


Patient Reported Outcomes Using Medical Cannabis for Managing Pain in Charcot-Marie-Tooth Disease

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Abstract

Objective: Chronic pain is a major problem for patients with Charcot-Marie-Tooth (CMT) disease. This exploratory study examined patient reported efficacy of medical cannabis for pain management in this population. **Methods:** Participants (N = 56; 71.4% female; Age = 48.9, SD = 14.6; 48.5% CMT1) were recruited through the Hereditary Neuropathy Foundation. The online survey contained 52 multiple choice questions about demographics, medical cannabis use, symptomology, efficacy, and adverse effects. **Results:** Nearly all (90.9%) of respondents reported experiencing pain, including all (100%) females and 72.7% of males (chi-square $P < .05$) with 91.7% of respondents indicating cannabis provided at least 50% pain relief. The most frequent response was an 80% reduction in pain. Moreover, 80.0% of respondents reported using less opiates, 69% noted using less sleep medication, and 50.0% reported using less anxiety/antidepressant medications. Negative side effects were noted by 23.5% of respondents. However, almost all (91.7%) of that subgroup did not have plans to stop consuming cannabis. One-third (33.9%) possessed a medical cannabis certificate. Patient perceptions of their physicians' attitudes regarding patient medical cannabis use greatly impacted whether respondents informed their providers of their usage. **Conclusion:** The vast majority of patients with CMT reported that cannabis was effective to manage pain symptoms. These data support the need for prospective, randomized, controlled trials using standardized dosing protocols to further delineate and optimize the potential use of cannabis to treat pain related to CMT.

Keywords

Charcot Marie Tooth, hereditary motor and sensory neuropathy, neuropathic pain, chronic pain, cannabis, marijuana

Introduction

Charcot-Marie-Tooth (CMT) disease is the most common genetic neuropathy affecting 1 in 2500 people.¹ Although the motor symptoms may attract the most attention, a large survey (N = 407) revealed that over three-quarters of patients with CMT experienced pain and over four-fifths numbness.² Among genetically diagnosed patients with CMT1A, 29% had neuropathic pain. Allodynia was the most specific neuropathic pain symptom.³ Complications of CMT include sleep apnea, restless legs syndrome, daytime sleepiness, and impaired sleep.⁴ Although there is no known cure for this slowly progressive disease, there are treatments such as physical and occupational therapy, orthotics, and pharmacotherapies to manage symptoms. The medications used for pain management are varied and included aspirin, nonsteroidal anti-inflammatory medications, acetaminophen, tricyclic antidepressants, anticonvulsants, and opioids.⁵

The National Academy of Sciences reported that there was conclusive evidence indicating that cannabis was effective for chronic pain among adults.⁶ There was also moderate evidence that cannabis was effective for improving short-term sleep outcomes in individuals with sleep disturbance

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associated with obstructive sleep apnea syndrome or chronic pain.⁶ Preclinical and observational studies demonstrate the potential opioid-sparing effects of cannabinoids in the context of analgesia.⁷ Surveys of cannabis dispensary members have identified a harm-reducing substitution effect where they reduce or stop using other medications, especially opioids,⁸ after starting cannabis. There is currently no published information about medical cannabis that is specific to CMT. The objective of this exploratory study was to obtain CMT patient's perspectives regarding the benefits and risks of medical cannabis.

Methods

All protocols were approved by the sponsoring institution Human Subjects Institutional Review Board (IRB) Committee prior to initiation of the study. Recruitment for this study was done through the Hereditary Neuropathy Foundation's (HNF) Global Registry for Inherited Neuropathies (<https://www.hnfcure.org/>). All registered members of the HNF received an e-mail invitation to participate in this study, which was also advertised on the website. The survey was available on the HNF website and data was collected for 1 year starting on September 01, 2018. Inclusion criteria included those affected by CMT or inherited neuropathy who were over the age of 18, and who used medical cannabis to cope. Participation was voluntarily and anonymous. Given the overall rarity of the disorder, the study was not limited to any one genetic subtype of CMT. Despite genotypic heterogeneity, there is a large degree of phenotypic similarity across most of the major forms of CMT. The survey used a branched logic approach to ensure that participants would only get follow-up questions that were relevant to them. The data is reported in both numerator/denominator form and as relative percentages. The online survey contained 52 multiple choice questions about demographics, medical cannabis use, symptomology, efficacy, and adverse effects ([Supplementary Material](#)). The survey used for this study included a subset of the items used previously⁸ but also many questions were tailored for the CMT population. The survey contained 52 multiple choice and short-answer items ([Supplementary Material](#)). The survey instrument gathered information on the utility, cannabis composition preferences (eg tetrahydrocannabinol (THC) vs cannabidiol (CBD)) and adverse effects of medical cannabis. The entire survey is included in [supplemental material Table 1](#).

Participants

A total of 56 subjects completed the survey (71.4% female, Age = 48.9, SEM = 2.0, Min = 22, Max = 87). Among the subset who reported a known CMT subtype (n = 33), there was 48.5% with a form of CMT type 1, 27.3% with hereditary neuropathy with liability to pressure palsies (HNPP), 18.2% CMT type 2, and 6.1% CMT type 4. Among those that reported using a motility device (N = 24), this included cane

(25.0%), braces (20.8%), walker (16.7%), and scooter (12.5%).

Procedures

Data-analysis

Data was imported into and analyzed using statistical software by International Business Machines (IBM, Armonk, New York, United States). The Statistical Package for Social Sciences (SPSS) package, version 26 was used to conduct all analyses, including chi-square tests. Figures were constructed with GraphPad Prism, version 8. The variability was reported as the Standard Error of the Mean (SEM). A $P < .05$ was considered statistically significant.

Results

All survey response data is included in the [supplemental data Table 2](#). When asked if they experienced pain associated with CMT, 30/33 (90.9%) of participants answered 'yes'. All females, 22/22 (100%) but only 8/11 (72.7%) of males reported pain associated with CMT (chi-square $P < .05$). In response to: 'How effective is medical cannabis in alleviating your symptoms with CMT?' respondents provided the percent of relief they experienced from medical cannabis (0 to 100% in 10% increments). The most frequently selected option was 80% relief. The vast majority 44/48 (91.7%) indicated cannabis provided at least 50% relief ([Figure 1A](#)).

Issues related to muscle weakness and atrophy were common in this sample. About three-quarters of respondents reporting weak ankles, 25/36 (72.2%), about one-third with muscle atrophy 13/36 (36.1%), tremors 12/36 (33.3%); 10/36 (27.8%) had poor or absent reflexes, clumsiness 9/36 (25.0%), coordination or balancing problems 9/36 (25.0%), restless leg syndrome 9/36 (25.0%), arm or leg weakness 8/36 (22.2%), difficulty with physical activity 8/36 (22.2%), rigid muscles 8/36 (22.2%); and a fifth had hammer or curled toes 7/36 (19.4%), spasticity 7/36 (19.4%), and weakness 7/36 (19.4%). Sensory concerns included temperature sensitivity 10/36 (27.8%), neuropathic pain 8/36 (22.2%), and numbness 8/36 (22.2%).

Preferred methods of cannabis consumption were smoking 18/53 (34.0%), vaporize 25/53 (28.3%), edibles 14/53 (26.4%), sublingual tinctures 4/53 (7.6%), and topical 2/53 (3.8%). Preferred cannabis compositions were indica dominant 12/54 (22.2%), 50/50 THC/CBD 11/54 (20.4%), high CBD 9/54 (16.7%), high THC strains 5/54 (9.3%), sativa dominant strains 3/54 (5.6%), and hybrid strains 2/54 (3.7%). One-third 19/56 (33.9%) reported possessing a medical cannabis certificate.

Participants were asked if they noticed a change in their use of other medications after they began using medical cannabis. Among the subset that used each drug class, 8/10 (80.0%) reported using less opiates, 11/16 (68.8%) with less sleep

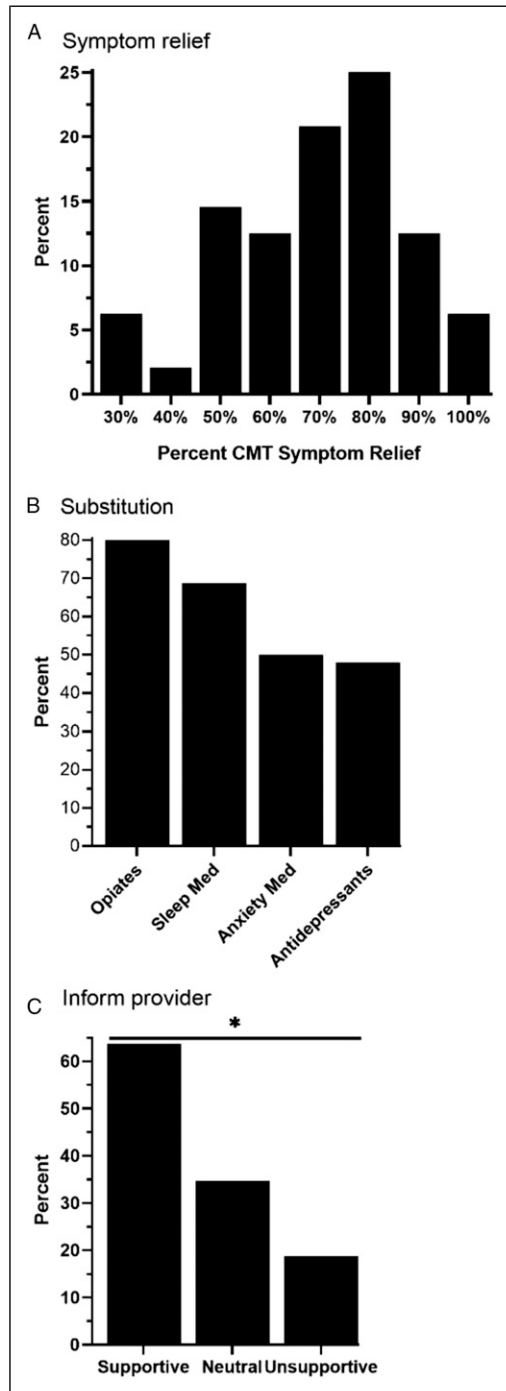


Figure 1. Charcot-Marie-Tooth patients' (N = 56) evaluations of medical cannabis. Percent symptom relief (mean = 69.6, SEM = 2.6) from medical cannabis (A). Percent reporting a reduction in medication use after using medical cannabis (B). Percent that informed health-care providers of cannabis use based on perceived support (C, *P < .05 vs unsupportive).

medication, and 6/12 (50.0%) with less anxiety medications and 11/23 (47.8%) with less antidepressants (Figure 1B).

Physicians' attitudes regarding patient medical cannabis use were examined. For those who reported receiving a

supportive response from providers, 7/11 (63.6%) indicated that they would inform them of their medical cannabis use. For those who reported unsupportive responses from providers for medical cannabis use, only 3/16 (18.8%) said they would inform providers of their cannabis use (P < .05, Figure 1C).

Overall 12/51 (23.5%) participants reported experiencing negative side effects due to cannabis use. When asked if they planned on halting their usage due to side effects, only 1/51 (2.0%) patient answered 'yes', with 5/51 (9.8%) being 'unsure'. However, almost all 11/12 (91.7%) of those who noted having negative side effects from medical cannabis reported that they did not have plans to stop consuming it. Of patients reporting adverse side effects, this included 3/12 (25%) noting asthma or breathing problems, 2/12 (17%) noted rapid heart rate/palpitations, and 2/12 (17%) reported unwanted weight gain. In addition, 1/12 (8.3%) patients each reported chest pain, sleep and mood changes, and visual changes.

Discussion

Pain is a well-studied and significant comorbid condition accompanying CMT.²⁻⁵ Due to inadequate relief from standard pain treatments, individuals with CMT may seek alternatives, such as cannabis. However this has not been previously investigated. The current study is the first to examine the perspectives of patients with CMT regarding the use MC to treat symptoms of pain. The results of this informal survey show that patients with CMT report marked symptom relief from using medical cannabis. Based on the substantial (70%) improvement in CMT symptoms, cannabis may be a promising therapeutic option if these findings are verified by prospective, randomized, controlled trials. These findings extend upon prior research with cannabinoids as complementary and alternative therapeutic agents for other neurological conditions.^{9,10} The results for multiple-sclerosis appear to be formulation dependent.^{11,12} The American Academy of Neurology reports that there is high quality evidence indicating that oral cannabis extract is efficacious in relieving symptoms of spasticity and pain in patients with multiple sclerosis. There were also concerns about adverse effects as well as the use of non-standardized cannabis extracts.¹³

Perceived provider attitudes may adversely affect patients' likelihood to inform providers of their medical cannabis use. There have been some, mostly regionally focused, efforts to characterize providers attitudes towards medical cannabis,¹⁴⁻¹⁶ particularly among medical oncologists.^{17,18} Medical cannabis is a controversial topic and the likelihood of an open-dialogue between patients and providers likely varies based on provider specialty, region of the country, and employer policies.^{8,17,19} Cannabis was viewed by these patients as a therapeutic drug and, as such, it is crucial that they are able to inform their medical providers of their use. Moreover, our data is really "patient perceptions of physician attitudes", which may not accurately reflect the opinions of the providers. It is also difficult to draw firm conclusions on the impact of patient location. This survey

did not ask enough specific questions on geographic location, or detailed status of local laws regarding cannabis, although that is an area worthy of further inquiry. Approximately 15% of the HNF registrants are from international locations, outside of the United States.

This report also determined that four out of five CMT patients reported decreasing their use of opiates after starting medical cannabis. Similarly, two-thirds (68.8%) reported less sleep medication, and half (50.0%) with less anxiety medications or less antidepressants (47.8%).

The identified substitution effect corroborates prior investigations including among New England dispensary patients primarily with chronic pain,⁸ a nationally representative survey,¹⁷ Prescription Drug Monitor Program records in New Mexico²⁰ and Medicare and Medicaid prescription records.^{21,22} However, recent ecological research has challenged whether this substitution effect meaningfully impacts opioid overdoses.^{23,24} Regardless, there would appear to be some harm reduction impact of cannabis by allowing patients to take less opioids. However, further attention is needed if those that use less prescription medications (e.g., antidepressants) are also not informing their health care providers.

Also noteworthy was that only one-third of participants in this study were certified for medical cannabis. The demarcation between medical and recreational cannabis use is complex⁸ as some “medical users” may use it for recreational purposes and some “recreational users” may be self-treating for therapeutic purposes. The cost of medical cannabis is non-trivial and is not covered by insurance.

There are a number of notable limitations to this study. Inherent to all survey studies is respondent bias. With the exception of a larger percentage of female responders, the survey population is felt to be a reasonable reflection of the overall population of patients with CMT. The 70% female make-up of our survey does suggest some gender bias, which is common in self-reported studies on chronic pain.^{25,26} In most populations, including CMT, women report pain more frequently than men, and this is likely a factor here. CMT is not a sex-linked trait. However, a prior report in CMT1A indicates that women report an earlier onset of symptoms than men, higher deterioration of their QoL and higher disability of their upper limb, assessed by Overall Neuropathy Limitation Scale.²⁷ All participants (N = 56) in this study use cannabis. Given the branched design of the survey, there were multiple questions where fewer than twenty respondents provided information. This would bias the dataset toward a positive cannabis experience as those who are more inclined to answer the survey generally have more favorable experiences with medical cannabis. Although the sample size (N = 56) was only moderate, CMT is a relatively rare disease¹ making these findings particularly novel relative to the absence, to our knowledge, of prior investigations. Cannabis not being used in a controlled setting (dosage, composition, methods of delivery, etc.) was also a limitation. Cannabis can be administered in many ways, whether it is inhaled through vapor or ingested

in food or drinks and each method has a different rate of absorption. Although some participants reported a decrease in their pain, there is no indication as to how much cannabis they consumed in order for them to see that decrease, which would require a much more controlled setting. It is possible that those who reported decreased levels of pain consumed an increased dose of cannabis and/or had a different method of administration that was faster at relieving pain than that of those participants who reported no change in their pain levels. We also did not attempt to differentiate any potential differential effects of cannabis on nociceptive and neuropathic pains, both of which impact patients with CMT. However that would be challenging to do under any setting as there is often considerable symptom overlap in patients with neuromuscular disease and chronic pain.^{25,26} The degree of side effects noted in our study are fairly consistent with what has previously been reported in the literature.²⁸

Conclusions

The findings from this survey indicate that patients with CMT report substantial relief of pain symptoms from the use of cannabis. These current survey results support the need for further investigation, including randomized, prospective, controlled trials of MC for pain management in patients with CMT, using standardized dosing paradigms and delivery methods.

Declaration of Conflicting Interests

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Disclosures

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Supplemental Material

Supplemental material for this article is available online.

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