TITLE: Cannabinoids for the Treatment of Post-Traumatic Stress Disorder: A Review of the Clinical Effectiveness and Guidelines

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CONTEXT AND POLICY ISSUES:

Post-traumatic stress disorder (PTSD) is a condition that can occur following a traumatic event.1 PTSD can develop immediately following the event or can be delayed.2 In Canada, the prevalence rate of lifetime PTSD is approximately 9.2%.1 The core symptoms of PTSD include avoidance of reminders of the traumatic event, re-experiencing aspects of the event, and hyperarousal (exaggerated startle responses, difficulty concentrating, and sleep problems).2

Current treatment approaches for the management of PTSD include psychological therapy and pharmacotherapy.2 Alternative drug therapy approaches are being considered including the use of cannabinoids. The term cannabinoids is used to describe the additional active ingredients found in cannabis other than Δ-9-tetrahydrocannabinol and cannabidiol.3 Two synthetic cannabinoids, dronabinol and nabilone, are currently available in Canada.3

This report will review the clinical effectiveness and the guidelines regarding the use of cannabinoids for the treatment of PTSD.

RESEARCH QUESTIONS:

1. What is the clinical effectiveness of cannabinoids for the treatment of post-traumatic stress disorder?

2. What are the guidelines regarding the use of cannabinoids for the treatment of post-traumatic stress disorder?

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METHODS:

A limited literature search was conducted on key health technology assessment resources, including OVID Medline, OVID PsycINFO, The Cochrane Library (Issue 4, 2009), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between 2004 and November 2009. No filters were applied to limit the retrieval by study type.

SUMMARY OF FINDINGS:

The literature search identified one observational study and three evidence-based guidelines regarding the use of cannabinoids for the treatment of patients with PTSD. No health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, or controlled clinical trials were identified.

Observational studies

Fraser (2009) reported results of an open label study that evaluated the effectiveness of the synthetic cannabinoid nabilone for the treatment of PTSD. The Canadian study recruited 47 patients (mean age, 44 years; 57% female) who had a confirmed diagnosis of PTSD by the DSM-IV-TR with a minimum two-year history of treatment-resistant nightmares. The types of trauma experienced by patients included repetitive childhood trauma [38% (sexual or physical abuse)], adult trauma [38% (accident, rape, injury, or life threatening illness)], and combat-associated trauma (23%). To be eligible for inclusion, patients had to experience at least one nightmare per week. All of the patients were on psychotropic medication throughout the study period. Prior to receiving the first dose of nabilone, the patients recorded the intensity of their nightmare using a scoring system that ranged from one to five with five being the most severe. This scoring practice as well as the patient’s thoughts about the previous night’s sleep continued throughout the treatment period. The initial dose of nabilone was 0.5 mg taken one hour before bedtime. The dose was titrated up or down until nightmare symptom control was achieved. The maximum dose used in the study was 6 mg.

The effective dose range was 0.2 mg to 4 mg and the average effective dose was 0.5 mg. Thirty-four patients (72%) had the nightmares stop entirely (n=28) or reduce in severity (n=6). Four of the patients were able to withdraw from nabilone treatment without the recurrence of nightmares following four to 12 months on nabilone. The remaining 28% of the patients (13/47) experienced mild to moderate side effects (lightheadedness, forgetfulness, dizziness, and headache) and discontinued treatment.

The study relied on a patient-reported subjective assessment of nightmare severity and frequency. The study did not include a placebo control group. These factors may represent limitations of the study. The author concluded that nabilone had reduced the severity and frequency of treatment-resistant nightmares in patients with PTSD. The author suggested that more studies should be done to further evaluate the clinical effectiveness of nabilone for the treatment of PTSD-associated symptoms.
Guidelines and recommendations

A clinical practice guideline for the management of anxiety disorders was developed by the Canadian Psychiatric Association. A systematic search of literature was performed and the evidence was reviewed by a sub-group of the guideline panel. Draft guidelines and recommendations were prepared and presented to the entire panel for consensus. The guideline evaluated psychological and pharmacological treatment approaches for anxiety. Cannabinoids were not discussed as part of the guideline. The guideline recommends the use of cognitive behavioural therapy (CBT) as a psychological treatment. The recommended first-line drug therapy includes selective serotonin reuptake inhibitors [SSRI; (sertraline, paroxetine, and fluoxetine)] and the selective serotonin/norepinephrine reuptake inhibitor (SNRI), venlafaxine.

The National Institute for Clinical Excellence (NICE) published clinical guidance for the management of PTSD. A systematic search of the literature was used to develop the guideline. Group consensus was used to formulate recommendations. If the available information on a particular clinical question was limited, a recommendation was made by informal consensus and subsequently sent for external peer review. The guideline was validated through two consultation processes that included stakeholders, the NICE Guidelines Review Panel, key experts, and the public. The guideline evaluated psychological and pharmacological treatment approaches for PTSD. Cannabinoids were not discussed as part of the guideline. The guideline recommends that trauma-focused CBT be offered to those individuals with PTSD. The guideline does not recommend drug treatment as a first-line therapy in the place of psychological therapy. Treatment with paroxetine and mirtazapine (or amitriptyline or phenelzine under the treatment supervision of a mental health specialist) may be considered for patients who would rather not participate in psychological therapy.

The American Psychiatric Association published clinical practice guidelines regarding the treatment of patients with acute stress disorder and PTSD. The guideline was developed following a systematic search of the literature. The quality and strength of the evidence was assessed by expert consensus. The recommendations were formulated based on expert consensus. The guideline was externally peer-reviewed. The practices for the initial assessment of patients with stress disorders and subsequent psychological or pharmacological therapy were assessed in the guideline. Cannabinoids were not discussed as part of the guideline. CBT is recommended for the treatment of PTSD when given two to three weeks following trauma exposure. SSRIs are recommended as a first-line drug therapy for the treatment of PTSD. Other antidepressants including monoamine oxidase inhibitors may also be beneficial as well as benzodiazepines.

Limitations

The evidence regarding the effectiveness of cannabinoids for the treatment of PTSD was limited. No health technology assessments or systematic reviews were identified. No studies typically associated with high internal validity (i.e. randomized controlled trials) were identified. One observational study was identified. Observational studies do not involve a control group and therefore may be subject to bias. The one observational study included in this report used a self-report measure to evaluate the effectiveness of treatment, which is subjective.
Three evidence-based guidelines were identified by the literature search including one developed in Canada. None of the guidelines discussed the use of cannabinoids in the management of PTSD.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

Overall, the evidence regarding the clinical effectiveness of cannabinoids for the treatment of PTSD is limited. The one included study concluded that the synthetic cannabinoid nabilone was effective in treating patients with PTSD who were experiencing treatment-resistant nightmares. Approximately 70% of patients enrolled in the trial experienced either a reduction in frequency or intensity, or complete cessation of nightmares while taking nabilone. None of the three evidence-based guidelines discussed the use of cannabinoids in the management of PTSD. All three of the guidelines recommended the use of CBT or SSRIs for the treatment of patients with PTSD.

Overall, the evidence regarding the clinical effectiveness of cannabinoids for the treatment of PTSD is limited. The paucity of information may wish to be considered when making decisions regarding coverage of cannabinoids or the clinical use of cannabinoids for PTSD.

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