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Knowledge, expectations and fears of cannabis use of epilepsy patients at a tertiary epilepsy center

Randi von Wrede *, Susanna Moskau-Hartmann, Nicola Amarell, Christian Erich Elger, Christoph Helmstaedter

University Hospital Bonn (UKB), Department of Epileptology, Germany

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ABSTRACT

Introduction: Medical cannabis is increasingly discussed as an alternative treatment option in neurological diseases, e.g. epilepsy. Supporters and opponents base their propositions mostly on subjective estimates, they confuse cannabis in whole versus extracts and botanical versus synthesized.
Methods: Two hundred seventy five patients with any kind of epilepsy (56% female, 44% seizure free, 91% on medication) answered a survey on the knowledge, expectations, fears, and willingness to be treated with medical cannabis. Data were analyzed with regard to patient characteristics and clinical data from patient files.
Results: Overall, 70.5% of the patients were familiar with the possibility of medical cannabis treatment, 36.7% with its use in epilepsy. A minority of 10.9% gained the information from their physicians. The majority knew about organic compared to synthetic cannabis. The interest in further information is high (71.3%). Regression analysis (explaining 53.8% of the variance) indicated that positive expectations (in the order of relevance) were seizure control, relaxation, mood, and tolerability whereas fears mostly concerned addiction and delirant intoxication. Men showed a greater interest than women.
Conclusion: Many epilepsy patients knew about medical cannabis, were interested in this treatment, and wanted more information. Expectations, however, appear to be based on the connotations of the whole substance cannabis with tetrahydrocannabidiol and its commonly known effects. Unfortunately, patients did not get their information from physicians, but mostly by other sources. In order to avoid prejudices and potentially harmful self-medication, physicians and healthcare providers are called to become familiar with the substance and to inform patients adequately.

1. Introduction

Epilepsy is the third most common chronic neurological disease with a prevalence of 0.5 to 1.0%. The disease is associated with increased morbidity and mortality, and implies a profound loss of quality of life for those affected. As much as one-third of epilepsy patients fails to achieve seizure freedom with at least two appropriately selected anticonvulsive drugs, i.e. are drug resistant. Even the development of new anticonvulsants has not led to a significant increase in the proportion of seizure-free patients, although the tolerability and interaction profiles of newer anticonvulsants may be more favorable [1,2]. The search for new and complementary treatment options remains a major challenge for patients and physicians.

Cannabis is one of the most commonly used psychoactive substances in the world with consumption by about 181 million people worldwide [3]. Although the assumed prevalence differs depending on age, cultural background, and legal status of cannabis, a trend towards rising prevalence of cannabis consumption can be observed in many countries [4].

The use of cannabis products in various medical conditions has been documented for centuries, with case reports showing the effect of medical cannabis on seizure control as early as the late 19th century. In the 1960s, the scientific work on isolation and mechanisms of cannabis and its receptors started. Cannabis contains more than 120 phytocannabinoids, of which tetrahydrocannabinol (THC) and cannabidiol (CBD) are the ones most thoroughly studied.

The anticonvulsant potency of cannabis has been anecdotally described in refractory epilepsies in small studies since last century [5]. Effects on seizures and epilepsies by medical cannabis in general are inconsistent. Considering the well-known psychoactive effects of THC, epilepsy research focussed on the abundant, nonpsychoactive component CBD. Animal studies showed promising anticonvulsant effects [6]. Furthermore, study-based evidence of efficacy in pediatric epilepsy syndromes (Lennox–Gastaut-Syndrome and Dravet-Syndrome) is available [7,8]. Therefore, purified CBD is approved for Lennox–Gastaut-Syndrome and Dravet-Syndrome in the USA. In Germany, CBD is a prescription and pharmacy-only medical product, it is not subject to the Narcotics Act and can be easily purchased from the Internet. Apart

* Corresponding author at: Department of Epileptology, University Hospital Bonn (UKB), Venusberg Campus 1, 53127 Bonn, Germany.
E-mail address: randi.von.wrede@ukbonn.de (R. von Wrede).

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from this, cannabis has far more active components which might contribute to cannabis effects [9].

Since 2017, there is the possibility of prescribing cannabis-containing preparations at the expense of the health insurance in Germany. Although a clear benefit of cannabis use in all epilepsy syndromes has not been proven so far [5], patients increasingly demand medical cannabis, and the treatment centers are challenged by the fact that social media and aggressive marketing strategies confuse cannabis abuse and recreational use with medical cannabis.

Since standardized surveys on the demand towards neurologists concerning medical cannabis are lacking, and since high demands are reported for general practioners [10], this study aims at capturing the knowledge, expectations, and fears patients with epilepsy have about medical cannabis. This knowledge might in particular help to develop strategies for an unbiased information of patients and their physicians.

2. Material and methods

2.1. Patients

Adult patients with epilepsy aged 16 years or over attending our ward or outpatient clinic between October and December 2018 were asked to participate in a written survey. In some cases, filling out in terms of patient history was assisted by the medical staff or by the treating physician in the presence of the participant. The questions about medical cannabis were answered by the patients themselves. All patients were given the opportunity to ask further questions. The paper survey was waived from ethic approval by the local medical ethical committee at the Medical Faculty of the Rheinische Friedrich-Wilhelms-University of Bonn.

2.2. Questionnaire

The questionnaire was composed of questions concerning knowledge about cannabis for medical conditions, interest in the use of medical cannabis, expectations, and fears about potential use of cannabis in the treatment of epilepsy (see Table 1). Cannabis was used as a general term, to get uninfluenced and unbiased answers from the patients. Further questions were put to assign what patients think medical cannabis is and how it is administered. It was composed of 11 questions, two of them nominal, nine of them ordinal.

Furthermore, the following demographic data were obtained: age, sex, duration of epilepsy, seizure frequency, seizure freedom (yes/no), anticonvulsant medication (yes/no), number of previously prescribed anticonvulsants, and highest level of education.

Seizure frequency was gathered on the basis of self-assessment and categorized into categories according to the Revised Seizure-based Outcome Classification System (Duke) with Analysis of Relationship to health-related quality of life (HRQOL), into three groups: seizure free, ≤10 seizures a year, and >10 seizures a year according to Vickrey et al. [11]. This classification system was used to map the close relation to quality of life.

2.3. Statistical analysis

Statistics were done using SPSS IBM statistics calculator. Information for missing data was given where necessary. P-values < 0.05 were regarded as statistically significant.

3. Results

A total of 275 participant questionnaires were included in the study. Four patients denied to participate. Filling out for demographic data was assisted in 12 cases. Patients' characteristics reflect the population a tertiary epilepsy center and can be seen in Table 2.

Table 1
Questionnaire concerning medical cannabis.

Have you heard about medical cannabis in general before? Have you heard about medical cannabis in general before?	Yes/no Yes/no
What do you think about medical use of cannabis?	Not important ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 very important
Have you heard about medical cannabis in treatment of epilepsy?	Yes/no
By whom did you hear about medical use of cannabis?	☐ Physician ☐ Internet/print media ☐ Family/friends ☐ Support group of people with epilepsy ☐ Other:
What do you think is meant by cannabis treatment?	☐ Known drug as tablet/capsule/oil ☐ Known drug as vapor/smoke ☐ Extracts/parts of the known drug as tablet/capsule/oil ☐ Extracts/parts of the known drug as vapor/smoke ☐ Synthesized drug as tablet/capsule/oil ☐ Synthesized drug as vapor/smoke ☐ Other:
Would you like to know more about this treatment?	Yes/no
Could you imagine such a treatment for yourself	In no case ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 absolutely
What would your expectations be?	☐ Seizure improvement ☐ Better tolerability ☐ Improvement of mood ☐ Exhilaration ☐ Relaxation ☐ Other:
If not/rather not, why not?	☐ Fear of side effects ☐ Fear of addiction ☐ Fear of exhilaration ☐ I am satisfied with my treatment ☐ Other:
Have you ever used cannabis? For what reason?:	Yes/no ☐ Recreation/relaxation ☐ Medical treatment ☐ Exhilaration ☐ Other:
Are you currently consuming cannabis? For what reason?:	Yes/no ☐ Recreation/relaxation ☐ Medical treatment ☐ Exhilaration ☐ Other:

Seventy-eight (28.4%) of the participants reported to have consumed cannabis in the past, most of them for relaxation (40 patients; 51.3% of the consumers) or exhilarating purpose (36 patients; 46.2% of the consumers), ten patients (12.8% of the consumers) used cannabis for medical reasons. Within the group of participants with medical reasons, only three used cannabis for medical reasons exclusively. At the time of the survey, cannabis was taken by 15 (5.5%) patients, some of them for relaxation (eight patients, 53% of the present consumers) or exhilarating purpose (seven patients, 46% of the present consumers), interestingly, just as many for medical reasons (seven patients, 46% of the present consumers), three of those for medical reasons only.

Overall 194 (70.5%) of the patients knew about use of cannabis in medical conditions, but only 101 (36.7%) of the patients knew about the possibility of using medical cannabis for epilepsy treatment. Information had mostly been gained by the Internet (36.7%), print media (25.8%), and family and friends (24.7%). Only 30 patients (10.9%) had received information about medical cannabis from their physician and only six patients (2.2%) were provided with the information by their support group of people with epilepsy.

Most of the patients who stated to know about medical cannabis thought it to be extracts or parts of the known drug as mainly referred to in social media (67.0%; 62% of all participants) or the known drug (whole cannabis) itself (45.5%; 42.3% of all participants). Knowledge about the possibility of synthesized medical cannabis products in all participants was lower (21.5%). As to formulation, 35% of the participants thought medical cannabis to be smoke or vapor of any origin. In the subanalysis patients who stated to be informed about medical cannabis more frequently thought medical cannabis to be consumed by smoke or vapor than those uninformed (41.5% vs 19.8%; $p = 0.001$). The same was found for patients with former cannabis use as compared to nonusers (47.4% vs 30.1%, $p = 0.05$).

Interest in further information on medical cannabis was high (196 patients, 71.3%), subanalysis revealed a significant trend towards more interest in further information by those who already knew about medical cannabis before in comparison to those who did not.

A total of 164 (59.6%) patients could imagine a treatment with medical cannabis for themselves. In the group of the patients informed about medical cannabis in epilepsy treatment, even 73.3% were willing to take medical cannabis.

Regression analysis explained 53.8% of the variance and revealed several prognostic factors for the willingness to use medical cannabis. (see Table 3). In the order of relevance, seizure control, relaxation, mood, and tolerability were positively valued, and fears of addiction and delirant intoxication were negatively valued. In addition, men showed a greater interest in the use of medical cannabis than women.

4. Discussion

Initiated by the lively discussion about the use of medical cannabis in neurological disorders in both social media and medical press, the present work investigated the preconceptions, experiences, expectations, and fears of epilepsy patients about these topics. The current discussion can be characterized well by confoundation of cannabis and cannabis extracts, such as CBD or THC. Supporters and opponents of medical cannabis base their propositions on personal estimates and experience. By the means of studies, efficacy in seizure control by whole cannabis, THC oder THC-rich extracts is not proven yet and side effects are well-documented. For CBD in contrast objective data for impact on seizure control were shown in drug studies with acceptable side effects. Relevant studies on seizure control in epilepsy patients on other phytocannabinoids are missing [7,8,12].

Table 2
Patients characteristics (n = 275).

Sex	
Male	121 (44%)
Female	154 (56%)
Age in years, mean (SD)	38.86 (±16.2)
Age in years, range	17–79
Age at onset of epilepsy, mean (SD)	24.2 (±17.4)
Age at onset of epilepsy, range	0–77
Duration of epilepsy in years, mean (SD)	14.7 (±15.3)
Duration of epilepsy in years, range	0–72
Seizure frequency	
Seizure free	146 (53.1%)
Seizure free in the last year	121 (44%)
Lower seizure frequency	120 (43.6%)
Higher seizure frequency	33 (12%)
Medical therapy	
Anticonvulsant medication	251 (91.3%)
Exposition to ≥3 different anticonvulsants	138 (50.1%)
Education	
Basic school education	113 (41.2%)
General qualification for university entrance, vocational diploma	82 (29.8%)
University degree	45 (16.4%)
No education/school for mentally or physically handicapped persons	6 (10.5%)

Of the 275 participants of this survey, two-thirds had already heard of medical cannabis, though merely one-third knew about a possible use in epilepsy. The most common way of information flow was via the Internet showing exemplarily the impact of digitalization on daily living and health information flow. The timely availability and convenient accessibility of Internet information makes information easier and quicker to obtain though, depending on health literacy of the user, misunderstandings, and potentially dangerous interpretations of health data might occur [13]. Especially the medical cannabis market is flooded by pseudoprofessional data and differentiation between professional and nonprofessional opinion leaders is difficult to perform. In our study, primary information provided by physicians was rare. Whether it reflects lack of information of physicians or some unwillingness to propose and prescribe medical cannabis because of the rejection of drug-associated substances would need to be determined in a separate study.

Physicians should be aware of the possibility of medical cannabis, as otherwise by the means of easy access (high street market, online trade) patients will start self-medication. These nonpharmaceutical products are not under legal control as pharmaceutical products are, so purity and safety are undetermined. Even for extracts of cannabis with specified content inaccurate labelling was shown, and unexpected levels of cocontents were found [14]. Patients often consider self-medication with herbal medicine as harmless and as complementary medicine, however drug interactions are well-known [15]. The interactions with comedication through similar pathways as well as liver enzyme induction may cause avoidable problems [16–19]. Therefore, knowledge about medical cannabis and willingness for further education on and information about medical cannabis is the physicians' crucial responsibility in order to avoid harm.

In this study, the majority of our patients seemed to connotate medical cannabis with the original plant or its extracts, whereas the possibility of synthetic cannabis is less known. Supporters of botanical cannabis focus on the “natural” background of botanical cannabis and hypothesize an entourage-effect due to dynamic interaction between the different compounds of cannabis. This entourage effect could not be finally proven [9,20,21]. Disadvantages of botanical cannabis might be impure extraction, the difficulty to define the composition of the drug by quantity and quality of any component at any time and despite possible changes in environmental conditions. Acceptance by patients is high [22], perhaps supported by the idea of natural and therefore nonharmful substances and possibly the connotation of illicitly synthetized full cannabis (“spice”) with high health risks [23]. In contrast, synthesized cannabis products can easily follow the established procedures of drug regulation. But as pivotal studies on extracts are carried out with botanical cannabis, a transfer to synthetic cannabis seems questionable. Nevertheless, the way of proving quality and efficacy in the pharmaceutical market is expensive and moving slowly, and patients make use of easily accessible cannabis (sold for recreational use) for self-medication alternatively. These facts make a structured cannabis research and valid data acquisition difficult and lead to potentially inefficient or insecure medication for patients as well as a difficult decision situation for healthcare providers on a confusing market.

Medical cannabis is provided as vapor, smoke, capsule, oil, or other liquid. In general, there is no recommendation for medical cannabis to be smoked. Interestingly, in our study a high percentage of participants thought that medical cannabis is smoke, especially those with former use and knowledge of the possibility of medical cannabis follow this estimation. An interpretation of these data is again a strong association between recreational cannabis (which is mostly smoked) and positive effects on different health conditions.

In our studied population, interest in medical cannabis is high. Two-thirds of the participants could imagine a treatment for themselves, especially those with former use and informed patients. Positive predictors for willingness were, as expected, a hope for better seizure control, but also ideas of relaxation and mood stabilization. This shows

Table 3
Stepwise regression analysis in willingness to take medical cannabis.

Dependent variable	Model	Predictors	Beta-coefficient	t-Value	Significance
Willingness to take medical cannabis	F = 34.2510	Sex	0.116	−2.739	0.000
	P = 0.000	Seizure improvement	0.346	7.200	0.000
	Square = 0.538	Relaxation	0.258.	5.877	0.000
		Mood	0.189	4.112	0.000
		Fear of addiction	−0.195	−3.900	0.000
		Fear of delirant intoxication	−0.172	−3.441	0.001
		Tolerability	0.127	2.750	0.006

Stepwise regression analysis. Analyzed variables: sex, age, education, duration of epilepsy, seizure freedom, seizure frequency (categories), number of previously prescribed anticonvulsants, knowledge of medical cannabis in general, fear of side effects, fear of addiction, fear of delirant intoxication, hope for seizure improvement, hope for relaxation, hope for mood improvement, tolerability, hope for delirant intoxication. Variables were entered for probability ≤ = ;0.050, variables were removed for probability ≥=; 0.100.

again that the perception of medical cannabis reflects the perception of recreational cannabis and perhaps the patients hope to profit from health issues as well as from additional recreational benefits.

Prevalence of cannabis use differs depending on legislative, culture, and religion. A population-based survey showed a life time prevalence of cannabis use of 4.3%. The majority uses it for recreational use only and just few for medical purposes only [24]. The frequency of life time cannabis use is lower in our population of patients with chronic neurologic disease than in the general population. Perhaps this is due to patients' comprehensive healthcare regulations which say 'no drugs', 'no alcohol'. Subanalysis in actual cannabis users on purpose (recreational only versus medical only) does not differ significantly from the general population data. Consistent to previous studies, the majority of medical cannabis users in our group reported corecreational use [24,25]. This suggests that wishes towards improvement of health condition go hand in hand with satisfaction of lifestyle wishes. Even though these reflections of patients can be well-understood, this mixture will stand against a way of providing larger groups with medical cannabis as insurances and health politicians will point at the well-being idea as a reason for contradiction or nonreimbursement.

As revealed by regression analysis, the willingness to be treated with medical cannabis appeared to be driven by beliefs of recreational cannabis, especially botanical cannabis, again reflecting the above mentioned hope of desired side effects. In line with this, negative predictors for willingness were attached to known adverse side effects of cannabis in general respectively. Concerning the study data, as least for some parts of cannabis, e.g. synthetized or botanical CBD, these hopes (relaxation, mood) and fears (addiction, delirant intoxication) lack basis. Interestingly, in our population, men were more often willing to be treated with medical cannabis than women. It is well-known that men are more likely to use cannabis than women, whereas data on sex difference in medical versus recreational use are not consistent [25,26].

5. Conclusion

Demand and interest in medical cannabis is high. A differentiation between cannabis in whole versus extracts as well as botanical versus synthetical origin needs to be carried out to understand the capability of medical cannabis as an acceptable alternative treatment for severely affected epilepsy patients. In order to avoid prejudices and potentially harmful self-medication, physicians and healthcare professionals are called to become familiar with the substance and to inform patients appropriately.

Conflict of interest

The authors declare that the research was conducted in the absence of any financial or commercial interest that could be a potential conflict of interest.

RvW has received fees as a speaker or consultant for Cerbomed, Desitin, Eisai, UCB.

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We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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