

Cannabinoid Use for Pain Relief Among People with Multiple Sclerosis

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Abstract

Aim

Pain is an often-reported symptom in Multiple Sclerosis (MS); however, pain management is often described as being inadequate. Emerging evidence suggests that cannabinoids may be effective in the treatment of MS related pain. This research aimed to determine the prevalence and patterns of use of cannabinoids for pain relief among a sample of Irish people with MS (PwMS).

Methods

101 individuals attending neurology outpatient appointments at Cork University Hospital completed questionnaires measuring demographics, nociceptive pain, neuropathic pain, and use of cannabinoids.

Results

Sixty people (59%, 95% CI 48–67.7%) had experienced MS related pain, while twenty-six (26%, 95% CI 17–34%) had experienced neuropathic pain. Almost a third (30%, 95% CI 18–42%) of PwMS experiencing pain had used cannabinoids. PwMS who had used cannabinoids compared to non-users were more likely to experience neuropathic pain, be of a younger age and to use cannabinoids recreationally ($p < 0.05$). In addition, the type of cannabinoids participants used appeared to influence how effectively they rated it as a pain reliever; with cannabis/hash being rated as more effective than CBD oil or a Sativex spray ($p < 0.05$).

Conclusion

Pain is a significant problem for PwMS. A substantial number of participants used cannabinoids to manage their pain, however, further research into the efficacy and long-term side effects of this substance is necessary.

Introduction

Multiple Sclerosis (MS) is the most common neurological disease among young adults.¹ A recent meta-analysis suggested that 63% of people with MS (PwMS) experience pain, while other studies have indicated that PwMS experience pain for on average 77 hours per week, with 25% enduring pain of severe intensity.²⁻⁴ MS related pain has been demonstrated to have a profoundly negative impact on many aspects of peoples' lives, affecting their ability to work and fulfil social roles.⁵

The pain experienced by PwMS has been classified by the W.H.O as nociceptive, neuropathic, or mixed. Nociceptive pain occurs due to actual or potential tissue injury.⁶ Neuropathic pain arises following damage to the somatosensory nervous system, while mixed pain includes both nociceptive and neuropathic elements. Neuropathic pain is a significant element of MS pain and has been noted by many studies as being particularly difficult to treat.⁶⁻⁸ Similarly, research has demonstrated that the medications utilized to manage MS related pain are often found to be inadequate.⁸ It is estimated that 11% of PwMS present to the emergency department for pain treatment, an expensive and unsuccessful method of controlling pain in a chronic illness.⁹

There is emerging evidence which suggests that cannabinoids may be effective in relieving pain. Cannabinoids refer to the 60-110 different chemicals found in the cannabis plant, the major components being the psychoactive element delta-9-tetrahydrocannabinol (THC) and the non-psychoactive component cannabidiol (CBD).¹⁰ Two cannabinoid receptors (CB1 and CB2) have been demonstrated to be involved in the regulation of pain. It has been shown that stimulation of these receptors results in the inhibition of pain responses.^{11, 12}

Furthermore, cannabinoids appear to be particularly effective in relieving pain that is neuropathic in origin, with several investigations having found it to be a successful analgesic for a variety of neuropathic conditions.^{12 and 13} The European Federation of Neurological Societies now supports the use of cannabinoids as a second line treatment for neuropathic pain.¹² However, the evidence regarding the efficacy of cannabinoids when used by PwMS pain is more conflicting. A systematic review conducted in 2014 found cannabinoids to be effective in alleviating central MS related pain.¹⁴ However, other research has suggested that while cannabinoids appear to be successful in reducing MS related pain in the short term, it is not effective in the long term.^{15 and 16}

Despite the inconclusive nature of results, research has demonstrated the use of cannabinoids to relieve MS related pain in a number of European countries. In the UK 30% of PwMS have used medical cannabinoids, while in Spain it is estimated to be 17% and in Denmark 49% of PwMS have used the drug for medical purposes.¹⁷⁻¹⁹ In Ireland, the Health Products Regulatory Authority (HPRA) recently carried out an assessment of cannabinoids for medical use and authorized its use for spasticity as a result of MS, certain forms of epilepsy as well as chemotherapy-related nausea. However, it was recommended that it remain illegal for the treatment of chronic pain. Although the report acknowledged the evidence base for cannabinoids in the management of chronic pain, it cited the sizable number of effective analgesics already available, as well as the large and diverse population of patients with chronic pain as factors which prevented its legalisation.²⁰ Nevertheless, a 2018 study conducted on Irish patients with chronic pain revealed that 22% had utilized cannabinoids for analgesic purposes.²¹ However, there is currently no study which examines the prevalence and patterns of use of cannabinoids among an Irish population of PwMS. This study aimed to explore the use of cannabinoids for pain management among an Irish cohort of PwMS.

Method

The study was a cross-sectional questionnaire-based survey. PwMS were invited to participate in the research when attending routine visits to the neurology outpatient departments of both Cork University Hospital (CUH) and CUH Consultants' Private Clinic. A total of 101 PwMS agreed to take part.

Individuals included in the study had a diagnosis of MS according to the McDonald criteria and were over 18 years of age.²² There were no exclusion criteria. Data was collected using anonymous self-report questionnaires. Four different questionnaires were administered as part of the survey. Demographic information such as: age, sex, type of MS, age diagnosed, employment status and education level attained were initially collected. The first questionnaire measured disability using the Patient Determined Disease Steps (PDDS) which strongly correlates with the Expanded Disability Status Scale (EDSS).²³ The second questionnaire explored pain severity and pain interference using the Brief Pain Inventory (short form).²⁴ The third questionnaire established the presence of neuropathic pain through the ID Pain questionnaire.²⁵ Only participants reporting MS related pain in the second or third questionnaires were administered the fourth questionnaire. The fourth questionnaire investigated participants' patterns of use of cannabinoids. IBM SPSS statistics V26.0 was used to analyse the collected data.

Results

Participant demographics

The survey was completed by 101/106 PwMS (95% response rate). The average age of participants was 51 years, 63% of participants were female, and 83% had relapse remitting MS. The average age people were diagnosed with MS was 36 years, 31% of participants were on disability payment and the leaving certificate was the highest education level achieved by 31% of participants. No disability was reported by 34% of participants, 15% reported mild disability, 12% moderate disability, 11% gait disability, 10% described themselves as early cane users, 6% late cane, 8% required bilateral support, 5% required a wheelchair and no participant described themselves as being bedridden.

Pain

Descriptive statistics revealed that 59% (60/101, 95% CI 48.4 - 67.7%) of people experienced MS related pain and 26% (26/101, 95% CI 17 - 34%) experienced neuropathic pain. The worst pain experienced by participants was on average 5.5/10 (range 1-10, SD 2.4). A Mann-Whitney U test demonstrated a significant difference in pain severity between individuals who experienced neuropathic pain and those who did not ($p = 0.00$, $r = 0.4$). The median pain severity for individuals with neuropathic pain was seven, while for individuals without neuropathic pain it was five. A statistically significant relationship was not found between pain severity and use of cannabinoids ($p = 0.88$, $r = 0.02$). The median pain score for cannabinoid users was six and for nonusers was also six.

Cannabinoids

Cannabinoids had been used by 30% (18/60, 95% CI: 18 - 42%) of participants with pain. Cannabis products were rated as 3.1/5 (SD = 1.5) in effectiveness. Table 1 illustrates participants' patterns of use of cannabinoids. The most frequently utilised form of cannabinoids was CBD (15%, 9/60), cannabis/hash were used by 11.7% (7/60) and Nabiximols (Sativex) by 3.4% (2/60) of individuals. The use of cannabinoids was 100% medical in the majority of PwMS (18.3%, 11/60), while 10% (6/60) indicated their use was a combination of recreational and medical. At the time of the survey 15% (9/60) of PwMS were still using cannabinoids. Most participants who used cannabinoids obtained them from friends and family (15%, 9/60). Frequency of use by most individuals utilising cannabinoids was several times a day (10%, 6/60). Only 3.4% (2/60) of people indicated that they had experienced any adverse effects from utilising cannabis products, with both participants reporting paranoia.

Table 1. Patterns of cannabinoid use.

Characteristics	Response % (n)
Used cannabinoids for pain relief	
Yes	30% (18/60)
No	70% (42/60)
Recreational cannabinoid use	
Yes	14% (14/101)
No	78% (78/101)
Medical/Recreational use	
100% Recreational	0% (0/60)
75% Recreational and 25% Medical	0% (0/60)
50% Recreational and 50% Medical	4% (4/60)
25% Recreational and 75% Medical	3.4% (2/60)
100% Medical	18.3% (11/60)
Currently using cannabinoids	
Yes	15% (9/60)
No	8% (5/60)
Preferred form of cannabinoids	
Sativex	3.4% (2/60)
CBD	13% (8/60)
Cannabis/Hash	10% (6/60)
Obtained cannabinoids	
Grow it myself	1.7% (1/60)
Health food store	8.3% (5/60)
Pharmacy	0% (0/60)
Internet	0% (0/60)
Friends/family	10% (6/60)
Underground market/dealer	3.4% (2/60)

Characteristics	Response % (n)
Years using cannabinoids	
Less than 1 year	13.3% (8/60)
1 to 5 years	6.7% (4/60)
6 to 10 years	1.7% (1/60)
11 to 15 years	3.4% (2/60)
16 to 20 years	1.7% (1/60)
More than 20 years	1.7% (1/60)
Preferred delivery method	
Smoked as a cigarette	11.7% (7/60)
Vaporiser	25% (15/60)
Dropper	13.3% (8/60)
Eat	1.7% (1/60)
Other delivery methods used	
Bong	1.7% (1/60)
Chillum	5% (3/60)
Drink	1.7% (1/60)
Dropper	3.4% (2/60)
Eat	3.4% (2/60)
Vaporiser	10% (6/60)
Most effective type	
Cannabis sativa	0% (0/60)
Cannabis indica	3.4% (2/60)
Don't know	23.3% (14/60)
Frequency of use	
Several times a day	10% (6/60)
6-7 times a week	3.4% (2/60)
3-5 times a week	1.7% (1/60)
1-2 times a week	3.3% (2/60)
Less than weekly	1.7% (1/60)
Very seldom	3.4% (2/60)
As required	3.4% (2/60)
Side effects	
Yes	3.4% (2/60)
No	23.3% (14/60)

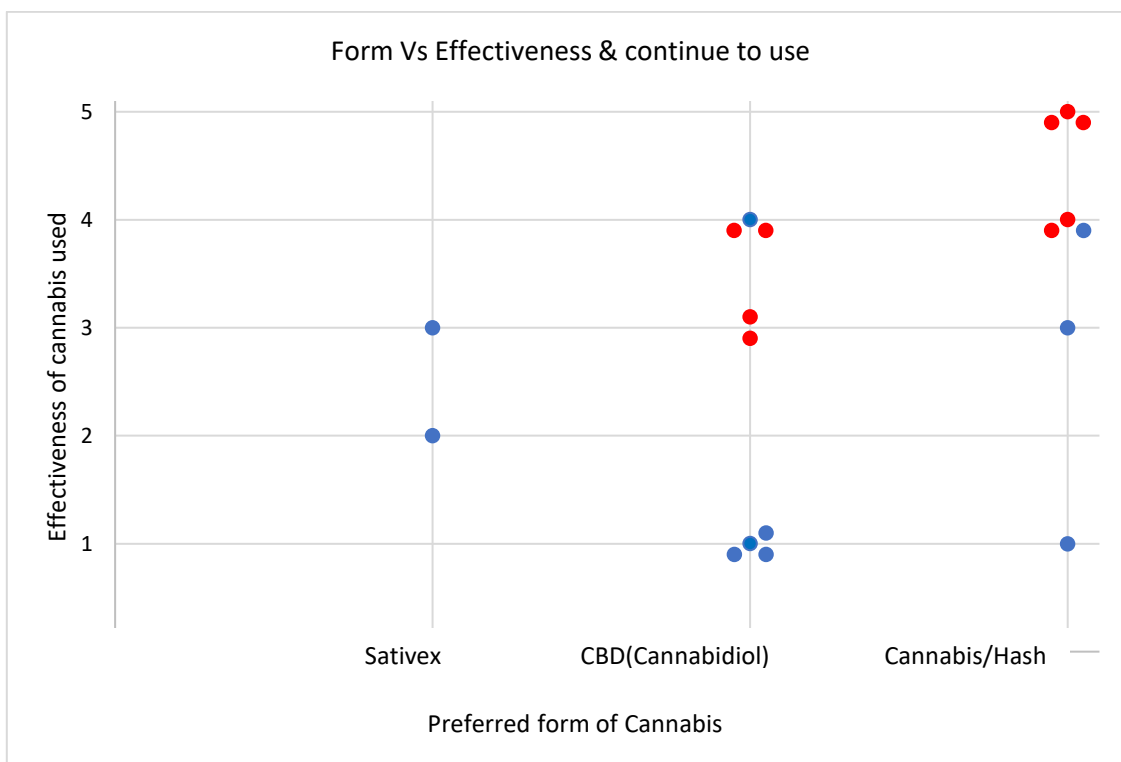
Several statistically significant differences were observed between PwMS who used cannabinoids for pain relief and those who did not (Table 2). A Mann - Whitney U test revealed that cannabinoid users were of a younger age than non-users ($p = 0.003$, $r = 0.3$). Median age of cannabinoid users was 39.5 years, while the median age of non-users was 51 years. A Chi square test demonstrated that cannabinoid users were more likely to experience neuropathic pain than non-users ($p = 0.01$ and $\phi = 0.3$). In addition, a Fisher's exact test indicated that medical cannabinoid users were more likely to use cannabinoids recreationally compared to non-users ($p = 0.00$, $\phi = 0.5$).

Table 2. Use of cannabinoids.

Participant group	Participant group	P-value
Cannabinoid user	Median Age	
- Yes (n=18)	39.5	0.00
- No (n=43)	51	
	Neuropathic pain	
Cannabinoid user	Yes	No
- Yes	n=11	n=5
- No	n=14	n=28
	Recreational use	
Cannabinoid user	Yes	No
- Yes	n=8	n=9
- No	n=2	n=38

Similarly, a number of statistically significant differences were demonstrated between the different forms of cannabinoids participants used (Figure 1). A Fisher's exact test revealed that cannabis/hash had higher efficacy ratings as a pain reliever than CBD oil or Sativex ($p = 0.03$, Cramer's $V = 0.73$). Likewise, a Fisher's exact test evidenced that PwMS using cannabis/hash were more likely to continue using cannabinoids than those using CBD oil or Sativex ($p = 0.02$, Cramer's $V = 0.74$).

Figure 1. Form of cannabinoids vs effectiveness.



Discussion

This was a cross-sectional study, 101 PwMS met the inclusion criteria and agreed to participate. Most participants experienced pain and a significant number of these individuals also experienced neuropathic pain. Greater pain severity was found to be associated with the presence of neuropathic pain however, it was not found to be associated with the use of cannabinoids. Cannabinoids were used for analgesic purposes by almost a third of participants and were evaluated as being moderately effective. The use of cannabinoids to relieve pain was found to be associated with the recreational use of cannabinoids, the presence of neuropathic pain and being of a younger age.

The prevalence of use of cannabinoids found in this study is consistent with similar research conducted in Spain and the UK, but lower than the numbers reported in Denmark. The discrepancy in these results is likely reflective of medical cannabis products having been made available to patients on prescription in Denmark since 2018.¹⁷⁻¹⁹ The factors found to be associated with the use of cannabinoids in this investigation are largely supported by previous literature. A number of studies have found the presence of neuropathic pain to be associated with use of cannabinoids, it is uncertain whether this is a result of the possibility that cannabis products work best for pain that is neuropathic in origin or because neuropathic pain tends to be more severe and is poorly controlled by the current treatment options, therefore leading to people being more open to trying alternative treatments.^{12 and 13} The finding that the use of cannabinoids is associated with PwMS of a younger age has also been demonstrated by past research, this may be due to the use of cannabinoids being more socially acceptable among those of a younger age or because people of a younger age may be more aware of the potentially beneficial effects of cannabis.¹⁴ This is also illustrated by the final association found between recreational use of cannabinoids and their medical use which may result as recreational users happen upon apparent medical benefits of cannabinoids by accident.⁹

Participants of this study reported the plant form of cannabis to be more effective than cannabinoid extracts in their experience. This coincides with the results of previous studies and is perhaps because the plant form of cannabis contains other potentially biologically active agents, such as terpenes and other phytocannabinoids, that may have analgesic properties which are not present in cannabinoid extract preparations.¹² Furthermore, the indication that the majority of participants obtained cannabinoids from informal networks such as through friends and family has been evidenced by a number of previous investigations. This discovery is concerning as it implies that PwMS are using unregulated products in which the reported strengths of THC and CBD may be wrong.^{12 and 18}

The strengths of this research include it being the first study to examine the use of cannabinoids among an Irish population of PwMS. Additionally, the majority of the questionnaires utilised in the survey have been previously demonstrated to be reliable and valid. The study achieved a substantial sample size and a high response rate, thus decreasing the impact of PwMS who were more motivated to participate.

However, this investigation was not without its limitations. One of the questionnaires was designed by the researcher and had not previously been evidenced to be reliable or valid. In addition, the

presence of neuropathic pain cannot be definitively established from a questionnaire - a clinical assessment is an essential part of diagnosis.²⁵ Likewise, the study was conducted at a single clinic visit and therefore, does not account for the variable nature of MS related pain.¹⁵ Data was collected in a busy outpatient clinic, with some PwMS requiring the assistance of the researcher and thus participants may have been reluctant to admit to the use of cannabinoids. In addition, the survey was largely conducted in the public hospital and therefore it is possible that results were influenced by socio-economic status.^{9,21} Furthermore, it is likely that people with very debilitating MS may stop attending regular outpatient appointments, therefore, the sample obtained may not be representative of the total population of PwMS.

In conclusion, pain, particularly neuropathic pain is a significant problem for PwMS. A significant number of PwMS attending an Irish neurology clinic have used cannabinoids to relieve their pain, with anecdotal evidence that different forms of cannabinoids appear to have different levels of efficacy. However, this research cannot seek to establish the veritable effectiveness of cannabis products. Clinical trials that compare the efficacy of cannabinoids in relieving pain with that of authorised analgesics are required. It is also necessary that future research examine the long-term safety of the use of cannabis products. The findings of this research suggest that healthcare professionals should be aware of the use of these products by PwMS and should be willing to discuss the utilisation of this substance with their patients. In addition, the researchers would query whether the use of cannabinoids should be permitted in cases of neuropathic pain given that it is poorly controlled with a smaller patient population and few available therapeutic alternatives.

Declaration of Conflicts of Interest:

The authors have no conflicts of interest to declare.

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