

COVID-19 and Cannabidiol (CBD)

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COVID-19 pandemic has resulted in devastating mortality and morbidity consisting of socioeconomic and health effects that have included respiratory/pulmonary, cardiovascular, mental health and neurological consequences such as anxiety, depression, and substance use. Extensive efforts are underway to develop preventive vaccines and therapeutics such as remdesivir, dexamethasone, convalescent plasma, and others to treat COVID-19 but many report residual mental health problems after recovery. Cannabis products such as cannabidiol (CBD) are being advertised for the treatment of COVID-19 associated mental health problems and substance use disorders. This commentary will briefly clear the myth that CBD can ameliorate a wide range of COVID-19 associated health effects including anxiety, depression, or any substance use disorder, and show that there is a clear lack of sufficient unbiased clinical evidence from well-designed double-blind, placebo-controlled clinical trials to prove the antianxiety or antidepressant therapeutic properties of CBD and support its wide use as medicine to treat COVID-19-associated mental health conditions or substance use disorders. Finally, we suggest that addiction physicians must play an important role in dealing with their patients requesting CBD prescription for treating any of these conditions.

Key Words: cannabidiol, CBD, COVID-19

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Today, the world is facing one of the most devastating viral pandemics of our time where almost 62 million people have been infected with a novel corona virus, known as severe acute respiratory syndrome coronavirus-2 (SARS-Cov2),

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and more than one million people have died from the corona virus induced disease (COVID-19).¹ The COVID-19 pandemic is also responsible for unprecedented loss of life, economic, social, and health consequences including severe acute respiratory syndrome (SARS),² cardiovascular,³ mental health including anxiety, depression, and neurological complications like tremors, seizures, and impaired consciousness.⁴ An estimated 45% of adults in the US reported that their mental health has been negatively impacted due to worry and stress over the virus.⁵ Further, people with preexisting health conditions including asthma, cerebrovascular disease, hypertension, diabetes, immunocompromised state, neurological conditions such as dementia and others might be at increased risk from COVID-19.⁶ The conditions such as imposed shelter-in-place, physical distancing, social isolation and potential financial distress from job loss might further lead to mental health problems, increased substance use, and possibly suicides. Furthermore, limited access to mental health care and addiction treatment health care providers for treating substance use disorder(s) may also in part exacerbate COVID-19 related complications, thereby necessitating the use of telemedicine to treat people with substance use disorder(s).

Extensive efforts worldwide are underway to develop vaccines and therapeutics including remdesivir, dexamethasone, and convalescent plasma to combat the coronavirus induced symptomatic disease (COVID-19) and associated complications. Even though long-term use of cannabis is associated with significant morbidity including increased risk of panic attacks,⁷ the internet is filled with suggestions for using cannabis or cannabinoids including cannabidiol (CBD) for the treatment of coronavirus infection induced inflammation and COVID-19 induced mental health conditions including anxiety, depression, PTSD, and panic attacks. The recent changes in legalization of CBD in many US states have made CBD products easily accessible to all as over the counter products. This commentary will briefly show that the use of CBD for the treatment of anxiety, depression and substance use disorder(s) are just myths and not a reality.

Though CBD may be a promising drug to treat panic disorders, generalized anxiety disorder, post-traumatic disorder (PTSD), social anxiety disorder, and depressive disorders⁸ via serotonergic pathways and endocannabinoid system, extensive literature search failed to find sufficient clinical evidence to support CBD for treating any of the above-mentioned mental conditions.⁹ Much more clinical research from well-designed clinical trials is needed to support the use of CBD in treating anxiety and depressive disorders and bipolar disorders.¹⁰ CBD may promote wakefulness via

triggering increased dopamine levels in areas of the brain and thereby treat narcolepsy, and in a case report,¹¹ CBD did improve the quality and quantity of sleep of a 10-year old young patient with PTSD, likely due to its anxiety-relieving benefits. But these data from one patient are clearly insufficient to support the use of CBD for treating sleep disorders.

Could CBD treat substance use disorders? The answer is *not yet*. Limited research suggests that CBD *could potentially* treat patients with substance use disorders like opioid-, cannabis-, and tobacco use disorders (OUD, CUD, TUD).¹² Earlier studies showed that legalization of medical marijuana reduced the number of over dose deaths from opioid pain relievers,¹³ and that medical marijuana laws significantly reduced prescribing of opioids for pain.¹⁴ More recently, Hurd et al¹⁵ reported that acute administration of CBD to heroin abstinent patients with OUD significantly reduced craving, anxiety, heart rate and salivary cortisol without causing adverse effects. But still additional clinical trials are needed to establish the efficacy of CBD in treating opioid use disorder.¹⁶ In a randomized, double blind, placebo-controlled trial,¹⁷ nabiximols (THC+CBD [Sativex]) combined with Motivational Enhancement Therapy and Cognitive Behavioral Therapy (MET/CBT), reduced cannabis use and craving but not withdrawal symptoms in persons that used cannabis chronically. CBD also reduced euphoria and depressive and psychotic-like symptoms, improved attention, verbal learning and memory without impairing cognition when smoking cannabis, suggesting that prolonged therapy with CBD may be a useful adjunct therapy for treating cannabis dependence.¹⁸ In a study of 24 tobacco smokers, CBD inhaler reduced the number of tobacco cigarettes by 40% when compared to placebo¹⁹; and a single dose of 800 mg oral dose of CBD reduced the salience and pleasantness of cigarette cues, but did not influence tobacco craving or withdrawal or any subjectively rated side effects.²⁰ Data from these studies with a small number of patients present a positive signal of CBD's potential to treat substance use disorders, but significantly much more research from well-designed clinical trials is needed to support its wide use as treatment for substance use disorder(s).

Thus, there is a clear paucity of data from well-designed clinical trials to support the use of CBD for treating anxiety, depression, other neurological complications associated with COVID-19 or substance use disorders. A careful systematic evaluation of CBD in large clinical trials is essential prior to endorsing its wider use for alleviation of mental health symptomatology. It is also of paramount importance that the clinicians treating patients with any of the above COVID-19 related mental or neurological conditions or substance use disorders inform their patients about the lack of sufficient unbiased clinical evidence for the use of CBD and discourage them from using CBD for COVID-19 related health problems during this COVID-19 related severe, unprecedented global health catastrophe.

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