Cannabidiol prescription requests in NZ: Describing patients and indications seen in a New Zealand cannabis clinic

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Abstract (284 words)

Background

In 2017, revision of the Misuse of Drugs Act in New Zealand (NZ) allowed all medical practitioners to prescribe cannabidiol (CBD), a non-euphoriant constituent of cannabis. More information is needed on its therapeutic potential. This is an audit of all patients prescribed CBD from a single private clinic (Cannabis Care, Henderson, New Zealand) from 7th December 2017 to 3rd June 2020. We describe the patient population seeking CBD prescriptions in routine care in NZ, indications for use and quality of life (QOL) indices.

Methods

Patient records were audited by the primary clinician, who had assessed indication for use and QOL indices (EuroQol-5D-5L and EQ-VAS). Indications were coded into four categories: non-cancer pain, emotional distress, neurological symptoms and cancer symptoms. Change in QOL and perceived patient efficacy was described where available. SAS version 9.4 was used. Data descriptions are by mean and standard deviation (SD). Categorical variables were described by counts and proportions expressed as percentages. Paired t-tests were used to compare V1 and V2 VAS scores.

Results

Of 1264 patient records reviewed the mean age was 51 years (SD 20.6), with 55.5% female. Non-cancer pain was the primary indication for use (49.4%). The mean EQ-VAS score at first visit in patients over 16 years (n=924) was 50 (SD 22.3) and 65 (n=384, SD 21.1) at follow up. The mean difference in VAS score in returning patients (n=332) was -11.1 (95% CI -13.2 to -9.0, p<.0001), indicating a positive change in health rating.

Conclusions

In NZ a range of patients are seeking CBD prescriptions, primarily for pain, with a sub-group reporting improved health following use. Further research into the clinical application of these products, especially dosage, precise indications and associated adverse events, is needed.

Keywords (6 words)

CBD, Cannabidiol, Indication, Quality of Life, Prescription, Cannabis

Tables/Figures (4/1)

Background

Cannabidiol (CBD) as a stand-alone product is becoming increasingly available world-wide and is perceived by many to have therapeutic potential in a wide range of conditions despite a relative paucity of scientific evidence outside of epilepsy. Overseas studies on CBD use are concentrated in the USA and primarily describe patients accessing CBD, often combined with delta-9-tetrahydrocannabinol (THC), independent of clinician input. New Zealand has limited CBD to a prescription only medication, with strict THC restrictions, presenting an opportunity to audit pure CBD prescriptions. This research adds further understanding to the use of CBD in the clinical setting, describing the patient population, indications for use, quality of life indices and perceived efficacy in returning patients, expanding on previous research published in 2020.

CBD is one of over 140 phytocannabinoids found across the *Cannabis* genus, others of which include delta-9-tetrahydrocannabinol (THC).[1] CBD is considered a non-euphoriant component of cannabis. Recent randomised controlled trials (RCT) and subsequent open-label extension trials have demonstrated evidence for its adjunctive use in the management of severe refractory epileptic syndromes such as Lennox-Gastaut and Dravet syndromes.[2–5] In addition, it is suggested that CBD may have further therapeutic potential, due to proposed anti-emetic, anti-

inflammatory, analgesic and anxiolytic properties, however RCTs exploring these effects are scarce.[6,7] The National Academies of Science, Engineering and Medicine (NASEM) report on the health effects of cannabis and cannabinoids in 2017 identified a gap in the evidence regarding the use of CBD in medical conditions.[8]

Despite this gap in the evidence for use, recent global changes have seen increased access to cannabis-based products such as CBD.[9,10] Perceived as 'natural', with many health benefits, patients seek out cannabis-based products for management of a range of medical conditions.[10] Such conditions are primarily difficult to treat and chronic in nature, for example, chronic pain, anxiety and depression.[10,11] CBD offers hope of a treatment solution that will work where other medications have been deficient.[12]

Unlike THC, CBD-only products meeting specific criteria have been removed from the controlled drugs legislation in many countries, including New Zealand (NZ), Australia and the United Kingdom (UK).[13,14] In NZ, CBD was removed from the Misuse of Drugs Act in 2017, allowing prescription by any medical practitioner in NZ for any medical condition but it cannot be sold over the counter. Those CBD products containing over 2% THC remain subject to more restrictive criteria, making them more difficult to prescribe.[15] As of October 2021, there were two CBD-only products available through the country's Medicinal Cannabis Scheme (MCS).[16] This scheme requires products to meet a set of minimum quality standards but they are not required to be pharmaceutical grade medications.[17] Despite their ability to prescribe CBD, many medical practitioners across specialties in NZ, such as general practice and oncology, still feel uncomfortable prescribing cannabis-based medical products, primarily due to lack of evidence and lack of understanding of the prescription process.[18,19]

Private clinics, whose clinicians have gained experience in prescribing cannabis-based products, offer opportunities for patients and medical practitioners to discuss the use of CBD for medical conditions. One such clinic, Cannabis Care, undertook an audit of the first 400 patients prescribed CBD in 2018.[20] This paper is a follow-up to this original audit, and aims to describe the patient population seeking CBD prescriptions in NZ, including the indications for use and baseline quality of life indices across the population. Further description of changes in quality of life indices following prescription of CBD are provided in a subset of patients who returned for further consultation.

Methods

This study is an audit of all patients presenting to the Cannabis Care clinic for the discussion of CBD for their medical condition between 7th December 2017 and 3rd June 2020. Patients were either referred by their primary care provider or self-referred to the service. All patients included in the analysis were prescribed cannabidiol.

Patient records were reviewed by the primary clinician involved in their care. The following data was collected at baseline for each patient: demographics (age and gender), date of initial consultation, short descriptive narrative for indication for use, and baseline EuroQol Quality of life scales (EQ-5D-5L) and visual analogue scale (EQ-VAS). The EQ-5D-5L includes five categories measuring mobility, ability to self-care, ability to complete usual activities, symptoms of pain/discomfort, and symptoms of anxiety/depression. Each category has five stages of classification that patients

may choose from: no problems, slight problems, moderate problems, severe problems and extreme problems. The EQ-VAS is a scale from 0-100, whereby zero equates to the 'worst health you can imagine' and 100 equates to the 'best health you can imagine' at the time of the assessment. Whilst all patients and their guardians were given the opportunity to complete the EQ-5D-5L/EQ-VAS by the primary clinician, these were developed for use for those over sixteen years of age, therefore only the scores of those over sixteen years old were reported.[21]

The primary clinician coded the primary indication for use into one of four categories, based on their dominant symptoms; chronic non-cancer pain symptoms, emotional distress and psychiatric symptoms, neurological symptoms and cancer-related symptoms. Further coding analysis of the short descriptive narrative for indication provided was undertaken by a secondary clinician reviewing the anonymised extracted data. This secondary analysis allowed more than one indication per patient, and provided more categories for coding of reasons for use.

EQ-5D-5L outcomes, EQ-VAS scores and a self-rated efficacy scales (Excellent, Very Good, Good, Neutral, No Good) for those patients who returned for review after a minimum period of three weeks use were also captured and reported.

Statistics: SAS version 9.4 was used. Data descriptions are by mean and standard deviation (SD). Categorical variables were described by counts and proportions expressed as percentages. Paired t-tests were used to compare V1 and V2 VAS scores. Missing data was excluded from the analysis. Denominators for each outcome variable are reported in the results to allow for transparency in results reporting.

Results

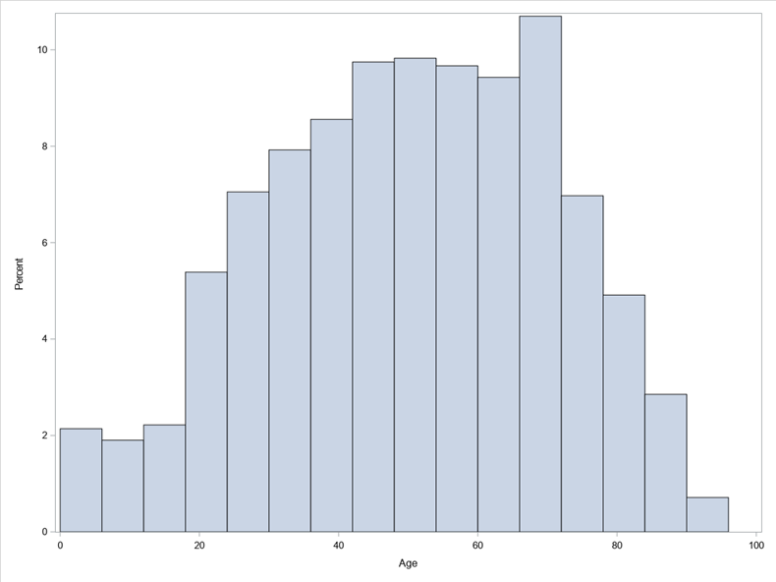
A total of 1264 patient records were reviewed during the audit process, including the 400 from the original audit. Patients were seen in the clinic between December 2017 and June 2020.

Patient demographics are reported in Table 1. The mean age was 51 years (SD 20.59), with 55.5% female. Figure 1 shows the distribution of ages of patients seen in the clinic.

Table 1. Patient Demographics

	Total	**Single consultation recorded (no-follow up)**	**Two consultations recorded**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**
	(N=1262)	(N=600)	(N=662)
Age (years)	51.0 (20.6)	48.7(20.8)	50.5(20.4)
	n (%)	**n (%)**	**n (%)**
	(N=1264)	(N=601)	(N=663)
Gender			
Male (%)	575 (45.5)	271(45.1)	291(43.9)
Female (%)	689 (55.5)	330 (54.9)	372 (56.1)

Figure 1. Age (years) distribution of patients presenting for CBD prescription



Indications for use categorised by the primary treating physician into one of the four main categories may be seen in Table 2. Non-cancer pain was the primary indication given, with 624 (49.4%) indicating this was the primary reason for seeking a CBD prescription. Emotional distress and psychiatric conditions were the second most common indications reported (20.3%). Patients mean age varied according to primary indication for use (Table 3), with patients presenting for pain and cancer indications older than those presenting with neurological, emotional distress and psychiatric conditions. Patients with a cancer indication were most likely not to have a follow up consultation (56.9%), followed by neurological conditions (51.3%), emotional distress and psychiatric conditions (48.4%), with those with a pain diagnosis most likely to return for review (43.1% not returning for a second visit).

Table 2. Indications for prescription of CBD products (n=1264)

Primary Physician Initial Indication (assigned to only one category)	**N (%)**
Non-Cancer Pain	624 (49.4)
Emotional Distress and Mental Health	256 (20.3)
Neurological Symptoms	189 (15)
Cancer symptoms	195 (15.4)
Expanded indications[a]	
Non-Cancer Pain	702 (55.5)
Emotional Distress and Mental Health	486 (38.4)
Neurological Symptoms	283 (22.4)
Cancer symptoms	214 (16.9)
Autoimmune condition	61 (4.8)
Drug management	75 (5.9)
Gastrointestinal disorders	72 (5.7)
Infection	3 (0.2)
Other	325 (25.7)

[a] more than one category could be chosen so percentages sum to more than 100%

Table 3. Mean age at first visit by primary indication

Indication	**Mean (SD)**

Non-Cancer Pain (N=623)	53.7 (19.2)
Emotional Distress and Mental Health	40.7 (16.8)
Neurological Symptoms (N=189)	39.5 (26.0)
Cancer symptoms (N=194)	58.4 (14.4)

Further categorisation of indication for use, which allowed more than one category to be chosen, provided an expansion on the reasons given above, with 55.6% patients having more than one possible indication for use. These other reasons, outside of the four primary categories, included reducing other drug use (illicit or prescribed) (5.9%), auto-immune disorders (4.8%), gastroenterology symptoms (5.7%), infection (0.2%) and other reasons, not defined (25.7%) (Table 2).

EQ-VAS responses were completed by 924 (73.1%) for patients over the age of 16 years at their first visit, with 384 (30.4%) participants completing a follow up EQ-VAS. The mean EQ-VAS score at first visit was 50 (SD 22.3). The mean EQ-VAS follow up score (n=384) was 65 (SD 21.1).

In those patients over the age of 16 years for whom two EQ-VAS scores were available (n=332, 26.3%) the mean difference score was calculated. The mean difference in VAS score from visit 1 to visit 2 was -11.1 (95% CI -13.2 to -9.0, p<0.0001). As a higher score reflects a better health status, a negative mean difference indicates a higher score at visit 2.

EQ-5D-5L questionnaires were completed by 627 patients or their guardians (49.6%) at their first visit. Of all patients included in the audit, 230 (18.2%) completed a follow-up EQ-5D-5L. EQ-5L-5D responses at the first visit for those patients 16 years or over are reported in Table 4. Patients rated high levels of moderate to severe problems in ability to undertake their usual activities and pain/discomfort, with a more equal spread across the anxiety/depression ratings. Self-care and mobility had fewer participants indicating these as problematic at a moderate to severe level.

Table 4. Reported EQ-5D-5L Scores at Visit 1 (over 16 years age)

Mobility (N=591)	N (%)
I have no problems in walking about	274 (46.4)
I have slight problems in walking about	110 (18.6)
I have moderate problems in walking about	136 (23.0)
I have severe problems in walking about	56 (9.5)
I am unable to walk about	15 (2.5)
Self-Care (N=593)	
I have no problems washing or dressing myself	374 (63.1)
I have slight problems washing or dressing myself	107 (18.0)
I have moderate problems washing or dressing myself	73 (12.3)
I have severe problems washing or dressing myself	24 (4.1)
I am unable to wash or dress myself	15 (2.5)
Usual Activities (N=587)	

I have no problems doing my usual activities	117 (19.9)
I have slight problems doing my usual activities	114 (19.4)
I have moderate problems doing my usual activities	188 (32.0)
I have severe problems doing my usual activities	111 (18.9)
I am unable to do my usual activities	57 (9.7)
Pain/Discomfort (N=575)	
I have no pain or discomfort	93 (16.2)
I have slight pain or discomfort	95 (16.5)
I have moderate pain or discomfort	168 (29.2)
I have severe pain or discomfort	164 (28.5)
I have extreme pain or discomfort	55 (9.6)
Anxiety/Depression (N=585)	
I am not anxious or depressed	137 (23.4)
I am slightly anxious or depressed	161 (27.5)
I am moderately anxious or depressed	166 (28.4)
I am severely anxious or depressed	81 (13.8)
I am extremely anxious or depressed	40 (6.8)

Self-reported effectiveness of CBD was indicated by patients or their guardians who had a follow-up consultation (n=587, 46.4%). Of this subset of patients, 18.6% indicated an 'excellent' response, 32.5% indicated a 'very good' response, and 30.8% a 'good' response, and 18.1% indicating a 'no-good' response.

Discussion

There is limited literature describing the use of CBD without THC in clinical practice, as in many jurisdictions CBD may be accessed without the need for prescription. This audit is an extension of a previously completed audit of the first 400 patients seen for CBD prescriptions in a NZ clinic, and further expands on the findings that patients using CBD for medical conditions who return for consultation report an improvement in their health condition.[20] Reasons for use identified in the prior audit and subsequently expanded on and described here include: chronic non-cancer pain from neuropathic pain syndromes, osteo-arthritis, fibromyalgia, autoimmune conditions, and migraines; cancer-related symptoms such as pain, nausea, appetite disturbances, and side effects from chemotherapy and radiotherapy; mental health symptoms such as anxiety, depressive disorder, post-traumatic stress-disorder and insomnia; and neurological symptoms such as multiple sclerosis, epilepsy, neuropathies, tremors and autism spectrum disorder with challenging behaviour. [20]

Overseas, where CBD is often accessed as a dietary supplement, there are a range of reasons for access reported. Corroon and Phillips, 2018, surveyed 2409 CBD users through social media, who indicated their main reasons for use were pain, anxiety and depression, with 36% reporting that CBD alone treated their condition "very well by itself".[10] Wheeler and colleagues, 2020, surveyed 340 participants, primarily between the ages of 18-24 years (75.5%) of which 135 reported using CBD only products. The primary reasons for use were stress relief, relaxation, sleep improvement and pain relief.[22] Fedorova and colleagues studied CBD use in youth who reported general cannabis

use; with CBD-dominant users reporting pain as the primary reason for use.[23] These reasons for access are consistent with the findings of indications for use seen in this audit.

The clinical efficacy of CBD is still unestablished.[8,24] Despite many patients accessing CBD for a multitude of medical conditions the evidence from clinical trials remains lacking, with small underpowered trials that are inconclusive in their findings.[24] Since the NASEM report of 2017, the most significant evidence established for CBD use has been in the severe refractory epilepsy syndromes.[24,25] Research in this area is further complicated due to the fact that many trials reporting on CBD effects in areas such as pain include products combined with THC, making extrapolation of CBD efficacy harder to determine.[24]

This audit has provided the opportunity to describe a large population of patients in NZ who have presented to clinic to discuss and obtain a prescription of CBD to manage their medical condition.

However, interpretation of efficacy and change in health scores is not without limitations. Less than half of the patients completed a follow- up consultation regarding self-reported efficacy of CBD, and the reason for this is unknown, as there was no follow up of non-returners. Potential reasons for non-return include patients who have had no effect from the CBD on their condition, inability to access prescription CBD due to cost, adverse effects, complete resolution of symptoms not requiring further management or death. While there was no difference in demographics of patients who were returners vs non-returners, patients with a cancer indication were more likely not to have a follow up consultation (56.9%) when compared with those with a pain diagnosis (43.1%). Due to potential response bias, interpretation of the results is necessarily limited and it may be that the self-reported effectiveness and change in EQ-VAS are not representative of the CBD-using population as a whole.

Conclusions

Over a two-and-a-half-year period, 1264 patients presented to a private clinic specialising in the use of cannabis as a medicine in New Zealand. Patients who were reviewed in the clinic came from a wide range of ages, with a slight trend towards female sex. The primary indication for seeking a CBD prescription was for the management of chronic non-cancer pain, followed by emotional distress and psychiatric conditions. Breaking this down further, other reasons patients sought assistance included re

duction of prescription and illicit drug use and managing auto-immune conditions.

Patients rated their overall health as average when first seen in clinic. In a subgroup of patients who returned and re-ranked their overall health following CBD use there was a significant improvement in their health self-rating. Returning patients also indicated that overall they found CBD effective for their medical conditions.

This audit has demonstrated that a wide range of patients, in age, gender and medical conditions, are seeking CBD prescriptions in NZ. With the introduction of the MCS in 2020, which aims to increase the access to quality-assured and affordable medical cannabis products, there is need for further research into the clinical application of these products, especially regarding appropriate dosage, precise indications and associated adverse events. This may be

achieved through both ongoing well-designed and powered RCTs of CBD for the primary conditions identified for seeking prescriptions, whilst concurrently running large real-world cohort studies of patients using CBD in the management of their symptoms.

List of abbreviations

New Zealand (NZ)

cannabidiol (CBD)

quality of life (QOL)

standard deviation (SD)

delta-9-tetrahydrocannabinol (THC)

randomised controlled trials (RCT)

The National Academies of Science, Engineering and Medicine (NASEM)

United Kingdom (UK)

Medicinal Cannabis Scheme (MCS)

EuroQol Quality of life scales (EQ-5D-5L)

visual analogue scale (EQ-VAS)

Declaration:

Ethics approval and consent to participate

As this is an audit, The NZ National Health and Disability Ethics Committee (HDEC) determined this project was out of scope and does not require HDEC approval as per Standard Operating Procedures for Health and Disability Ethics Committees (SOPs). In NZ patient consent is not required for routinely collected data presented anonymously.[26]

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due commercial sensitivity but are available from the corresponding author on reasonable request.

Competing interests

KO declares that she has previously received funding through a Clinical Research Training Fellowship from the Health Research Council of New Zealand (HRC). IB and KO have undertaken unrelated consultant work for RuaBio, ZHM,

Whakaora Pharma and Helius Therapeutics and are members of the Medicinal Cannabis Research Collaborative. The Medical Research Institute of New Zealand in funded by the HRC by way of an Independent Research Organization (IRO) grant. AE has no conflicts to report. JS is the recipient of a Western Sydney University Postgraduate Research Scholarship and is employed by Australian Natural Therapeutics Group. JS also sits on the board of the Australian Medicinal Cannabis Association (*pro bono*) and the scientific advisory board of United in Compassion (*pro bono*). JS and MA are part of NICM Health Research Institute. As a medical research institute, NICM receives research grants and donations from foundations, universities, government agencies, individuals and industry. Sponsors and donors provide untied funding for work to advance the vision and mission of the Institute. The project that is the subject of this article was not undertaken as part of a contractual relationship with any organisation.

Funding

No funding was received for the purposes of undertaking this research.

Acknowledgement

The authors would like to acknowledge and thank Matej Minic for his contribution to this research project.

Authors' contributions

GG was the primary clinician, collecting data, writing early drafts and editing final drafts. KO was involved in the planning of the manuscript for publication, cleaned, coded and assisted in the interpretation of the analysed data, and was the primary writer of the draft manuscript. AE cleaned the data and undertook the data analysis and interpretation. IB was involved in the planning of the manuscript for publication, and initial review of the data. JS was involved in the planning of the manuscript for publication and assisted in the interpretation of the analysed data. WX was involved in the study design, collection and processing of data and manuscript reviewing. BA was involved in the original idea to set up the audit and advised on the quality of life scoring, data collection analysis and writing of various drafts. MA was involved in the planning of the manuscript for publication, and assisted in the interpretation of the analysed data. All authors read and approved the final manuscript.

Authors' information

Not applicable.

Footnotes

Not applicable.

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