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Efficacy of different varieties of medical cannabis in relieving symptoms in post-traumatic stress disorder (PTSD) patients

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Abstract

Post-traumatic stress disorder (PTSD) is a crippling condition that affects individuals who have experienced severe traumatic event(s). Cannabis is emerging as a treatment option for patients experiencing PTSD. The objective of this study is to determine which varieties of cannabis PTSD patients perceive to be most effective for relieving their symptoms. PTSD patients using medical cannabis from a Canadian licensed provider voluntarily completed an online survey at baseline, 4 and 10 months, which collected information pertaining to their medical conditions, symptoms, and use of medical cannabis. The majority of PTSD patients reported improvement in all most commonly reported symptoms, including depression, anxiety, sleep problems, and pain, following the use of medical cannabis ($p < 0.0001$). *Sedamen*^{MR} was reported to be effective in relieving overall PTSD at 4 and 10 months, and also helped manage each of the four common symptoms. *Luminarium*^{MR} was also reported to be beneficial for PTSD at 4 and 10 months, as well as for depression, anxiety, and pain. *Alaska*^{MR} was reported beneficial for PTSD after 4 months as well as for depression, anxiety, and sleep problems. *Midnight*^{MR} was reported to be effective in relieving PTSD after 10 months, and also was reportedly beneficial for all four common symptoms. Study results demonstrated that PTSD patients perceived notable differences in the effectiveness of cannabis varieties for managing their symptoms. Further research in a controlled clinical setting to determine which varieties manage PTSD symptoms most effectively will help clinicians make better recommendations to patients.

Keywords: Medical cannabis, cannabis varieties, post-traumatic stress disorder, survey

Introduction

Post-traumatic stress disorder (PTSD) is a debilitating mental health condition with several manifestations that occurs in some people after experiencing a traumatic event. Predisposing factors have been identified, as not all individuals who are exposed to

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trauma will develop this condition (1). Several different types of psychotherapy and pharmacotherapy treatment options are available for PTSD and its associated symptoms such as hyperarousal, re-experiencing traumatic events, and avoidance (2, 3). The multifaceted physiology of PTSD must be taken into consideration when developing treatment plans.

The PTSD brain presents with modified circuitry and structural changes (1, 4, 5). Patients with PTSD also experience altered endocrine and neurochemical activity compared to non-PTSD patients. The neurochemical changes in PTSD patients often manifest as a dysregulation of several neurotransmitters including catecholamines and serotonin. As neurochemical regulation plays an important role in a wide range of brain functions, including the ability to form memories and process emotion, neurochemical imbalances can disturb the emotional control of PTSD patients.

Major dysregulation of the endocrine system also occurs in PTSD patients, specifically dysregulation of the glucocorticoid and thyroid hormone systems. The hypothalamic-pituitary-adrenal (HPA) axis is the body's stress regulation system. Each part of the axis works together to modulate the stress response through the release of a cascade of various hormones and ultimately, the release of glucocorticoids, including the body's main stress hormone, cortisol (1,6). In a healthy brain, a negative feedback system regulates cortisol release to suppress the stress response after a stressful stimulus is no longer present. Studies have shown that PTSD patients have an increased negative feedback response however, leading to the release of lower levels of cortisol during periods of stress (1, 7). In addition, low cortisol levels before exposure to a traumatic event may predispose a person to developing PTSD (1, 8, 9). Some studies have also indicated that abnormal levels of thyroid hormones in PTSD patients can be associated with increased anxiety (1, 10).

Medical cannabis is emerging as a viable treatment option for patients with PTSD, as an alternative to, or in conjunction with, traditional psychotherapy and pharmacotherapy. Many different strains of medical cannabis exist, each with unique profiles of active compounds, namely cannabinoids. The two most well studied cannabinoids thought to be predominantly responsible for the physiologic effects of cannabis are tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is the main psychoactive constituent, whereas CBD is non-psychoactive and thought to possess antipsychotic, anti-inflammatory, and anxiolytic properties (3, 11).

Medical cannabis varieties are derived from two main subspecies of cannabis - *Cannabis sativa* and *Cannabis indica*. In general, anecdotal evidence suggests that *sativa* dominant strains produce a more stimulating effect, whereas *indica* dominant varieties tend to be more sedative in nature (3). Varieties available to medical patients contain unique cannabinoid and *indica*/*sativa* properties, as well as profiles of other potentially physiologically active, but less well studied compounds such as terpenes. These different characteristics are likely to contribute to variations in the efficacy of strains for the management of various symptoms. As patients have access to such an array of cannabis strains, it is important to establish which are most effective for PTSD symptom management from a clinical perspective. The varieties of medical cannabis in this study were classified per their relative composition of *indica* and *sativa*. For example, varieties were categorized as *sativa*-leaning (consisting of 50-60% *sativa*), *sativa*-dominant (61-70% *sativa*), or very *sativa*-dominant (>70% *sativa*); *indica* varieties were categorized similarly.

Methods

Patients registered with a Canadian licensed cannabis provider were invited to complete a voluntary online survey upon registration with the provider (baseline), and at 4- and 10-month follow-up intervals.

Study design

The online survey was developed by a licensed cannabis producer in consultation with various healthcare professionals with knowledge of medical cannabis, for the purpose of gathering information about patient demographics, quality of life, current symptoms and conditions, and the use and preference of different medical cannabis varieties. Surveys were

dynamic, and follow-up questions were customized based on answers to previous questions. Patients were able to skip questions, and could select more than one answer for several questions. As a result, each patient answered a unique set of questions. The average completion time was between 15-25 minutes.

Baseline

Patients were invited to complete an intake survey at the time of registration with the licensed provider (baseline). Questions were designed to collect information pertaining to demographics, current conditions and symptoms, and corresponding severities. Patients were also asked to report on their quality of life, which related to their experience with a number of key activities of daily living (ADLs).

Follow-up

At 4 and 10 months from baseline, patients were invited to complete follow-up surveys, in which they were asked questions about any changes to their symptoms or conditions, their experience with cannabis treatment, and which varieties they perceived to have had the greatest effect. There were no restrictions on the number of varieties each respondent could select.

Patient population

All surveys included in this analysis were completed between January 2015 and December 2016. 3076 patients in total completed the survey at baseline, of which 647 patients reported having PTSD.

Statistical analysis

Descriptive and inferential statistical analyses were performed. Along with basic statistics such as mean and range calculations, the Fisher exact test was performed to determine significance of symptom improvement and volume of usage of medical cannabis when comparing PTSD with non-PTSD patients. A p-value of less than 0.05 was considered statistically significant.

Results

3076 patients completed baseline surveys, 647 of which reported experiencing PTSD. At baseline, the four most commonly reported symptoms for all patients including those with PTSD were pain (74.3%), anxiety (74.0%), sleep problems (71.4%), and depression (60.4%).

Improvement of PTSD and its common symptoms

Perceived changes in the condition (PTSD) and commonly experienced symptoms following medical cannabis use are shown in Table 1. Of 171 patients with PTSD reporting a change in their condition following the use of cannabis, 12.3% responded that their condition deteriorated between baseline and 4-month follow-up. 10.5% of PTSD patients reported no change in their condition, while the remaining 77.2% indicated that their condition had improved following the use of cannabis ($p = 0.0031$).

143 PTSD patients experiencing depression reported a change at the 4-month follow-up. 11.2% indicated that this symptom had deteriorated after using cannabis, 10.5% reported no change, and 77.6% responded that they had experienced improvement in their depression following the use of cannabis ($p < 0.0001$). Additionally, 0.7% indicated that they no longer experienced this symptom. Of respondents experiencing anxiety ($n = 157$), 11.5% indicated that their symptom deteriorated, 9.6% reported no change, 78.3% reported improvement, and 0.6% responded that they no longer experienced anxiety after 4 months ($p < 0.0001$). 142 patients reported experiencing a change in their sleep problems at follow-up. 11.3% experienced a deterioration of this symptom, 14.1% reported no change, 70.4% reported experiencing an improvement, and 4.2% no longer experienced sleep problems ($p < 0.0001$). Finally, 124 patients indicated experiencing a change in their pain following cannabis use. Of these patients, only 8.1% reported deterioration, and 9.7% reported

experiencing no change in their pain levels. 80.6% of patients previously experiencing pain indicated that their symptom had improved, and 1.6% reported no longer experiencing pain after using cannabis ($p < 0.0001$).

Preferred varieties for relief of PTSD

At the 4-month follow-up, 38 patients with PTSD indicated which varieties of cannabis they felt were most effective for their overall condition. 35 of these patients also provided responses at the 10-month follow-up. At 4-month follow-up, 39.5% of these respondents preferred *Stellio*^{MR} (very *indica*-dominant, 23-26% THC, 0% CBD), while 31.6% indicated that *Sedamen*^{MR} (very *indica*-dominant, 21-24% THC, 0% CBD), *Alaska*^{MR} (very *sativa*-dominant, 20-23% THC, 0% CBD), and *Luminarium*^{MR} (very *sativa*-dominant, 25-28% THC, 0% CBD) were most beneficial for managing their PTSD (Table 2).

At the 10-month follow-up, responses differed slightly. 48.6% of PTSD patients reported *Sedamen*^{MR} to be most effective, 45.7% chose *Luminarium*^{MR}, 42.9% chose *Midnight*^{MR} (*sativa*-leaning, 8-11% THC, 11-14% CBD), and 34.3% chose *Avidekel*^{MR} (*indica*-leading, 0.1-0.8%, THC, 15-18% CBD). The compositions of *indica* and *sativa* species in each variety, as well as the levels of THC and CBD, are included in Table 2.

Preferred varieties for relief of common PTSD symptoms

The most common symptoms experienced by all respondents at baseline, including PTSD patients, were depression, anxiety, sleep problems, and pain. Reported strain efficacy for each of these symptoms is shown in Table 3.

Table 1. Change in severity of PTSD and the four most commonly experienced symptoms of PTSD patients

	Deterioration n (%)	**No change n (%)**	**Improvement n (%)**	**No longer experiencing this symptom n (%)**	**p-value***
PTSD (Total n = 171)	21 (12.3%)	18 (10.5%)	132 (77.2%)	N/A	**0.0031**
Depression (Total n = 143)	16 (11.2%)	15 (10.5%)	111 (77.6%)	1 (0.7%)	**< 0.0001**
Anxiety (Total n = 157)	18 (11.5%)	15 (9.6%)	123 (78.3%)	1 (0.6%)	**< 0.0001**
Sleep problems (Total n = 142)	16 (11.3%)	20 (14.1%)	100 (70.4%)	6 (4.2%)	**< 0.0001**
Pain (Total n = 124)	10 (8.1%)	12 (9.7%)	100 (80.6%)	2 (1.6%)	**< 0.0001**

PTSD – post traumatic stress disorder.
*Bolded p-values are statistically significant.

Table 2. Varieties most helpful for PTSD at 4 months and 10 months and composition of each variety (% *indica*, *sativa*, THC, CBD)

Variety	**Number of patients who reported variety to be helpful n (%)**	**Composition**	**% THC**	**% CBD**
4 months (Total n = 38)				
Stellio^{MR}	15 (39.5%)	very *indica*-dominant	23 - 26%	0
Sedamen^{MR}	12 (31.6%)	very *indica*-dominant	21 - 24%	0
Alaska^{MR}	12 (31.6%)	very *sativa*-dominant	20 - 23%	0
Luminarium^{MR}	12 (31.6%)	very *sativa*-dominant	25 - 28%	0
10 months (Total n = 35)				
Sedamen^{MR}	17 (48.6%)	very *indica*-dominant	21 - 24%	0
Luminarium^{MR}	16 (45.7%)	very *sativa*-dominant	25 - 28%	0
Midnight^{MR}	15 (42.9%)	*sativa*-leaning	8 - 11%	11 - 14%
Avidekel^{MR}	12 (34.3%)	*indica*-leaning	0.1 - 0.8%	15 - 18%

PTSD – post traumatic stress disorder; THC – tetrahydrocannabinol; CBD – cannabidiol.

Table 3. Varieties most helpful for PTSD symptoms and composition of each variety

Variety	Number of patients who reported variety to be helpful n (%)	Composition	% THC	% CBD
Depression (Total n = 93)				
Luminarium^{MR}	37 (39.8%)	very *sativa*-dominant	25 - 28%	0
Midnight^{MR}	21 (22.6%)	*sativa*-leaning	8 - 11%	11 - 14%
Sedamen^{MR}	21 (22.6%)	very *indica*-dominant	21 - 24%	0
Alaska^{MR}	20 (21.5%)	very *sativa*-dominant	20 - 23%	0
Voluptas^{MR}	20 (21.5%)	very *sativa*-dominant	20 - 23%	0
Elevare^{MR}	20 (21.5%)	very *sativa*-dominant	24 - 27%	0
Anxiety (Total n = 110)				
Sedamen^{MR}	33 (30.0%)	very *indica*-dominant	21 - 24%	0
Luminarium^{MR}	32 (29.1%)	very *sativa*-dominant	25 - 28%	0
Midnight^{MR}	29 (26.4%)	*sativa*-leaning	8 - 11%	11 - 14%
Alaska^{MR}	28 (25.5%)	very *sativa*-dominant	20 - 23%	0
Sleep problems (Total n = 89)				
Sedamen^{MR}	31 (34.8%)	very *indica*-dominant	21 - 24%	0
Midnight^{MR}	21 (23.6%)	*sativa*-leaning	8 - 11%	11 - 14%
Remissio^{MR}	21 (23.6%)	very *indica*-dominant	24 - 27%	0
Alaska^{MR}	16 (18.0%)	very *sativa*-dominant	20 - 23%	0
Pain (Total n = 91)				
Sedamen^{MR}	33 (36.3%)	very *indica*-dominant	21 - 24%	0
Midnight^{MR}	31 (34.1%)	*sativa*-leaning	8 - 11%	11 - 14%
Luminarium^{MR}	27 (29.7%)	very *sativa*-dominant	25 - 28%	0
Avidekel^{MR}	27 (29.7%)	*indica*-leaning	0.1 - 0.8%	15 - 18%

THC – tetrahydrocannabinol; CBD – cannabidiol.

Table 4. Dosage of medical cannabis in PTSD versus non-PTSD patients

Dose	Responses n (%)	p-value*
PTSD (Total n = 195)		**< 0.0001**
0.0-2.0g	79 (40.51%)	
2.1-4.0g	42 (21.54%)	
4.1-6.0g	19 (9.74%)	
6.1-8.0g	14 (7.18%)	
8.1-10.0g or more	41 (21.03%)	
Non-PTSD (Total n = 509)		
0.0-2.0g	356 (69.94%)	
2.1-4.0g	83 (16.31%)	
4.1-6.0g	43 (8.45%)	
6.1-8.0g	18 (3.54%)	
8.1-10.0g or more	9 (1.77%)	

PTSD – post traumatic stress disorder.

*Bolded p-values are statistically significant.

Of 93 PTSD patients experiencing depression at the 4-month follow-up, 39.8% reported *Luminarium*^{MR} to be most effective, 22.6% selected *Midnight*^{MR} and *Sedamen*^{MR}, and 21.5% indicated *Alaska*^{MR}, *Voluptas*^{MR} (very *sativa*-dominant, 20-23% THC, 0% CBD), and *Elevare*^{MR} (very *sativa* dominant, 24-27% THC, 0% CBD) to be most effective in relieving this symptom. At 4 months from baseline, there were 110 patients with PTSD who indicated that they experienced anxiety. These

patients reported that *Sedamen*^{MR} (30.0%), *Luminarium*^{MR} (29.1%), *Midnight*^{MR} (26.4%), and *Alaska*^{MR} (25.5%) were most effective in relieving this symptom. The third most common symptom experienced by PTSD patients was sleep problems (n = 89). Patients who reported experiencing problems with sleep indicated that *Sedamen*^{MR} (34.8%), *Midnight*^{MR} (23.6%), *Remissio*^{MR} (very *indica*-dominant, 24-27% THC, 0% CBD; 23.6%), and *Alaska*^{MR} (18.0%) were most effective in relieving this symptom. Finally, PTSD patients experiencing pain (n = 91) indicated that *Sedamen*^{MR} (36.3%) was most beneficial in alleviating this symptom, followed by *Midnight*^{MR} (34.1%), *Luminarium*^{MR} (29.7%) and *Avidekel*^{MR} (29.7%).

Usage of medical cannabis

Patient reported daily usage of medical cannabis (in grams) is shown in Table 4. At 4 month follow-up, a total of 195 PTSD and 509 non-PTSD patients responded to the question asking them to specify the amount used per day. Significantly more PTSD patients reported taking higher doses than non-PTSD patients (21.03% using 8.1g or more vs. 1.77%, $p < 0.0001$).

Discussion

Different varieties of medical cannabis were reported to be effective for managing PTSD as an overall condition, and for managing common condition-related symptoms, namely depression, anxiety, sleep problems, and pain. Notably, *Sedamen*^{MR} was reported to be beneficial for PTSD after 4 and 10 months, as well as for the four PTSD symptoms most commonly experienced by surveyed patients. Other popular varieties included *Luminarium*^{MR}, which was reported to provide relief from all symptoms except sleep problems, *Midnight*^{MR}, which was effective in managing all symptoms but not the overall condition after only four months, and *Alaska*^{MR}, which was present in the list of effective varieties for all symptoms except pain and PTSD as an overall condition after 10 months. These trends are important to understand when determining which varieties are best suited for patients depending on the symptoms they are experiencing.

The two varieties reported to be most effective for managing PTSD at 4 and at 10 months were *Sedamen*^{MR} and *Luminarium*^{MR}. Interestingly, *Sedamen*^{MR} is an *indica* dominant variety whereas *Luminarium*^{MR} is *sativa* dominant. The THC and CBD contents of the two varieties, however, are similar. It is thought that the *indica/sativa* properties of different cannabis varieties play a role in their physiological effects, so these results may either suggest that patients prefer a combination of the two for the management of PTSD, or that due to the complicated nature of the disease, with varying phenotypically distinct symptoms, different patients have different needs which are reflected in their reported preferences for cannabis varieties.

In addition to identifying preferred varieties, this study also revealed several other important trends. Notably, PTSD patients reported significant improvement compared to deterioration in their condition following the use of medical cannabis ($p = 0.0031$). Additionally, significant improvements were observed in all of the common symptoms of PTSD ($p < 0.0001$ for all symptoms). These observations suggest that medical cannabis is a highly effective treatment option for PTSD patients, either in addition to or as an alternative to traditional psychotherapy and pharmacotherapy, and should be further investigated in controlled efficacy studies.

Within the limits of what is prescribed by their physicians, many patients self-titrate their dose to be able to optimally manage their symptoms. It was observed in this study that patients with PTSD consume significantly more cannabis than non-PTSD patients ($p < 0.0001$). One explanation for this difference in dosing may be that a large proportion of patients with PTSD in this population are military veterans who receive insurance coverage through Veteran's Affairs Canada for their medication. Because other patient populations do not yet have access to coverage for this medication, cost can be a limiting factor in terms of products selected and amount consumed. This could have contributed to the observation of the higher quantities used and varieties preferred by PTSD patients compared to non-PTSD patients. This factor should be further investigated to give clinicians a better understanding of the optimal

daily dose of cannabis that is both safe and efficacious for managing PTSD. Additionally, since patients were often ordering multiple varieties at a time, it is likely that they often medicated with several different strains on a daily basis. This may have made it difficult for them to differentiate which strains were responsible for improvements in particular symptoms, especially if a combination of strains provided a unique cumulative effect. This does not call into question the efficacy of cannabis as a treatment option for PTSD patients, but rather suggests that further research in a controlled clinical setting is needed to provide further insight into the efficacy of individual strains for treating specific symptoms.

Conclusion

Several varieties of medical cannabis have been reported by PTSD patients to provide effective relief from their condition and associated symptoms. The most preferred strain for managing PTSD and all related symptoms was *Sedamen*^{MR}. Among respondents at 4 and 10 month follow-up intervals, many also reported *Luminarium*^{MR} to be an effective variety for managing this condition. Additionally, *Midnight*^{MR} was found to be effective in relieving each of the four most common symptoms associated with PTSD (depression, anxiety, sleep problems, and pain). As cannabis becomes a more widely available treatment option for PTSD, this data will become increasingly valuable for helping physicians and patients select varieties that are best suited for them to more quickly and effectively manage the symptoms they are experiencing. In addition, it is important for informing the effective design of controlled efficacy studies that will be conducted in the future to further investigate the clinical utility of medical cannabis in this patient population.

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