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Case Report

Effectiveness of Cannabinoids Treatment in Pain Management and Other Fibromyalgia-Associated Symptoms: A Case Series

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Abstract

Pharmacological therapies for FM are still ineffective in many patients, involving adverse effects that hinder their long-term use.

We aimed to assess the effectiveness of cannabinoids (Tilray Dried Flower THC18) in the management of chronic pain and other FM-associated symptoms according to patient-reported outcomes, in a series of three FM patients.

We observed improvements after one and three months of cannabinoids treatment in Brief Pain Inventory (BPI), Visual Analogue Scale (VAS), Insomnia Severity Index (ISI), SF-36 Health Survey, and Fibromyalgia Impact Questionnaire (FIQ) allowing pain relief, and improvements in sleep quality, performance of daily life activities, and quality of life.

Keywords: Cannabinoids; Case series; Chronic pain; Fibromyalgia; Nociplastic pain

Introduction

Fibromyalgia (FM) is classified as chronic primary pain, being a form of chronic and nociplastic widespread pain that is associated with sleep disorders, cognitive dysfunction, and somatic symptoms, leading to significant emotional distress and/or significant functional disability [1].

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The European League Against Rheumatism (EULAR) currently recommends nonpharmacological treatment as first-line therapy and, in case of ineffectiveness, individualized treatment according to patient needs, which may include pharmacological therapies for individuals with severe pain or sleep disturbance [2]. Nevertheless, pharmacological therapies for FM are ineffective in many patients and involve adverse effects that can hinder their long-term use [3].

Although the pathophysiology of FM is still largely unknown, some studies suggest that the modulation of pain in pathological conditions such as in FM may be at least partially related to the endocannabinoid system's deregulation [4]. This system is fundamentally composed by endocannabinoid signalling molecules, G-protein-coupled cannabinoid receptors (CB1 and CB2), and enzymes involved in ligand biosynthesis and inactivation [5].

Cannabis flowers contain more than 100 types of cannabinoids [4], being tetrahydrocannabinol (THC) and cannabidiol (CBD) the main compounds of cannabis with analgesic and anti-inflammatory properties [6]. The analgesic properties of cannabinoids and their ligands are primarily mediated by the cannabinoid receptor CB1 by inhibiting presynaptic gamma-aminobutyric acid and glutamatergic transmission [5].

Several studies already supported the efficacy and effectiveness of Medical Cannabis (MC) in the management of chronic pain and other FM-related symptoms [4,6-8] including two systematic reviews comprising both observational studies and clinical trials.

In Portugal, there is still lack of evidence regarding cannabinoids treatment in FM patients. In this work, we aimed to assess the effectiveness of cannabinoids (Tilray Dried Flower THC18) in the management of chronic pain and other FM-associated symptoms according to patient-reported outcomes, in a series of three FM patients. Tilray Dried Flower THC18 is the only commercially available medical cannabis product available in Portugal.

Patients Information and Clinical Findings

We present the course of three patients followed at inDOLOR unit, between July 2021 and September 2022, with refractory pain associated with FM diagnosed according to the criteria from Portuguese General Directorate of Health [9]. The baseline demographic and clinical characteristics of patients are presented in table 1. Two patients were female and the age ranged from 22 to 72 years (Table 1). All patients were of Caucasian ethnicity.

Therapeutic interventions, diagnostic assessments, follow-up, and outcomes

Tilray dried flower THC18 (18%THC) was administered to all patients by inhalation/vaporization for three months, according to Table 2. No intercurrences and/or major adverse effects were reported after the introduction and consequent adjustments of cannabinoids treatment (Table 2).

Patient	Age (yrs)	Sex	Occupation	Height (cm)	Weight (kg)	BMI (kg/m2)	Medical, family, and psychosocial history	Main symptoms	Clinical findings
1	72	Female	Retired	160	80	31.3	Hypertension, obesity, diabetes Mellitus type II, depression, chronic depression. Surgical history of total hysterectomy, mastectomy and lymph node emptying due to breast carcinoma, with radiotherapy and oral chemotherapy for 5 years, bariatric surgery, and anal fissure. FM diagnosis at 62 years	Generalized pain for > 1 year. Neuropathic pain characterized as: pins, tingling, stabbing and burning.	Inadequate diet, unsatisfactory water intake, little physical exercise, irregular intestinal transit. Consciousness and orientation in time and space with occasional inconsistent speech. Poor sleep quality (4 hours/night) and social isolation (given the reduced mobility) due to pain. Quality of life extremely affected. Current therapy included metformin+sitagliptin, quetiapine, bromazepam, venlafaxine, losartan+amlodipine with no pain relief.
2	62	Female	Secretary	164	62	23.1	No surgical history or known allergies. Anxiety and dysfunctional family dynamics. FM diagnosis for several yrs.	Generalized and mixed pain with predominance at the lumbar, cervical and dorsal spine levels. The pain started > 1 year ago, after trauma to the left knee. Pain characterized as sharp spasm, piercing; crawling over ski, stabbing; burning, red-hot iron, and barbed wire.	Adequate diet, little physical exercise, regular intestinal transit. Consciousness and orientation in time and space. Current therapy included amitriptyline, zolpidem as SOS, and diazepam as SOS with 50% of pain relief.
3	22	Male	Student	175	113	36.9	No history of surgery and known allergies. FM diagnosis in childhood. Past therapy included Palexia, gabapentin, pregabalin, metamizol, elontril, sirdalud, cholecalciferol, thiamine, folic acid, zaldiar, metanor, flexiban, mirtazapine, diazepam, paracetamol, duloxetine, transtec, and triticum with no effect on pain control, and acupuncture with some effect on pain control.	Constant low back pain - migratory in several places, that started at age 7. Pain characterized as sharp spasm, nerve pinching, stabbing, burning, and electric shock.	Obesity. Inadequate diet, little exercise, regular bowel movements. Poor sleep quality due to pain and social isolation. School education and interaction with peers extremely affected. Current therapy included zolpidem, quetiapine, duloxetine, neurobion, folic acid with 10% of pain relief.

Table 1: Baseline Demographic and Clinical Characteristics of the patients.

BMI: Body Mass Index; FM; Fibromyalgia; SOS: Saviour Drug; Yrs: Years.

The following patient-reported outcomes were assessed prior to (baseline) and after one and three months of cannabinoids treatment: Brief Pain Inventory (BPI), Visual Analogue scale (VAS), Insomnia Severity Index (ISI), SF-36 Health Survey, and Fibromyalgia Impact Questionnaire (FIQ). The individual clinical outcomes are presented in table 3.

Patient 1

At baseline, this patient presented severe pain interference in daily activities (mean score, 9.3) that decreased one (mean score, 3.6) and three (mean score, 2.7) months after cannabinoids treatment. At three months the patient reported decreased pain intensity by 90%.

At baseline, this patient presented severe clinical insomnia that improved to subthreshold insomnia after one and three months of cannabinoids treatment.

FM-associated symptoms had a relevant impact in both physical and mental domains of SF-36 at baseline, mainly in role-physical, vitality, and role-emotional components, which improved after one and three months of cannabinoids treatment. FIQ also showed a great impact of FM in daily life (score, 10), morning tiredness (score, 9), anxiety and depression (score, 10) at baseline, which decreased both after one and three months of cannabinoids treatment (Table 3). At the end of follow-up, depression was still evident, and a negative impact on anxiety was found.

Patient 2

At baseline, this patient presented severe pain interference in daily activities (mean score, 7.6) that decreased one month after cannabinoids treatment (mean score, 4.1). At one month, this patient also reported decreased pain intensity by 60%.

	Daily Vaporisations[a]	Equivalence of THC18 bioavailability (mg/Kg/day)
Patient 1[b]		
1st week of FUP	1+1+1+1	0.33
1st month of FUP	1+1+2+2	0.51
3rd month of FUP	2+2+2+0	0.51
Patient 2[c]		
1st week of FUP	0+0+2+2	0.44
1st month of FUP	2+2+2+2	0.87
3rd month of FUP	Discontinued treatment	---
Patient 3[d]		
1st week of FUP	0+0+1+2	0.18
1st month of FUP	2+1+1+3	0.42
3rd month of FUP	2+1+1+3	0.42

Table 2: Doses of administration of Tilray dried flower THC18 (18%THC) per patient.

FUP: follow-up.

a The vaporisations were administer after breakfast, lunch, afternoon meal, and dinner, respectively.

b No intercurrences and/or major adverse effects were reported after the introduction and consequent therapeutic adjustments of cannabinoids. At the second week of treatment (1+1+2+2) the patient reported motor agitation after vaporization at night, interfering with sleep onset. Therefore, the dosage was adjusted, reducing the number of vaporizations at the end of the day (to 1+1+2+0 and after 4 days to 1+1+2+1). After one month of cannabinoids treatment, the patient reported increased pain and stiffness, increasing again the dosage at night (1+1+2+2). During the second month, the dosage was readjusted, and the patient became autonomous in managing the vaporizations needed at night.

c No intercurrences were reported after the introduction and consequent therapeutic adjustments of cannabinoids during the first month of treatment. The patient interrupted cannabinoids treatment at week 5 due to family reasons and re-started it at week 6, with a dosage of 2+2+3+3. However, after this adjustment, the levels of anxiety of the patient increased, leading to the adjustment to 1+1+3+3. Due to anxiety and pain complaints, the patient discontinued cannabinoids treatment at 8 weeks after the initiation.

d No intercurrences and/or major adverse effects were reported after the introduction and consequent therapeutic adjustments of cannabinoids. After the therapeutic adjustment at second week of treatment (1+0+2+2), the patient reported discomfort related to psychotropic effects and somnolence associated with vaporization after afternoon meal, leading to dosage adjustments. The dosage was readjusted at month 1 to 2+1+1+3, and since the therapeutic goal was reached it was maintained until the end of the third month.

Patient-reported outcomes	Patient 1			Patient 2			Patient 3		
	Baseline	1 mo	3 mos	Baseline	1 mo	3 mosa	Baseline	1 mo	3 mos
BPI									
Pain interference, mean score	9.3	3.6	2.7	7.6	4.1	---	7.1	1.1	0.6
Pain severity, mean score	5.0	3.3	2.3	4.8	2.5	---	5.8	4.0	2.5
VAS, total score	5	3	2	4	1	---	5	3	2
ISI, total score	25	12	12	19	5	---	24	6	4
SF-36 Health Survey, %									
Physical functioning	5	25	35	40	100	---	35	80	90
Role-Physical	0	25	56	0	46	---	19	69	75
Bodily Pain	23	46	46	24	65	---	13	69	82
General Health	25	30	30	60	50	---	65	65	72
Vitality	0	44	44	31	50	---	44	50	56
Social Functioning	25	50	63	63	50	---	13	75	75
Role-Emotional	0	25	25	0	50	---	8	75	83
Mental Health	15	50	40	35	55	---	70	80	85
FIQ, total score	59.2	45.4	41.2	60.3	29.6	---	69.9	40.1	26.7

Table 3: Individual clinical outcomes at baseline, and after one and three months of cannabinoids treatment.

BPI: Brief Pain Inventory; FIQ: Fibromyalgia Impact Questionnaire; ISI: Insomnia Severity Index; mo: month; mos: months; VAS: Visual Analogue Phase.
a The patient discontinued cannabinoids treatment after 8 weeks.

At baseline, this patient presented clinical insomnia of moderate severity, that improved to no clinical insomnia after one month of cannabinoids treatment (Table 3).

FM-associated symptoms had a relevant impact in both physical and mental domains of SF-36 at baseline, mainly in role-physical and role-emotional components, which improved after one month of cannabinoids treatment. FIQ also showed a great impact of FM in pain (score, 7), fatigue (score, 8), morning tiredness (score, 5), stiffness (score, 10), anxiety (score, 8) and depression (score, 8), which improved after one month of cannabinoids treatment. Despite the pain and stiffness relief, improved sleep quality and ability to perform daily tasks, reduced co-medication, and improved quality of life, cannabinoids treatment had negative effects on anxiety, leading to non-compliance with treatment instructions and to treatment discontinuation 8 weeks after initiation, being the patient referred to psychiatric consultations.

Patient 3

At baseline, this patient presented high pain interference (mean score, 7.1) that decreased one (mean score, 1.1) and three (mean score, 0.6) months after cannabinoids treatment. At three months, the patient reported complete pain relief with no pain interference with general activity (score, 1), reporting improved sleep (score, 0).

This patient presented severe clinical insomnia at baseline, that improved to no clinical insomnia after one and three months of cannabinoids treatment (Table 3).

At baseline, FM-associated symptoms had a relevant impact in both physical and mental domains of SF-36, mainly in role-physical, bodily pain, social functioning, and role-emotional components, which improved after one and three months of cannabinoids treatment. FIQ also showed a great impact of FM in work (score, 10), pain (score, 8), morning tiredness (score, 10), stiffness (score, 7), and anxiety (score, 7) at baseline, which improved after one and three months of cannabinoids treatment, with no interference of FM in the performance of several daily activities (score, 0) after three months.

Discussion and Conclusion

In this work, we aimed to assess the effectiveness of cannabinoids in the management of chronic pain and other FM-associated symptoms in a series of three patients. In general, we observed improvements after treatment in BPI, VAS, ISI, SF-36, and FIQ in these patients, allowing pain relief, improved sleep quality, improved performance of daily life activities, and improved quality of life.

Cannabinoids treatment allowed decreased co-medication in patients 1 and 2, suggesting that it may allow to decrease the chronic use of several pharmacological therapies associated with severe adverse effects.

Improvements of social interaction were also found after cannabinoids treatment in patients 1 and 3. Importantly, intercurrences and/or major adverse effects were not observed in any patient, but the tolerated doses varied greatly among these patients, indicating the need for a careful individual titration. Our results are in line with the literature suggesting the safety and beneficial effects of MC in FM patients [6,7] Nevertheless, adverse effects on anxiety levels were observed in two patients, one of which discontinued from treatment after 8 weeks. The incidence of nonserious adverse events was already reported as a possible limitation for the use of MC, including mental confusion, nausea/vomiting, restlessness/irritation, and palpitations [6,8]. Importantly, development of tolerance was not observed.

This work had some limitations that should be acknowledged: in Portugal, the only cannabinoids formulations available are administered by inhalation/vaporization, which is associated with a higher frequency of side effects [7] and which effects present high intra- and inter-individual variability; the cannabinoids administered were difficult to titrate, given the very high THC concentration; in Portugal, many patients may not benefit from MC as a last-line treatment due to the high costs and the lack of reimbursement.

This work had also some strengths that should be acknowledged: our patients presented a FM diagnosis based on well described criteria; the cannabinoids administered present a high concentration of THC, which is one of cannabis' main compounds with analgesic and anti-inflammatory properties [7]; the inclusion of several patient-reported outcomes measures, allowing a broader evaluation of each patient.

In conclusion, although more studies are needed, in our series of FM patients, cannabinoids treatment showed promising results in the management of chronic pain and other FM-associated symptoms, improving the quality of life of these patients.

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Author contributions

Soraia Tomás and Pedro Trincão were involved in data collection, analysis, and interpretation, and in the critical revision of the manuscript. Soraia Tomás was involved in the drafting of the manuscript.

All authors discussed the results and commented on the manuscript, approved its final version and take responsibility for the accuracy or integrity of any part of the work.

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Conflicts of Interest

The authors declare no conflicts of interest.

Ethics

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 1983. Informed consent was obtained from all patients for being included in the study.

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