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Therapeutic use of cannabidiol-based products in Brazil: a descriptive study, 2014-2017

Uso terapêutico de produtos à base de canabidiol no Brasil: estudo descritivo, 2014-2017

Daniel Marques Mota*

Renata de Morais Souza

Thiago Brasil Silverio

Augusto César Alves Arifa Coelho

Gabriella Hamú Giudice

Fernanda Maciel Rebelo

Agência Nacional de Vigilância Sanitária (Anvisa), Brasília, DF, Brasil

* **E-mail:** dmarques2003@yahoo.com.br

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ABSTRACT

Introduction: Little is known about the characteristics and clinical conditions of patients on therapeutic use of cannabidiol-based products in combination with other cannabinoids, despite a growing number of countries that have authorized the use of these products. **Objective:** This study describes the characteristics and clinical conditions of patients who obtained exceptional authorization from Anvisa to import cannabidiol-based products in combination with other cannabinoids for therapeutic use in Brazil. **Method:** A descriptive and retrospective study based on records of patients who obtained authorization from Anvisa to import cannabidiol-based products in association with other cannabinoids, between December 2014 and May 2017. The characteristics of the patients studied were: i) demographic (sex and age); ii) geographical (region and Federation Unit); iii) medical diagnoses of patients by ICD-10 codes; iv) medical specialties that prescribed the products to patients; and v) products intended for import by patients or caregivers (main products and country of importation). **Results:** 1,713 patients were identified, of whom 61.7% were aged ≤ 19 years. Epilepsy (62.9%), chronic pain (3.8%) and Parkinson's disease (3.6%) were the most frequent ICD-10 codes. Of the products requested for therapeutic use, 15 (57.7%) were not included in the Anvisa's Resolution. **Conclusions:** Patients who have obtained authorization from Anvisa to import cannabidiol-based products in combination with other cannabinoids are mostly under the age of 20 and suffering from epilepsy. These findings are in accordance with the determinations provided for in Resolution No. 2,113 / 2014 of the Federal Council of Medicine.

KEYWORDS: Brazilian Health Regulatory Agency; Cannabidiol; Cannabis; Epidemiology, Descriptive; Pharmaceutical Preparations

RESUMO

Introdução: Pouco se conhece sobre as características e as condições clínicas dos pacientes em uso terapêutico de produtos à base de canabidiol, apesar de um número crescente de países ter autorizado o uso desses produtos. **Objetivo:** Descrever as características e as condições clínicas dos pacientes que obtiveram autorização excepcional da Anvisa para importação de produtos à base de canabidiol em associação com outros canabinoides para uso terapêutico no Brasil. **Método:** Estudo descritivo e retrospectivo baseado nos registros de pacientes que obtiveram autorização da Anvisa para importação de produtos à base de canabidiol em associação com outros canabinoides, entre dezembro de 2014 e maio de 2017. As características dos pacientes estudadas foram: i) demográficas (sexo e idade); ii) geográficas (região e Unidade de Federação); iii) diagnósticos médicos dos pacientes por códigos da CID-10; iv) especialidades médicas que prescreveram os produtos aos pacientes; e v) os produtos com pretensão de importação pelos pacientes ou responsáveis (principais produtos e país de importação). **Resultados:** Foram 1.713 pacientes identificados, dos quais 61,7% apresentaram idade ≤ 19 anos. Os quadros de epilepsia (62,9%), dor crônica (3,8%) e doença de Parkinson (3,6%) foram os códigos da CID-10 mais frequentes. Entre os produtos solicitados para uso terapêutico, 15 (57,7%) não constavam em Resolução

da Anvisa. **Conclusões:** Os pacientes que obtiveram autorização da Anvisa para importação de produtos à base de canabidiol em associação com outros canabinoides são, na sua maioria, menores de 20 anos e que sofrem de epilepsia. Tais achados estão de acordo com as determinações da Resolução nº 2.113/2014 do Conselho Federal de Medicina.

PALAVRAS-CHAVE: Agência Nacional de Vigilância Sanitária; Canabidiol; Cannabis; Epidemiologia Descritiva; Preparações Farmacêuticas

INTRODUCTION

Cannabis sativa (popularly known as marijuana, hereafter referred to as Cannabis) is a plant with psychoactive properties containing at least 750 chemicals, including 104 cannabinoids like delta-9-tetrahydrocannabinol (THC) and cannabidiol[1]. Because it is included in the United Nations drug control list, under the treaties of the Single Convention on Narcotic Drugs of 1961, the Convention on Psychotropic Substances of 1971, and the Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988[2], Cannabis is considered illegal in many countries[3].

Despite this recommendation, movements for the legalization of Cannabis for therapeutic purposes in countries like Canada, the Netherlands, and Israel have encouraged the scientific development of purified preparations, especially with regard to their concentrations of THC and cannabidiol[4], resulting in the marketing authorization of some medicines by regulatory agencies of several countries[3,5]. Denmark, Sweden, Norway, Finland and England have not legalized the use of Cannabis for therapeutic purposes. However, their regulatory agencies have authorized the sale of medication containing cannabidiol and other prescription cannabinoids[3]. The authorization was granted in 2010 and 2011 in England and Sweden, respectively[3].

In 2014, Brazil began discussing access to cannabidiol-based products for therapeutic use with the case of a five-year-old child with severe and rare epilepsy. Ever since then, significant changes in the regulation of access control to such products have been made by the Brazilian National Health Surveillance Agency (Anvisa)[6,7,8,9,10] to provide legal protection to patients and physicians and the regulation of access through imports, including only cannabidiol-based products in association with other cannabinoids. For example: Collegiate Board Resolution (RDC) n. 3, of January 26, 2015 was responsible for including cannabidiol in List C1 of substances under special control of the Ordinance of the Ministry of Health's Health Surveillance Secretariat (SVS/MS) n. 344, of May 12, 1998. Previously, cannabidiol was part of the banned substances for importation, exportation, marketing, compounding and use in Brazil, as per Lists E and F2 of said Ordinance. RDC n. 17, of May 6, 2015 defined the criteria and procedures for the exceptional importation of cannabidiol-based products in association with other cannabinoids by individuals for their own use, as long as they have a prescription signed by a legally qualified professional for health treatment.

In January 2017, Anvisa granted marketing authorization to Mevatyl® (THC, 27 mg/ml + cannabidiol, 25 mg/ml), as an oral solution (spray), making it the first Cannabis-based drug legally available in Brazil. This medication, marketed in other countries under the trade name of Sativex®, is indicated for the symptomatic treatment of moderate to severe multiple sclerosis-related spasticity[11]. Mevatyl® began to be marketed in the second half of 2017 with a black band on its package (indicating controlled substance) and its dispensation is subject to medical prescription through prescription A notification, as provided for in SVS/MS Ordinance n. 344/1998, and the patient's Informed Consent[11].

Little is known about the characteristics of patients and the clinical conditions in which they make therapeutic use of cannabidiol-based products in Brazil, despite the increasing demand observed in the Brazilian territory and in other countries, mainly due to their potential use in chronic diseases[3].

The objective of this study was to describe the characteristics and clinical conditions of patients who obtained exceptional authorization from Anvisa to import cannabidiol-based products in combination with other cannabinoids for therapeutic use in Brazil.

METHOD

This is a descriptive and retrospective study in which we used Anvisa's database of requests and exceptional authorizations to import cannabidiol-based products in association with other cannabinoids.

The data recorded between December 12, 2014 and May 11, 2017 were analyzed. The choice of the starting date coincides with Anvisa's internal technical guidance to grant a one-year import authorization for these products, which took place shortly thereafter, with the publication of Service Guideline n. 07, in December 19, 2014[6]. This regulation details the criteria for issuing an exceptional authorization for the importation of cannabidiol-based products in association with other cannabinoids, by individuals, for their own use, through an exception report previously approved by Anvisa's board chair[6].

The database was reorganized into a spreadsheet (Microsoft Office Excel®) where each patient was recorded in one row and each variable that characterized him/her occupied one column. The reorganization provided for two steps: 1) initial exploration of the data; and 2) standardization and creation of new variables in the database.

Initial exploration of the data

At this stage, aspects that needed to be corrected for proper data analysis were identified, thus minimizing the loss of

analyzed records: a) elimination of repeat (duplicate) records in the database, preserving important data for analysis; and b) incompleteness of data that triggered the insertion of necessary information from research in data sources, such as documents from the technical area of Anvisa and the electronic portal of the Brazilian Federal Council of Medicine (CFM), where medical specialties were searched[12].

Standardizing and creating variables in the database

Database standardization included the correction of misspelled data and typos. Medical specialties were checked, and if there were differences for the same professional, priority was given to the most specific specialty registered in the CFM website. For example, if a physician was registered as a pediatrician and a pediatric neurologist, we decided to make the standardization based on the latter. New variables were created, such as age group, geographical region, place of origin of the product, medical specialty, and chapters of codes of the International Classification of Diseases and Related Health Problems, 10th edition (ICD-10)[13].

The country's population average in the period (2014-2017) was used to compare the distribution of patients by gender with that of the general population, as well as to estimate the national and state average of patients who obtained Anvisa's exceptional authorization to import cannabidiol-based products in combination with other cannabinoids for every million inhabitants. The population projections were obtained from the website of the Department of Information Technology of the Brazilian Unified Health System (SUS) of the Ministry of Health (Datasus/MS)[14].

PesqCID software, version 2.4, of Datasus/MS was used to search and confirm the ICD-10 codes registered in Anvisa's database.

Patient characteristics were studied according to the following variables: i) demographics (gender and age); ii) geographical (region and state – UF); iii) medical diagnoses of patients by ICD-10 codes; iv) medical specialties that prescribed the products to patients; and v) products imported by patients or guardians (main products and country of importation). The imported products were identified by capital letters of our alphabet, aiming to minimize possible induction of the demand for one product or another.

Statistical analysis included central tendency and dispersion values and was performed using Gretl software, version 2017b. The proportional equality test based on Pearson's x^2 statistic was used to verify whether the response categories of each variable were equally distributed. A 5% significance level was used in the analyses.

The analyzed data were obtained in the context of health surveillance actions, a situation in which consideration by the Research Ethics Committee is not required. Ethical aspects of the National Health Council (CNS) Resolution n. 510, of April 7, 2016 were observed[15]. Results were presented without any individual identification of participants.

RESULTS

We found 1,713 patients registered in Anvisa's database, which means an approximate mean of 59 patients per month (1,713 patients/29 months). The age of 1,710 patients ranged from 0 to 101 years, with a median of 12 years and a mean of 22 years (standard deviation ± 22 years). There was no record of age information for three patients.

Table 1 shows the distribution of patients and the general population of Brazil during the study period, by age group and gender. Male predominance was found in the patient population (53.2%) and in most age groups. In the general population of Brazil there is a slight predominance of females (50.6%) and equal

Table 1. Distribution of patients and the general population of Brazil during the study period, by age group and gender. Brazil, 2014 to 2017 (N = 1,710 patients).

Age range (years)*	Patients %**		Total	Population % (mean 2014-2017)		Total (mean 2014-2017)
	Female	Male		Female	Male	
0 to 4	45.5	54.5	365	51.1	48.9	14,645,535
5 to 9	48.8	51.2	367	51.1	48.9	15,667,613
10 to 14	40.4	59.6	203	51.0	49.0	16,762,207
15 to 19	48.3	51.7	120	50.8	49.2	17,150,278
20 to 29	50.3	49.7	161	50.4	49.6	34,196,183
30 to 39	44.1	55.9	118	49.9	50.1	33,645,424
40 to 49	46.0	54.0	87	49.2	50.8	26,984,380
50 to 59	44.7	55.3	114	48.1	51.9	21,731,879
60 to 69	52.0	48.0	98	46.4	53.6	13,929,244
≥ 70	51.9	48.1	77	41.4	58.6	10,527,652
Total	46.8	53.2	1,710	50.6	49.4	205,240,393

* Three records did not provide data on patient age.
** Test equality of proportions: $x^2 = 7.559$ (9 gl, p = 0.581).

distribution of genders in the studied age groups. The percentage observed for both genders did not change according to the age of the patients, i.e., it is equally distributed across all age groups (p = 0.581). There was a predominance of patients aged ≤ 19 years (61.7%).

In terms of geographical origin, patients came mainly from the Southeast (56.0%), South (18.5%) and Northeast (11.2%) regions. The five states with the largest number of patients were, in this order: São Paulo (N = 451), Rio de Janeiro (N = 318), Minas Gerais (N = 173), Paraná (N = 136) and Rio Grande do Sul (N = 100).

The Federal District (22.4/1 million inhabitants), Rio de Janeiro (19.2/1 million inhabitants), Mato Grosso do Sul (13.1/1 million inhabitants), Paraná (12.1/1 million) and Santa Catarina (11.7/1 million) had the highest ratios of patients per 1 million inhabitants. The national mean from 2014 to 2017 was 8.3 patients/1 million inhabitants. Another five states recorded values higher than the national mean: Goiás (11.1/1 million), Piauí (10.3/1 million), São Paulo (10.1/1 million), Paraíba (9.0/1 million) and Rio Grande do Sul (8.9/1 million inhabitants).

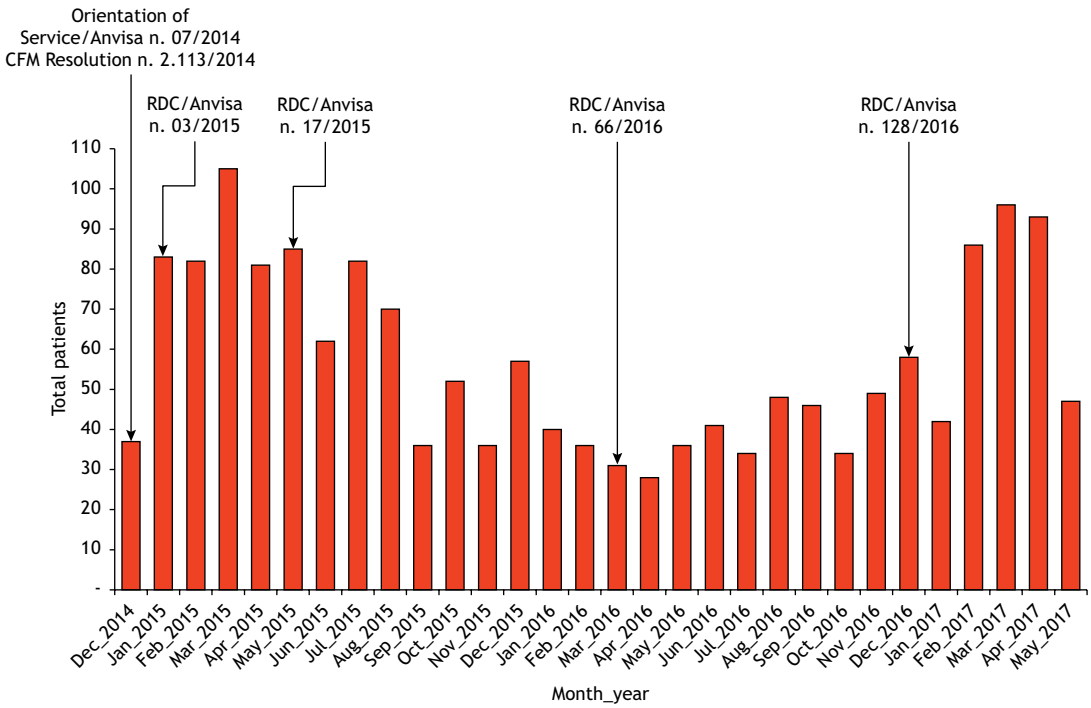
Figure 1 shows the distribution of patients by month-year of importation of cannabidiol-based products in association with other cannabinoids. We noticed that after the first regulatory and professional standards published in December 2014 by Anvisa and the CFM, respectively, there was an increase in the number of patients who requested the importation of these products, with the most substantial surge in March 2015 (N = 105 patients) in the period studied.

We identified 212 ICD-10 codes that characterized the clinical conditions of patients with prescription for therapeutic use of cannabidiol-based products in combination with other cannabinoids. Figure 2 presents the 14 ICD-10 codes most frequently recorded by the medical assessment. Epilepsy (62.9% - an aggregate percentage of eight ICD-10 codes), chronic pain (3.8%) and Parkinson's disease (3.6%) were the most frequent codes. The total ICD-10 codes in patient records ranged from 1 to 5, and 1,562 (91.2%) of the records contained only one ICD-10 code, followed by 138 records (8.1%) that contained two codes.

Physicians of at least 22 medical specialties prescribed cannabidiol-based products in combination with other cannabinoids. Of the 1,683 fields filled in with the physician's name and his/her CFM record, 487 (28.9%) physicians did not have any record of their specialty in the CFM. The medical specialties that most prescribed the products were, in this order: neurology (N = 555; 33.0%), pediatric neurology (N = 381; 22.6%), psychiatry (N = 68; 4.0%) and orthopedics and traumatology (N = 55; 3.3%).

Among the patients who most demanded care from a neurologist are those from 0 to 9 (46.3%) and 20 to 59 years of age (25.0%). The patients who most sought assistance from pediatric neurologists were those aged 0 to 9 (69.3%) and 10 to 19 years old (24.1%) (Table 2).

In the analyzed period, 35 (0.9%) patients replaced the first physician informed to Anvisa with another physician. In these cases, neurology was the most requested medical specialty (N = 15; 42.9%).



CFM: Federal Council of Medicine; RDC/Anvisa: Resolutions of the Collegiate Board of the National Health Surveillance Agency.

Figure 1. Distribution of patients by month-year of import request for cannabidiol-based products in association with other cannabinoids over the period of December 12, 2014 to May 11, 2017. Brazil, 2014 to 2017 (N = 1,713 patients).

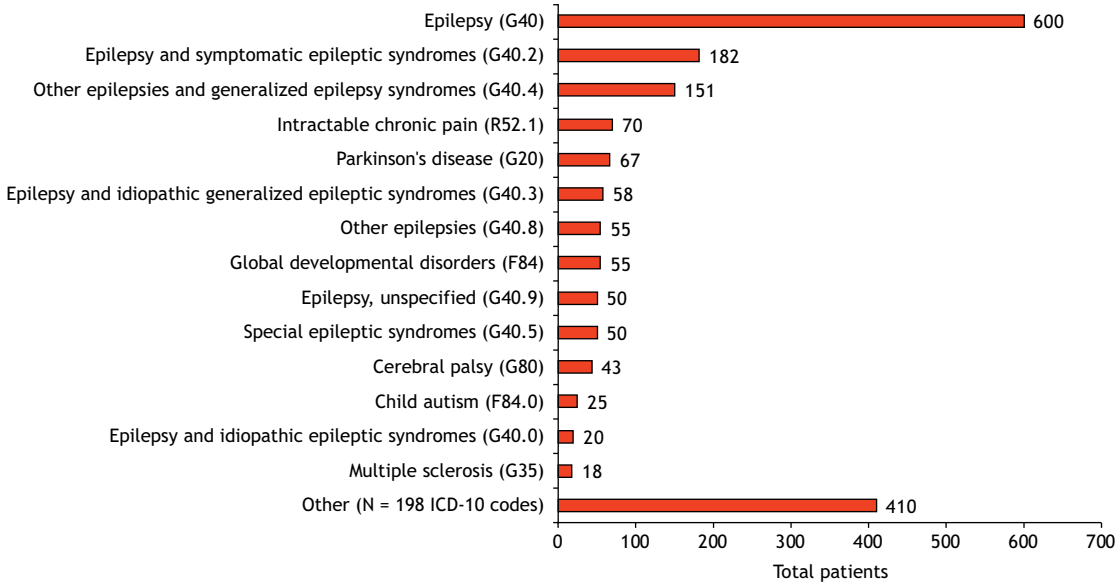


Figure 2. Main clinical conditions, according to ICD-10 codes, of patients with prescription for therapeutic use of cannabidiol-based products in combination with other cannabinoids. Brazil, 2014 to 2017 (N = 1,854 patients with ICD-10 code).

Table 2. Medical specialties that most prescribed cannabidiol-based products in combination with other cannabinoids, by age group. Brazil, 2014 to 2017 (N = 1,682 patients)*.

Medical specialty	Age range (years/%)				Total
	0-9	10-19	20-59	≥ 60	
Neurology	46.3	21.3	25.0	7.4	555
Not registered**	31.7	17.3	37.3	13.8	486
Pediatric neurology	69.3	24.1	6.6	0.0	381
Psychiatry	5.9	16.2	61.8	16.2	68
Orthopedics and Traumatology	0.0	0.0	61.8	38.2	55
Pediatrics	73.3	20.0	6.7	0.0	45
Neurosurgery	23.3	11.6	46.5	18.6	43
General practice	5.3	0.0	52.6	42.1	19
General surgery	11.1	0.0	22.2	66.7	9
Cancerology	0.0	0.0	50.0	50.0	4
Homeopathy	0.0	0.0	50.0	50.0	4

* Thirty records did not provide information about the professional council number, making it impossible to search the Federal Medical Council portal, and one record did not include the age of the patient.
** The physician's record did not include his/her medical specialty on the website of the Federal Council of Medicine.

Most physicians whose records did not include their specialty came from the Southeast (77.2% of 487), while the South obtained the lowest percentage (3.1%). Of the medical specialties that were most demanded by patients, pediatrics was the only one that was not dominated by the Southeast (22.2% of 45). In this case, the Northeast region achieved the highest percentage (62.2%).

Medical specialties with the highest number of patients treated were neurology (94.4% of 553), pediatric neurology (93.9% of 379), pediatrics (100% of 45), neurosurgery (74.4% of 43) and general practice (73.7% of 19), who prescribed cannabidiol-based products in combination with other cannabinoids for patients with "nervous system disorders" (ICD-10 Chapter VI), like epilepsy. The exceptions were mainly physicians specialized in psychiatry (Chapter V – Mental and behavioral disorders – 44.8% of 67) and orthopedics and traumatology (Chapter XVIII – Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified – 81.8% of 55). Of the 484 physicians without identification of specialty, 70.0% also prescribed cannabidiol-based products in combination with other cannabinoids for patients diagnosed with "nervous system disorders."

Table 3. Percentage of cannabidiol-based products in association with other cannabinoids most commonly referred to in the first import by patients or their guardians into Brazil, by age group. Brazil, 2014 to 2017 (N = 1,649 patients)*.

Product	Age range (years/%)**				Total
	0-9	10-19	20-59	≥ 60	
A	50.6	22.5	19.6	7.2	932
B	37.8	15.1	34.6	12.5	312
C	23.3	15.0	42.5	19.2	120
D	22.4	18.4	42.9	16.3	49
E	47.9	10.4	29.2	12.5	48
Other (N = 21)***	31.9	13.8	39.4	14.9	188

* Sixty-two records did not provide information about the imported product and in two of them there was no information on the patient's age.
**Proportion equality test: $x^2 = 125.474$ (15 gl, p = < 0.0001).
***Other types of cannabidiol-based products in combination with other cannabinoids.

During the period analyzed, 537 patients renewed the import request for cannabidiol-based products in association with other cannabinoids, of which 408 (76.0%) maintained the previously imported product. A total of 26 different imported products were identified in the database, mainly coming from the United States (N = 1,566 patients; 94.8%) and the United Kingdom (N = 77 patients; 4.7%). Of this total, 15 (57.7%) products, which were imported for the first time, were not included in Annex I of RDC n. 128, of December 2, 2016.

Products "A" (50.6%) and "E" (47.9%) were the most prescribed in the age group from 0 to 9 years, while products "C" (19.2%) and "D" (16.3%) were the most indicated for the age group ≥ 60 years. The percentage values of the products for first-time importation were not equal in the studied age groups (p < 0.0001) (Table 3). Most of the main products prescribed by physicians were used for ICD-10 Chapter VI diseases, like "A" (92.8% of 930), "E" (85.4% of 48) and "B" (74.5% of 310). Only product "C" had a higher number of indications for diseases linked to Chapters V (41.7% of 120) and II – Malignancies (28.3%).

DISCUSSION

This was the first pharmacoepidemiologic study to provide descriptive information about patients who obtained exceptional authorization from Anvisa to import cannabidiol-based products in combination with other cannabinoids for therapeutic use in Brazil. The regulation of the import of these products enabled a larger number of people, who might have not responded to conventional health treatment strategies for some diseases, to have access to this therapeutic alternative in the country.

The study presented a quantitatively similar distribution for both genders, according to age group. Apparently this distribution was slightly equal to that of the Brazilian population. Demographic data also revealed a slight tendency for men to use cannabidiol-based products in combination with other cannabinoids more often than women. However, this difference between genders was not statistically significant.

A cross-sectional study of a self-selected convenience sample of 2,774 individuals from over 40 countries on the use of cannabis as a substitute for prescription drugs primarily for pain, anxiety and depression found that most respondents were male (55.7%), aged ≤ 50 years (84.7%), living in the United States (83.0%) and users of medicinal cannabis (59.8%)[16]. In our study, which involved cannabidiol-based preparations in combination with other cannabinoids and not necessarily prescribed for individuals suffering from pain, anxiety and depression, 83.1% (N = 1,421) of the study population was < 50 years old.

A study of patients enrolled in the Dutch government's medical cannabis program found a predominance of females (56.8%) and those aged 41 to 60 years (46.0%). The population aged ≤ 20 years accounted for only 1.7% of the study population[17]. It is noted that the program offers physician-prescribed medical cannabis to chronic patients suffering from multiple sclerosis, cancer, HIV/AIDS, chronic pain, therapy-resistant glaucoma, and Tourette syndrome[17]. In our study, which, unlike the Dutch research, involved cannabidiol-based preparations in combination with other cannabinoids, the population of patients aged ≤ 19 years was the most prevalent, whereas for the age group of 40 to 59 years we found a value of 11.7%.

The special arrangement of the process of regulating access to cannabidiol-based products in association with other cannabinoids in Brazil[6,7,8,9,10,18] produced an initial prevalence of use of these products for therapeutic purposes with medical prescription of 0.83/100,000 inhabitants in the analyzed period. In spite of the particularities of each country's regulatory framework regarding the legalization of cannabis and preparations containing cannabinoid concentrations for medicinal use[1,2,3,19], data from a study revealed the prevalence of cannabis use for medicinal purposes with prescription between 5 and 8/100,000 inhabitants from 2003 to 2010[17].

Most indications for the use of cannabidiol-based products in combination with other cannabinoids appear to have been reasonably appropriate, according to ICD-10 codes recorded by medical assessment. The products were mainly used to treat epilepsy, chronic pain and Parkinson's disease. These products have also been recommended by physicians for other clinical conditions and patient groups not defined in CFM Resolution n. 2.113, of December 16, 2014[18].

A total of 234,075 people from seven US states reported 19 clinical conditions for the medicinal use of cannabis. A very small proportion of patients reported serious medical conditions (HIV/AIDS, glaucoma, cancer, Alzheimer's disease), whereas almost all users (91.0%) reported using cannabis rather than cannabidiol-based products in combination with other cannabinoids (as addressed in our study) to relieve severe or chronic pain. Epilepsy cases were reported by only 0.07% of patients[20].

In addition to the specialties established by CFM Resolution, neurology, neurosurgery and psychiatry[18], other medical specialties like orthopedics and traumatology, cancerology, homeopathy and dermatology have prescribed cannabidiol-based products for several clinical conditions. The high number of specialties not registered in the CFM should be carefully interpreted, since the information of "unregistered specialty" may either mean non-existent specialty or existing specialty, but not registered with the professional association.

As part of the regulatory actions for access to cannabidiol-based products in association with other cannabinoids in Brazil, Anvisa began to inform the names of preparations marketed in other countries in its normative acts (RDC n. 17/2015 and RDC n. 128/2016). Even though it seems that Anvisa's main intention was to simply facilitate the identification of these products, possibly still unknown to many patients and their families, our study found, for the most part, products authorized for import that were not listed in Annex I of RDC n. 128/2016. Note that this Resolution was published two years after the analyzed period of this study.

Many of the cannabidiol-based products in combination with other imported cannabinoids described in this study are not registered as medicines in their home countries and therefore have not been evaluated by any health authority. Therefore, it is not possible to guarantee the proper dosage, known composition and the absence of contaminants, nor is it possible to predict adverse events, which may pose risks to the health of patients. Converting cannabis preparations into medicines increases safety for physicians and patients, lowers logistical costs in patient and family purchases, and strengthens health control, including the availability of pharmaceutical formulation information[21].

One of the limitations of the study is that we could not confirm the use of cannabidiol-based products in combination with other cannabinoids for which patients obtained exceptional import authorization from Anvisa. Moreover, it is difficult to generalize the findings and assess the "causal association" of the variables.

However, it is noteworthy that descriptive studies complement other types of analyses and are often the first attempt to address a new event or clinical condition. They can, therefore, be used to monitor trends and generate hypotheses for the conduction of future analytical epidemiological studies[22].

The results help fill some gaps of patient-related information in the Brazilian and international literature by serving as a proxy for the use of cannabidiol-based products in combination with other cannabinoids. These findings can also be used to support assessment initiatives on the need for care and education programs for patients and their families in Brazil.

The regulation of access to cannabidiol-based products in combination with other cannabinoids for therapeutic use met an emergency demand from society and enabled this study, which is a great opportunity to improve our understanding of the characteristics and clinical conditions of these patients. It can also support the regulatory process in health surveillance on the subject, although important knowledge gaps remain in terms of the efficacy and safety of cannabis for medicinal purposes[23].

CONCLUSIONS

Patients who obtained exceptional authorization from Anvisa to import cannabidiol-based products in combination with other cannabinoids are mostly under the age of 20 and suffering from epilepsy. These findings are in line with the provisions of CFM Resolution n. 2.113/2014, which approved the compassionate use of cannabidiol for the treatment of epilepsy in children and teenagers who are refractory to conventional treatments[18].

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Conflict of Interest

Authors have no potential conflict of interest to declare, related to this study's political or financial peers and institutions.