Cannabidiol

Knowledge, beliefs, and experiences of patients with cancer

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BACKGROUND: Cannabidiol (CBD) is purported for a variety of therapeutic indications. Interest in CBD products has significantly increased as patients with cancer seek ways to improve symptom control and quality of life.

OBJECTIVES: The purpose of this study was to explore patients' knowledge of and experience with CBD.

METHODS: A panel of oncology nurse practitioners, an oncologist, and oncology pharmacy specialists developed a survey to capture information about patient knowledge and use of CBD. The initial survey was pilot tested and further refined, resulting in the final item survey. The final survey was administered to 100 participants undergoing or having completed cancer treatment and being followed in a supportive oncology care clinic at a large academic medical center.

FINDINGS: Most patients learned about CBD through a family member or friend. The majority of patients had never tried CBD. The most common reported indications were pain, anxiety, and nausea. Of those who had not tried CBD, the most common reasons included lack of knowledge about CBD and providers not recommending CBD.

KEYWORDS
cannabidiol; cancer; patients; CBD; symptom; pain; quality of life

CANCER INCIDENCE CONTINUES TO RISE, with 1,898,160 new cases and 608,570 cancer deaths estimated to occur in the United States in 2021 (Siegel et al., 2021). Cancer has the potential to greatly impair quality of life if symptoms are not well controlled (Tateo, 2017; van den Beuken-van Everdingen et al., 2016). More than half of all patients with cancer experience uncontrolled distressing symptoms and associated loss of function (Nipp et al., 2017). The most common and/or severe patient-reported symptoms are uncontrolled pain, anxiety, and depression (Basch et al., 2016; Deshields et al., 2014; Donovan et al., 2012; Hwang et al., 2016). These symptoms may increase the physical burden of disease and exacerbate emotional, spiritual, or psychosocial distress (Koesel et al., 2019).

Patients with cancer who have pain are frequently prescribed opioid analgesics. Given the potential side effects and the social stigma from opioid therapy, patients often seek adjunct treatments to mitigate their pain (Feinberg et al., 2021). Such therapies include a variety of medications, including a combination of nonsteroidal anti-inflammatory drugs, corticosteroids, anticonvulsants, and antidepressants (Tateo, 2017). If these medications are inadequate or produce concerning side effects, patients will sometimes turn to supplementation to improve symptomatology (Tank et al., 2021). Patients may also seek alternative medications for treatment of other symptoms, including nausea, anxiety, insomnia, and fatigue.

Eighty-five percent of patients with cancer reported using complementary or alternative treatments (Buckner et al., 2018). For a case study, see Figure 1. Patients for whom conventional treatments provide insufficient results may seek alternative treatments, such as cannabidiol (CBD), to mitigate symptoms, enhance quality of life and well-being, boost the immune system, or treat a disease (Richardson et al., 2000; Sparber et al., 2000). Biologic products, or natural health products, such as chaga mushrooms, green tea, curcumin, or CBD, are used by 52%–65% of patients after a cancer diagnosis, in comparison to 15% of patients before a cancer diagnosis (Buckner et al., 2018; National Center for Health Statistics, 2008). Methodologically sound studies demonstrating safety and efficacy are lacking; however, patients are enticed by success stories of patients who endorse use of unconventional, alternative, and natural therapies (Kanimozhi et al., 2021). Anecdotal reports of positive results, religious or cultural factors, attempts to self-regulate symptoms, or improved immune function (Buckner et al., 2018) may further prompt patients to perceive alternative therapies as natural and safe approaches.

CBD, a compound found in the cannabis plant, has become increasingly popular as a complementary or alternative therapy for mitigating symptoms related to cancer, as well as a myriad of other health conditions (Hande, 2019). After extraction from the cannabis plant, CBD is added to oils, mixed into creams and lotions, and sold in various formulations, such as candies or liquid drops (Hazekamp, 2018). The U.S. Food and Drug Administration (FDA) has approved a single commercial product that contains CBD, Epidiolex®, for pediatric seizures, but this product would be unlikely to be covered by insurance for cancer-related symptom management (Vlad et al., 2020).

Most recently, the use of CBD products has captured the attention of patients with cancer, family members, healthcare providers, and scientists. These treatments are derived from the *Cannabis sativa* plant and show promise in alleviating multiple symptoms associated with cancer and chemotherapy treatments. Use of cannabinoids has demonstrated positive effects in relieving pain, as well as chemotherapy-induced nausea and vomiting (Abrams, 2018; Tateo, 2017). In addition, products such as topical CBD have demonstrated a low side effect profile (Häuser et al., 2017; Tateo, 2017; VanDolah et al., 2019).

Sufficient data to recommend the use of CBD products as part of the standard of care are lacking (Abrams, 2018; Häuser et al., 2017; Mohiuddin et al., 2020; Tateo, 2017; van den Beuken-van Everdingen et al., 2017; VanDolah et al., 2019). According to the National Cancer Institute (2018), the only documented benefits of CBD include anxiolytic, antiemetic, and anti-inflammatory effects. Studies to determine toxicologic parameters and the effects of CBD are still needed (Hande, 2019; Iffland & Grotenhermen, 2017).

FIGURE 1.
CASE STUDY

A 62-year-old man with a history of multiple myeloma presents with fatigue, chemotherapy-induced peripheral neuropathy, and back pain. An oncology nurse practitioner (NP) in a supportive oncology care clinic has been managing his symptoms for the past four years. His symptoms are well managed with gabapentin and hydrocodone. Recently, he reported increased pain related to a new pathologic vertebral body fracture. His wife purchased cannabidiol (CBD) oil from an online retailer to help manage his pain after she read an advertisement about the benefits of the product. She encouraged him to apply the oil to his areas of pain twice a day. He was hesitant to apply the CBD oil because he had never heard of CBD and was unsure of what the oil was made from, who processed it, and if it would interact adversely with his other medications. He feared telling his NP about using CBD oil because he did not want her to discontinue his pain regimen. During his next visit, the NP asked if he was taking any new medications. His wife responded that he would like to use CBD oil. The NP explained that CBD is a compound extracted from the cannabis plant and is often added to oils or mixed into creams and lotions and then sold in a variety of applications. The U.S. Food and Drug Administration has not approved any commercial products that contain CBD for the diagnosis, cure, mitigation, treatment, or prevention of cancer or cancer-related symptoms.

"Of the participants surveyed in this study, almost one-third of patients reported using CBD currently or previously."

Clinical trials published to date using CBD monotherapy for symptom management include anxiety, peripheral neuropathy, and opioid consumption (Bergamaschi et al., 2011; Crippa et al., 2011; Xu et al., 2020). These studies did not specifically examine cancer-related symptoms. Clinical trials examining the effect of CBD on anxiety have limited applications because of small sample sizes and trial designs of one-time administrations (Bergamaschi et al., 2011; Crippa et al., 2011). Xu et al. (2020) conducted a study of 29 patients randomized to receive four weeks of topical CBD versus placebo for peripheral neuropathy. Only three participants had medication-induced peripheral neuropathy, although it is unclear if this was secondary to chemotherapy. When compared to placebo, CBD showed a decrease in intensity, sharpness, cold, and itchiness in participants' lower extremities (Xu et al., 2020). Another clinical trial studied open-label CBD softgels in 91 participants with chronic pain. The results demonstrated mixed improvement when examining multiple quality-of-life scales, and 53% of participants reduced opioid use within eight weeks (Capano et al., 2020). Reported outcomes of the participants with pain were inconclusive, particularly in the context of emerging data that opioid tapering may improve quality of life (Capano et al., 2020; Fishbain & Pulikal, 2019). Two additional studies examined participants' pain relief during kidney transplantation and acute graft-versus-host disease after a bone marrow transplantation; again, the results were inconclusive because of sample size (Cuñetti et al., 2018; Yeshurun et al., 2015).

The lack of oversight by drug manufacturers also contributes to inconclusive studies. One study examined the contents of CBD products bought from online retailers (Bonn-Miller

TABLE 1.
SAMPLE CHARACTERISTICS (N = 100)

CHARACTERISTIC	n
Gender	
Female	63
Male	37
Age (years)	
25–34	8
35–44	9
45–54	38
55–64	28
65–74	16
75 or older	1
Ethnicity[a]	
White	77
Black or African American	18
Hispanic or Latino	3
Native American or American Indian	2
Prefer not to answer	1
Education	
No schooling completed	2
Nursery school to 8th grade	1
Some high school, no diploma	7
High school graduate or GED	20
Some college credit, no degree	26
Trade school	6
Associate degree	8
Bachelor's degree	19
Master's degree	6
Professional degree	2
Doctorate degree	2
Prefer not to answer	1

Continued in the next column

TABLE 1. *(CONTINUED)*
SAMPLE CHARACTERISTICS (N = 100)

CHARACTERISTIC	n
Employment[a]	
Unable to work	60
Retired	20
Employed for wages	14
Self-employed	6
Homemaker	2

[a] Participants could choose more than one response.

et al., 2017). The majority of CBD products were mislabeled (69%), and 21% of products contained higher levels of tetrahydrocannabinol (THC) than intended (Bonn-Miller et al., 2017). Another study revealed similar results, underscoring the difficulty of finding unadulterated sources of CBD (Gurley et al., 2020).

Healthcare providers of patients with cancer are challenged by the popularity of CBD (Highet et al., 2020). Patients desire information about cannabis from their healthcare providers (Karanges et al., 2018; Pergam et al., 2017). In this vulnerable population, effective regulation and long-term effects and risks of CBD remain unclear (Hazekamp, 2018). Oncology nurses are well positioned to educate patients about the lack of evidence to support popular uses of CBD, possible contaminants, misleading advertising, and legal issues (Hande, 2019). However, differences in treatment philosophy, as well as lack of provider knowledge, comfort, and information about complementary therapies (Carlini et al., 2017; Karanges et al., 2018), pose threats of poor communication between patients and healthcare providers (Stub et al., 2016). Feeling unequipped to counsel patients about cannabis products (Cyr et al., 2018) may impede healthcare providers' important conversations about potential interactions, side effects, and benefits related to use. Because of stigma, patients may hesitate to report their use of CBD to their cancer team, fearing that they will not approve or will even discontinue current conventional treatments.

The purpose of this study was to explore the reported use and effects of CBD among adult patients with cancer or a history of cancer who were cared for at the Vanderbilt-Ingram Cancer Center supportive oncology care (SOC) clinic in Nashville, Tennessee. Study objectives were as follows: (a) understand patients' knowledge about CBD; (b) identify the number of patients who use CBD in the clinic; (c) assess patients' rationales for taking, or not taking, CBD; and (d) record patients' reported responses and any side effects from taking CBD.

TABLE 2.
RESPONSES OF PARTICIPANTS WHO HAVE USED OR CURRENTLY USE CBD

QUESTION	PREVIOUS CBD USERS (N = 21) n	CURRENT CBD USERS (N = 10) n
Why did you stop CBD?[a]		
Advised to stop by HCP	5	–
Cost	6	–
No benefit	6	–
Forgot	1	–
Loss of interest	1	–
Other	7	–
Have you told your HCP(s) that you use CBD?		
Yes	11	7
No	10	3
How have you used CBD?[a]		
Orally	14	8
Topically	7	5
Inhaled	3	2
Edibles	1	3
How often do you take CBD?		
Daily	7	2
2 times per day	3	2
3 times per day	2	–
3–4 times per week	1	1
Other	8	5
How much CBD do you take each time?		
Milligram (include how many)	3	1
Other (e.g., 1 dropper, thin film)	9	9
Unknown	9	–
How much do you spend on CBD per month?		
Free	6	3

Continued in the next column

TABLE 2. *(CONTINUED)*
RESPONSES OF PARTICIPANTS WHO HAVE USED OR CURRENTLY USE CBD

QUESTION	PREVIOUS CBD USERS (N = 21) n	CURRENT CBD USERS (N = 10) n
How much do you spend on CBD per month? *(continued)*		
$1–$25	5	1
$25–$50	2	2
$50–$100	5	1
$100–$200	2	2
$200–$1,000	–	1
Unknown	1	–
How long have you been taking CBD?		
Less than 1 month	10	1
1–6 months	10	3
More than a year	1	6
Where do you buy CBD?[a]		
Family member or friend	8	3
CBD store	6	6
Supplement store	3	3
Internet	2	–
Pharmacy	2	–
Other	2	3
Why are you taking CBD?[a]		
Joint pain	10	8
Nerve pain	8	7
Muscle aches	8	4
Somatic/visceral pain	8	1
Anxiety	4	7
Sleep	4	5
Mood	3	3

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TABLE 2. *(CONTINUED)*
RESPONSES OF PARTICIPANTS WHO HAVE USED OR CURRENTLY USE CBD

QUESTION	PREVIOUS CBD USERS (N = 21) n	CURRENT CBD USERS (N = 10) n
Why are you taking CBD?[a] *(continued)*		
Headaches	2	1
Nausea	1	4
Appetite	1	2
Attack my cancer	1	2
Prevent cancer	–	3
Other	2	–

[a] Participants could choose more than one response.
CBD—cannabidiol; HCP—healthcare professional

Methods

Project Development

PHASE I (TOOL DEVELOPMENT): The study co-investigators designed a closed-ended survey. The survey was pilot tested by colleagues in addition to the first 10 participants who completed the survey. Feedback informed further revision of the survey. Every participant completed nine questions in part 1 of the survey. If participants indicated that they had never tried CBD in part 1, they answered one additional question in part 2 of the survey. If participants responded that they had used or currently use CBD in part 1, then the participants answered either 11 or 12 additional questions, depending on current use.

PHASE II (CROSS-SECTIONAL SURVEY): The final survey was administered in paper form to a convenience sample of 100 patients who were recruited between July and December 2019. After survey completion, the co–principal investigators counseled participants about the available evidence on CBD and offered to respond to their concerns or questions.

Participants were screened for inclusion and exclusion criteria, which were the same for phases I and II. Participants were established patients who were receiving treatment for cancer-related symptoms in the SOC clinic and were aged 21 years or older. All participants spoke and read English. Exclusion criteria included any newly referred patients to the supportive oncology team because of time constraints. They were eligible if they needed a return visit.

Sample and Setting

Patients referred to the SOC clinic generally have uncontrolled cancer pain and other symptom management issues, which may need aggressive medical management and follow-up. The Vanderbilt University Medical Center Institutional Review Board and Vanderbilt-Ingram Cancer Center Scientific Review Committee approved the study as exempt.

Data Collection and Analysis

The survey responses were recorded on paper forms. Data were entered into an electronic spreadsheet to be analyzed. Categorical variables were summarized using frequency (percentage), and all statistical analyses were performed in R software, version 3.6.0.

Results

One hundred participants completed the survey. The majority of participants were White, female, and unable to work. Further participant demographics are described in Table 1.

The most common sources of information about CBD were from a family member or friend (47%), social media (36%), and television programs (31%). Most patients (93%) became aware of CBD prior to the survey, and only 13% of patients learned about CBD from a healthcare professional.

Most of the participants (69%) had never tried using CBD, and 31% had used or currently were using CBD products. Common selected barriers reported by patients who had never tried CBD included the lack of a recommendation from a healthcare professional and not knowing enough information about CBD. Thirteen of the 31 participants (42%) who had used or who were currently using CBD did not disclose their CBD use to their provider. Of those who had used or were currently using CBD (31%), eight (26%) of the participants had their CBD use documented in their medical record.

The most common believed benefits of CBD reported from the 100 participants were decreased pain (n = 63), anxiety (n = 54), and nausea (n = 45). Twenty-six participants (26%) reported uncertainty of the alleged benefits of using CBD. When asked about the risks associated with taking CBD, 17% of participants thought there were low or no risks to taking CBD, and 45% of participants were unsure of any risks. Other concerns for using CBD included drug interactions (34%), lack of FDA regulation (31%), and unlabeled substances in the product (31%). Although CBD is a legal product in the state of Tennessee, 17% of participants believed it was illegal.

The most widely used CBD formulations were oral (n = 22, 71%) and topical (n = 12, 39%) (see Table 2). The frequency and dose varied among all the participants, and 9 (29%) did not know the dose used. Participants (n = 25, 81%) paid less than $100 per month, and some (n = 9, 29%) obtained the product for free via samples or from family and friends. Cost for 11 of the 100 participants hindered trying or continuing CBD.

Participants who quit using CBD used the product for six months or less (n = 20, 95%), and current users usually used CBD for more than a year (n = 6, 60%). The most common indications for using CBD were pain (n = 26, 84%), anxiety (n = 11, 35%), and

sleep (n = 9, 29%). For current CBD users, 6 of 10 reported some to a lot of benefit and 9 of 10 would recommend CBD to family and friends. Of the 21 participants who previously used CBD, most reported limited to uncertain benefit (n = 12, 57%), but 11 (53%) would still recommend it to family and friends. Three of the 31 participants (10%) reported a possible side effect from CBD.

Discussion

Most of the 100 patients who participated in the study were aware of CBD products, but only a small percentage of them (13%) had been educated by a healthcare professional. This finding emphasizes the external influence and patient education by the media, friends and family, and the internet about CBD. However, these sources of information can sometimes be unreliable and inaccurate, resulting in misinformed patients. Johnson et al. (2018) described how misinformation with complementary medicine in this vulnerable population may lead to negative outcomes, including poorer five-year survival. The limited knowledge about risks associated with CBD in this vulnerable population is concerning for healthcare providers because optimal treatment would include examining risk versus benefit prior to starting any therapy.

Currently, there are 66 active or recently completed studies using CBD for symptom management, which will provide greater direction for alleged indications of CBD (U.S. National Library of Medicine, n.d.). The majority of studies are in non–cancer-related conditions, but there are several that are recruiting patients with symptoms from cancer, radiation therapy, and chemotherapy. With many trials expected to be completed and published in the next several years, oncology healthcare professionals need to stay up to date on the current literature and may investigate patient knowledge about CBD. CBD education may represent an opportunity for nurses to establish stronger relationships and improve patient education about CBD.

Of the participants surveyed in this study, almost one-third of patients reported using CBD currently or previously. There was no statistical difference between CBD use and any demographic. In addition, almost half (n = 13, 41%) of the participants who had tried CBD did not tell their healthcare provider. This finding prompts more in-depth investigation because of the educational and clinical consequences of not telling a healthcare provider about CBD use. The lack of disclosure of CBD use is noted in a study by Boehnke et al. (2019), who found that CBD users were 20 times more likely to discuss CBD with dispensary employees than medical professionals. Nurses can have a role in reducing barriers for patients to share their CBD use with a professional via addressing the topic early on in symptom management, providing accurate education, and establishing trust and a sense of comfort with a patient (Jones & Saad, 2017).

Possible interactions between CBD and other medications and/or side effects that a patient could experience may be wrongly attributed to another medication (Hande, 2019). The magnitude of risk associated with drug interactions with CBD is unknown. CBD is a known substrate of CYP3A4 and is believed to inhibit CYP3A4, CYP2D6, CYP2C19, and CYP2C9. These enzymes are pertinent for many commonly used medications in oncology (e.g., opioids, vincristine, paclitaxel, antidepressants, tamoxifen). More studies are needed to fully understand the clinical significance of these interactions (Balachandran et al., 2021).

IMPLICATIONS FOR PRACTICE

- Provide evidence-based patient education about the benefits and risks of cannabidiol (CBD).
- Inquire about CBD among patients with cancer to assess their knowledge and interest.
- Document CBD use in the electronic health record to screen for possible drug–drug interactions.

Although the participant-reported side effect burden was minimal, only 2 of 31 patients (6%) reported a lot of benefit from CBD. Woolridge et al. (2005) conducted a patient-reported survey of cannabis products for symptom management in patients with HIV. This study examined each symptom and found that appetite, pain, nausea, and anxiety were reported to be much better in greater than 50% of participants who had that complaint (Woolridge et al., 2005). This study was focused on patient knowledge rather than efficacy of CBD, but the difference in patient-reported benefits is interesting to note. To the authors' knowledge, no randomized studies of CBD/THC in comparison to CBD have been conducted.

This study was informative regarding patient education and perception about CBD. To the authors' knowledge, no studies focus on CBD use in a similar patient population and setting, making it difficult for comparisons to be made. In addition, because of the sample size (N = 100), absolute conclusions about the effects of CBD cannot be made. However, the study highlights the need for improvement in education about CBD use in the healthcare setting and prompts further research. An additional future implication from this study is the need for more expansive research on CBD use in the population of patients with cancer, given CBD's growing popularity.

Limitations

This study had several limitations. The study population included only 100 patients with cancer at a single center, which limited the statistical analysis and strengths of the conclusions. This study was conducted in an SOC clinic, which tends to be consulted on more complex symptom management cases and may not reflect all other oncology practices and cancer centers with different demographics. Finally, the study did not test poststudy education as an intervention to improve patient education, and the recommended intervention to discuss CBD with patients with cancer is primarily based on the authors' consensus.

Implications for Nursing

Although this survey is unable to determine whether CBD is efficacious, it does highlight that a portion of patients are interested and trying CBD products. Participants in this survey appeared to

have limited evidence-based education about the risks of CBD. The lack of regulated CBD products available to the public, the vulnerability of patients with cancer, and the potential for contamination and harm should urge oncology nurses to actively educate patients about these unregulated supplements, which may be a prime initiative for nursing.

Conclusion

Participants had a variety of beliefs about CBD use and limited knowledge regarding the risks of treatment. This knowledge primarily derives from family members and friends or social media. Almost one-third of this patient population had used CBD products for purported indications of pain, anxiety, and nausea, among others. The patients who had never tried CBD primarily reported a lack of understanding or recommendation from a healthcare professional. Although reported side effects were low, benefit in an outpatient oncology population may be limited and should be further investigated. Results from this survey may highlight a prime opportunity for nurses to discuss the information known about CBD with patients with cancer.

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The authors take full responsibility for this content and did not receive honoraria or disclose any relevant financial relationships. The article has been reviewed by independent peer reviewers to ensure that it is objective and free from bias. Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Oncology Nursing Society.

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