Prevalence of Cannabidiol (CBD) consumption and cancer patients' expectations in one Oncology Day-Hospital: A cross-sectional study and questionnaire validation

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Abstract

Purpose: The growing interest of cannabidiol (CBD) in medical care prompted french health authorities to explore the potential of CBD in cancer-related severe symptoms. This study aimed to assess the prevalence of CBD use among cancer patients with potential associated factors and to measure the cancer patient's health literacy (HL) on CBD consumption.

Methods: In a prospective study in oncology day-care hospital including patients from October 29th to December, 20th 2021, we collected demographic, biological and oncological characteristics. Patient CBD HL was measured by the hetero-questionnaire 8-item-CBD HL scale (HLS-8-CBD) whose conception has been validated by a psychometric analysis.

Results: Among 363 participants, 20 patients (5.5%) reported CBD use. Factors associated with CBD use were: age <60yrs (Odd Ratio=7.80[1.36-13.32], $p<10^{-4}$ versus ≥60yrs), smoking history (OR=5.53[1.81-16.88], p<0.01) and no smoking cessation (OR=5.07[1.66-15.46], p<0.01). CBD use was also associated with a better CBD total HL score than non-users (pvalue=0.02).

Conclusion: Identification of factors associated with CBD use and a relatively high patient CBD HL in CBD users showed that CBD use in cancer patients care represented a new concern and should enhance health professionals to consider CBD with its associated drug-related problems.

Introduction

Despite substantial advances in supportive care in oncology, many patients still suffer from symptoms caused by cancer and anticancer treatment. Some patients diagnosed with cancer use complementary and alternatives medicines (CAM) to manage cancer-associated disorders (e.g. pain, gastrointestinal, sleep disorders…), and anticancer treatment-related adverse effects (AE). CAM could lead to Drug-Related Problems (DRP) such as AE and Herb-Drug Interaction (HDI) with anticancer treatment (Bar-Sela et al. 2020; Bradish et Cheng 2014). The use of medicinal cannabis has been widely studied and debated for cancer patients(Subbiah et al. 2020). Different countries have implemented experimental and sometimes full access to medical cannabis (Ablin et al. 2016; Krcevski-Skvarc et al. 2018). More recently, France has launched experiments on the use of medical cannabis in five therapeutic indications (refractory neuropathic pain, refractory or treatment resistant epilepsy, non-resolutive symptoms caused by cancer or anticancer treatments, palliative care and severe spasticity) and for the management of targeted symptoms (pain, fatigue, nausea and vomiting, sleep disorders, loss of appetite, stress and anxiety). At the same time, Cannabidiol (CBD) was approved by French Parliament in February 2022 leading to the prompt emergence of several CBD products in open access shops and declared by their owners for medical or recreational care.

The main phytochemicals extracted from *Cannabis sativa* are CBD and Δ9-tetrahydrocannabidiol (THC). Compared to THC, CBD has psychoactive properties without intoxicating effect that could be welcomed for a potential use in supportive care for cancer patients (Pertwee 2004; Russo et Guy 2006). Meanwhile,

several studies have advocated CBD use as CAM for its sedative, anti-inflammatory, antispasmodic, appetite stimulant, and anticonvulsant activities and mood improving qualities (Abrams 2016; Fortin et al. 2021). Indeed, CBD has several mediators in the nervous system and gastrointestinal tract that regulate neural, digestive, and immunologic systems (Guindon et Hohmann 2009; Starowicz et Przewlocka 2012; Vučković et al. 2018). HDI have already been described and could enhance health professionals' awareness regarding CBD use (Micallef et al. 2022; Opitz et al. 2020; Pourroy et al. 2017). Moreover CBD-based products are proliferating in our country regarding french regulatory changes and to date, there is no available data regarding the use of CBD in this specific subpopulation. A first study related the issue of predictive factors of CBD use and explored the potential impact of health literacy (HL) in this consumption in oncological context (Sukrueangkul et al. 2022). Indeed, it is now well-knowed that health information can be used by people in order to improve their understanding of their own health and engage in self-management. HL is a concept which corresponds to adequate cognitive and social skills underlying the motivation and ability of individuals. It helps understanding how to promote and maintain good health in the general population.

This study aimed to describe CBD use among cancer patients receiving anticancer treatment in oncology Day-care unit. Furthermore, we also assessed cancer patients' knowledge about the CBD medical use in the literacy scope by the use of a HL questionnaire validated by psychometric analysis (NCT05407298).

Material And Methods

Study design and participants

A prospective cross-sectional study was conducted from 29th October 2021 to 20th December 2021 in one oncology day-hospital of a tertiary center receiving adult cancer patients with blood, digestive or thoracic cancers. All patients (> 18 years old) who received anticancer treatment were asked by pharmacists to complete a hetero-questionnaire anonymously. Patients who received an anticancer drug with a very short administration time (typically subcutaneous 5-azacitidine, bortezomib or monoclonal antibodies), patients who could not speak and understand French or were unable to communicate clearly or refused to participate were excluded.

Variables assessed

Morphological characteristics were collected: age, sex, body mass index (BMI). Tumor characteristics such as anticancer therapy indication, primary solid tumor location or type of blood cancer, curative or palliative care strategy, presence of metastases, anticancer treatment strategy were collected. Biological data collected at baseline (before the first cycle of anticancer therapy) were Serum Glutamate Pyruvate Transaminase (SGPT), Serum Glutamo-oxaloacetate Transferase (SGOT), gamma-GT, bilirubinemia, albuminemia, alkaline phosphatases, serum creatinine and renal clearance. We also collected administrative data as distance from hospital to patient home, type of housing (rural, urban) and socio-professional category definied by the INSEE (French National Institute for Statistics and Economic Research).

Development of the questionnaire: Content validity

The 8-item-CBD HL scale (HLS-8-CBD) was built by a multidisciplinary focus group constituted of oncologists, clinical pharmacists, oncology nurses and one onco-psychologist to identify the most important CBD HL-related factors to capture in a questionnaire. This was a hetero-questionnaire with 8 questions and five-point Likert-type answers (see in Supplementary data). Pharmacists conducted the interviews and completed the surveys. Four questions dealt with the informative dimension of CBD: evaluation of the information on CBD received from health-professionals, relatives or the media, and ability to assess the information received. Four questions dealt with their feelings about a drug-related aspect (the occurrence of adverse effects related to cancer treatment, HDI, suboptimal anticancer treatments or intoxication (occurrence of CBD adverse effects) of their anticancer treatments). The second part of the survey aimed to describe CBD users (desired effects, type of supply and form, frequency of use, start of use and if if the oncologist was aware about this consumption).

Cannabidiol health literacy evaluation

To quantify HL, we performed a questionnaire structured in distinct parts that explored dimensions of the object or instrument being measured. Answers constituted an overall score of the scale that was analyzed in this study. Answers to each question (all have 5-point Likert-type responses) were allocated a value with a range of 1 (worst) to 5 (best) as follows according to the type of response: Never = 1; to Often = 5 or Very unlikely = 1; to Very Likely = 5 or Very unsatisfactory = 1; to Very satisfactory = 5. These response were configured as a 5-point scale that indicated the extent to which the respondent was aware/informed/agrees or not with the item (Ishikawa et al. 2008; Suka et al. 2013). Higher scores indicated a higher level of CBD knowledge, use and skills.

Statistical analysis

Descriptive and logistic regression analyses

Quantitative variables were described as mean with standard deviation (SD) or median with interquartile range and minimum and maximum according to the distribution of the variable and qualitative variables as number and percentage. Student test was used to compare means standard deviation and Fischer's exact test to compare percentages between CBD users and non-users. Prevalence, odds ratios (ORs) and 95% confidence intervals (CIs) were used to determine factors associated of CBD use. Univariate and multivariate logistic regression models were used to obtain unadjusted OR_s and adjusted OR_s.

Health literacy score (HLS-8-CBD) validation: psychometric analysis and construct validity

An exploratory Factor Analysis (EFA) was performed to identify the latent relational structure among the 8 items of the HLS-8-CBD score as suggests literature (Suka et al. 2013). We retained all factors that accounted for at least 5% of variance, if confirmed by the scree plot. We retained all questions with at least modestly loadings on each factor ($r \geq 0.30$). Subscale scores were determined (Informative Score

(Score-I), Critical Score (Socre-C)) based on each factor and internal consistency was assessed for all subscales' score.

Reliability

EFA with promax rotation was performed to examine the factor structure of the HLS-8-CBD. Internal consistency was purchased by Cronbach's alpha (a value ≥ 0.7 means a satisfactory consistency) (Terwee et al. 2007). Floor and ceiling effects have been determined for subjects with the lowest and highest scores. A percentage > 15% in lowest or higher score indicated that the effect has to be considered (Terwee et al. 2007).

Validity

The construct validity of the HLS-8-CBD was achieved by confirmatory factor analysis. The adequacy of the model was assessed by the comparative fit index (CFI), Tucker Lewis Index of factoring reliability (TLI), standardized root mean square residuals (SRMR) and root mean square error of approximation (RMSEA) (see Supplementary Methods). All statistical analyses and confirmatory factor analysis were performed using R v4.1.0 software®.

Results

Subjects

Population Characteristics

363 patients were included in this study (Fig. 1). Mean age was 65.2 ± 12.1 years with a male/female ratio of 1.5. 44% of patients had a history of tobacco smoking, of whom 66.2% had quit. The majority of patients were retired (65.9%) and married (55.0%). The most frequent types of cancers were blood cancers (40.7%), non-small cell lung cancers (18.1%) and colorectal cancers (15.1%). The prevalence of CBD users in the population study was 5.5% (n = 20) (see Table 1).

Table 1
Characteristics of population study

CHARACTERISTICS	GLOBAL COHORT *n (%)*	UNMATCHED PATIENTS		
		CBD USERS n (%)	CBD NON-USERS n (%)	P-VALUE*
Patients	363	20 (5.5)	343 (94.5)	-
Socio-demographic characteristics				
Age (means ± standard deviations) in years	65.20 ± 12.10	52.30 ± 12.48	65.95 ± 11.67	$< 10^{-3}$
18–59 yrs	93 (25.6)	14 (70.0)	79 (23.0)	$< 10^{-5}$
60–69 yrs	119 (32.8)	4 (20.0)	115 (33.5)	
>70 yrs	151 (41.6)	2 (10.0)	149 (43.5)	
Male	219 (60.3)	16 (80.0)	203 (59.2)	0.50
Smoking history	160 (44.1)	16 (80.0)	144 (42.0)	$< 10^{-2}$
Smoking cessation	104 (66.2)	5 (25.0)	99 (28.9)	$< 10^{-2}$
Distance from home to the hospital less than 50 km	190 (52.2)	11 (55.0)	179 (51.9)	0.98
Housing				
Rural	228 (62.8)	12 (60.0)	216 (63.0)	0.98
Urban	135 (37.2)	8 (40.0)	127 (37.0)	
Socio-professional categories				
Farmers	10 (2.8)	2 (10.0)	8 (2.3)	$< 10^{-2}$
Craftsmen, merchants and company managers	12 (3.3)	1 (5.0)	11 (3.2)	
Executives and higher intellectual professions	7 (1.9)	1 (5.0)	6 (1.7)	
Employees	14 (3.9)	1 (5.0)	13 (3.8)	
Workers	24 (6.6)	4 (20.0)	20 (5.8)	
Intermediate professions	12 (3.3)	1 (5.0)	11 (3.2)	

**Student t-test have been made to compare mean and standard deviations between both groups. Fisher exact test have been made to compare percentages of each group.*

¶ *Renal clearance have been estimate by the MDRD (Modification of diet in renal disease) equation*

CHARACTERISTICS	GLOBAL COHORT *n (%)*	UNMATCHED PATIENTS		
Retired	240 (66.1)	5 (25.0)	235 (68.5)	
No professional activity	27 (7.4)	4 (20.0)	23 (6.7)	
No information	17 (4.7)	1 (5.0)	16 (4.8)	
Marital status				
Single	25 (6.9)	3 (15.0)	22 (6.4)	$< 10^{-2}$
Partner	37 (10.2)	8 (40.0)	29 (8.5)	
Divorced	7 (1.9)	1 (5.0)	6 (1.7)	
Married	200 (55.0)	5 (25.0)	195 (56.9)	
Separated	6 (1.6)	0 (0.0)	6 (1.7)	
Widowed	20 (5.8)	0 (0.0)	20 (5.8)	
Not known	68 (18.6)	3 (15.0)	65 (19.0)	
Oncological characteristics				
Tumor location				
Colorectal	55 (15.1)	3 (15.0)	52 (15.2)	0.74
Stomach	7 (1.9)	1 (5.0)	6 (1.7)	
Hematological	148 (40.7)	8 (40.0)	140 (40.8)	
Hepatic	24 (6.6)	1 (5.0)	23 (6.7)	
Esophagus	9 (2.5)	0 (0.0)	9 (2.6)	
Pancreas	44 (12.1)	1 (5.0)	43 (12.5)	
Thoracic	66 (18.1)	5 (25.0)	61 (17.8)	
Other	10 (3.0)	1 (5.0)	9 (2.7)	
Strategy				
Curative	236 (65.0)	14 (70.0)	222 (64.7)	0.87
Palliative	127 (35.0)	6 (30.0)	121 (35.3)	
Metastases	125 (34.4)	7 (35.0)	118 (34.4)	0.90

**Student t-test have been made to compare mean and standard deviations between both groups. Fisher exact test have been made to compare percentages of each group.*

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CHARACTERISTICS	GLOBAL COHORT *n (%)*	UNMATCHED PATIENTS		
Surgery	120 (33.1)	8 (40.0)	112 (32.7)	0.67
Morphological characteristics (mean ± standard deviation)				
Weight(kg)	75.38 ± 17.34	77.47 ± 13.72	75.55 ± 17.53	0.35
Size(m)	1.70 ± 0.092	1.73 ± 0.10	1.70 ± 0.0092	0.23
BMI(kg/m²)	25.95 ± 5.36	24.25 ± 3.46	26.05 ± 5.43	0.04
Underweight (< 18,5)	16 (4.5)	1 (5.0)	15 (4.4)	0.24
Normal (18,5–24,9)	152 (41.9)	11 (55.0)	141 (41.1)	
Overweight (25–29,9)	119 (32.7)	7 (35.0)	112 (32.7)	
Obese (≥ 30)	76 (20.9)	1 (5.0)	75 (21.8)	
Biological characteristics				
Serum creatinine value (µmol/l)	84.97 ± 52.30	75.62 ± 17.52	85.51 ± 53.60	0.05
Renal clearance (ml/min)¶	100.24 ± 39.45	106.59 ± 27.78	99.86 ± 40.03	0.32
Renal dysfunction				
Stade I (≥ 90 ml/min)	204 (56.2)	14 (70.0)	190 (55.4)	0.56
Stade II (60–89 ml/min)	118 (32.5)	5 (25.0)	113 (32.9)	
Stade III-IV (< 60 ml/min)	41 (11.3)	1 (5.0)	40 (11.7)	

**Student t-test have been made to compare mean and standard deviations between both groups. Fisher exact test have been made to compare percentages of each group.*

¶ *Renal clearance have been estimate by the MDRD (Modification of diet in renal disease) equation*

Knowledges of patients about CBD

Included patients had never or rarely received information about CBD from a health professional (2.5%, n = 9), in opposition with relatives (84.0%, n = 305) or other sources (69.1%, n = 251). The quality of information about CBD use was considered to be very unsatisfactory or unsatisfactory for 34.2% (n = 124) of patients and was satisfactory for only 8.3% (n = 30) of respondents. CBD impact on the occurrence of cancer treatments-related AE was considered more likely/very likely than very unlikely/improbable (14.0% vs. 6.1%). The same results were found for other drug dimension's questions (see Table 2).

Table 2
Patient knowledge

INFORMATION DIMENSION	Never n (%)	Rarely n (%)	No idea n (%)	Sometimes n (%)	Often n (%)
Health professional	350 (96.4)	4 (1.1)	0 (0.0)	8 (2.2)	1 (0.3)
A relative	286 (78.5)	20 (5.5)	0 (0.0)	48 (13.2)	9 (2.8)
Other source	190 (52.3)	61 (16.8)	1 (0.3)	103 (28.4)	8 (2.2)
	Very unsatisfactory n (%)	**Unsatisfactory n (%)**	**No opinion n (%)**	**Satisfactory n (%)**	**Very satisfactory n (%)**
Quality of information on CBD use	47 (12.9)	77 (21.2)	209 (57.6)	30 (8.3)	0 (0.0)
DRUG DIMENSION	**Very unlikely n (%)**	**Unlikely n (%)**	**No opinion n (%)**	**Likely n (%)**	**Very likely n (%)**
Impact on the occurrence of adverse events related to cancer treatments	9 (2.5)	13 (3.6)	290 (79.9)	40 (11.0)	11 (3.0)
Be the cause of drug interactions	6 (1.7)	10 (2.8)	288 (79.3)	47 (12.9)	12 (3.3)
Represent a risk of treatment ineffectiveness	10 (2.8)	16 (4.4)	284 (78.2)	41 (11.3)	12 (3.3)
Represent a risk of treatment overdose	5 (1.4)	10 (2.8)	294 (81.0)	43 (11.8)	11 (3.0)

Factors associated with CBD use

There were significant differences between CBD users and non-users. CBD users were younger (p_{value} = 0.001), more likely to have smoking history (p_{value} = 0.01) and a smoking cessation (p_{value} = 0.01). Socio-professional categories (p_{value} = 0.01) and marital status repartition (p_{value} = 0.01) also differed between the two groups as shown in details in Table 1. Logistic regression models revealed various factors associated with CBD use: age < 60 years (OR = 7.80[1.36–13.32], $p < 10^{-4}$ vs ≥ 60yrs), smoking history (OR = 5.53 [1.81–16.88], p < 0.01) and not being weaned (OR = 5.07 [1.66–15.46], p < 0.01). In the multivariate analysis, being 60 (OR = 6.40[2.34–17.47], $p < 10^{-3}$ vs ≥ 60yrs) and with a smoking history (OR = 4.26[1.36–13.32], p = 0.013) were confirmed as potential predictors for CBD use (see Table 3).

Table 3
Univariate and multivariate logistic regression results

VARIABLE*	CODAGE (N OF PATIENTS)	UNIVARIATE ANALYSIS OR NON-ADJUSTED	P-VALUE	MULTIVARIATE ANALYSIS OR ADJUSTED	P-VALUE
Age	continuous variable (363)	0.93 [0.90–0.96]	$< 10^{-5}$		
Age	> 70 yrs (270)	1	$< 10^{-4}$	1	$< 10^{-3}$
	18–59 yrs (93)	7.80 [1.36–13.32]		6.40 [2.34–17.47]	
Smoking history	No (203)	1	10^{-2}	1	0.013
	Yes (160)	5.53 [1.81–16.88]		4.26 [1.36–13.32]	
Smoking cessation	Yes (104)	1	10^{-2}		
	No (54)	5.07 [1.66–15.46]			
Socio-professional categories	Retired (240)	1	10^{-2}		
	No professional activity (27)	8.17 [2.05–32.58]	0.20		
	Craftsmen, merchants and company managers (12)	4.27 [0.46–39.76]	0.08		
	Executives and higher intellectual professions (7)	7.83 [0.79–77.73]	0.26		
	Employees (14)	3.62 [0.39–33.24]	10^{-2}		
	Workers (24)	9.40 [2.34–37.81]	10^{-2}		
	Farmers (10)	13.43 [2.21–81.56]	0.20		
	Intermediate professions (12)	0.46 [0.03–39.76]			

* Only variables with significant p-value in univariate analysis have been presented in this table. All OR_s of categorical variables are presented with a reference category to assess the risk of CBD use according each category.

VARIABLE*	CODAGE (N OF PATIENTS)	UNIVARIATE ANALYSIS OR NON−ADJUSTED	P-VALUE	MULTIVARIATE ANALYSIS OR ADJUSTED	P-VALUE
Marital status	Single (25)	1	0.37		
	Partner (37)	1.93 [0.46–8.16]	0.90		
	Divorced (7)	1.17 [0.10-13.36]	0.02		
	Married (200)	0.18 [0.04–0.80]			

* Only variables with significant p-value in univariate analysis have been presented in this table. All OR_S of categorical variables are presented with a reference category to assess the risk of CBD use according each category.

Oncological characteristics had no significant impact on CBD use (see Table 4). The main expectations from CBD effects by users were pain reduction (n = 8) and sleep disorders reduction (n = 8). Most CBD users (n = 11) consumed CBD once or several times a day, including n = 5 since the announcement of the disease diagnosis and n = 4 since the start of anticancer treatment. Finally, only n = 5 patients informed their referring oncologist about the CBD use.

Table 4
Description of CBD user's characteristics

CHARACTERISTICS	CBD USERS* N (%)
Desired effects	
Reduction of pain	8 (42.1)
Reduction of undesirable effects linked to treatments	1 (5.3)
Stimulation of immunity	0 (0.0)
Promote the effectiveness of treatments	0 (0.0)
Treatment of cancer	1 (5.3)
Other	13 (68.4)
Supply	
Specialist shop	7 (36.8)
Donated by a relative	4 (21.1)
Pharmacy	2 (10.5)
Internet	2 (10.5)
Other	4 (21.1)
Frequency of use	
1 to several times a day	11 (57.8)
At least once a week	4 (21.1)
At least once a month	4 (21.1)
Form	
Vaped	5 (26.3)
Sprayed	2 (10.5)
Tablet	2 (10.5)
Flower	2 (10.5)
Oil	4 (21.1)
Herbal tea	4 (21.1)
Start of consumption	
Before the disease	9 (47.4)

**Characteristics of 19 CBD users collected because one didn't want to share these information*

CHARACTERISTICS	CBD USERS* N (%)
Since the announcement of the disease	5 (26.3)
Since the start of treatment	4 (21.1)
Since a change in the disease	1 (5.2)
Information to your oncologist	
Yes	5 (26.3)
No	14 (73.7)
**Characteristics of 19 CBD users collected because one didn't want to share these information*	

Exploratory factor analysis validation

Reliability

The EFA hypotheses were completed to consider the HLS-8-CBD items as appropriate for factor analysis. The scree plot of EFA analysis confirmed that HLS-8-CBD items should be separated into two dimensions (Fig. 2), namely the "Informative Dimension" (score-I) and the "Critical Dimension" (score-C). We divided the score results in two parts: score-I and score-C as shown in Table 5. Internal consistency reliability analysis of the HLS-8-CBD using the 8 items revealed a Cronbach's alpha of 0.69. We obtained Cronbach's alphas for each score as follows: score-I = 0.40; score-C = 0.87(see Table 5 and Supplementary Methods).

Table 5
Internal consistency of the 8-item-CBD health literacy scale (HLS-8-CBD)

CBD Literacy scale Score	Mean ± standard deviation	Coefficient Cronbach's α	Lowest score n (%) / Highest score n (%)
Informative dimension score Q1 – Q4	7.37 ± 2.40	0.40	4(6.6) / 16(0.8)
Critical dimension score Q5 – Q8	12.42 ± 2.00	0.87	4(0.3) / 20(2.5)
Total health literacy score Q1 – Q8	19.75 ± 3.50	0.69	8(0.3) / 36(0.3)

Validity

The confirmatory factor analysis revealed an acceptable fit of the two-factor model (Supplementary Methods). We found no floor or ceiling effects in the response of all items of the HLS-8-CBD score. We obtained a mean total HL score of 19.75 (SD = 3.75). CBD users have a significant higher score-I and total HL score than CBD non users (see Table 6). No significant differences were found in mean score-I, score-C and overall score when age and sex were taken into account (see Supplementary Table S2). There were significant differences in score-C (p = 0.04) and total HLscore (p = 0.01) according to the type of primary cancer. Patients with gastric cancer and hepatocellular carcinoma had the highest literacy scores (see Supplementary Table S3).

Table 6
CBD Literacy Scale Score according to the CBD consumption

CBD Literacy scale Score	**CBD users (n = 20)**	**CBD NON-USERS (n = 343)**	**p_{value}***
Mean ± standard deviation			
Informative dimension score Q1 – Q4	10.00 ± 3.52	7.22 ± 2.23	0.002
Critical dimension score Q5 – Q8	12.50 ± 2.93	12.42 ± 1.94	0.90
Total health literacy score Q1 – Q8	22.50 ± 4.84	19.63 ± 3.26	0.02
* *Student t-test have been made to compare mean and standard deviations between each group*			

Discussion

We found a prevalence of 5.5% of CBD users among cancer patients receiving anticancer treatment in our study. To our knowledge, this is the first study exploring CBD use in the cancer population in France since the beginning of the experiment. This prevalence is lower than reported in a recent published Danish study with 13% of patient that report cannabis use, but without distinction between CBD alone and other cannabis extracts (Nielsen et al. 2022). Subbiah et al. reported 24.7% of users among 154 cancer patients treated in one California hospital but CBD use was found in only 58% of cases (Subbiah et al. 2020). The greater access to cannabis products in California could have enhanced its use in comparison with France. Indeed, France has just authorized medical experimentation of CBD/THC products while medical cannabis has been authorized and promoted in California over than 25 years. The French Observatory of Drugs and Addictive Behaviors found that 44.8% of the French population had at least one experience with cannabis use, including 11% of which were regular users. Finally, only 25% of the cancer patients in the present study disclosed CBD use to their referring oncologist, probably in relation with the current strict regulation.

The present study reports associated factors of CBD use in the study population. Cancer patients < 60 or with smoking history were more likely to use CBD with no correlation between smoking cessation and CBD use in multivariate analysis. These results have to be confirmed by larger studies but the trend of the association between both may indicate the potential relation between multiple addictions and CBD use in cancer patients. Regarding the initiation to CBD, more than half of CBD users (52.6%) started CBD after the cancer diagnosis.

Motivations in the present study were pain and nausea/vomiting (NV) prevention, similar to other studies. Indeed cancer-related pain is one of a leading concern in supportive care in cancer that could explain interest of CBD or THC extract use to relief burden. A multicenter randomized controlled trial including 43 patients showed a decreasing pain severity in the THC/CBD patients group but with no significant results(Johnson et al. 2013). A recent systematic review revealed three studies treated cancer-related pain and showed improvement in pain measures with cannabinoids use compared with placebo(Whiting et al. 2015). Many cancer patients also experienced neuropathic cancer-related or anticancer treatment-related. Deshpande et al. found a positive impact of medical cannabis use in refractory neuropathic pain (Deshpande et al. 2015). Regarding cannabis use for nausea, results appear contradictory among studies. A systematic review including thirty randomized controlled trials also found that cannabinoids were more effective than placebo or conventional antiemetics in reducing chemotherapy-induced NV (Machado Rocha et al. 2008). However, in Johnson et al. study, there were no significant decrease of NV in CBD/THC and THC group (Johnson et al. 2013). All these studies or trials included small number of patients in their design which may affect the interpretation of the result.

The consumption of CAM during an anticancer treatment procedure increases the risk of HDI. CBD is known as a weak or moderate inhibitor of CYP3A4, 2C19, 2C8 and 2C9 as well as P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) (Holland et al. 2006; Iffland et Grotenhermen 2017; Jiang et al. 2013; Yamaori et al. 2011). Furthermore, CBD is mainly metabolized in the liver, by the major isoenzymes CYP2C19 and CYP3A4, and to a lesser extent by CYP1A1, CYP1A2, CYP2C9, and CYP2D6 (Zendulka et al. 2016). Therefore the scoping review by Brandon J et al. identified various HDI between cannabidiol and anticancer drugs (Opitz et al. 2020).

The present study proposed one HL scale to measure the knowledge about CBD use and potential risks and impact on CBD use in oncological context. The recent Danish study found similar results in associated factors (smoking history) (Nielsen et al. 2022; Vitetta et al. 2022). By using validated scales for health-related quality of life, they focused on potentials quality of life and psychiatric dimensions to explain CBD consumption in cancer patients. Cancer-related pain management was identified as the most desired effect by CBD users (Vitetta et al. 2022). This study also showed a correlation between CBD use and a low quality of life. Indeed, low literacy has negative impacts on various patient behaviors and health outcomes, and HL can be considered a protective factor for optimal care (Marciano et al. 2019; Soones et al. 2017). Some studies have already used HL to determine whether it could be a factor influencing demand for CAM or specifically medical cannabis use among cancer patients (Sharoni et al.

2019; Sukrueangkul et al. 2022). They showed that increased demand and CBD use was correlated with high HL in cancer care.

Despite the acceptable model fit from the EFA, the “Informative dimension” (score-I) was unsatisfactory with a Cronbach α of 0.4. This could be explained by the item Q4 which had the lowest factor load among the 8 items (r=-0.03). We kept this item in our psychometric analysis but this sentence should be rewritten to better capture this informative dimension. No significant differences in health scores were found according to sex and age. This is in contradiction with literature describing women with significantly higher scores than men regardless of age due to a greater sensitivity to information seeking (Galdas et al. 2005; Verbrugge 1982). Higher HL scores were observed among CBD users showing a better knowledge of potential risks and benefits among consumers. Similar results were obtained by Sukrueangkul et al. who showed that demand for CBD use increased with HL scores regarding medical cannabis use (Sukrueangkul et al. 2022). However, sex (40% women vs 62% men) and socio-cultural differences differ from our study. HLS-8-CBD results may encourage health professionnals to promote more communication and informations about CBD use as part of potential supportive care in cancer. However, these also may engage them to prior identify at initial oncological consultation patients who eventually could be interested and to give verified and validated informations concerning CBD use and risks.

The prospective design of the study represents a real strength ensuring the selection of a representative sample of cancer patients and making it possible to propose and collect the answers to a questionnaire previously drawn up by a multidisciplinary group and validated. This study has some limitations. First, the information bias (or collecting bias) represented an important limitation to our study because it was a hetero-evaluation. Furthermore, in our psychometric analysis, we didn’t explore the test-retest reliability that could have minimized these biases. Another limitation concerned the statistical power of our small sample size comparisons, particularly in the CBD user group (20 subjects). Although we used adapted statistical test to the small number of subjects (χ2test with Yates’s correlation, Fischer exact test, Student test). We are aware that our results represent a potential trend that must be confirmed by larger-scale study.

Conclusion

In the present study, we highlighted a low prevalence of CBD consumption in cancer patients. Our 8-item-CBD HL scale also highlighted the importance of patients’ access to information and dialogue with referring health professionals.

Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

Antoine Le Bozec, Marie Guedon, Mathias Brugel, Olivier Bouché, Marine Perrier, Léa Aubert and Maeliss Laurent contributed to the study conception and design. Material preparation was realized by Antoine Le Bozec, Marie Guedon, Céline Mongaret, Mathias Brugel and Florian Slimano. Data analysis were performed by Antoine Le Bozec and Marie Guedon. The first draft of the manuscript was written by Antoine Le Bozec and Marie Guedon. Céline Mongaret and Florian Slimano commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

All data have been completed in accordance with the ethical principles from the Declaration of Helsinski. In accordance with the French regulatory related to clinical studies, the approval by an independent committee was not required. Database has been registered with the reference MR00425072022 according to the General Data Protection Regulation (RGPD register). The institutional review board at Reims University Hospital approved this study and the CANPADIOL study is registered on ClinicalTrials.gov (NCT05407298)

Consent to participate

Informed consent was obtained from all individual participants included in the study

Consent to publish

Consent to publish has been received from all participants should appear in the manuscript

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Figures

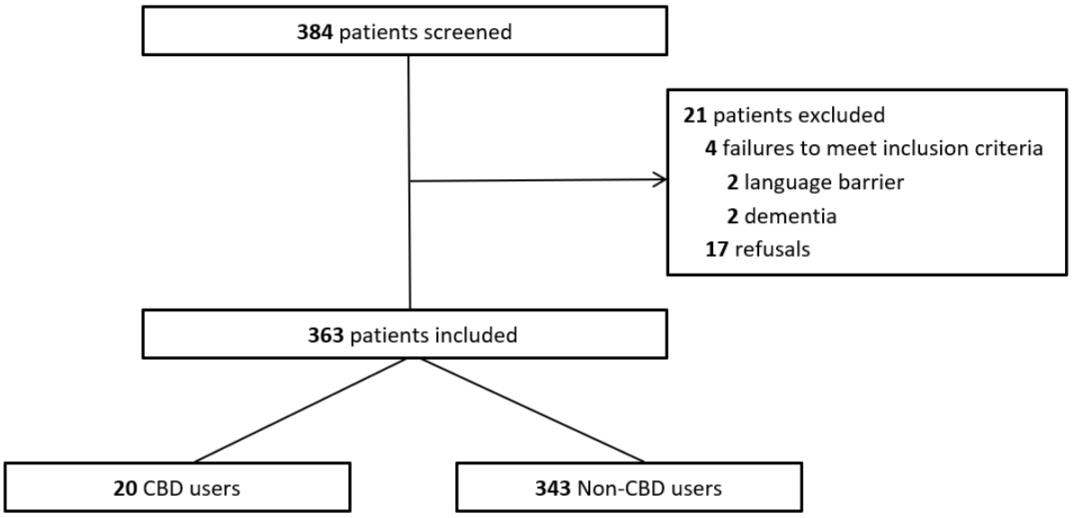

Figure 1 : Flow chart of population study

Figure 1

See image above for figure legend

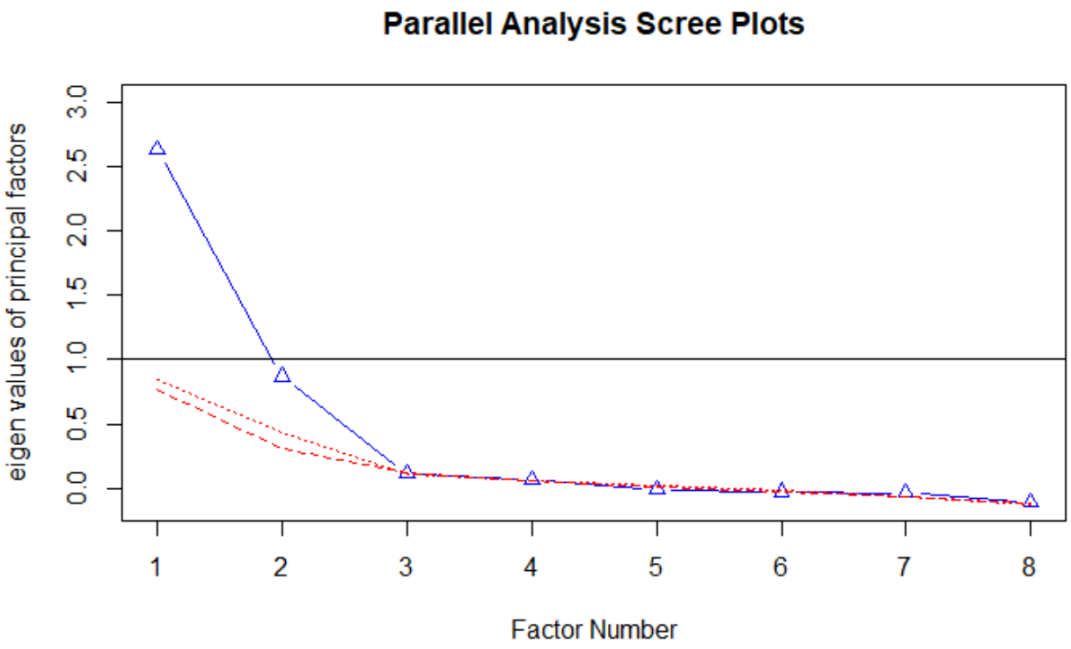

Figure 2: Scree plot of exploratory factor analysis

Figure 2

See image above for figure legend

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