Lancet Neurol. 2016 Mar;15(3):270-8. doi: 10.1016/S1474-4422(15)00379-8. Epub 2015 Dec 24.

Cannabidiol in patients with treatment-resistant epilepsy: an open-label interventional trial.

Devinsky O[1], Marsh E[2], Friedman D[3], Thiele E[4], Laux L[5], Sullivan J[6], Miller I[7], Flamini R[8], Wilfong A[9], Filloux F[10], Wong M[11], Tilton N[6], Bruno P[4], Bluvstein J[3], Hedlund J[3], Kamens R[2], Maclean J[2], Nangia S[5], Singhal NS[6], Wilson CA[10], Patel A[12], Cilio MR[6].

Author information

Erratum in
Corrections. [Lancet Neurol. 2016]

Abstract

BACKGROUND: Almost a third of patients with epilepsy have a treatment-resistant form, which is associated with severe morbidity and increased mortality. Cannabis-based treatments for epilepsy have generated much interest, but scientific data are scarce. We aimed to establish whether addition of cannabidiol to existing anti-epileptic regimens would be safe, tolerated, and efficacious in children and young adults with treatment-resistant epilepsy.

METHODS: In this open-label trial, patients (aged 1-30 years) with severe, intractable, childhood-onset, treatment-resistant epilepsy, who were receiving stable doses of antiepileptic drugs before study entry, were enrolled in an expanded-access programme at 11 epilepsy centres across the USA. Patients were given oral cannabidiol at 2-5 mg/kg per day, up-titrated until intolerance or to a maximum dose of 25 mg/kg or 50 mg/kg per day (dependent on study site). The primary objective was to establish the safety and tolerability of cannabidiol and the primary efficacy endpoint was median percentage change in the mean monthly frequency of motor seizures at 12 weeks. The efficacy analysis was by modified intention to treat. Comparisons of the percentage change in frequency of motor seizures were done with a Mann-Whitney U test.

RESULTS: Between Jan 15, 2014, and Jan 15, 2015, 214 patients were enrolled; 162 (76%) patients who had at least 12 weeks of follow-up after the first dose of cannabidiol were included in the safety and tolerability analysis, and 137 (64%) patients were included in the efficacy analysis. In the safety group, 33 (20%) patients had Dravet syndrome and 31 (19%) patients had Lennox-Gastaut syndrome. The remaining patients had intractable epilepsies of different causes and type. Adverse events were reported in 128 (79%) of the 162 patients within the safety group. Adverse events reported in more than 10% of patients were somnolence (n=41 [25%]), decreased appetite (n=31 [19%]), diarrhoea (n=31 [19%]), fatigue (n=21 [13%]), and convulsion (n=18 [11%]). Five (3%) patients discontinued treatment because of an adverse event. Serious adverse events were reported in 48 (30%) patients, including one death-a sudden unexpected death in epilepsy regarded as unrelated to study drug. 20 (12%) patients had severe adverse events possibly related to cannabidiol use, the most common of which was status epilepticus (n=9 [6%]). The median monthly frequency of motor seizures was 30.0 (IQR 11.0-96.0) at baseline and 15.8 (5.6-57.6) over the 12 week treatment period. The median reduction in monthly motor seizures was 36.5% (IQR 0-64.7).

INTERPRETATION: Our findings suggest that cannabidiol might reduce seizure frequency and might have an adequate safety profile in children and young adults with highly treatment-resistant epilepsy. Randomised controlled trials are warranted to characterise the safety profile and true efficacy of this compound.