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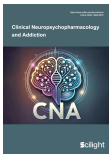

Article

Improved Migraine Disability, Sleep Quality, and Well-Being in Individuals with Chronic Migraine Self-Administering Artisanal or Industrial Full-Spectrum Cannabidiol-Rich Oils: An Observational Cohort Study

Linério Ribeiro de Novais Júnior [1,*], Larissa Mendes da Silva [1], Vicente Meneguzzo [1], Suelen de Souza Ramos [1], Lara Rodrigues da Rosa [1], Tiago Odilio de Souza [1], João Victor Simão [1], Alisson Reuel da Silva [1], Josiel Mack [1], Kelser de Souza Kock [1], Mariana Pereira de Souza Goldim [1], Antonio Inserra [1,2] and Rafael Mariano de Bitencourt [1]

[1] Behavioral Neuroscience Laboratory, University of Southern Santa Catarina—UNISUL, Avenida José Acácio Moreira, 787, Dehon, Tubarão CEP 88704-900, SC, Brazil
[2] Department of Neuroscience, Imaging and Clinical Sciences, G. d'Annunzio University of Chieti-Pescara, Via dei Vestini, 38, 66100 Chieti, Italy
* Correspondence: linerionovaisjr@gmail.com

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Abstract: Background: Migraine is a highly prevalent neurological disorder. Conventional therapies may be limited by side effects and suboptimal efficacy. Cannabidiol (CBD) has emerged as a potential alternative therapy with a more favorable safety profile. **Methods**: In this 12-week prospective observational cohort study, we evaluated the safety, feasibility, and preliminary efficacy of two full-spectrum CBD-rich oils—industrial and artisanal—for chronic migraine in 40 individuals that began self-medicating with either oil (N = 20 per group), provided through an existing initiative by an industrial company and a patient association. The oil was titrated individually to reach a target dose of 100 mg/day of CBD. Assessments were conducted using the Migraine Disability Assessment Questionnaire (MIDAS), Headache Impact Test (HIT-6), Mini Sleep Questionnaire (MSQ), and the World Health Organization Quality of Life—5-item version (WHOQOL-5). **Results**: Both formulations led to improvements in migraine-related disability, headache impact, quality of life, quality of sleep, and subjective well-being. Adverse events occurred at similar rates across groups. **Conclusions**: In sum, full-spectrum CBD-rich oil—both industrial and artisanal—appears effective in reducing migraine burden in individuals with chronic migraine, while maintaining an acceptable side effects profile. These findings support the need for randomized controlled trials to determine the lowest and most effective regimens, and cannabinoid compositions.

Keywords: cannabidiol; cannabinoids; chronic migraine; migraine disorders; full-spectrum; cannabis oil; observational study; prospective cohort; artisanal; industrial

1. Introduction

Migraine is a neurological disorder affecting approximately 1 billion people worldwide, with higher prevalence in females [1,2]. It is characterized by moderate to severe headache attacks lasting from 4 to 72 h, which are typically unilateral and pulsatile. Symptoms such as nausea, vomiting, phonophobia, and photophobia

may be associated. The pain can be preceded by aura, a reversible focal neurological symptom that often presents visual impairment or sensory disturbances [2,3].

Migraine is generally treated with nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, triptans, ergotamines, β-blockers, and antiepileptics, which are not always satisfactorily efficacious. Additionally, excessive medication use can lead to the progression to chronic migraine, involving pain occurring on 15 or more days per month, and migraine symptoms on at least 8 of those days. Psychiatric disorders, excessive caffeine consumption, obesity, and temporomandibular joint disorders can also contribute to the chronification process [4,5].

Given that available pharmacotherapies do not always provide satisfactory results, novel, more effective treatments with fewer side effects are needed. The endocannabinoid system (ECS) plays a crucial role in maintaining homeostasis, and migraine has been linked to dysfunctions within this system [6,7]. In particular, alterations in the ECS system have been implicated in pain modulation, neuroinflammation, and central sensitization, all of which are key mechanisms in migraine pathophysiology. Therefore, the ECS may prove as a valuable therapeutic target for the treatment of migraine. The clinical endocannabinoid deficiency theory, although still debated, proposes that migraine is associated with low levels of endocannabinoids; therefore, low doses of exogenous cannabinoids could help manage pain [8]. Phytocannabinoids interact primarily with the cannabinoid type 1 (CB1) and type 2 (CB2) receptors, which are predominantly found in the central nervous system and peripheral tissues, respectively. The two most well-studied exogenous cannabinoids are cannabidiol (CBD) and Δ-9-tetrahydrocannabinol (Δ9-THC) [9]. Through these receptors, phytocannabinoids may influence nociceptive processing, cortical excitability, and trigeminovascular signaling, providing a mechanistic rationale for their potential use in migraine. Some studies have shown preliminary benefits of using vaporized, edible, topical, and smoked Cannabis preparations to treat migraines, with generally acceptable side effects profiles [10–18].

Despite this preliminary clinical evidence, real-world data directly comparing different sources and production methods of CBD-rich cannabis oils—such as industrially produced versus artisanally produced preparations—remain scarce. Against this background, the present study sought to explore the potential utility of full-spectrum CBD-rich cannabis oils, produced either industrially or artisanally, as a self-administered treatment for chronic migraine. Specifically, the study aimed to assess their effects on migraine-related disability, headache burden, and associated quality-of-life measures. Based on accumulating evidence implicating ECS dysregulation in migraine pathophysiology, it was hypothesized that self-administered full-spectrum CBD-rich cannabis oils would be associated with improvements in migraine-related disability, headache burden, and quality-of-life outcomes in individuals with chronic migraine.

2. Materials and Methods

2.1. Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki. Data collection and processing were approved by the Brazilian National Research Ethics Committee (protocol number 55614022.0.0000.5369). The study adhered to the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).

2.2. Study Design

This is an observational prospective cohort study of an existing treatment initiative. The project was initially implemented by the company Natyva Care (Cambridge, MA, USA), in partnership with a patient Brazilian association that has judicial authorization for the cultivation and extraction of medicinal cannabis (Associação Santa Cannabis, Florianópolis, SC, Brazil), to provide cannabinoid-based medication for 40 individuals diagnosed with migraine. Participation was voluntary and based on patient self-selection following public advertisement of the initiative. As part of the program, participants received the medication at no cost and were followed by an independe nt physician at a private clinic. Participants were responsible for covering the costs of their medical consultations and underwent treatment for a period of 12 weeks. The research team monitored patient outcomes through standardized questionnaires without interfering in the clinical management.

2.3. Inclusion Criteria

Participants met the following inclusion criteria: a diagnosis of chronic migraine, characterized by headaches occurring on at least 15 days per month and exhibiting at least two of the following four features—unilateral pain, pulsatile quality, duration between 4 and 72 h, or worsening with physical activity—accompanied by at least one of the following symptoms: photophobia or phonophobia, nausea, and/or vomiting. Eligible individuals were

between 18 and 59 years of age and had independently initiated treatment with CBD-rich oil between July and October 2022 through a specialized medical clinic for cannabinoid therapy accessed via Telemedicine.

2.4. Exclusion Criteria

Exclusion criteria included the use of any cannabis-derived products in the month preceding the study; a known history of intolerance or hypersensitivity to components of the cannabis plant; women of childbearing potential who were pregnant, planning to become pregnant, or breastfeeding; and individuals who were unable or unwilling to provide informed consent by signing the Informed Consent Form.

2.5. Recruitment

Participants were selected by the private medical clinic responsible for conducting the consultations. Social media platforms were used to advertise consultations and treatment for 40 individuals suffering from chronic migraine. Interested participants were required to complete an online questionnaire to assess the presence of chronic migraine based on the criteria established by the Headache Classification Committee of the International Headache Society [2,6]. Final diagnostic confirmation was performed by a physician during the initial telemedicine consultation, based on established IHS criteria.

2.6. Group Allocation

After screening for eligibility, 40 participants were systematically allocated into two groups based on enrollment order. Each participant was assigned a unique identification number from 1 to 40 in the order of enrollment; thus, group allocation was systematic and non-random, based on order of enrollment. The distinction between artisanal and industrial CBD-rich oils was based on source and manufacturing process. The twenty participants with odd identification numbers were assigned to self-administer treatment with an industrially manufactured full-spectrum, CBD-rich cannabis oil (50 mg/mL CBD, <0.3% THC, CBD:THC ratio ~17:1) produced by a U.S. pharmaceutical company (Natyva Care, Cambridge, MA, USA) (group 1, “Industrial”). The twenty participants with even numbers were assigned to self-administer treatment with an artisanally produced, full-spectrum, CBD-rich cannabis oil (20 mg/mL CBD, 1 mg/mL THC, CBD:THC ratio 20:1) manufactured by a Brazilian association that has judicial authorization for the cultivation and extraction of medicinal cannabis (Associação Santa Cannabis, Florianópolis, SC, Brazil) (group 2, “Artisanal”).

2.7. Informed Consent

All participants were informed about the study objectives, procedures, potential risks, and benefits, and their right to withdraw at any time without penalty. Written informed consent was obtained prior to inclusion in the study.

2.8. Data Collection Timepoints

The data collection process involved questionnaires that were self-administered online three times:

(1) Time 0, baseline. Immediately before starting treatment with the CBD-rich oil.
(2) Time 1, 4-week follow-up: Four weeks after starting treatment.
(3) Time 2, 12-week follow-up: Twelve weeks after starting treatment.

2.9. Evaluation Instruments

The sociodemographic profile, lifestyle factors, and analgesic use were assessed using a researcher-developed questionnaire covering the following aspects: sex, age, marital status, income, physical exercise, smoking habits, presence of comorbidities, and analgesic consumption (see Supplementary Material for the Portuguese Version of the Scales and Questionnaires Administered).

The following questionnaires were administered: (i) The Migraine Disability Assessment Questionnaire (MIDAS), a well-established instrument that evaluates headache-related disability over the past three months. It assesses loss of work or school days, reduced performance at work or school, inability to perform household tasks, and loss of family, social, or leisure activities—factors commonly affected by headaches [19]. (ii) The Headache Impact Test (HIT-6), which assesses the impact of headaches on disability in work, school, and social activities, as well as headache intensity and the presence of fatigue, frustration, and difficulty concentrating over the past four weeks [20]. (iii) The Mini Sleep Questionnaire (MSQ), consisting of 10 items, which assesses symptoms related to excessive daytime sleepiness and sleep quality [21]. (iv) The World Health Organization Quality of Life—5-item

version (WHOQOL-5), which assess individuals' subjective psychological well-being and quality of life [22]. Additionally, participants were asked to rate their perceived sleep quality and quality of life on a 0–10 scale.

2.10. Safety

Adverse events were self-reported by participants. No formal severity grading scale was applied.

2.11. Statistical Analysis

All statistical analyses were conducted using GraphPad Prism®® version 10.3.1 (GraphPad Software Inc., San Diego, CA, USA). The study employed a modified intention-to-treat approach, in which all participants who completed at least two of the three timepoints (baseline, 4-week, and 12-week follow-ups) were included in the analysis, regardless of adherence or dropout status.

Given the repeated-measures design involving the same participants assessed across three timepoints (T0, T1, T2), a mixed-model analysis of variance (ANOVA) was used to assess changes over time and between groups. This method was chosen due to its robustness in handling missing data and within-subject correlations in longitudinal data [23]. A Greenhouse–Geisser correction was applied to adjust for potential violations of sphericity assumptions. The fixed factors included Time (within-subject: T0, T1, T2), Group (between-subject: Industrial vs. Artisanal), and the Time × Group interaction. When the ANOVA indicated significant effects, post hoc analyses were conducted using Tukey's multiple comparison test. All p-values reported are two-sided, and $p < 0.05$ was considered statistically significant. For categorical data (e.g., adverse events), Fisher's exact test was used to compare frequencies between the Industrial and Artisanal groups. Data are reported as mean ± standard error of the mean (SEM). The number of observations (n) is reported for each outcome measure.

3. Results

3.1. Recruitment and Retention

One thousand one hundred fifty-eight individuals were assessed for eligibility to participate in the study. Of these, 1102 did not meet the inclusion criteria, 6 declined to participate, and 10 were unable to be contacted. Forty individuals with a diagnosis of chronic migraine, aged between 18 and 59 years, were enrolled from July to October 2022 and self-initiated treatment with either the industrial or the artisanal full spectrum, CBD-rich, cannabis oil.

The initial CBD dosage ranged from 5 to 20 mg per day, adjusted individually based on factors such as symptom severity, previous cannabis or CBD use, body weight, metabolic rate, comorbid conditions, concomitant medications, sensitivity to side effects, age, patient preference, and the physician's clinical impressions during the consultation. The dose was progressively increased by 5 to 10 mg every 2 to 7 days, administered two to three times per day. The target dosage of 100 mg per day of CBD was typically reached within 30 days.

Thirty-two participants (retention rate 80%, drop-out rate 20%) completed all three assessments, 15 from group 1, (Industrial), and 17 from group 2 (Artisanal). Eight participants (three from group 1—15%-, and five from group 2—25%-) did not complete the second and third assessment. Of these, two participants from group 1 dropped out during the first month of treatment respectively due to drowsiness and diarrhea, and two participants from group 2 dropped out during the first month of treatment respectively due to drowsiness and anxiety. The other four participants (10% of the initial sample, three from group 1 and one from group 2) were lost to follow-up, and it was not possible to determine the causes leading to the discontinuation of the study (Figure 1).

3.2. Demographic Characteristics

Baseline demographic and clinical characteristics, including age, sex distribution, migraine duration, and baseline headache burden, were comparable between the industrial and artisanal CBD-rich oil groups, with no statistically significant differences observed. The enrolled participants were predominantly assigned female at birth (37/40, 92.5%), identified as Caucasian (33/40, 82.5%), and were largely between 30 and 49 years old (31/40, 77.5%). Most participants completed higher education (28/40, 70%) and reported a monthly income between two to four minimum wages (31/40, 77.5%). Most participants reported that the migraine-related headache was greater than 5 on a scale from 1 to 10 (28/40, 70%), and that they had taken medications in the past month to alleviate migraine-related pain (39/40, 97.5%). Most participants were non-smokers (38/40, 95%) and did not consume alcohol three or more times a week (39/40, 97.5%) (Table 1).

Table 1. Sociodemographic profile of study participants. N = 40.

Sociodemographic Variable	n (%)
Sex	
Male	3 (7.5)
Female	37 (92.5)
Age	
18–29 years	7 (17.5)
30–49 years	30 (75)
50–59 years	3 (7.5)
Ethnicity	
Caucasian	32 (80)
Mixed race	7 (17.5)
Black	1 (2.5)
Asian	0 (0)
Indigenous	0 (0)
Marital status	
Single	17 (42.5)
Married	21 (52.5)
Divorced	2 (5)
Education	
Completed high school	8 (20)
Incomplete higher education	4 (10)
Completed higher education	28 (70)
Monthly income	
Up to 1.5 minimum wages	7 (17.5)
1.5–3 minimum wages	11 (27.5)
3–5 minimum wages	13 (32.5)
6–10 minimum wages	7 (17.5)
>10 minimum wages	2 (5)

All participants had a prior medical diagnosis of migraine and had undergone previous treatment. Additionally, 50% of participants (20/40) had at least one associated diagnosis, such as fibromyalgia or hypertension. Participants reported high rates of symptoms of anxiety (29/40, 72.5%), depression (24/40, 60%), and disturbed sleep (23/40, 57.5%).

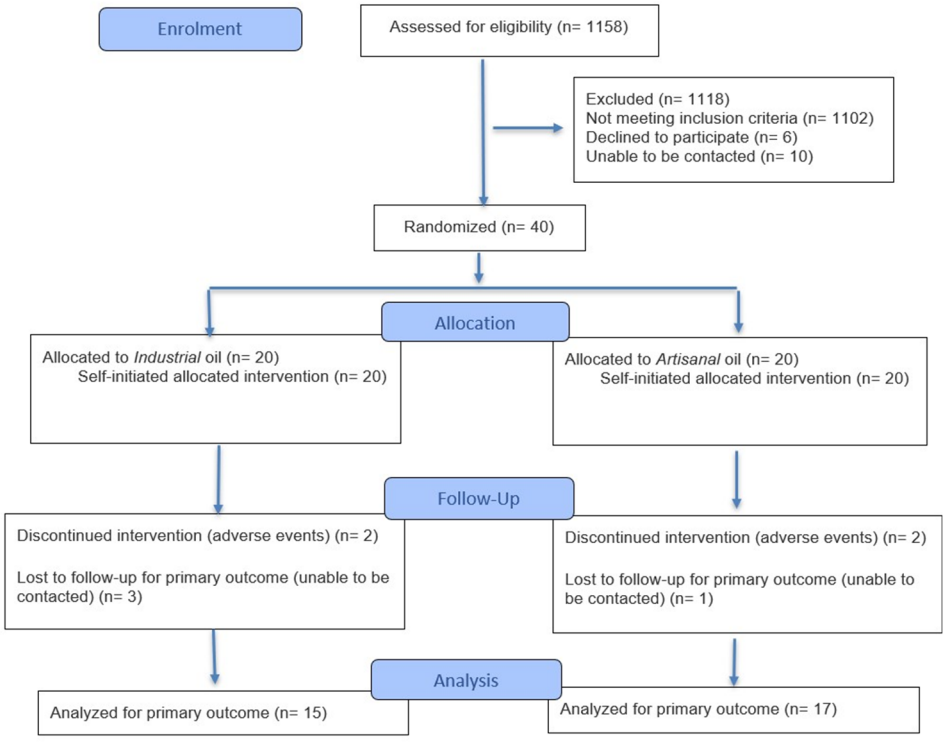

Figure 1. Overview of the study design.

3.3. Migraine Disability Assessment (MIDAS) Questionnaire

In the MIDAS questionnaire (Figure 2A), mixed-model repeated-measures ANOVA identified a significant effect of Time (F (2, 122) = 24.48, $p < 0.0001$), but no effect of Group or Time × Group interaction ($p > 0.05$). When considering all participants, decreases were observed at T1 and T2 compared to T0 (respectively $p = 0.0087$ and $p < 0.0001$). In the group taking the industrial oil, a decrease was observed at T1 and T2 compared to T0 (respectively $p = 0.0292$ and $p < 0.0001$). In the group taking the artisanal oil, a decrease was detectable only T2 compared to T0 ($p = 0.0078$). No statistically significant differences were observed at any timepoint between groups (post-hoc $p > 0.05$).

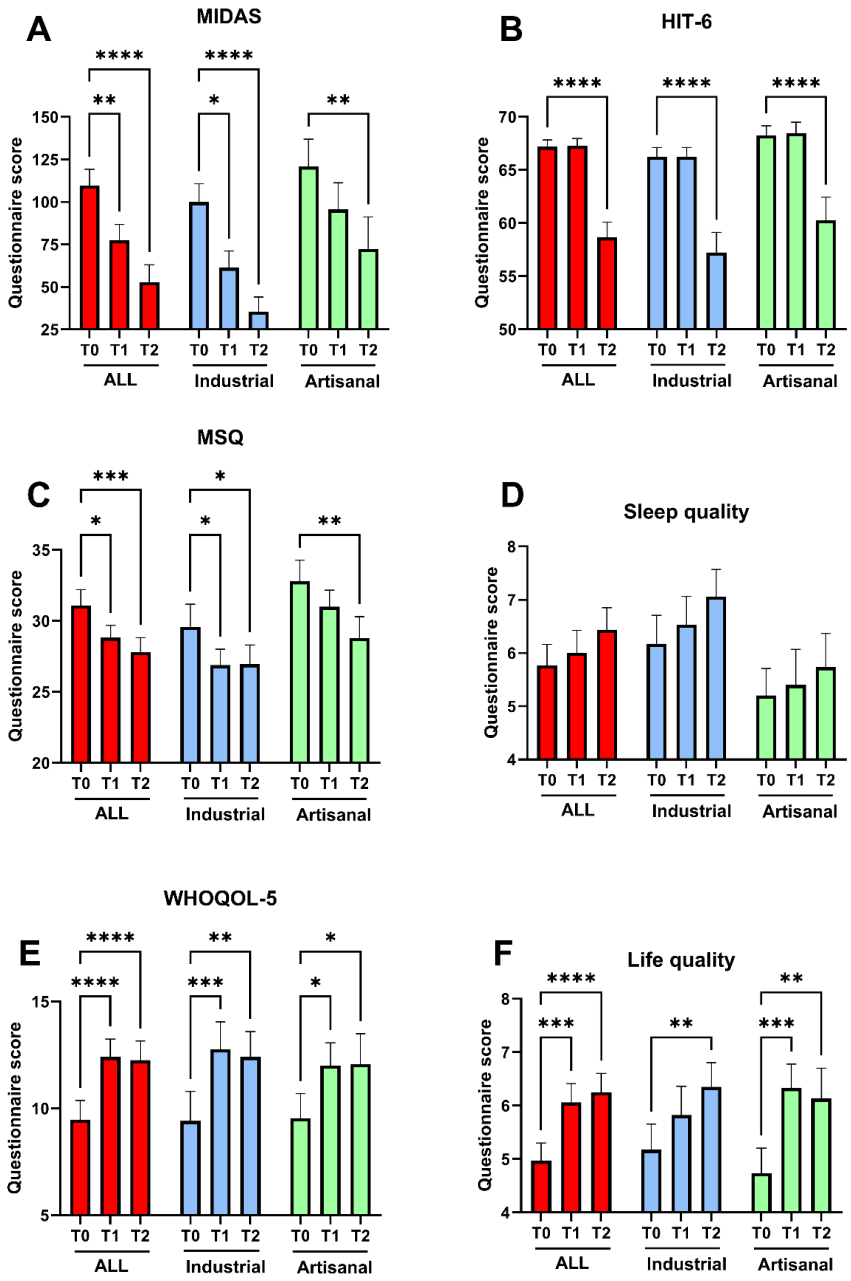

Figure 2. Effect of industrial and artisanal CBD oil on migraine-related disability, headache impact, quality of life, and subjective well-being. (**A**) Migraine Disability Assessment Questionnaire (MIDAS) results; (**B**) Headache Impact Test (HIT-6); (**C**) Mini Sleep Questionnaire (MSQ); and (**D**) Self-reported sleep quality on a scale from 0 to 10; (**E**) World Health Organization Quality of Life—5-item version WOQOL5? (**F**) Self-reported life quality on a scale from 0 to 10. (X axis) T0: baseline assessment; T1: 4-weeks of CBD oil administration; T2: 12-weeks of CBD oil administration. (Y axis) questionnaire score. All: all participants (N = 32); Industrial: participants receiving the industrial CBD oil (N = 15); Artisanal*:* participants receiving the artisanal CBD oil (N = 17). Mixed model ANOVA followed by Tukey's post-hoc test. * indicates Tukey's post-hoc *p* value < 0.05; ** *p* value < 0.01; *** *p* value < 0.001; **** *p* value < 0.0001.

3.4. Headache Impact Test-6 (HIT-6)

In the HIT-6 questionnaire (Figure 2B), mixed-model repeated-measures ANOVA identified a significant effect of Time ($F(2, 122) = 61.52$, $p < 0.0001$), but no effect of Group or Time × Group interaction ($p > 0.05$). When considering all participants, a decrease was observed at T2 compared to T0 ($p < 0.0001$). The two groups showed a remarkably similar pattern. No differences were present at any of the timepoints between groups ($p > 0.05$).

3.5. Mini Sleep Questionnaire (MSQ)

In the MSQ questionnaire (Figure 2C), mixed-model repeated measures ANOVA identified a significant effect of Time ($F(2, 122) = 16.68$, $p < 0.0001$), but no effect of Group or Time × Group interaction (post-hoc test $p > 0.05$). When considering all participants, a decrease was observed at T1 and T2 compared to T0 (respectively $p = 0.0120$ and $p = 0.0002$). In participants taking the industrial oil, a decrease was observed at T1 and T2 compared to T0 (respectively $p = 0.0351$ and $p = 0.0403$). In the group taking the artisanal oil, a decrease was detectable only at T2 compared to T0 ($p = 0.0019$). No differences were present at any of the timepoints between groups ($p > 0.05$).

3.6. Self-Reported Sleep Quality

Mixed-model repeated measures ANOVA identified a significant effect of Time ($F(2, 120) = 4.231$, $p < 0.0168$) but no effect of Group or Time × Group interaction ($p > 0.05$) in improving the self-reported sleep quality on a scale from 0 to 10 (Figure 2D). However, despite a trend towards increased quality of life, no statistically significant post-hoc differences emerged.

3.7. World Health Organization Quality of Life—5-Item Version (WHOQOL-5)

In the WHOQOL-5 questionnaire (Figure 2E), mixed-model repeated measures ANOVA identified a significant effect of Time ($F(2, 122) = 25.67$, $p < 0.0001$), but no effect of Group or Time × Group interaction ($p > 0.05$). When considering all participants, increases were observed at T1 and T2 compared to T0 (both $p < 0.0001$). In the group taking the industrial oil, an increase was observed at T1 and T2 compared to T0 (respectively $p = 0.0004$ and $p = 0.0015$). Similarly, in the group taking the artisanal oil an increase was detectable at T1 and T2 compared to T0 (respectively $p = 0.0189$ and $p = 0.0153$). No differences were present at any of the timepoints between groups ($p > 0.05$).

3.8. Self-Reported Life Quality

Mixed-model repeated measures ANOVA identified a significant effect of Time ($F(2, 122) = 25.33$, $p < 0.0168$) but no effect of Group or Time × Group interaction ($p > 0.05$) in increasing the self-reported life quality on a scale from 0 to 10 (Figure 2F). When considering all participants, increases were observed at T1 and T2 compared to T0 (respectively $p = 0.0002$ and $p < 0.0001$). In the group taking the industrial oil, an increase was observed only at T2 compared to T0 ($p = 0.0040$). However, in the group taking the artisanal oil, an increase was detectable at both T1 and T2 compared to T0 (respectively $p = 0.0002$ and $p = 0.0011$). No differences were present at any of the timepoints between groups ($p > 0.05$).

3.9. Safety

Fifty percent (N = 18) of the participants for which data was available (36/40) experienced mild adverse events. The five most common were sleepiness (18/36, 50%), tiredness and anxiety (each 10/36, 27.8%), increased appetite (9/36, 25%), and dry mouth (7/36, 19.4%). The incidence of adverse events did not differ significantly between groups (Table 2).

Table 2. Frequency of adverse events.

Adverse Event	n	% of Sample	n Industrial Group	% Industrial Group	n Artisanal Group	% Artisanal Group	Fisher Exact Test *p*
YES	18	50.0	8	44.4	10	55.6	>0.9999
NO	18	50.0	9	50.0	9	50.0	>0.9999
Sleepiness	18	50.0	8	44.4	10	55.6	0.5050
Anxiety	10	27.8	5	27.8	5	27.8	>0.9999
Tiredness	10	27.8	4	22.2	6	33.3	0.7112
Increased appetite	9	25.0	6	33.3	3	16.7	0.4430
Dry mouth	7	19.4	3	16.7	4	22.2	>0.9999

Table 2. *Cont.*

Adverse Event	n	% of Sample	n Industrial Group	% Industrial Group	n Artisanal Group	% Artisanal Group	Fisher Exact Test p
Nausea	5	13.9	2	11.1	3	16.7	>0.9999
Lightheadedness	5	13.9	2	11.1	3	16.7	>0.9999
Constipation	4	11.1	2	11.1	2	11.1	>0.9999
Sadness	4	11.1	3	16.7	1	5.6	0.6026
Diarrhea	3	8.3	3	16.7	0	0.0	0.2286
Disorientation	2	5.6	1	5.6	1	5.6	>0.9999
Euphoria	0	0.0	0	0.0	0	0.0	-

4. Discussion

This 12-week observational cohort study focused on the effects of industrial and artisanal CBD-rich full-spectrum oils in individuals with chronic migraine, exploring migraine-related disability, headache burden, quality of life, sleep quality, and subjective well-being. Statistically significant improvements across all these domains were observed, with both formulations demonstrating apparent comparable therapeutic benefits and overlapping side effects profiles.

These observations broadly align with previous clinical and observational studies indicating that cannabis-based treatments can reduce migraine frequency and severity, improve quality of life, and decrease headache-related disability [10–18]. The present observations support the growing body of evidence suggesting that cannabis-based products might hold promise as adjunct or alternative therapies for migraine. It could be speculated that the therapeutic effects observed may be driven by CBD, which acts as a partial agonist at serotonin (5-HT)1A receptors [24]—a subtype of serotonin receptor known to modulate pain perception, anxiety, and vascular tone [25–28]. In migraine, dysregulation of serotonergic pathways—particularly involving 5-HT1 receptors—is a well-established mechanism, with current frontline treatments like triptans acting as 5-HT1B/1D agonists to induce vasoconstriction and inhibit neuropeptide release [29,30]. By activating 5-HT1A receptors, CBD may exert anxiolytic, anti-hyperalgesic, and vascular stabilizing effects, potentially contributing to the observed reduction in headache burden and improvements in well-being.

In parallel, given that CBD interacts with TRPV1 (vanilloid) ion channels, which are involved in nociceptive transmission and central sensitization—processes central to the chronification of migraine [31,32], it cannot be excluded that TRPV1-dependent mechanisms might be involved in the apparent improvements in migraine severity and burden observed in this study. Additionally, CBD may act as a negative allosteric modulator of CB1 and 5-HT2A receptors [33,34], possibly tempering the psychoactivity of THC while allowing it to exert analgesic and anti-inflammatory effects via CB1 and CB2 receptor pathways. Even at low doses, THC may contribute therapeutic benefit through partial agonism at CB1 and CB2 receptors, which are expressed in both central and peripheral regions implicated in migraine [35,36].

Both groups exhibited a similar side effect profile, with no statistically significant differences observed in the incidence of adverse events. Adverse events—such as drowsiness, increased appetite, fatigue, and anxiety symptoms—were reported by a comparable proportion of participants in each group and primarily occurred within the first two weeks of treatment. This side effect profile is consistent with existing literature, including recent studies and a systematic review and meta-analysis of randomized clinical trials on cannabidiol use, which reported these side effects in approximately 50–70% of participants. In most cases, the effects were mild to moderate in severity (90%), with the most common being loss of appetite, diarrhea, sedation, and drowsiness. Side effects typically manifest at the start of treatment or following increases in cannabinoid dosage and, as demonstrated in our study, are often temporary and do not hinder continued treatment with cannabis extract.

In a randomized, double-blind, placebo-controlled crossover trial, vaporized treatments of 6% THC, 11% CBD, a 6% THC/11% CBD combo, and placebo were tested for acute migraine. The THC/CBD combination was significantly more effective than placebo in pain relief (67.2% vs. 46.6%), pain freedom (34.5% vs. 15.5%), and relief from the most bothersome symptom (60.3% vs. 34.5%) at 2 h, with benefits lasting up to 48 h. THC alone improved pain relief, while CBD alone had no effect [18]. A large retrospective study from the Strainprint app showed inhaled cannabis reduced headache and migraine intensity by about 50%. Men and users of cannabis concentrates reported greater relief. However, tolerance developed over time, requiring higher doses and reducing effectiveness, indicating short-term benefits but potential long-term limitations [12]. In a survey of medicinal cannabis users, migraine was a primary condition treated, with 88% of respondents screening positive for probable migraine. Many respondents reported substituting cannabis to prescription medications like opioids (43.4%), antidepressants/anxiolytics (39%), NSAIDs (21%), and triptans (8.1%) [17]. In an observational study, cannabis sessions were screened via the Releaf App, finding that 94% of users experienced headache and migraine relief

within two hours, with an average pain reduction of 3.3 points on a 0–10 scale. Greater relief occurred in males and younger users. THC levels ≥ 10% were the strongest predictor of improvement, especially for headache sufferers, females, and younger individuals. Cannabis indica strains showed greater efficacy in these groups [16]. In a retrospective review of individuals with migraine at two Colorado clinics, medical cannabis significantly reduced monthly migraine frequency from 10.4 to 4.6 episodes. About 40% reported benefits, while 11.6% experienced side effects, mainly from edibles, such as somnolence and dose-titration difficulties [15]. In a large online survey of self-identified medical cannabis users in Washington State, 35.5% reported using cannabis to treat headache or migraine [14]. A cross-sectional study of individuals with migraine taking medical cannabis found that over 60% had a ≥50% reduction in monthly attacks. Responders reported less disability and used fewer opioids and triptans [10]. Lastly, in a survey of individuals with cluster headache from two French centers, 45.3% had used cannabis. Of the 27 who used it for cluster headache attacks, 25.9% reported benefit, over half had variable or uncertain effects, and 22.3% experienced negative outcomes [11].

Together, the available preliminary evidence highlights the potential of cannabis-based treatments to alleviate migraine frequency, intensity, and associated symptoms. While variations exist in individual responses and long-term efficacy, the overall trend suggests a meaningful therapeutic role for cannabinoids. Building on this growing body of evidence, our findings align well with the observed benefits across both controlled studies and real-world settings. Like previous clinical trials and observational research, we observed meaningful reductions in migraine burden and symptom severity, reinforcing the potential of cannabinoid-based treatments to improve patient quality of life. Several clinical trials investigating the use of cannabis for migraine are listed on ClinicalTrials.gov. Among them, a completed randomized, double-blind, placebo-controlled crossover trial evaluated the efficacy of inhaled cannabis for acute migraine treatment (NCT04360044). Currently, an open-label tolerability trial is recruiting adolescents with chronic headaches to assess the administration of a CBD-rich cannabis herbal extract (NCT05337033). A randomized, double-blind, placebo-controlled trial is planned but not yet recruiting, which aims to investigate the prophylactic use of CBD at doses of 100 mg and 200 mg over 12 weeks for migraine prevention (NCT03972124). Another randomized, double-blind trial assessing the combination of cannabidiol, cannabigerol, and THC versus placebo as an adjuvant treatment for chronic migraine was terminated early due to interim futility assessment (NCT04989413). Lastly, a pilot randomized, double-blind, placebo-controlled, crossover, dose-ranging trial evaluating inhaled cannabis versus placebo for acute migraine treatment was suspended due to inadequate funding (NCT05427630).

Against this backdrop of ongoing but methodologically heterogeneous clinical research, the findings of the present study should be interpreted in light of several limitations: no placebo group was included; therefore, it is not possible to rule out placebo effects. The full phytocannabinoid composition of the oil was not investigated. No pharmacokinetic or bioavailability experiments were performed. The study was open label. The majority of participants were female; therefore, the results may not be generalizable to males. The majority of participants were Caucasian; therefore the findings may not reflect the experiences of individuals from other ethnic backgrounds, including Indigenous individuals. Concomitant medication use during the CBD treatment period was not systematically assessed. While participants reported prior use of acute migraine medications, the potential influence of ongoing pharmacological treatments on study outcomes cannot be excluded and should be monitored in future studies. Lastly, events were self-reported by participants, and no formal severity grading scale was applied, which may have affected the consistency and comparability of safety data.

5. Conclusions

In conclusion, this study offers exploratory and preliminary evidence suggesting that CBD-rich cannabis extracts—whether industrially or artisanally produced, including those sourced through patient associations—may be well tolerated and potentially beneficial for individuals with chronic migraine. These findings should be regarded as hypothesis-generating rather than confirmatory. The observational, open-label design, lack of a control group, and other methodological limitations limit causal inference, and the results should therefore be interpreted with considerable caution. Definitive conclusions regarding safety, tolerability, efficacy, therapeutic range, and optimal cannabinoid composition await confirmation in double-blind RCTs for acute and preventive migraine management.

Supplementary Materials

The additional data and information can be downloaded at: https://media.sciltp.com/articles/others/26011214 47103009/CNA-25110019-Supplementary-material.pdf.

Author Contributions

L.R.d.N.J.: Conceptualization, Methodology, Investigation, Formal Analysis, Writing—Original Draft; L.M.d.S.: Investigation, Data Curation, Formal Analysis, Writing—Original Draft; V.M.: Investigation; S.d.S.R.: Investigation, Writing—Original Draft; L.R.d.R.: Investigation; T.O.d.S.: Investigation; J.V.S.: Investigation; A.R.d.S.: Investigation; J.M.: Writing—Review & Editing; K.d.S.K.: Formal Analysis; M.P.d.S.G.: Formal Analysis; A.I.: Formal Analysis, Writing—Original Draft, Writing—Review & Editing; R.M.d.B.: Conceptualization, Methodology, Supervision, Writing—Review & Editing, Project Administration. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study protocol was approved by the Brazilian National Research Ethics Committee (protocol number 55614022.0.0000.5369).

Informed Consent Statement

All participants provided written informed consent prior to enrollment in the study.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

The artificial intelligence tool ChatGPT by OpenAI was used to improve language clarity and correct typographical errors. No AI tools were used for generating content, analysis, or interpretation of results.

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