% reported using cannabis products following their diagnosis and an additional 36% were interested in doing so if facilitated by their treating physician (Blake et al., 2019). A survey of 36 patients in Connecticut with gynecologic cancer who were prescribed MM found 83% experienced relief of at least one cancer or treatment-related symptom (Webster et al., 2020).

As of November 10, 2020, 40 states and territories have approved medical marijuana/cannabis programs (State Medical Marijuana Laws, 2020). Medical marijuana was legalized for patients with cancer and other serious medical conditions in New York in 2016; New Jersey legalized cannabis for recreational use in 2020.

Gynecologic cancer patients commonly report nausea, vomitinand pain associated with both thei cancer itself and cancer-directed treatments. The Society of Gynecologic Oncology recently published a clinical practice statement summarizing the evidence for MM for chemotherapy-induced nausea/vomiting, prevention of neuropathy secondary to taxanes, and cancer-related pain (Whitcomb et al., 2020). Despite this guidance, relatively little is known about the utilization and efficacy of MM in this population. We evaluated the effect of MM for symptom management in gynecologic cancer patients at our institution.

2. Methods

Women with gynecologic cancer who used MM between May 2016 and February 2019 were identified through our institution's electronic medical record. Medical marijuana was prescribed by one gynecologic oncologist at our institution (BP) or an authorized palliative care physician.

Clinicopathologic and demographic data, including age, race/ethnicity, insurance status, cancer diagnosis, and treatment information were collected. Detailed information regarding dosage form, including the ratio of THC to CBD, quantity prescribed, self-reported usage, and length of treatment were collected from the electronic medical record.

Prior to MM prescription, patients were asked what symptoms they hoped to alleviate with cannabinoids. Follow-up questions to assess efficacy and tolerance in clinic were routinely implemented with the use of a standardized EPIC smart phase after starting MM. This queried if patients had used MM, how long they used it for, efficacy for specific symptoms, and any side effects experienced. For patients where information on efficacy and tolerance was not obtained, follow-up data was not considered to be available.

This study was approved by the institutional review board at our institution and the requirement for obtaining informed consent was waived. Descriptive statistics were calculated. Categorical variables were compared using Fisher's exact test and a p-value of <0.05 was considered statistically significant.

3. Results

From May 2016 to February 2019, 45 gynecologic cancer patients at our institution were prescribed MM. Table 1 shows the baseline clinicopathologic and demographic characteristics of the study cohort. Patients were a median of 60 years old (range 46–79) when MM was first prescribed. The majority of patients (73%) were non-Hispanic White; 9% each were non-Hispanic Black or Asian, and 7% of patients were Hispanic and White. Just over half of patients (51%) had Medicare insurance, with 33% insured privately and 16% insured by Medicaid. Those with ovarian, fallopian tube, or primary peritoneal cancer (56%) made up the majority of the patient population, with the remainder split between cervical and uterine cancer. Almost all patients (89%) were receiving chemotherapy when prescribed MM and just over half were undergoing primary treatment (56%).

Table 1
Demographic and clinicopathologic characteristics of patients prescribed medical marijuana.

	Patients, n (%)
Age when medical marijuana first prescribed, median (range)	60 (46–79)
Race/ethnicity	
White, non-Hispanic	33 (73%)
White, Hispanic	3 (7%)
Black, non-Hispanic	4 (9%)
Black, Hispanic	0 (0%)
Asian	4 (9%)
Other	1 (2%)
Insurance type	
Private	15 (33%)
Medicare	23 (51%)
Medicaid	7 (16%)
Disease site	
Cervix	5 (11%)
Uterus	15 (33%)
Tubo-ovarian	25 (56%)
Cancer stage	
I/II	5 (11%)
III	16 (36%)
IV	24 (53%)
Undergoing primary treatment	25 (56%)
Recurrent disease	20 (44%)
Receiving chemotherapy when prescribed MM	40 (89%)

There was significant heterogeneity in the formulation and THC:CBD ratio prescribed, as shown in Table 2. The majority of patients (55%) were prescribed formulations with a 1:1 THC:CBD ratio, but this data was missing for almost a quarter of patients. Administration route also varied: while inhaled and sublingual formulations were most commonly prescribed (over 70% of patients), free form, edible, and oil preparations were also utilized. Many patients were prescribed more than one formulation, either initially, or following a trial period of another formulation.

Among 41 patients with follow-up information available, MM was used for a median of 5.2 (range 0.6–25.4) months. The most common indications for MM in patients were: pain, 25 (56%); nausea/vomiting, 21 (47%); anorexia, 15 (33%); and insomnia, 12 (27%). Fig. 1 illustrates commonly prescribed indications and self-reported effectiveness by symptom. More than 70% of patients reported that use of marijuana

Table 2
Prescribed formulation and length of medical marijuana use.

	Patients, n (%)
THC: CBD ratio*	
1:1	25 (55%)
High: Low	3 (7%)
Low: High	7 (16%)
Missing	11 (24%)
Route of administration*	
Inhaled	17 (38%)
Sublingual	17 (38%)
Free form	8 (18%)
Edible	4 (9%)
Dronabinol	2 (4%)
Oil	1 (2%)
Missing	1 (2%)
Length of use, months, median (range)	5.2 (0.6–25.4)

* Some patients prescribed more than one formulation.

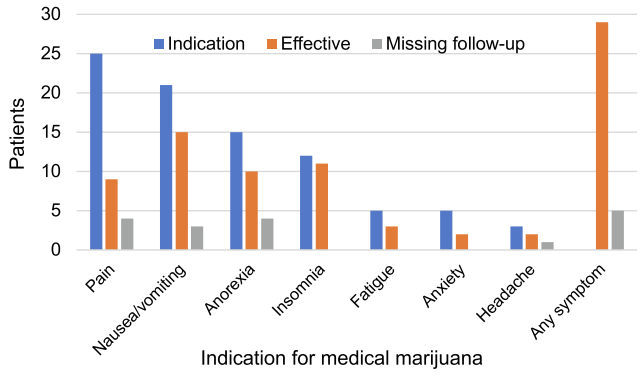

Fig. 1. Indications for medical marijuana and self-reported effectiveness for individual symptoms.

improved nausea/vomiting, while only 36% of patients using MM for pain reported symptom improvement ($p = 0.02$). Among the 41 patients with follow-up information, 29 (71%) reported medical marijuana improved at least one symptom.

The most common reasons for discontinuation were death from disease progression (10 patients, 24%) and no improvement in symptoms (6 patients, 15%). Only one patient specifically cited side effects (fatigue and paranoia) as a reason for stopping use of MM. Other reported side effects included: euphoria, dizziness, feeling 'high', nausea, headache, and fatigue. Four patients were still using MM at the time of last follow-up. The reason for discontinuation was missing for 17 patients (41%).

4. Conclusions

Among gynecologic cancer patients prescribed MM for symptom management, follow-up indicated symptom relief for the majority of patients and minimal therapy-related side effects. Almost 90% of patients were receiving chemotherapy when first prescribed MM, most of whom were undergoing primary treatment. Patients used MM for a median of almost six months, with significant variation in length of use; some patients had continued to use it for more than two years at time of last follow-up.

Although MM use is legal in a majority of states and commonly utilized by cancer patients, few oncology providers feel comfortable prescribing it. Braun and colleagues surveyed a nationally representative population of medical oncologists; only 29% felt sufficiently knowledgeable to prescribe MM. Of providers surveyed, 56% recommended MM to their patients (Braun et al., 2018). A follow-up survey by Braun and colleagues found the most perceived benefit for patients at the end of life (83%) compared to those with early stage disease (33%) and cancer survivors (26%) (Braun et al., 2019). Given the prevalence of MM use among cancer patients, improved education of both patients and providers may help increase its utilization for symptom management throughout the disease continuum.

This data provides one of the initial reports of the symptom relief profile of MM among patients on cancer-directed therapy in women with gynecologic malignancy. In this limited cohort of gynecologic oncology patients, MM was effective for the relief of nausea/vomiting, anorexia, and insomnia in a majority of patients but was less helpful for pain management. This is consistent with the findings of Webster et al, where the majority of patients reported symptom relief with medical cannabis use, but details were not provided on efficacy for specific symptoms. Patients were not, however, queried on the adjunctive use of other medications or interventions for cancer-associated symptoms while using MM. Although patients reported MM provided symptom relief, this could have been affected by recall bias and we did not assess for the relative efficacy of any other approaches (other medications, supplements, or behaviors) compared to MM.

Patients were also not queried on the specific type or location of pain they hoped to improve with MM use. Additionally, there was no standardized collection of the type and frequency with which other pain medications were used concurrent with MM. The use of cannabis products as an adjunct has been shown to improve pain control in patients with severe cancer-associated pain, but has not been associated with a decrease in opioid use (Johnson et al., 2010; Portenoy et al., 2012; Lichtman et al., 2018). While there is preclinical data and studies in other diseases associated with neuropathic pain (O'Hearn et al., 2017; King et al., 2017), we did not specifically query patients on the use of MM for the prevention or treatment of taxane-induced neuropathy.

The heterogeneity of preparations and administration methods prescribed, with many patients being prescribed more than one formulation, limits our ability to comment on the effectiveness of specific THC: CBD ratios or preparations for specific symptoms. For patients prescribed more than one formulation, we did not assess whether or not they were used simultaneously or query why an alternate preparation was not effective. We also did not explicitly exclude patients who used marijuana recreationally. Larger, prospective, and more standardized studies in gynecologic cancer patients will hopefully provide further clarity on this question. Prior studies have found that many of the undesirable side effects of MM are related to high amounts of THC and optimizing the ratio between THC and CBD may maximize symptom relief while minimizing side effects (MacDonald and Farrah, 2019).

Among a small cohort of gynecologic cancer patients prescribed MM for symptom management, the majority reported improvement in at least one disease or treatment-related symptom and reported minimal side effects. Given the relatively widespread approval for MM in the United States as well as high rates of patient interest and increasing utilization of medical marijuana in cancer patients in general, this data can prove useful for counseling gynecologic cancer patients on the efficacy and side effects of MM. Further larger prospective studies are needed to investigate specific formulations and indications in this patient population, but our data indicate that it is a safe and useful adjunct for symptom management among a diverse cohort of women with gynecologic cancer.

Declaration of Competing Interest

Julia Fehniger, Allison Brodsky, and Arum Kim have nothing to disclose. Bhavana Pothuri reports grants, personal feels and non-financial support outside the submitted work; institutional PI for industry sponsored trials from Tesaro/GSK, AstraZeneca, Merck, Genentech/Roche, Mersana, and Clovis Oncology. Compensated advisory boards include Tesaro/GSK, AstraZeneca, Merck, Mersana, Eisai, Elevar, Sutro and Toray.

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