A review and meta-analysis of the efficacy and safety of cannabidiol in epilepsy. - GreenMedInfo Summary

BACKGROUND: Approximately one-third of patients with epilepsy presents seizures despite adequate treatment. Hence, there is the need to search for new therapeutic options. Cannabidiol (CBD) is a major chemical component of the resin of Cannabis sativa plant, most commonly known as marijuana. The anti-seizure properties of CBD do not relate to the direct action on cannabinoid receptors, but are mediated by a multitude of mechanisms that include the agonist and antagonist effects on ionic channels, neurotransmitter transporters, and multiple 7-transmembrane receptors. In contrast to tetra-hydrocannabinol, CBD lacks psychoactive properties, does not produce euphoric or intrusive side effects, and is largely devoid of abuse liability.

OBJECTIVE: The aim of the study was to estimate the efficacy and safety of CBD as adjunctive treatment in patients with epilepsy using meta-analytical techniques.

METHODS: Randomized, placebo-controlled, single- or double-blinded add-on trials of oral CBD in patients with uncontrolled epilepsy were identified. Main outcomes included the percentage change and the proportion of patients with ≥ 50% reduction in monthly seizure frequency during the treatment period and the incidence of treatment withdrawal and adverse events (AEs).

RESULTS: Four trials involving 550 patients with Lennox-Gastaut syndrome (LGS) and Dravet syndrome (DS) were included. The pooled average difference in change in seizure frequency during the treatment period resulted 19.5 [95% confidence interval (CI) 8.1-31.0; p = 0.001] percentage points between the CBD 10 mg and placebo groups and 19.9 (95% CI 11.8-28.1; p < 0.001) percentage points between the CBD 20 mg and placebo arms, in favor of CBD. The reduction in all-types seizure frequency by at least 50% occurred in 37.2% of the patients in the CBD 20 mg group and 21.2% of the placebo-treated participants [risk ratio (RR) 1.76, 95% CI 1.07-2.88; p = 0.025]. Across the trials, drug withdrawal for any reason occurred in 11.1% and 2.6% of participants receiving CBD and placebo, respectively (RR 3.54, 95% CI 1.55-8.12; p = 0.003) [Chi squared = 2.53, degrees of freedom (df) = 3, p = 0.506; I = 0.0%]. The RRs to discontinue treatment were 1.45 (95% CI 0.28-7.41; p = 0.657) and 4.20 (95% CI 1.82-9.68; p = 0.001) for CBD at the doses of 10 and 20 mg/kg/day, respectively, in comparison to placebo. Treatment was discontinued due to AEs in 8.9% and 1.8% of patients in the activeand control arms, respectively (RR 5.59, 95% CI 1.87-16.73; p = 0.002). The corresponding RRs for CBD at the doses of 10 and 20 mg/kg/day were 1.66 (95% CI 0.22-12.86; p = 0.626) and 6.89 (95% CI 2.28-20.80; p = 0.001). AEs occurred in 87.9% and

72.2% of patients treated with CBD and placebo (RR 1.22, 95% CI 1.11-1.33; p < 0.001). AEs significantly associated with CBD were somnolence, decreased appetite, diarrhea, and increased serum aminotransferases.

CONCLUSIONS: Adjunctive CBD in patients with LGS or DS experiencing seizures uncontrolled by concomitant anti-epileptic treatment regimens is associated with a greater reduction in seizure frequency and a higher rate of AEs than placebo.