Survey of cannabis use in patients with amyotrophic lateral sclerosis

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Abstract

Cannabis (marijuana) has been proposed as treatment for a widening spectrum of medical conditions and has many properties that may be applicable to the management of amyotrophic lateral sclerosis (ALS). This study is the first, anonymous survey of persons with ALS regarding the use of cannabis. There were 131 respondents, 13 of whom reported using cannabis in the last 12 months. Although the small number of people with ALS that reported using cannabis limits the interpretation of the survey findings, the results indicate that cannabis may be moderately effective at reducing symptoms of appetite loss, depression, pain, spasticity, and drooling. Cannabis was reported ineffective in reducing difficulties with speech and swallowing, and sexual dysfunction. The longest relief was reported for depression (approximately two to three hours).

Key words: pain, palliative care, cannabis, medicinal marijuana, amyotrophic lateral sclerosis

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Introduction

Amyotrophic lateral sclerosis (ALS), with an incident rate of five to seven per 100,000 population, is the most common form of adult motor neuron disease.[1-3] ALS is a rapidly progressive neuromuscular disease that destroys both upper and lower motor neurons, ultimately causing death, typically from respiratory failure. The vast majority of ALS is acquired and occurs sporadically. There is not yet a known cure for ALS.[4-6]

ALS patients may present with any number of clinical symptoms, including weakness, spasticity, cachexia, dysarthria and drooling, and pain secondary to immobility, among others.[7,8] Previous studies have reported both direct and theoretical applications for using cannabis to manage some of these ALS symptoms.[9-11] Cannabis has easily observable clinical effects with rapid onset (e.g., analgesia, muscle relaxation, dry mouth). Moreover, some components of marijuana (not inhaled smoke) have been shown in laboratory studies to have neuroprotective properties that may help prolong neuronal cell survival over extended time.[12-16]

Marijuana is a complex plant, containing over 400 chemicals.[17] Approximately 60 are cannabinoids, chemically classified as 21 carbon terpenes.[17,18] Among the most psychoactive of these is delta-9-tetrahydrocannabinol (THC).[17,18] Because of this biochemical complexity, characterizing the clinical pharmacology of marijuana is difficult. The clinical pharmacology of marijuana containing high concentrations of THC may well

differ from plant material containing small amounts of THC and higher amounts of the other cannabinoids. The bioavailability and pharmacokinetics of inhaled marijuana are also substantially different from those taken by ingestion. The cannabinoids are all lipid soluble compounds and are not soluble in water.[19] Besides THC, which is the active ingredient in dronabinol, varying proportions of other cannabinoids, mainly cannabidiol (CBD) and cannabinol (CBN), are also present in marijuana and may modify the pharmacology of THC as well as have distinct effects of their own. CBD is not psychoactive but has significant anticonvulsant and sedative pharmacologic properties and may interact with THC.[20,21]

The concentration of THC and other cannabinoids in marijuana varies greatly depending on growing conditions, plant genetics, and processing after harvest.[21] In the usual mixture of leaves and stems distributed as marijuana, concentration of THC ranges from 0.3 percent to 4 percent by weight.[21,22] However, specially grown and selected marijuana can contain 15 percent or more THC. Thus, one gram of marijuana might contain as little as three milligrams of THC or more than 150 mg.[21] THC is a potent psychoactive drug, and large doses may produce mental and perceptual effects similar to hallucinogenic drugs.[23,24] Despite this, THC and other cannabinoids have low toxicity, and lethal doses in humans have not been described.[25,26]

Despite risk for bronchitis, the main advantage of smoking is rapid onset of effect and easy dose titration. When marijuana is smoked, cannabinoids in the form of an aerosol in the inhaled smoke are rapidly absorbed and delivered to the brain, as would be expected of a highly lipid-soluble drug.[27,28] However, smoking anything, including marijuana, carries health risks for the lungs and airway system. A healthier option is vaporization. Because the cannabinoids are volatile, they will vaporize at a temperature much lower than actual combustion.[24] Heated air can be drawn through marijuana and the active compounds will vaporize, which can then be inhaled. This delivers the substance in a rapid manner that can be easily titrated to desired effect.[29] Vaporization therefore removes most of the health hazards of smoking.[27]

The medicinal use of cannabis is better documented in multiple sclerosis (MS) than in other clinical conditions, although evidence tends to be anecdotal, and no controlled clinical trials of medicinal marijuana use in MS have been published.[30-39] With respect to pain, the concomitant use of cannabis with narcotics may be beneficial, because the cannabinoid receptor system appears to be discrete from that of opioids.[40-45] In that regard, the antiemetic effect of cannabis may also help with the nausea sometimes associated with narcotic medications. Untoward effects of cannabis include potentially significant psychoactive properties, which may produce a sense of well-being or euphoria but can also induce anxiety, confusion, paranoia, and lethargy.[46]

To date there have not yet been any empirical studies to investigate the use of cannabis for medicinal purposes in ALS. The purpose of this survey was to gather preliminary data on the extent of use of cannabis among persons with ALS (PALS) and to learn which of the symptoms experienced by PALS are reported to be alleviated by the use of cannabis.

Methodology

Participants in this survey were recruited from the ALS Digest (the Digest), an electronic discussion list published weekly to serve the worldwide ALS community, including patients, families, caregivers, and providers. The Digest serves as a forum for discussion of issues related to ALS and is not intended to provide medical advice on individual health matters. The Digest can be viewed at *www.alslinks.com*. Currently there are over 5,600 subscribers in 80 countries worldwide. However, the number of subscribers with ALS is not known. The editor is not a physician and the Digest is not peer reviewed. An e-mail invitation to participate was posted to the Digest four times over two months.

The survey was available online from January 6 through March 2, 2003, approximately eight consecutive weeks. Any subscriber with ALS was invited to participate on a voluntary and anonymous basis. The sponsoring institution human subjects review board approved the study protocol. A Web-based survey tool developed by the University of Washington was used to collect responses. The tool uses SSL encryption for transferred data, and all identifying information was stored in a code translation table separate from the actual data to protect the privacy of respondents. The University of Washington human subjects review board has approved this tool for research purposes.

PALS who wanted to participate were given a Web site address that introduced the survey and provided a link to the survey site. The invitation to participate did not mention cannabis or marijuana, in order to discourage participation by individuals who do not have ALS but might otherwise be interested in promoting legalization of marijuana. The survey was titled "A survey of ALS Patients Who Use Alternative Therapies to Treat Symptoms."

It was presumed by the investigators that the diagnostic information provided by the survey participants was accurate (i.e., no medical records were reviewed to confirm their diagnosis). In addition to a series of questions related to the ALS symptoms, the use of cannabis, and its effectiveness in

alleviating the symptoms of ALS, participants were also asked to provide demographic and diagnostic information. The survey was anonymous and it is therefore impossible to conclusively determine whether all respondents were individuals with ALS. However, the first six questions of the survey asked about how and when the respondent was diagnosed with ALS and specifically asked those who were not diagnosed with ALS by a physician to not fill out the survey. The authors carefully studied the demographic and diagnostic information provided by each respondent for completeness, consistency, and plausibility. Records with the diagnostic information missing were excluded from the analysis. Many participants offered extensive information about other alternative therapies they use, and the general comments appeared to reflect experiences of individuals living with ALS.

Results

A total of 137 responses were received. Four responses were excluded because of duplicate submission (i.e., the same person inadvertently submitting more than one survey by hitting the submit key more than once) and two because of failure to complete most of the questions of the survey. Electronic logs of all submissions were inspected for repeated entries from the same Internet protocol (IP) address. None were found. A total of 131 responses were retained for analysis.

The demographics of the sample are shown in Table 1. Seventy-five percent of the respondents were male and 90 percent were Caucasian. The average age of participants was 54 years [standard deviation (SD) = 11], with no significant difference between the genders [Mean (M) = 54 for males, SD = 10.7; M = 53 for females, SD = 12.5]. Eighty-four percent of the respondents were married or living with a significant other, 17 percent were employed (full time or part-time), 64 percent were unemployed or retired due to disability, and 18 percent were retired due to age. Respondents reported high levels of education, with only 13 percent with high school education or less and 62 percent with college education or higher. The time since ALS diagnosis ranged from one month to 24 years. The median time since diagnosis (i.e., duration) was three years, the mean duration was approximately four years (M = 4.4, SD = 4.0). About a half of the sample reported they used a wheelchair usually or always, and about 20 percent reported no restrictions in mobility. Eighty-one percent of the respondents filled out the survey independently while 19 percent reported that they required assistance from others. One-half of the participants were taking Riluzole. The majority of participants (69 percent) reported that they live in the United States, 8 percent in Canada, and 5 percent in Australia. Six percent of the participants live in Europe, while the rest (12 percent) of the respondents reported that they were from Africa, India, Israel, Brazil, Ecuador, Guatemala, or Argentina. Fifty-three participants (41 percent) reported drinking alcohol, 14 (11 percent) reported that they used tobacco, and four (3 percent) reported consuming both alcohol and tobacco.

Use of cannabis

Seventy-seven respondents (60 percent) reported that they never used cannabis, and 41 (31 percent) used cannabis in teenage or college years only. Thirteen respondents (10 percent) reported using cannabis in the last 12 months, and their demographics are outlined in Table 2.

Those who reported using cannabis in the last 12 months were all male and all lived in the US. Ten of those who reported using cannabis in the last 12 months also responded affirmatively to the question that asked about the use of cannabis during the teenage, college, and adult years. All of those who reported using cannabis in the last 12 months also reported that they used cannabis at some point in their lives before they were diagnosed with ALS. Six of the cannabis users reported that they lived in a state where medical cannabis is legal, and four lived in a state where medical cannabis is illegal. The remaining three respondents were not sure whether medical cannabis was legal in their state. There were no statistically significant differences between the cannabis users and non-users (see Table 2) on any demographic variable (age, marital status, employment status, education level, time since diagnosis, mobility status).

None of those who reported using cannabis in the past 12 months reported tobacco use, but all reported drinking alcohol.

Eight cannabis users reported smoking cannabis in the last three months. Two respondents reported smoking cannabis infrequently (less often than once a month), one reported smoking one to two times a week, and three reported daily use.

No respondents reported only breathing vaporized cannabis, although one participant reported using vaporized cannabis in addition to smoking and using medicinal cannabis. Two participants reported eating cannabis, one in addition to smoking it. Three respondents used medicinal cannabinoids (i.e., Dronabinol). Of the three respondents who used medicinal cannabinoids, one reported using only medicinal cannabinoids, one also smoked cannabis, and one both smoked as well as breathed vaporized cannabis.

Symptoms

The intensity of ALS-related symptoms was quantified by asking respondents to rate how much they experience each of the symptoms on a

Table 1. Sample demographics			
		Minimum	**Maximum**
Age		25	82
Duration of ALS in years		.05	23.43
		Number	**Percent**
Gender	Male	98	75
	Female	33	25
	Total	131	100
Race	African American	1	1
	Asian	4	3
	White	118	90
	Other	8	6
	Total	131	100
Employment	Full time	16	13
	Part time	5	4
	Retired due to disability	56	43
	Retired due to age	23	18
	Unemployed due to disability	27	21
	Homemaker	1	1
	Total	128	100
Education	Less than high school	3	2
	High school graduate	14	11
	Vocational school/some college	33	25
	College graduate	38	29
	Graduate/professional degree	42	33
	Total	130	100
Marital status	Married/living with significant other	110	84
	Single/divorced/separated/widowed	21	16
	Total	131	100
Type of ALS	Inherited	5	4
	Acquired	45	35
	Unsure	79	61
	Total	129	100
Mobility	No restrictions	27	21
	Some difficulty walking on uneven surfaces	16	12
	Use canes, crutches, or walkers	18	14
	Usually use wheelchair	30	23
	Always use wheelchair	38	30
	Total	129	100
Required assistance with filling out survey	Yes	25	19
	No	105	81
	Total	130	100
Riluzole	Yes	65	50
	No	66	50
	Total	131	100

Table 2. Demographics of cannabis users			
		Minimum	Maximum
Age		35	59
Duration of ALS in years		.8	10.4
		Number	**Percent**
Gender	Male	13	100
	Female	0	0
	Total	13	100
Race	African American	0	0
	Asian	0	0
	White	13	100
	Other	0	0
	Total	13	100
Employment	Full time	2	15
	Part time	1	8
	Retired due to disability	6	46
	Retired due to age	0	0
	Unemployed due to disability	4	31
	Homemaker	0	0
	Total	13	100
Education	Less than high school	0	0
	High school graduate	1	8
	Vocational school/some college	4	33
	College graduate	6	51
	Graduate/professional degree	1	8
	Total	12	100
Marital status	Married/living with significant other	12	92
	Single/divorced/separated/widowed	1	8
	Total	13	100
Type of ALS	Inherited	0	0
	Acquired	6	42
	Unsure	7	54
	Total	13	100
Mobility	No restrictions	1	8
	Some difficulty walking on uneven surfaces	4	31
	Use canes, crutches, or walkers	2	15
	Usually use wheelchair	2	15
	Always use wheelchair	4	31
	Total	13	100
Required assistance with filling out survey	Yes	2	15
	No	11	85
	Total	13	100
Riluzole	Yes	4	31
	No	9	69
	Total	13	100

Table 3. Symptoms reported by cannabis users										
Symptom	Cannabis nonusers					Cannabis users				
	Minimum	Maximum	Mean intensity	SD	N	Minimum	Maximum	Mean intensity	SD	N
Weakness	0	4	2.87	1.05	118	1	4	2.85	0.99	13
Speech difficulties	0	4	1.93	1.55	118	1	4	2.22	1.09	9
Drooling	0	4	0.97	1.15	118	1	4	2.00	1.15	7
Swallowing difficulties	0	4	1.36	1.33	118	1	4	2.00	1.20	8
Shortness of breath	0	4	1.11	1.14	118	1	4	1.80	1.03	10
Pain	0	4	1.14	1.15	118	1	4	1.67	1.21	6
Spasticity	0	3	1.77	1.25	118	1	3	1.63	0.92	11
Appetite loss	0	3	0.73	1.06	118	1	3	1.56	0.88	9
Depression	0	3	1.20	1.07	118	1	3	1.50	0.85	10
Sexual dysfunction	0	2	.97	1.38	118	1	2	1.25	0.50	4

five-point scale ranging from "not at all" (0) to "very much" (4). The most frequent symptom was weakness (reported by all cannabis users). The mean intensity was highest for weakness, followed by speech difficulties, drooling, and swallowing difficulties. The intensity of symptoms reported by respondents who did not use cannabis was not statistically significantly different from the symptom intensity reported by the cannabis users [$F(10, 120) = 1.07$, $P = .39$]. A summary of symptoms and their intensity is listed in Table 3.

The amount of relief attributed to cannabis use was assessed by asking the respondents to rate the degree to which cannabis alleviates each symptom on a five-point scale ranging from "not at all" (0) to "completely relieves the symptom" (4). Respondents reported that the use of cannabis helped moderately for depression, appetite loss, spasticity, drooling, and pain. All cannabis users who reported symptoms of appetite loss and depression also reported that cannabis reduced these symptoms. None of the cannabis users reported any reduction in difficulties with swallowing and speech or sexual dysfunction.

The duration of symptom relief was measured on a scale from 0 (no relief) to 6 (more than nine hours). Respondents reported the most lasting relief (on average two to three hours) for depression. The loss of appetite, drooling, shortness of breath, spasticity, and pain were reported to be relieved on average for approximately one hour or less. Table 4 provides a summary of symptoms reported by the cannabis users. Level of relief was reported on a five-point scale ranging from "not at all" (0) to "completely relieves the symptom" (4). The duration of symptom relief was measured on a scale from "no relief" (0), "less than one hour" (1), "two to three hours" (2), "four to five hours" (3), "6 to 7 hours" (4), "eight to nine hours" (5), "more than nine hours" (6).

Discussion

There is an increasing amount of research concerning the medicinal effects of cannabinoids. For example, cannabinoids have been reported to reduce chemotherapy-induced nausea and vomiting, lower intraocular pressure in patients with glaucoma, reduce anorexia in patients with cancer and AIDS-associated weight loss, and reduce pain and spasticity in MS.[30-39] Cannabinoids, the active ingredients in marijuana, may also have properties that may be applicable to the management of ALS.[9,10] However, to date no empirical studies of use and effectiveness of cannabis for symptom management by PALS have been published.

Approximately 10 percent of the survey respondents reported using cannabis. This is a lower rate than the

Table 4. Level and duration of relief following use of cannabis									
Symptom	Minimum	Maximum	Average relief	SD	Reported no relief	Percent	Reported some relief	Percent	Total N
Weakness									
degree of relief	0	2	0.75	0.71	3	37.50	5	62.50	8
length of relief	0	3	1.60	1.14					5
Speech difficulties									
degree of relief	0	0	0.00	0.00	6	100.00	0	0.00	6
length of relief									
Drooling									
degree of relief	0	3	1.75	1.25	1	25.00	3	75.00	4
length of relief	2	2	2.00	0.00					3
Swallowing difficulties									
degree of relief	0	0	0.00	0.00	6	100.0	0	0.00	6
length of relief									
Shortness of breath									
degree of relief	0	3	0.60	1.34	4	80.00	1	20.00	5
length of relief	2	2	2.00	0.00					1
Pain									
degree of relief	0	3	1.67	1.21	1	16.67	5	83.3	6
length of relief	1	3	2.00	0.71					5
Spasticity									
degree of relief	0	4	1.86	1.46	2	28.57	5	71.43	7
length of relief	1	3	2.00	0.71					5
Appetite loss									
degree of relief	1	4	2.13	1.13	0	0.00	8	100.00	8
length of relief	2	3	2.17	0.40					6
Depression									
degree of relief	1	4	2.13	1.13	0	0.00	8	100.00	8
length of relief	1	4	2.67	1.03					6
Sexual dysfunction									
degree of relief	0	0	0.00	0.00	3	100.00	0	0.00	3
length of relief									

frequency of use reported by other patient populations, including MS, AIDS, and cancer patients.[10,30,31] However, the pattern of symptom relief reported by the small number of PALS who reported using cannabis[13] was consistent with the reported effects of cannabis for symptom management by people with other conditions, including MS.[30,35,36] Cannabis users reported that cannabis smoking was most effective at reducing depression, appetite loss, pain, spasticity, drooling, and weakness. The factor that most predicted current use of cannabis by PALS was reported previous use (presumably recreational).

The survey had a number of limitations. First, the survey results reported here are based on a relatively small number of respondents (131) and on reports of 13 cannabis users, and may not be representative of the patterns of cannabis use in the ALS population by people with ALS in general. Second, 75 percent of the respondents were male, 25 percent were female. Men appear to be about 1.5 times more likely to be affected with ALS than women,[7,8] so the percentage of female participants is slightly lower than expected in the general ALS population (about 33 percent). Published studies of Internet use consistently report that females are less likely to use the Internet for reasons that may be independent of income and estimate that only about one-third of Internet users are women.[47,48] This may account for the lower than expected participation by women with ALS.

A third limitation of the study is that a disproportionate number of the survey respondents were white (90 percent) and all cannabis users were white. There is some evidence that whites may be at higher risk for ALS, though most researchers agree that ALS equally affects people of all races.[49,50] Racial discrepancies in rates of ALS may be due to poorer access to healthcare for minority populations in the US, particularly access to tertiary referral centers, where the ALS diagnosis is often made. Published studies report that over 80 percent of Internet users are white;[48] this is the most likely explanation for the disproportionate participation by Caucasians in this survey.

Fourth, Internet users tend to be highly educated. Almost 60 percent report having at least one degree.[48] Those with higher education are more likely to own computer equipment and to use it to connect to the Internet.[51] The results of the survey we report here provide further evidence for this trend, with only 13 respondents (10 percent) reporting having high school education or less.

Finally, none of the participants from the countries where cannabis use is prevalent (India) or legal for medical uses (Australia, Canada) reported using cannabis. The most likely explanation for this finding is the small number of participants from these countries; only one respondent was from India, six from Australia, and eleven from Canada.

In general, professionals with university degrees living in households with disposable incomes sufficient to purchase technology tools are likely to be over-represented in Internet surveys. Women, minorities, the elderly, those who live on social assistance disability payments, or who earn minimum wages, are much less likely to participate.[48,51]

Privacy is a major issue associated with Web-based methodology. When the Internet is used for research, especially for research on sensitive issues (such as using substances that are illegal under federal law and most state laws), protecting the privacy of the participants is paramount. By making the survey anonymous, the authors protected the privacy of the respondents but gave up the ability to verify respondents' diagnoses or prevent repeated or malicious submittals. Although the records showed that no two responses were submitted from the same IP address, the IP address identifies the computer, not the user. Therefore, it cannot be conclusively determined that one respondent did not submit more than one response using different computers.

The low response rate might be explained by many factors. First, we do not know how many participants in the electronic discussion list that was used to recruit participants have ALS. It is possible, even likely, that a large majority of the participants are family members, service providers, and advocates. Second, the respondents who do not use alternative therapies may have been less likely to respond. It is unclear what percentage of people with ALS use alternative therapies. A recent survey from Germany suggests that about half of the ALS patients there use complementary and alternative medicine.[52] Some respondents who do not use alternative therapies such as vitamins and supplements, but do use cannabis to manage their symptoms may not have considered cannabis to be an "alternative therapy" and decided not to participate. Many respondents provided information on vitamins, supplements, and other alternative therapies in the write-in spaces of the survey even though they were not asked about these therapies directly, probably because the respondents had anticipated the survey would gather information on those topics. Third, even though the invitation as well as the introduction to the survey clearly stated that the survey was anonymous and there was no way for the researchers to associate a specific response with a specific respondent, many may have been individuals who are generally suspicious of providing information via the Internet and may have decided not to participate for this reason.

Despite the limitations of this study noted above, these preliminary findings support the need for further

research into the potential benefits of cannabis use for the clinical management of some ALS symptoms. These include pain, which was one of the symptoms identified in a recent study as not being sufficiently addressed in ALS.[53] Further research is needed to see if the current findings can be confirmed using non-Internet-based survey methodology with a defined sample. It would also be informative to inquire about cannabis use within the context of subject beliefs about the efficacy of various alternative and complimentary approaches and their engagement and satisfaction with those approaches.

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