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Medical cannabis use in military and police veterans diagnosed with post-traumatic stress disorder (PTSD)

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Abstract

Post-traumatic stress disorder (PTSD) is a mental illness with intrusive symptoms related to a traumatic event(s), usually treated with pharmacotherapy and psychotherapy. This study aimed to assess outcomes in military and police veterans with PTSD treated with medical cannabis, through a retrospective chart review. Veterans with PTSD using medical cannabis after unsuccessful pharmacotherapy and psychotherapy treatment were assessed in a single centre review at baseline and follow-up. Changes in outcomes and PTSD medications from baseline to follow-up were reported with percent change and effect size (ES) and then compared to the minimal clinically important difference. A total of 100 patients (97% male, average age 43 years old) were assessed from January 2014 to January 2016. The aggregate score of PTSD symptoms was reduced from a mean score of 7.0 at baseline to 2.9 at follow-up (59% reduction, ES 1.5, very large effect; $p < 0.0001$). Suicidal thoughts decreased from 4.1 to 0.9 (77% reduction, ES 1.0, large effect; $p < 0.0001$). The aggregate score for the impact of PTSD on social and family life was reduced from 6.6 to 2.7 (59% reduction, ES 1.2, large effect; $p < 0.0001$). Pain severity decreased from an average of 6.6 to 3.4 (48% reduction, ES 1.5, very large effect). Consumption of PTSD-related medications reduced by 50% from baseline to follow-up. Treatment with medical cannabis in military and police veterans with PTSD who had failed conventional therapy resulted in significant improvements across all PTSD symptoms, as well as social and family impact outcomes and pain severity.

***Keywords*:** Post-traumatic stress disorder, medical cannabis, veterans, medical cannabis, suicide

Introduction

Post-traumatic stress disorder (PTSD) is a mental illness originating from experiencing or witnessing a severe traumatic event(s), resulting in debilitating symptoms in each of the four symptom clusters defined by the "Diagnostic and statistical manual of mental disorders, 5th Edition" (DSM-5). These

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symptom clusters include re-experiencing, avoidance, negative cognitions and mood, and arousal, and persist longer than one month, causing social or occupational impairment (1). In a study by Rapaport et al. (2), 59% of PTSD patients were found to have clinically severe impairment in QOL (defined by two or more standard deviations under the community norm), even more so than patients with panic disorder (20%), obsessive compulsive disorder (26%), and social phobia (21%) (2).

In Canada, a telephone survey of a nationally representative sample of 2991 patients revealed that 76.1% of participants had been exposed to one or more traumatic events that could potentially cause PTSD (3). This same study found the lifetime prevalence of PTSD to be 9.2% and the 1-month prevalence to be 2.4% (3). In a study of 1002 participants from Winnipeg, Manitoba, the 1-month prevalence of full or partial PTSD was 1.2% and 8.2% in men and women, respectively (4). A lifetime prevalence of PTSD of 10.7% was observed in a sample of 3062 Ontario women (5).

Amongst war veterans, the prevalence of PTSD is higher than in the civilian population. In a literature review of mental health in the Canadian Armed Forces, the point prevalence of PTSD ranged from 2.1% to 8.1%, and 12-month prevalence was reported at 2.8% (6). Over a 4-year follow-up, studies reported 8% to 20% of Canadian Forces veterans were diagnosed with PTSD at some point (6).

PTSD is conventionally treated with pharmacotherapy and psychotherapy. Traditional pharmacotherapy for PTSD includes selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, adrenoceptor agonists or antagonists, anticonvulsants, antipsychotics and monoamine oxidase inhibitors (MAOIs) (7). However, findings from pharmacotherapy trials in combat-related PTSD, which tends to be more chronic, have been inconsistent and less effective compared to civilian PTSD (8–15). For instance, one double-blind, placebo controlled trial investigating SSRI efficacy in combat-related PTSD saw only a 25-33% reduction in PTSD symptom clusters (16), compared to 40-53% in civilian PTSD, although the combat-related PTSD patients had more severe symptoms at baseline (17,18). Additionally, a study by van der Kolk et al. saw that PTSD patients using fluoxetine (an SSRI used to treat PTSD) had significantly improved PTSD symptoms compared to patients on a placebo after 5 weeks (n = 64) (15). However, a study by Hertzberg et al. also conducted to establish the efficacy of fluoxetine in treating PTSD reported that patients with combat-related PTSD did not have improved PTSD symptomatology when using fluoxetine compared to a placebo (n = 12) (14).

Recently, medical cannabis has emerged as a potential alternative treatment option for managing PTSD symptoms when traditional methods are unsuccessful. However, the current literature lacks strong evidence demonstrating the efficacy of medical cannabis within this patient group (19,20). The objective of this study was to assess if medical cannabis improved the quality of life and reduced PTSD-related symptoms in Canadian military and police veterans with PTSD through a retrospective chart review.

Methods

The present study was a retrospective chart audit conducted at a single medical practice experienced in treating military veterans diagnosed with PTSD. 100 consecutive veteran patients who had begun cannabis treatment were assessed. These patients were initially referred to the clinic by the physician(s) managing their prior treatment after failing both pharmacotherapy and psychotherapy. Patients were included in the present review if they had a confirmed diagnosis of PTSD, were military or police veterans, and initiated the use of medical cannabis between January 2014 to January 2016. Patients were started on a dose of 1 gram/day, and self-titrated until desired results were met with instructions of a ceiling dose of 10 grams/day.

Data collection

Patient charts were retrospectively reviewed by a single individual prior to initiation of medical cannabis treatment, referred to as baseline, and at their first follow-up visit.

At baseline, demographic information including age, gender, marital status, employment status, length

of military or police service, alcohol and tobacco use, family history of medical conditions, and patient's history of medical conditions was reviewed. Additionally, patients were asked to score their pain severity on a scale of 0 to 10, with 10 being the worst possible pain on the data collection form. Current medication use and dosages were extracted, if available.

In the patient charts, several PTSD-related symptoms were scored on a scale of 0 to 10, with 10 being the most severe. These symptoms included anger and irritability, anxiety, avoidance of trigger-related people and situations, depression, distorted sense of blame for events, easily startled, depersonalization, flashbacks or intrusive memories, hyper-vigilance, nightmares, poor concentration, sense that one's surroundings are not real, severe emotional state, and suicidal thoughts. Patients were also asked to rate how PTSD affected their social and family life, including drug and alcohol overuse, marital/relationship harmony, relationship with siblings and parents, and several religious or personal beliefs on a scale from 0 to 10, where 10 indicated an extremely negative effect. Finally, the efficacy of other attempted treatments was recorded using a scale from 0 to 10, with 10 representing the most success.

At follow-up, data on dose and strains of medical cannabis used, and the method of administration was recorded. In addition, current medications, alcohol and tobacco use, pain severity, PTSD symptoms, previous treatments, and effect of PTSD on social and family life were also documented in patient charts. These results were compared to those obtained at baseline.

Statistical methods

Changes in the average score for each outcome across all participants from baseline to follow-up were analyzed. For each outcome, responses were included in the average only if patients had information available at both the baseline and follow-up. The percentage change in the average score of each outcome and magnitude of effect as measured by effect size (ES) was reported. Effect size is a quantitative measure of how strong the differences between average outcomes at baseline and follow-up are. An ES of 0.8 to 1.29 was considered large, and an ES of 1.3 or higher was very large. ES was calculated using Cohen's term d (21). Paired t-test was also used to compare baseline and follow-up scores for each outcome. A p-value < 0.05 was considered statistically significant.

The minimal clinically important difference (MCID) is the minimal change associated with a significant benefit from a clinical perspective, rather than a statistical perspective. The MCID was calculated for each outcome and changes from baseline to follow-up were compared against the corresponding MCID (22).

Changes in other PTSD related medications used were detailed in terms of average number of PTSD-related medications and percent change for patients with information available at both baseline and follow-up. Medications considered related to PTSD include medications for pain, depression, anti-psychotic medications, medications for bipolar disorder, anxiety, ADHD, seizures, muscle relaxants, nightmares, sleep and related effects, such as erectile dysfunction and nausea.

This study did not capture details of adverse events, hospitalization, or other physician visits that occurred while using medical cannabis. All analyses were conducted using Statistical Analysis Software (SAS version 9.4 for Windows, Cary, NC).

Results

A total of 100 patients were assessed. They were primarily male (97%) and on average 43 years old. Two-thirds of patients were unable to work or had retired (see Table 1).

Medical cannabis use

Results collected at baseline were compared to those obtained at follow-up for each scored outcome. Time to follow-up ranged from less than 3 months to 18 months, with follow-up occurring most commonly less than 3 months or 11-12 months after baseline. Table 2 shows the distribution of time to follow-up. Patients were taking 9.4 grams of medical cannabis per day on average at follow-up. Table 3 shows the

distribution of doses of medical cannabis used at follow-up. Many varieties of medical cannabis were used by these patients including *Luminarium*^{MR}, *Sedamen*^{MR}", *Midnight*^{MR}, *Avidekel*^{MR} and others supplied by MedReleaf Corp. Patients were often using multiple strains simultaneously with varying cannabidiol (CBD) and tetrahydrocannabinol (THC) content. Table 4 summarizes the strain composition of several medical cannabis varieties used by patients.

Table 1. Demographic Information (n = 100)

Demographics	n (%)
Average age (years)	43
Male	97 (97%)
Age distribution	
<40 years	34 (34%)
40-49 years	41 (41%)
50-59 years	21 (21%)
60+ years	4 (4%)
Employment Status at Time of Baseline Visit	
Working	21 (21%)
Student	2 (2%)
Retired/unable to work	63 (63%)
Unknown	14 (14%)

Table 2. Time to follow-up (n = 100)

Distribution of Time to Follow-Up Visit	n (%)
≤3 months	25 (25%)
4-6 months	12 (12%)
7-10 months	11 (11%)
11-12 months	25 (25%)
13-15 months	20 (20%)
16-18 months	7 (7%)

Improvement in PTSD-related symptoms and pain

From baseline to follow-up, a highly significant reduction greater than the MCID was observed in the mean severity of all PTSD symptoms ($p < 0.0001$) (Table 5). The aggregate score of PTSD symptoms were reduced from a mean score of 7.0 to 2.9 (59% reduction, ES 1.5, very large effect; $p < 0.0001$). Notably, suicidal thoughts decreased from a baseline score of 4.1 to a follow-up score of 0.9 (77% reduction, ES 1.0, large effect; $p < 0.0001$). Additionally, anxiety was reduced from a mean score of 7.8 to 3.3 (59% reduction, ES 9.0, very large effect; $p < 0.0001$) and depression was reduced from 7.3 to 2.9 (60% reduction, ES 2.1, very large effect; $p < 0.0001$). A 63% reduction in the mean score for anger and irritability was observed (7.9 to 3.0, ES 2.4, very large effect; $p < 0.0001$). Pain severity decreased from an average of 6.6 (standard deviation (SD) 2.1) to 3.4 (SD 2.1) (48% reduction, ES 1.5, very large effect; n = 80).

Table 3. Dose of medical cannabis at follow-up (n = 99)

Dose of Medical Cannabis	n (%)
< 5 grams	5 (5%)
5 to 9 grams	20 (20%)
10 grams	66 (67%)
More than 10 grams	8 (8%)

Table 4. Composition of medical cannabis varieties

Variety Name	THC%	CBD%	Composition
Avidekel^{MR}	0.1 - 0.8	15 - 18	*sativa*-leaning
Midnight^{MR}	8 - 11	11 - 14	*indica*-leaning
Sedamen^{MR}"	21 - 24	0	*indica*-dominant
Luminarium^{MR}	25 - 28	0	*sativa*-dominant

THC: tetrahydrocannabinol.
CBD: cannabidiol.

Impact of PTSD on social and family life

The severity of the impact of PTSD on social and family life was significantly reduced across all domains, with reductions in severity ranging from 46% to 82% ($p \leq 0.0001$) (Table 6). For all domains, improvement from baseline to follow-up was larger than the MCID. The aggregate score for the impact of PTSD on domains of social and family life decreased from 6.5 to 2.7 (59% reduction, ES 1.2, large effect; $p < 0.0001$). Specifically, the mean score for the impact of PTSD on drug and alcohol overuse decreased from 6.0 to 1.1 (82% reduction, ES 1.4, very large effect; $p < 0.0001$) and marital/relationship harmony was reduced from 8.1 to 2.8 (65% reduction, ES 2.6, very large effect; $p < 0.0001$). A 48% reduction in the severity of the impact of PTSD on relationships with siblings and parents was also observed (7.1 to 3.7, ES 1.2, large effect; $p < 0.0001$).

Table 5. Severity of symptoms at baseline and follow-up (Scale of 0-10)

Symptom	Number of Responses	Mean Baseline Score ± SD	Mean Follow-Up Score ± SD	Improvement (%)	Effect Size	p-value*
Anger and irritability	93	7.9 ± 2.1	3.0 ± 2.1	5.0 (63%)	2.4	**<.0001**
Anxiety	93	7.8 ± 1.5	3.3 ± 1.5	4.6 (59%)	9.0	**<.0001**
Avoidance of trigger related people and situations	90	8.1 ± 2.3	3.7 ± 2.3	4.3 (54%)	1.9	**<.0001**
Depression	92	7.3 ± 2.1	2.9 ± 2.1	4.4 (60%)	2.1	**<.0001**
Distorted sense of blame for the events	78	6.7 ± 2.8	2.9 ± 2.8	3.8 (57%)	1.4	**<.0001**
Easily startled	90	7.5 ± 2.3	3.3 ± 2.3	4.2 (57%)	1.8	**<.0001**
Feeling disconnected from oneself (depersonalization)	78	7.0 ± 2.7	2.5 ±2.7	4.4 (64%)	1.6	**<.0001**
Flashbacks and intrusive memories	89	6.9 ± 2.4	2.8 ±2.4	4.2 (60%)	1.7	**<.0001**
Hyper-vigilance	84	7.4 ± 2.2	3.0 ± 2.2	4.4 (59%)	2.0	**<.0001**
Nightmares	87	6.8 ± 2.5	2.5 ± 2.5	4.2 (62%)	1.7	**<.0001**
Poor concentration	92	8.0 ± 1.8	4.2 ± 1.8	3.8 (47%)	2.0	**<.0001**
Sense or feeling that one's surroundings are not real	76	4.8 ± 3.4	1.9 ± 3.4	2.9 (60%)	0.9	**<.0001**
Stuck in severe emotions related to the event	79	6.8 ± 2.5	2.6 ± 2.5	4.3 (63%)	1.7	**<.0001**
Suicidal thoughts	80	4.1 ± 3.3	0.9 ± 3.3	3.1 (77%)	1.0	**<.0001**
Aggregate score		7.0 ± 2.7	2.9 ± 2.7	4.1 (59%)	1.5	**<.0001**

SD: standard deviation.

*Bolded p-values indicate significance.

Table 6. Impact of PTSD on several domains of social and family life at baseline and follow-up (Scale of 0-10)

Impacted Domain	Number of Responses	Mean Baseline Score ± SD	Mean Follow-Up Score ± SD	Improvement (%)	Effect Size	p-value*
Drug and alcohol overuse	66	6.0 ± 3.6	1.1 ± 1.7	4.9 (82%)	1.4	**<.0001**
Marital or relationship harmony	70	8.1 ± 2.0	2.8 ± 2.4	5.3 (65%)	2.6	**<.0001**
Relationship with brothers/sisters/parents	73	7.1 ± 2.8	3.7 ± 2.6	3.4 (48%)	1.2	**<.0001**
Your belief that good things will happen in the future	72	6.1 ± 3.1	3.0 ± 2.3	3.1 (50%)	1.0	**<.0001**
Your belief that you are a valuable and appreciated member of society	47	6.1 ± 2.9	3.3 ± 2.5	2.8 (46%)	1.0	**<.0001**
Your belief that you belong in the "human race" or your concepts of society	35	5.8 ± 3.1	2.3 ± 2.0	3.4 (59%)	1.1	**<.0001**
Your relationship with children	66	6.7 ± 2.9	2.3 ± 2.3	4.3 (65%)	1.5	**<.0001**
Your trust in the relationship with "the creator" or your concept of "God"	51	5.7 ± 3.8	3.0 ± 2.9	2.8 (48%)	0.7	**0.0001**
Aggregate Score		6.5 ± 3.1	2.7 ± 2.5	3.9 (59%)	1.2	**<.0001**

SD: standard deviation.

*Bolded p-values indicate significance.

Table 7. Number of PTSD-related medications at baseline and at follow-up for patients with medication lists available (n = 87)

Number of PTSD-Related Medications	Number of Patients on Medications at Baseline Visit	Number of Patients on Medications at Follow-Up Visit
0	28 (32%)	43 (49%)
1	11 (13%)	17 (20%)
2	13 (15%)	11 (13%)
3	12 (14%)	4 (5%)
4	13 (15%)	8 (9%)
5 or more	10 (11%)	4 (5%)

Reduction in PTSD-related medication use

PTSD related medication information was available for 87 of 100 patients (Table 7). Of these 87 patients, 59 (68%) were using an average of 3.2 (SD 1.9) PTSD-related medications at baseline. At follow-up, the number of medications for these patients was reduced to an average of 1.6 (SD 1.8). The percentage of patients on two or more medications dropped from 55% at baseline to 31% at follow-up. Correspondingly, the percentage of patients on zero or one medication increased from 45% to 69% between baseline and follow-up. Of those 59 patients on PTSD-related medications at baseline, 21 (36%) had discontinued all PTSD related medications at follow-up, 19 (32%) had discontinued some of their PTSD medications, 14 (24%) had no change to their PTSD related medications, and 5 (8%) added some PTSD related medications.

Discussion

PTSD is a debilitating disorder with a lifetime prevalence of 9.2% in Canada (3). This trauma- and stressor-related disorder is even more prevalent in military and police veterans as they may be exposed to many traumatic events during their service (6). However, traditional treatment options are not always effective in this population. Preliminary clinical research suggests that medical cannabis may be an effective alternative therapy for these patients. Therefore, the aim of the present study was to assess the clinical utility and efficacy of medical cannabis in Canadian military and police veterans with PTSD following initiation of cannabis use, by examining a variety of relevant patient outcomes through a retrospective chart review.

Patients in the study used multiple strains of cannabis containing varying amounts of cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC). Specifically, THC is the most common constituent of the Cannabis plant, and is most known for its psychoactive effects. Additionally, THC is used in a clinical setting for its analgesic and anti-nausea effects (23). In comparison, CBD is a non-intoxicating cannabinoid with anti-epileptic, anti-inflammatory, anti-emetic, and muscle relaxing properties. As a result, cannabis strains with differing CBD and THC ratios may offer a variety of medical benefits to patients.

These cannabinoids bind with CB-1 and CB-2 receptors that are a part of the mammalian endocannabinoid system. This system is involved in the regulation of mood, appetite, sleep, memory, and emotional state (24). Therefore, activation of CB-1 and CB-2 receptors via cannabinoid binding produce the desired clinical effects associated with cannabis use, such as appetite stimulation, muscle relaxation, pain and anxiety reduction, and mood regulation (24). Furthermore, PTSD patients may have abnormalities in CB-1 receptors and low levels of the endogenous cannabinoid, anandamide (19). Therefore, stimulation of the CB-1 pathway through medical cannabis is a potential treatment option for reducing PTSD related symptoms.

A literature review conducted by Walsh et al. on the use of medical cannabis in the management of mental health found very few studies reporting the effects of cannabis on PTSD symptoms (20). A

retrospective chart review by Greer et al. (25) examined changes in CAPS (Clinically Administered PTSD Scale) scores of 80 PTSD patients and observed a greater than 75% reduction in CAPS symptom scores in patients when they were using medical cannabis compared to when they were not using cannabis (25). However, patients included in this study were pre-screened for entry to the New Mexico Medical Cannabis Program having already used cannabis, therefore knowing that their PTSD symptoms were reduced with its use. Additionally, cannabis-withdrawal syndrome may have exacerbated their PTSD symptoms when they were not on cannabis, possibly contributing to their positive findings. Therefore, these results are not representative of the effects of cannabis in the general PTSD population (25). Fraser observed a 72% cessation of nightmares or reduction in nightmare severity after nabilone treatment in 47 PTSD patients with a 2-year history of PTSD-related nightmares who didn't respond to standard treatment previously (26). In an open pilot study by Roitman et al. (27), significant reductions in symptom severity were observed in the CAPS hyperarousal symptom cluster, sleep quality, and frequency and severity of nightmares after 10 Israeli PTSD patients were treated with oral Δ9-tetrahydrocannabinol (THC) as an add-on treatment (27). The present study also observed improvements in PTSD symptoms following medical cannabis use. In particular, a decrease in suicidal thinking post-initiation of medical cannabis was observed. Additionally, patients experienced significant improvements in social and family life through the reduction of their PTSD symptoms.

In the present study, a majority of patients reduced the number of PTSD-related medications used between baseline and follow-up, while 21 patients (24%) had discontinued all PTSD-medications at follow-up. Upon pharmacoeconomic evaluation, the estimated annual savings from these 21 patients discontinuing these prescription medications would range from $48,600 to $78,600 based on average daily dose for these medications, the price of generic versus brand name products, and assuming a dispensing fee of $10 per month. This translates into an average savings of $2,300 to $3,800 per year per patient. If medical cannabis can be used as an equally effective first line treatment option or replacement for other conventional pharmaco-therapies, the health-care costs and financial burden associated with PTSD treatment can be significantly reduced.

Several limitations exist in the present study. First, this study was limited to a single centre under the supervision of a single physician, to which patients were only referred if they failed pharmaco-therapy and psychotherapy. Thus, this sample may not be representative of all veterans with PTSD. Additionally, information regarding hospital admissions or adverse events while using medical cannabis was not available, preventing any determination of the risks or side effects associated with cannabis use. Since this was a retrospective chart review, some patients were missing data for certain outcomes, and dosages of PTSD related medications were not always specified. This study also did not use a validated tool for assessment of PTSD symptoms, nor was information regarding patients' history of cannabis use or duration of PTSD collected.

Conclusion

The results of a retrospective chart review presented in this study indicate that medical cannabis may be an effective treatment option for military and police veterans with PTSD, particularly those for whom conventional pharmacotherapy and psychotherapy was ineffective. Cannabis use resulted in improvements across all PTSD symptoms, social and family outcomes, and pain severity. Furthermore, these improvements were associated with a 50% reduction in the use of PTSD-related medications between baseline and follow-up, providing significant cost-savings to both the patient and greater health care system. In addition, less drug or alcohol overuse was observed following the initiation of medical cannabis use. Given the widespread use of medical cannabis among Canadian PTSD patients, it is essential that the safety, efficacy and clinical utility of medical cannabis be validated through thorough clinical investigations. Future studies should consider involving larger sample sizes and controls to determine the efficacy of medical cannabis in reducing PTSD-related symptoms, both as a first-line and alternative treatment option.

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