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Marijuana use among patients with epilepsy at a tertiary care center

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Abstract

The expansion of medical and recreational marijuana legalization facilitates patient access to cannabis, and many patients with epilepsy pursue marijuana as a treatment for seizures. We administered a nine-item survey on marijuana use to patients seen in an epilepsy clinic over a 9 month period at a tertiary care center in Oregon where recreational use was legalized in 2015. The majority of respondents (n = 39) reported cannabis use for the purpose of treating epilepsy (87.2%, n = 34), and strongly agreed (53.8%, n = 21) or agreed (28.2%, n = 11) that cannabis use improved seizure control. The most commonly selected cannabis strains were high cannabidiol (CBD) (30.8%, n = 12) or multiple types (30.8%, n = 12), with administration methods of smoking (66.7%, n = 26), edibles (48.7%, n = 19), and concentrates (43.6%, n = 17). More participants reported using marijuana with primarily CBD than primarily tetrahydrocannabinol (THC) or equal CBD:THC content, and very few women reported using marijuana with primarily THC compared with men (10% of female versus 47% of male respondents). Only 2 of 39 participants were able to give an exact dosage used in milligrams. Medical and recreational dispensaries were the most common cannabis sources, followed by homegrown and friends/family members. Although pharmaceutical CBD extract is now Food and Drug Administration (FDA)-approved for certain epilepsy types, access remains limited. Further research is needed to understand recreational cannabis use among patients with epilepsy while clinical research for pharmaceutical cannabis products continues.

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Declarations of interest

None.

Keywords

Cannabis; Medical marijuana; Clinical survey; Cannabidiol; Epilepsy

1. Introduction

Since Oregon's legalization of recreational marijuana in 2015, many patients have been supplementing their prescribed seizure medication regimen with marijuana products containing cannabidiol (CBD), a component of marijuana that has been researched as a treatment for epilepsy. As of January 2019, 30 states and Washington D.C. allow marijuana for medical purposes [1]. An additional 10 states and Washington D.C. have legalized recreational marijuana. Because of its federal classification as a Schedule I controlled substance, research on its efficacy and appropriate dosage in treating various medical conditions remains limited. Three randomized controlled double-blind clinical trials investigating CBD in specific types of severe epilepsy syndromes showed clinically significant results and resulted in Food and Drug Administration (FDA) approval of purified CBD extract (Epidiolex, GW Pharmaceuticals, London, UK) for severe epilepsy syndromes including Lennox–Gastaut syndrome and Dravet syndrome [2–4]. Food and Drug Administration approved drugs that contain CBD derived from cannabis and no more than 0.1% tetrahydrocannabinols (THC) are now Schedule V [5]. There is ongoing research investigating CBD as a treatment for other forms of epilepsy, but for now, the FDA-approved indications remain limited, and exclude the majority of patients with epilepsy.

The drive to pursue alternative treatments for epilepsy stems in part from the fact that around 30% of patients with epilepsy continue to have seizures despite appropriate medical treatment. Marijuana as treatment for epilepsy is a popular topic in lay media as well as social media, and many patients with epilepsy become aware of cannabis' potential benefits via the internet or other lay sources [6–9]. A recent online survey in Australia with 976 responses showed that 15% of adults with epilepsy were using or had used cannabis products to treat epilepsy, and 90% of those using cannabis reported its success in reducing seizure frequency. Primary motivations given for using cannabis included presence of medically refractory epilepsy and desire for treatments with fewer adverse effects [10]. Previous studies have uncovered fallacies among patients regarding their attitudes toward marijuana, including the belief that natural products are by definition safe, acceptance of anecdotal evidence as fact, and belief that sufficient scientific evidence for marijuana's safety and efficacy has already been established [11–13].

Until more research is done, and pharmaceutical grade CBD oil becomes available to more patients, the majority of patients with epilepsy who desire treatment with cannabis products will not be eligible for prescriptions from their doctors, and many decide to seek marijuana through marijuana dispensaries and other legal means. Many questions remain unanswered concerning the use of medical marijuana including the consistency and safety of unregulated, commercially available products at marijuana dispensaries. Patients who choose to use unregulated marijuana products to manage their seizures encounter challenges such as inconsistent CBD/THC content, inaccurate labeling, and high tax rates. In addition,

recommendations from dispensary staff may be discordant with current research, for example, in recommending contraindicated high THC products for the treatment of epilepsy [14,15]. While CBD is not psychoactive, THC produces psychoactive effects that are desired by recreational users to feel “high.” THC has been linked to neuropsychological problems in the developing brain and has been shown in some animal studies to have a proconvulsive effect [16,17].

The aim of this clinical survey was to ascertain how patients with epilepsy at a tertiary care clinic in Oregon are using marijuana outside of the medical system, and to explore their perceptions about marijuana use and efficacy.

2. Methods

2.1. Data collection

Approval was obtained from the Oregon Health & Science University (OHSU) Institutional Review Board in advance of survey administration. Participants over age 21 were recruited from the OHSU Epilepsy Clinic from October 2017 to June 2018. All patients seen in the clinic during this time period were screened for marijuana use as per standard clinical care. If they screened positive for marijuana use, they were asked if they would be willing to participate in the survey. A nine-item survey was administered to consenting patients who reported the use of medical and/or recreational cannabis to the physician, and agreed to participate in the study. Consent was obtained by the treating physician or other members of the research team. All surveys were anonymous and were assigned a number, corresponding to a numbered consent form. Surveys were kept in a locked cabinet, and results were entered into Excel for storage and subsequent analysis.

2.2. Statistical analyses

Descriptive statistics were calculated using Microsoft Excel 2016 software.

3. Results

3.1. Demographics

A total of 39 patients participated, with demographics and survey responses in Table 1. In addition to overall trends, responses were analyzed by age (21–66 years), gender (male, female), and cannabis strain selection (high CBD, high THC, equal CBD:THC, multiple types). The greatest proportion of patients was age 31–40 years (35.9%, n = 14), with a mean sample age of 38 years and standard deviation of 12.4 years. Respondents identified as 51.3% female (n = 20) and 48.7% male (n = 19).

3.2. Seizure control

In the overall sample, the majority (87.2%, n = 34) reported using cannabis for the explicit purpose of treating epilepsy (see Table 1). Patients who reported selecting strains high in THC were less likely (50%, n = 4) to report using cannabis to treat seizures, whereas those selecting high CBD strains universally used cannabis for that purpose (100.0%, n = 12). Patients age 31–40 (n = 14) reported the greatest perceived efficacy, strongly agreeing that

cannabis improves their seizure control (78.8%, n = 11) more frequently than any other age group. Similarly, men strongly agreed with that statement (63.2%, n = 12) at a higher rate than women (45.0%, n = 9). Patients age 21–30 (n = 12) more often selected “neither agree nor disagree” when asked whether cannabis improved their seizure control; they also consumed high THC strains (33.3%, n = 4) at a higher rate than other age groups. Fifty-five percent of respondents from the group with high CBD consumption (41.7%, n = 5) strongly agreed that cannabis improved seizure control, whereas 37.5% of the respondents from the group with high THC consumption strongly agreed.

3.3. Administration methods

Smoking marijuana was the primary administration method (66.7%, n = 26) followed by edible products (48.7%, n = 19) and concentrates (43.6%, n = 17). Drinks (teas, sodas) and topicals were the least frequently reported methods (Fig. 1). Among patients over age 50, vaping was selected more frequently than smoking (Table 2). While smoking was the most common choice for both men and women, they differed in the distribution of methods: men utilized edibles, concentrates, and bongs/waterpipes (in order of frequency) whereas women were equally likely to choose vaping, edibles, and tinctures, followed by concentrates.

3.4. Sources

Medical dispensaries, commonly licensed for both medical and recreational sales in Oregon, were the most common cannabis source reported (61.5%, n = 24), followed by recreational shops (35.9%, n = 14). Homegrown and friends/family members as cannabis sources were equally prevalent (28.2%, n = 11). The majority of patients (87.1%, n = 34) find cannabis easier to obtain now than before the legalization of recreational marijuana. Only one respondent, in the 21–30 age bracket, reported greater difficulty obtaining cannabis, attributed to high tax rates. Others (12.8%, n = 5) reported that it is now as easy to obtain cannabis as before recreational legalization; of those patients, nearly all listed friends/family members and homegrown as (tax-free) sources.

3.5. Administration frequency

More than half of patients (53.8%, n = 21) reported administering cannabis several times daily. Seventy-two percent of patients age 40 and under (n = 18) administered cannabis several times daily, while only 23.1% of patients over age 40 administered cannabis several times per day. Frequency of use by age is shown in Fig. 2.

3.6. CBD and THC content

About 1/3 of participants (30.8%, n = 12) reported choosing strains with more CBD than THC, and about 1/3 reported using multiple types (30.8%, n = 12), e.g., a variety of CBD and THC ratios. A smaller segment selected strains with more THC (20.5%, n = 8), an equal ratio of CBD to THC (6.9%, n = 2), or did not know 12.8% (n = 5) the content of their cannabis products. Those who selected high THC strains were less likely (63.6%, n = 7) to use it for the purpose of treating epilepsy than the group with high CBD consumption (100.0%, n = 12) or the sample as a whole (87.1%, n = 34). The group with high THC consumption reported utilizing inhalation as opposed to oral ingestion. All groups had a high

rate of reporting agreement or strong agreement with the statement “cannabis improved my seizure control,” and no one disagreed with the statement. Seven participants reported that they neither agreed nor disagreed with the statement “cannabis improved my seizure control,” and among that group, 4 reported using cannabis products with more THC, 2 reported more CBD, and 1 reported using multiple types. It is worth noting that some patients gave verbal explanations for how marijuana improved their epilepsy via indirect means, such as “being more relaxed” or “sleeping better.” Women selected high CBD products (55.0%, n = 11) or multiple types (45.0%, n = 9) more frequently than men (Fig. 3), who primarily chose high THC products (47.4%, n = 9). When asked an open (nonmultiple choice) question about dosage taken in milligrams, the majority of patients (64.1%) did not know the dosage they were taking in milligrams. Some patients quantified the amount used in other ways, such as weight in flower, amount of liquid taken (e.g., “1 dropper full”), or approximation of size (e.g., “pea-sized amount”). Only two patients were able to give exact dosages in milligrams by active ingredient (THC:CBD).

4. Summary

The majority of patients surveyed in this study reported successfully using cannabis to improve seizure control, despite using varied combinations of THC:CBD as opposed to exclusively high CBD strains. All patients who selected high CBD products reported engaging in cannabis use to manage seizures. Of patients who reported using high THC strains, half agreed that cannabis use improved their seizures, and half neither agreed nor disagreed. Patients with epilepsy may report that marijuana strains high in THC are helpful for seizures as a way of justifying their recreational use, or may be influenced by a strong desire for marijuana to be an effective treatment. An open-label, retrospective study done in Colorado (CO) in 2015 highlighted one aspect of self-reporting bias among patients taking medical marijuana for epilepsy treatment [18]. Patients in the study who moved to CO for the purpose of obtaining legal medical marijuana were 3 times more likely to report significant marijuana benefit than patients who were native to CO. This finding showed that the amount of effort that patients put forth to obtain medical marijuana affects their perception of treatment efficacy.

Patients surveyed did not have a clear understanding of the potential risks and benefits of marijuana use and its components. Most patients surveyed used marijuana strains that contained THC in varying amounts. Although there are preparations of pure or nearly pure CBD oil available in some marijuana dispensaries in Oregon, the least expensive option for patrons is to buy whole plant strains that have been bred to have a high CBD to THC ratio. Cost is an important factor limiting use of CBD oil at dosages comparable to those used in clinical trials. Commercial CBD oil prices vary widely in price, but can be prohibitively expensive. For example, “Charlotte’s Web” CBD oil, which is derived from a strain of marijuana plant with a 30:1 CBD:THC ratio, popularized by a patient named Charlotte Figi who has Dravet syndrome, is available for purchase online at a price of $274.99 for 100 mL with 50 mg/mL [19]. The recommended maintenance dosage for patients taking Epidiolex CBD oil is 10 mg/kg/day. If a 70 kg adult wanted to replicate the recommended dose from Epidiolex clinical trials by buying commercial “Charlotte’s Web” CBD oil, the cost would be $1,150.80 per month.

Cannabis use varied with age, with patients age 40 and younger more commonly administering several times daily by inhalation. Smoking, edibles, and concentrates (in that order) were the most prevalent administration methods in the overall sample, with vaping replacing smoking as the primary method after age 50. Smoking was the most common delivery method among patients surveyed, which has potential health risks. Although studies on smoking marijuana and development of lung cancer have been inconclusive [20], there is evidence that smoking marijuana contributes to airway inflammation and chronic bronchitis [21]. Data on the long-term effects of smoking marijuana are incomplete, but suggestive of potential harm. The physician's role in counseling patients regarding means of administration has not been defined by professional organizations, and remains unclear. Neurologists could potentially play an active role in counseling patients to use lower risk cannabis administration methods, such as tinctures, edible products, or oils.

Medical and recreational dispensaries were the main cannabis sources, closely followed by homegrown and friends/family members as sources. No patients reported using prescription THC (dronabinol), and at the time of survey administration, pharmaceutical grade CBD (Epidiolex) was not yet available for prescription. Patients generally found cannabis more accessible now than before recreational legalization. Men and women demonstrated different selection behaviors, with men using high THC strains at higher rates than women, and women using high CBD strains at higher rates than men. Men were more likely than women to strongly agree that cannabis improved their seizure control. Gender differences in medical marijuana use may reflect epidemiologic gender differences in recreational marijuana use, since more men than women use marijuana for recreational purposes in a sustained manner over time, and men are more likely than women to be diagnosed as having cannabis use disorder [22,23].

The majority of patients were unable to quantify the exact dosage of active ingredient they were using, which can be explained in part by the fact that the majority of patients reported smoking as their primary means of administration which does not allow for precise dosage measurement. Even among patients who used marijuana in other forms, they more often reported the instructions for administration (e.g., "1 dropper full" or "pea-sized amount") rather than the intended dosage in milligrams. This detail highlights the knowledge gap among many patients regarding appropriate dosing for medical marijuana, and a potential area where patient education may be beneficial in the future. Even when patients intend to use CBD oil similarly to the dosing used in clinical trials for epilepsy, they tend to use a subtherapeutic dose, or to not understand how much they are actually taking. Many marijuana dispensaries do list or label products with respect to THC and CBD content, but multiple studies have demonstrated that labeling can be wildly inaccurate [24,25]. The number of doses per day also varied greatly between patients in the study. Just over half of patients reported using cannabis multiple times per day, 20.5% reported daily use, and 25.6% reported less than daily use. Although only 53.8% of patients were using cannabis products more than once per day, 87.2% of patients reported they were using it for the purpose of treating epilepsy. If cannabis were being treated as a medication, then one would expect it to be taken regularly in the same manner as other epilepsy medications. Cannabidiol oil was dosed twice daily in clinical trials. There are many factors that may influence the way that patients are using cannabis products on a different schedule than in

the trials, which may include cost, poor understanding of appropriate medical dosing, desire to use cannabis more frequently for recreational reasons, or conversely, desire to avoid using cannabis during the day to avoid feeling "high."

This study was limited by small number of participants, and was underpowered to measure efficacy among subgroups with epilepsy. The responses highlight the wide gap between patient desire to use cannabis products for epilepsy treatment and their knowledge about how to use cannabis as an epilepsy treatment. We propose that a future research direction could be to assess the efficacy of physician counseling regarding risks and benefits of medical marijuana. A study could be designed that randomized patients to in-clinic counseling on risks and benefits of medical marijuana vs online cannabis and epilepsy tutorial, with pre- and posttutorial survey on attitudes toward cannabis. One study that is currently being discussed among a multidisciplinary team at OHSU is a survey given to "budtenders" (the name for workers at marijuana dispensaries) to explore attitudes of people in the marijuana industry and types of counseling given to medical marijuana customers. This proposed study would expand on a previous study that investigated levels of training and sources of information given to patients obtaining medical marijuana from the Oregon Medical Marijuana Dispensary (OMMD) program [14]. Another direction for future research could be randomized controlled study of Epidiolex versus placebo as an adjunctive medication in patients with focal or generalized epilepsies who do not have syndromes such as Lennox–Gastaut, tuberous sclerosis, or Dravet syndromes.

5. Conclusion

As legislation on medical and recreational marijuana use evolves, open communication between medical providers and patients is essential to understanding the potential risks and benefits of marijuana use in epilepsy. Patients with epilepsy may benefit from CBD use, but currently have limited access to prescribed pharmaceutical grade CBD extract. Further research is needed regarding practical recreational and medical use of cannabis products in patients with epilepsy. Some patients will continue to seek legal (and illegal) marijuana products outside of the medical system to treat their epilepsy as long as 1) clinical research continues to lag behind potential medical applications and 2) FDA-approved indications for CBD extract remain limited. Both patients and providers would benefit from further study of recreational and medical marijuana use. Until epileptologists engage in discussions and education with patients regarding cannabis use in epilepsy, patients will pursue medical cannabis use through unregulated means, and will continue to receive misinformation from nonmedical sources.

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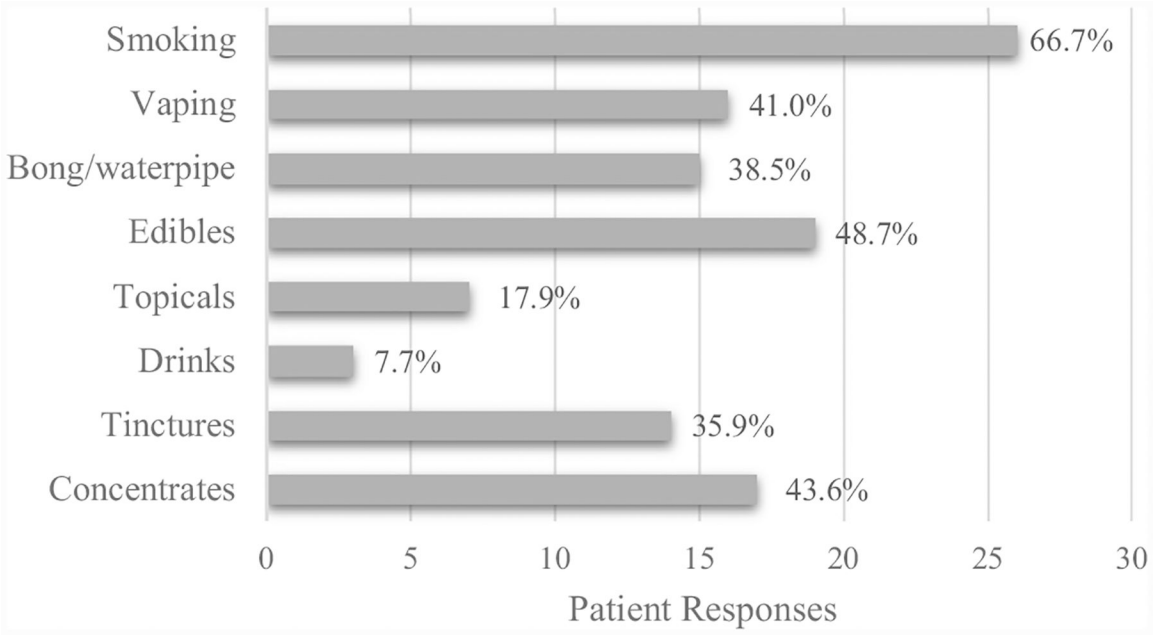

Fig. 1.
Overall sample frequency of cannabis administration methods (select as many as apply).

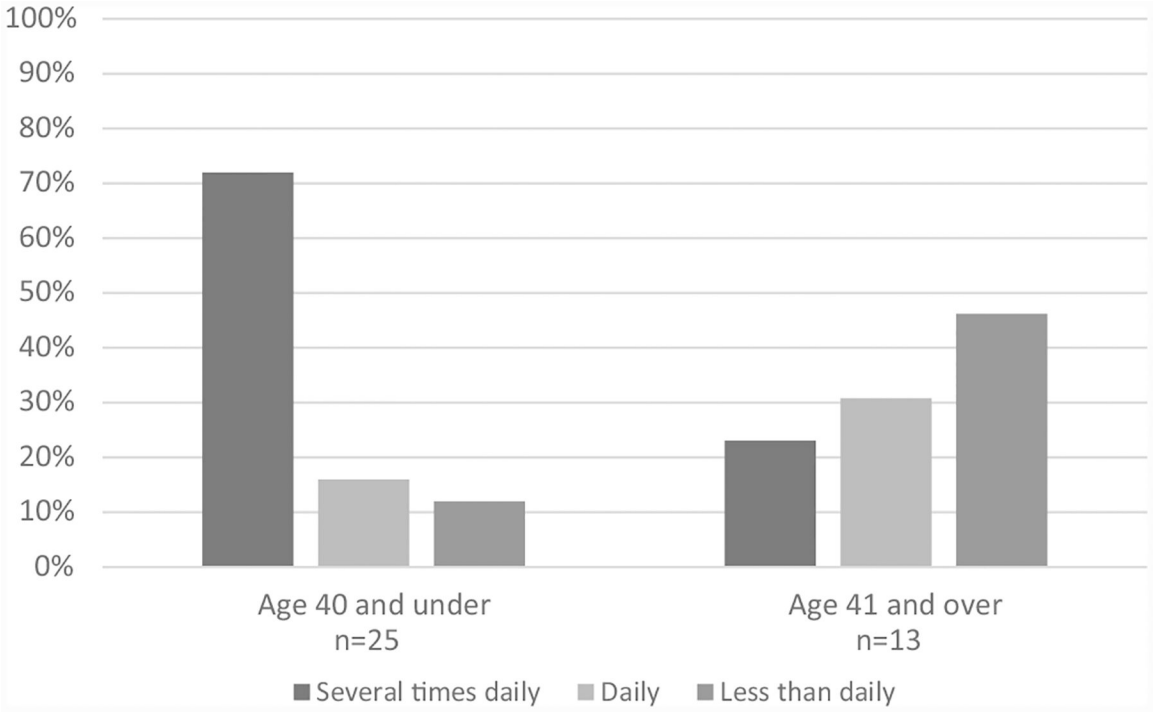

Fig. 2.
Administration frequency of marijuana products by age group.

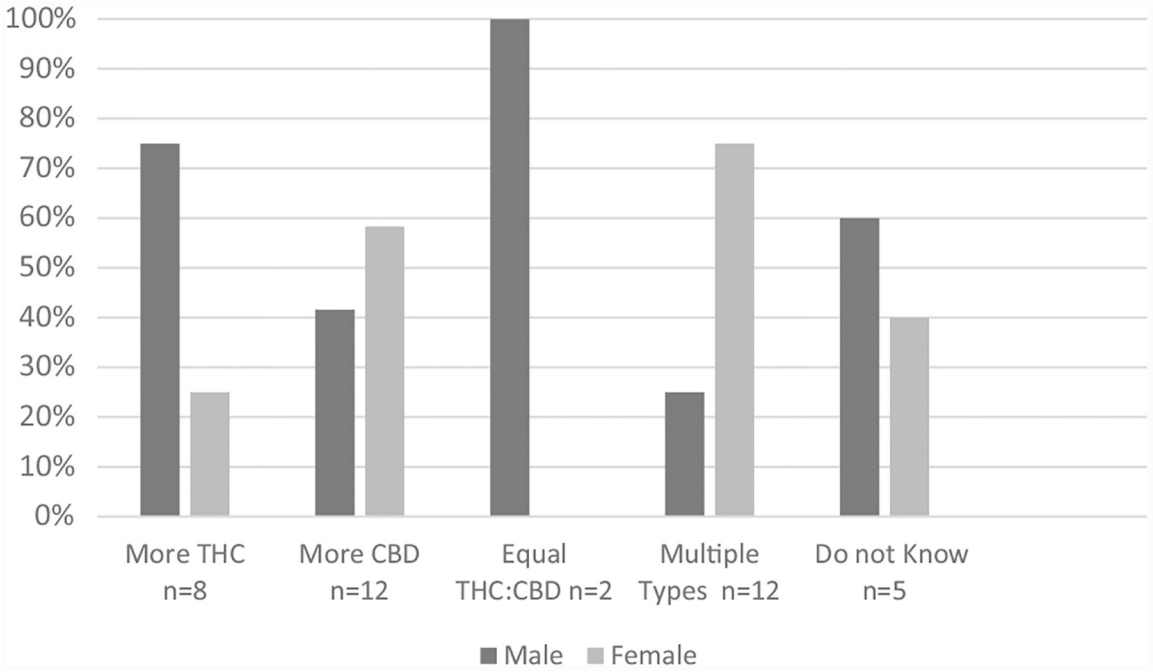

Fig. 3.

Distribution of CBD:THC ratio selection by gender. A higher percentage of men than women chose high THC products, and a higher percentage of women than men chose high CBD products.

Table 1

Summary of survey responses (n = 39) by question.

Question	Answer option	Responses (n = 39)	Percent n
Gender	Female	20	51.3%
	Male	19	48.7%
Do you use cannabis to treat yourseizures?	Yes	34	87.2%
	No	5	12.8%
How do you use cannabis? Check as many as apply	Smoking	26	66.7%
	Vaping	16	41.0%
	Bong/waterpipe	15	38.5%
	Edibles	19	48.7%
	Topicals	7	18.0%
	Drinks (tea, soda)	3	7.7%
	Tinctures	14	35.9%
	Other concentrates	17	43.6%
Where do you get cannabis from?	Medical dispensary	24	61.5%
	Home grown	11	28.2%
	Friend/family member	11	28.2%
	Pharmacy (i.e., prescription Marinol)	0	0
	Recreational shop	14	35.9%
Since recreational marijuana became legal in Oct 2015 in OR, do you think it is…	Easier to get	34	87.1%
	Harder to get	1	2.6%
	Same as before	4	10.3%%
Do you know if your cannabis has more CBD or THC?	More CBD	12	46.2%
	More THC	8	28.2%
	Equal CBD and THC	2	15.4%
	I use multiple types	12	30.8%
	I do not know	5	12.8%
In a typical week, how many times do you use cannabis? (check one)	Less than once a week	6	15.4%
	1–2 times	2	5.1%
	3–6 times	2	5.1%
	Once a day	8	20.5%
	Several times daily	21	53.8%
	I do not know	0	0.0%
How many milligrams do you use each time?	I do not know or indistinct measurement	25	64.1%
	0.5–10 mg	4	10.3%
	10–100 mg	2	5.1%
	100–1000 mg (flower weight)	6	15.4%
	>1 g (flowerweight)	1	2.6%
To what extent do you agree or disagree with the following statement: “cannabis improved my seizure control.”	Strongly agree	21	53.9%

Question	Answer option	Responses (n = 39)	Percent n
	Agree	11	28.2%
	Neither agree nor disagree	7	18.0%
	Disagree	0	0.0%
	Strongly disagree	0	0.0%

Table 2

Primary methods of administration by age.

Age 21 −30 (n = 12)	Age 31–40 (n = 14)	Age 41–50 (n = 7)	Age 51–60 (n = 2)	Age 61–70 (n = 4)	All ages (n = 39)
Smoking (83.3%)	Smoking (71.4%)	Smoking (57.1%)	Vaping (100%)	Vaping (50%)	Smoking (66.7%)
Concentrates (58.3%)	Edibles (57.1%)	Edibles (57.1%)	Smoking (50%)	Tinctures (50%)	Edibles (48.7%)
Bong/waterpipe (50.0%)	Vaping (50.0%)	Concentrates (42.9%)	Bong/waterpipe (50%)	Smoking (25%)	Concentrates (43.6%)
Edibles (50.0%)	Concentrates (50.0%)	Bong/waterpipe (28.6%)	Edibles (50%)		Vaping (41.0%)
			Tinctures (50%)		Bong/waterpipe (38.5%)
			Drinks (50%)		