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Cannabinoids for Post-Traumatic Stress Disorder: A Systematic Review

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ABSTRACT:

A complicated mental health disease known as post-traumatic stress disorder (PTSD) may arise following exposure to traumatic situations. Many patients suffer from unfavorable side effects or insufficient symptom alleviation despite the availability of numerous therapeutic alternatives. Cannabis contains active molecules called cannabinoids, which have drawn interest due to their possible PTSD treatment benefits. The purpose of this systematic review is to assess the body of knowledge about the safety and effectiveness of cannabis in the treatment of PTSD.

KEYWORDS: Active molecules**,** Effectiveness, Therapeutic alternatives, Safety,

INTRODUCTION:

Posttraumatic stress disorder (PTSD) include intrusive, involuntary, distressing memories or recollections, avoidance, negative changes in mood and cognition, and changes in arousal and reactivity after the person has witnessed, experienced, or learned about actual or threatened death, serious injury, or sexual violence from a close friend or family member. The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) is the basis for the most recent nationally representative estimates of PTSD prevalence in the UN.[1] Posttraumatic stress disorder (PTSD) affects 6.8% to 12.3% of Americans during the course of their lifetimes, with significant racial and ethnic disparities reported in multiple studies Compared to non-Latino whites (7.4%) or Asians (4.0%), there is evidence that the lifetime prevalence of PTSD is higher among African Americans (8.7%). Other research indicates that there is either no difference in the prevalence rates of PTSD among African Americans, Latinos, and non-Latino whites, or that there is only a minimal correlation between race and ethnicity.[2] Racial and cultural disparities in PTSD are not fully understood, even when they are discovered. Even though African Americans report less traumatic event exposures than non-Latino whites, after controlling for gender, age, and kind of exposure, their chance of getting post-traumatic stress disorder (PTSD) is higher.[3] Various psychotherapies and non-pharmacological methods, like cognitive-behavioral therapy, are the main treatments for PTSD.[4] Other non- pharmacological treatment includes Desensitization and reprocessing of eye movements. Furthermore, a variety of pharmaceutical treatments, including selective serotonin reuptake inhibitors (SSRIs), [5] Dysregulation of the hypothalamic-pituitary axis and changes in the activity of the amygdala (fear conditioning), prefrontal cortex (emotional regulation) and hippocampus (memory consolidation) have been observed in brain morphometric investigations of PTSD patients.[6] This systematic review's goals were to evaluate the impact of cannabis on PTSD, quality of life, social function, return to work, and harm effects like adverse effects and dropout rates. It also aimed to critically evaluate the body of research on cannabis's effects on PTSD treatment [7].

MECHANISM OF ACTION:

Human cannabinoid pathways were unknown. Signaling pathways were discovered as a result of the discoveries of Tertahydro Cannabinol (THC) and Cannabidiol (CBD) When exposed to THC or its synthetic equivalents, murine neuroblastoma cells showed elevated expression of adenylate cyclase, providing evidence that the molecule interacts with a specific mammalian target. [8] Because of this discovery, a G protein-coupled receptor known as cannabinoid receptor type 1 (CB1) was isolated and cloned. Later, human leukemia cells were found to contain cannabinoid receptor type 2 (CB2). It was demonstrated that CBD directly activates the CB2 receptor. [9] Following the discovery of these receptors, it was postulated that the mammalian body may also contain an endogenous cannabinoid system called endocannabinoids. N-arachidonoylethanolamine (AEA), often known as anandamide, was the first endogenous cannabinoid ligand to be identified when it was extracted from pig brain. 2-arachidonoylglycerol (2-AG) is the name of the second endogenous ligand that was also extracted from intestinal tissue.[10] Activity-dependent activation of particular phospholipase enzymes yields the

arachidonic acid derivatives AEA and 2-AG from phospholipid substrates. N-arachidonoyl dopamine, N-arachidonoyl glycerol ether, and O-arachidonoylethanolamine are among the several endogenous ligands that have since been identified.[11]

EFFECTIVENESS:

The overall impact of cannabis on health shows major, moderate, or mild improvement, no change, and slight, moderate, or major deterioration were the seven possible answers. Treatment success was defined as (a) at least moderate or significant improvement in the patient's condition and (b) none of the following: treatment cessation or serious side-effects, which are defined as 9–10 on the severity scale and incidence of often or always.[12] Other anxiety disorders, such as social anxiety disorder and particular phobia disorder, have been linked to hyperactivations of certain brain areas, referred to as the "limbic" brain, but not hypoactivations. The brain areas linked to emotion experience or control showed hypoactivations during PTSD symptoms, which further suggests that defective fear extinction is involved. PTSD sufferers have also been found to have lower levels of 2-AG and AEA, which provides more proof of aberrant CB1 receptor signaling. The ability of synthetic cannabinoids to alter prefrontal-limbic circuits during fear extinction and extinction memory consolidation.[13] It's also critical to understand that prolonged usage of cannabinoids may reduce their clinical effectiveness.[14]

SAFETY:

It was discovered that cannabis medication was highly safe in this diverse group of patients, particularly when contrasted with the safety of long-term opiate treatment. The side effects of medical cannabis were rare, mild, and rarely the reason for stopping use. [15] These consequences include cognitive impairments, heightened mood, paranoia, relaxation, and changes in perception. Regardless of the various negative consequences, stress reduction is the main cause of chronic cannabis use. Although it can also be derived from cannabis, cannabidiol (CBD) does not have the same intoxicating effects as THC. In addition to its interactions with CB receptors, there is mounting evidence that CBD primarily operates through the 5HT1A receptor. [16] Many illnesses have been treated using synthetic cannabinoids, including as sleep difficulties, muscular spasms and pain from multiple sclerosis, and anti-emetic effects. anxiolytic symptoms, pain, and inflammation. They have also been demonstrated to lessen cannabis withdrawal symptoms in those who are trying to stop using it. The medications carry some hazards, particularly when abused, including the possibility of tachycardia, seizures, and hallucinations. [17]

INDICATION:

Cannabinoids are recommended to treat PTSD symptoms like anxiety, sleeplessness, and hyperarousal. For certain PTSD patients, they might lessen nightmares and enhance the quality of their sleep. Evidence for their effectiveness is still developing, though, and their use is often regarded as off-label. When traditional therapies are not enough to treat PTSD, clinicians may think about using marijuana as part of a comprehensive therapy plan. [18]

Limitations:

Cannabis therapy users may not be a representative sample of patients with a particular illness (self-selection bias). But their use is limited by a lack of large-scale, conclusive clinical trials. Additionally, concerns about potential dependency, cognitive impairment, and adverse side effects restrict their widespread adoption. Regulatory restrictions and variability in individual responses further complicate their application as a treatment option for PTSD.[19]

CONCLUSION:

The systematic review suggests that cannabinoids may offer potential therapeutic benefits for individuals with post-traumatic stress disorder (PTSD). Evidence from various studies indicates that cannabinoids, particularly those targeting the endo cannabinoid system, may help alleviate symptoms such as anxiety, hyperarousal, and intrusive memories commonly associated with PTSD. However, the variability in study designs, cannabinoid formulations, dosages, and treatment durations highlights the need for more rigorous, large-scale randomized controlled trials to solidify efficacy and safety profiles. Additionally, the potential for side effects and the psychoactive properties of certain cannabinoids, notably THC, necessitate careful consideration in clinical application. Future research should aim to explore the long-term effects of cannabinoid use in PTSD treatment and examine the specific mechanisms by which they may confer their therapeutic effects. Overall, while cannabinoids present a promising avenue for intervention, further investigation is essential to establish consensus guidelines for their use in PTSD management.

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