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PTSD Symptom Reports of Patients Evaluated for the New Mexico Medical Cannabis Program

George R. Greer, M.D.[a]; Charles S. Grob, M.D.[b] & Adam L. Halberstadt, Ph.D.[c]

Abstract — *Background*: New Mexico was the first state to list post-traumatic stress disorder (PTSD) as a condition for the use of medical cannabis. There are no published studies, other than case reports, of the effects of cannabis on PTSD symptoms. The purpose of the study was to report and statistically analyze psychometric data on PTSD symptoms collected during 80 psychiatric evaluations of patients applying to the New Mexico Medical Cannabis Program from 2009 to 2011. *Methods*: The Clinician Administered Posttraumatic Scale for DSM-IV (CAPS) was administered retrospectively and symptom scores were then collected and compared in a retrospective chart review of the first 80 patients evaluated. *Results*: Greater than 75% reduction in CAPS symptom scores were reported when patients were using cannabis compared to when they were not. *Conclusions*: Cannabis is associated with reductions in PTSD symptoms in some patients, and prospective, placebo-controlled study is needed to determine efficacy of cannabis and its constituents in treating PTSD.

Keywords — cannabis, post-traumatic, stress, tetrahydrocannabinol, THC, treatment

INTRODUCTION

In 2009, New Mexico became the first state to explicitly authorize the use of medical cannabis for people with PTSD. Approved patients are allowed to purchase cannabis from licensed, non-profit growers/producers or to grow their own supply. The new regulation of cannabis use for PTSD required evaluation by a psychiatrist certifying: "(1) the aforementioned patient has a debilitating medical condition and the potential health benefits of the medical use of marijuana would likely outweigh health risks for the patient. 2) the aforementioned patient has

[a]Private practice, Santa Fe, NM.
[b]Professor, Department of Psychiatry and Biobehavioral Sciences and Department of Pediatrics, and Director, Division of Child and Adolescent Psychiatry, Harbor-UCLA Medical Center, Torrance, CA.
[c]Assistant Research Scientist, Department of Psychiatry, University of California San Diego, La Jolla, CA.

Please address correspondence to George R. Greer, M.D., 2019 Galisteo, Bldg. N2, Santa Fe, NM 87505; phone and fax: +1 505 982 0312; email: george@newmexico.com

current unrelieved symptoms that have failed other medical therapies" (New Mexico Department of Health 2012). Later, psychiatric nurse practitioners were authorized to conduct the evaluations. As of the most recent report available at this writing, there were 5,495 active medical cannabis patients, of whom 1,854 (34%) had PTSD and 1,355 had chronic pain (New Mexico Department of Health 2011).

A literature search of "cannabis AND PTSD" through PubMed yielded 42 references, some of which reported a positive association of PTSD with cannabis use (Bonn-Miller, Vujanovic & Drescher 2011; Cougle et al. 2011), or abuse and dependence (Cornelius et al. 2010). One article reviewed the anxiolytic properties of the cannabinoid, cannabidiol (Schier et al. 2012), and one included a case report and a thorough discussion on the use of cannabis as a PTSD treatment and possible mechanisms of action (Passie et al. 2012).

In one unpublished, open-label pilot study, smoked medical cannabis containing 23% tetrahydrocannabinol

(THC) and less than 1% cannabidiol was administered to 29 male Israeli combat veterans with PTSD, with instructions to smoke it daily (Mashiah 2012). The baseline score on the Clinician Administered Posttraumatic Scale for DSM-IV (CAPS) was 98 for the entire group, and post-treatment scores in three subgroups after four to 11 months of treatment ranged from 54 to 60.

Soon after the New Mexico PTSD regulation went into effect, one of the authors [GG] began receiving unsolicited phone calls in his private practice from people asking to be evaluated as part of their application to the Program. In order to avoid evaluating patients who would be unlikely to qualify, telephone screening was conducted to determine whether they met the following criteria by self-report: (1) the experience of and emotional response to a trauma that met the DSM-IV Criterion A for PTSD; (2) the presence of several of the major symptoms in Criteria B, C, and D (reexperiencing, avoidance, and hyperarousal) of PTSD when not using cannabis; (3) significant relief of several major PTSD symptoms when using cannabis; and (4) lack of any harm or problems in functioning resulting from cannabis use. All patients who met these screening criteria were evaluated.

The CAPS was utilized during the evaluation to quantify the patients' symptoms retrospectively with and without cannabis use. The CAPS is a frequently used instrument in PTSD research that was developed by the National Center for PTSD and two Veterans Affairs medical centers (Blake et al. 1995). The instrument asks questions about the presence of traumatic experiences and the immediate emotional response to them described in DSM-IV Criterion A for PTSD, and asks for a rating of the frequency and intensity of all 17 symptoms in Criteria B, C, and D on a scale of 0 to 4. On the CAPS scoring form, the frequency and intensity scores are added to create a total score for that symptom; then a total score for all the symptoms within each criterion, and for all symptom criteria, are calculated.

During the evaluation, patients were asked to answer the symptom questions for Criteria B, C, and D retrospectively for a time period when they were not using cannabis, and for a period when they were using it, and scores were recorded for each period. No urine drug screens were collected to verify recent cannabis use.

After conducting over 80 such evaluations between mid-2009 and the end of 2011, all with adults over age 18, CAPS scores were analyzed to assess differences in PTSD symptoms with vs without cannabis use. The null hypothesis was that there would be no significant difference in CAPS scores between the cannabis and no-cannabis conditions.
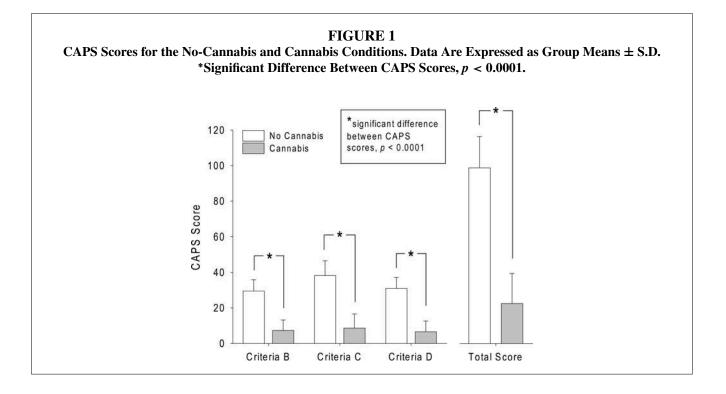
MATERIALS AND METHODS

Study procedures were approved by the Institutional Review Board (IRB) of the Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center. Retrospective chart review procedures were conducted for the first 80 patients evaluated by GG for participation in the New Mexico Department of Health's Medical Cannabis Program for PTSD. The data collection procedure began with GG scanning each of the CAPS scoring forms for Criteria B, C, and D to a file in .pdf format. The .pdf files and spreadsheet were then sent to the two other investigators, CG and AH. Per IRB rules, no identifying information was extracted from patient records, or seen or retained by any of the investigators.

CAPS symptom cluster (re-experiencing, avoidance, and arousal) scores were analyzed using two-way analysis of variance (ANOVA) with time period (no-cannabis vs. cannabis) as a within-subject factor. When the two-way ANOVA detected significant main effects of time period or interactions between time period and symptom cluster, post-hoc pairwise comparisons were performed by one-way ANOVA. CAPS scores in patients using cannabis were also analyzed as %baseline (no-cannabis) scores using two-tailed one-sample t-tests. Statistical significance was demonstrated by surpassing an α level of .01.

In addition to statistically analyzing the Criteria B, C, and D symptom scores, the initial plan was to record whether the patient met diagnostic criteria for PTSD with and without cannabis use. However, no single scoring rule or method of the nine suggested by the CAPS Manual (Weathers, Ruscio & Keane 1999) was appropriate for this study. Determining whether someone has or does not have a PTSD diagnosis based solely on any of the nine CAPS scoring methods would exaggerate the perception of a difference that did not reflect the clinical condition of the person, because the frequency and intensity of all the symptoms exist on a continuum. Therefore, a patient who barely qualified for the diagnosis according to one of the scoring rules/methods would not be very different from someone who almost qualified.

RESULTS

CAPS scores for the no-cannabis and cannabis conditions are shown in Figure 1. Within-subject analysis showed that there was a significant reduction of total CAPS scores ($F(1,79) = 1119.55$, $p < 0.0001$) when patients were using cannabis (22.5 ± 16.9 (mean $\pm$ S.D.)) compared with the no-cannabis condition (98.8 ± 17.6). There were also significant reductions in CAPS symptom cluster scores (Cannabis $\times$ Cluster: $F(2,158) = 39.87$, $p < 0.0001$) in patients using cannabis. Post-hoc analysis confirmed that scores were reduced during cannabis use for Criterion B (core symptom cluster of re-experiencing), which decreased from 29.5 ± 6.4 to 7.3 ± 5.9 ($F(1,79) = 734.98$, $p < 0.0001$); Criterion C (numbing and avoidance), which decreased from 38.2 ± 8.4 to 8.7 ± 8.0 ($F(1,79) = 783.73$, $p < 0.0001$); and Criterion D (hyperarousal), which

FIGURE 1
CAPS Scores for the No-Cannabis and Cannabis Conditions. Data Are Expressed as Group Means ± S.D.
*Significant Difference Between CAPS Scores, $p < 0.0001$.

decreased from 31.0 ± 6.2 to 6.6 ± 6.0 ($F(1,79) = 910.79$, $p < 0.0001$).

CAPS scores in patients using cannabis were also analyzed as %baseline (no-cannabis) scores. Use of cannabis was associated with a reduction of total CAPS scores to $22.7 \pm 15.9\%$ of baseline ($t(79) = -43.48$, $p < 0.0001$); similar reductions occurred in Criterion B ($24.8 \pm 18.9\%$; $t(79) = -35.59$, $p < 0.0001$), Criterion C ($22.5 \pm 19.5\%$; $t(79) = -35.59$, $p < 0.0001$), and Criterion D ($21.0 \pm 17.6\%$; $t(79) = -40.12$, $p < 0.0001$) scores.

One finding was that only 19 of the 80 patients reported any score at all for Criterion C3 (inability to recall an important aspect of the trauma) with no cannabis, and the mean score for C3 was much smaller than the mean scores for the other 16 criteria (main effect of criteria for the no cannabis condition: $F(16,1264) = 43.18$, $p < 0.0001$). As shown in Table 1, post-hoc analysis confirmed that the Criterion C3 values for the no-cannabis time period were significantly different than the values for all other criteria during the same time period.

DISCUSSION

Patients in this sample reported over 75% reduction in all three areas of PTSD symptoms while using cannabis. Because this was a highly select group of pre-screened patients who had already found that cannabis reduced their PTSD symptoms and who sought entry to the NM Medical Cannabis Program to avoid criminal penalties for cannabis

TABLE 1
DSM IV Criteria B, C, and D Scores During the No-Cannabis Time Period

Criteria	Mean	S.D.	N	Comparison Versus C3
B1	6.7	1.2	80	$F(1,79) = 362.53$, $p < 0.0001$
B2	5.7	2.5	80	$F(1,79) = 123.80$, $p < 0.0001$
B3	4.1	2.9	80	$F(1,79) = 48.62$, $p < 0.0001$
B4	6.5	1.5	80	$F(1,79) = 273.24$, $p < 0.0001$
B5	6.5	1.4	80	$F(1,79) = 279.16$, $p < 0.0001$
C1	6.7	1.7	80	$F(1,79) = 266.72$, $p < 0.0001$
C2	6.5	1.6	80	$F(1,79) = 308.42$, $p < 0.0001$
C3	1.2	2.4	80	
C4	6.2	2.1	80	$F(1,79) = 211.79$, $p < 0.0001$
C5	6.2	2.0	80	$F(1,79) = 229.73$, $p < 0.0001$
C6	5.9	2.3	80	$F(1,79) = 185.00$, $p < 0.0001$
C7	5.6	2.8	80	$F(1,79) = 118.92$, $p < 0.0001$
D1	7.1	1.7	80	$F(1,79) = 339.92$, $p < 0.0001$
D2	5.9	2.2	80	$F(1,79) = 153.62$, $p < 0.0001$
D3	5.9	1.7	80	$F(1,79) = 214.04$, $p < 0.0001$
D4	6.3	2.1	80	$F(1,79) = 221.47$, $p < 0.0001$
D5	5.8	2.0	80	$F(1,79) = 178.75$, $p < 0.0001$

possession, reports of significant symptom reduction could be expected. Some degree of intentional or unintentional exaggeration of symptom differences on the part of the patients is likely, and some unintentional bias on the part of the psychiatrist conducting the evaluations is also possible.

Another factor is that some patients may have reported their no-cannabis PTSD symptoms when they were also experiencing a cannabis-withdrawal syndrome. Nightmares, anger, and insomnia have been reported as common symptoms of cannabis withdrawal (Allsop et al. 2011). Those three symptoms are among the 17 symptoms of PTSD, and so could have resulted in higher no-cannabis CAPS scores for those symptoms. However, in this retrospective chart review, no information was collected on the length of the time periods without cannabis use. Therefore, there is no valid way to quantify the degree to which cannabis-withdrawal symptoms may have increased the CAPS scores for those three PTSD symptoms. However, even with the above confounding variables, the amount of reported symptom relief is noteworthy.

Furthermore, the variability in scores with cannabis use was relatively high, with the standard deviation being almost equal to the mean total scores and the scores of the three symptom clusters. If patients had consistently reported frequent and severe symptoms without cannabis and almost no symptoms with cannabis in order to make sure they qualified for the Program, one would expect less variability in the cannabis scores. Finally, the relatively consistent reporting of low or "0" scores on Criterion C3 without cannabis (see Table 1) is another indication that most patients were not malingering by exaggerating their no-cannabis scores for every single symptom in order to qualify for the program. In fact, their reporting low scores for this symptom is consistent with psychometric literature on the CAPS: "Finally, with the exception of amnesia, the prevalence of each of the 17 core PTSD symptoms on the CAPS was significantly greater in participants with PTSD than in those without PTSD, indicating robust discrimination between the two groups" (Weathers, Keane & Davidson, 2001).

Because only patients who reported benefit from cannabis in reducing their PTSD were studied, no conclusions can be drawn as to what proportion or type of PTSD patients would benefit from treatment with cannabis or its constituents. The reported anxiolytic properties of cannabidiol may partly explain the reported benefit, though the cannabis in the Israeli study reportedly contained almost no cannabidiol (Mashiah 2012). That small, open-label prospective study comes closer to showing a benefit, at least for people with combat-related PTSD. It has also been reported that the synthetic cannabinoid nabilone can reduce the incidence and severity of nightmares in PTSD patients (Fraser 2009).

The finding that use of cannabis can reduce symptoms of PTSD is consistent with preclinical evidence showing that the endocannabinoid system is involved in the regulation of emotional memory. There is extensive evidence that cannabinoids may facilitate extinction of aversive memories (de Bitencourt, Pamplona & Takahashi 2013). For example, in rodents, the full CB1 receptor agonist WIN 55,212-2 (Pamplona et al. 2006; Pamplona, Bitencourt & Takahashi 2008) and the fatty acid amide hydrolase inhibitor AM404 (Pamplona et al. 2006; Chhatwal et al. 2005) facilitate extinction of conditioned fear. Given the role that the endocannabinoid system plays in fear extinction, it is possible that the marked reduction in PTSD symptomatology reported with cannabis use in the present study was due to facilitated extinction of fear memories. Additional studies are necessary to identify the specific mechanism by which cannabis use attenuates the symptoms of PTSD.

CONCLUSION

Though currently there is no substantial proof of the efficacy of cannabis in PTSD treatment, the data reviewed here supports a conclusion that cannabis is associated with PTSD symptom reduction in some patients, and that a prospective, placebo-controlled study of cannabis or its constituents for treatment of PTSD is warranted.

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