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EPILEPSY

Cannabidiol reduces seizure frequency in Dravet syndrome

> This trial represents the beginning of solid evidence for the use of cannabinoids in epilepsy

Cannabidiol is effective in treating drug-resistant seizures in Dravet syndrome, according to a new clinical trial. For the first time, a multinational, randomized, double-blind, placebo-controlled trial has confirmed controversial anecdotal evidence supporting the efficacy of cannabinoids in epilepsy.

Throughout history, anecdotal reports have suggested that cannabis is effective in the treatment of epilepsy, but reliable evidence has been lacking: vested interests in favour of or against the legalization of medicinal cannabis in some countries have made interpretation of the evidence especially difficult for clinicians. Furthermore, the proposed use of cannabinoids in the vulnerable population of children with Dravet syndrome has added to the controversy.

Cannabidiol was previously shown to be effective in preclinical models of epilepsy, but small clinical trials from the past few decades have produced inconsistent results. "Definitive evidence has been lacking, so the well-performed double-blind, controlled trial of Devinsky *et al.* …showing the effectiveness of cannabidiol in the Dravet syndrome is welcome," comments Samuel Berkovic in an editorial accompanying the new paper.

The new study involved 120 individuals with Dravet syndrome, aged 2–18 years. The patients were randomly assigned to receive either 20 mg of oral cannabidiol per kilogram of body weight per day or placebo. The primary endpoint was the change in convulsive seizure frequency during 14 weeks of treatment, compared with a baseline measurement taken over the 4 weeks preceding the trial. "We decided to count only convulsive seizures for our primary outcome measure, as these were the only seizures that parents or caregivers could reliably count," explains lead author Orrin Devinsky.

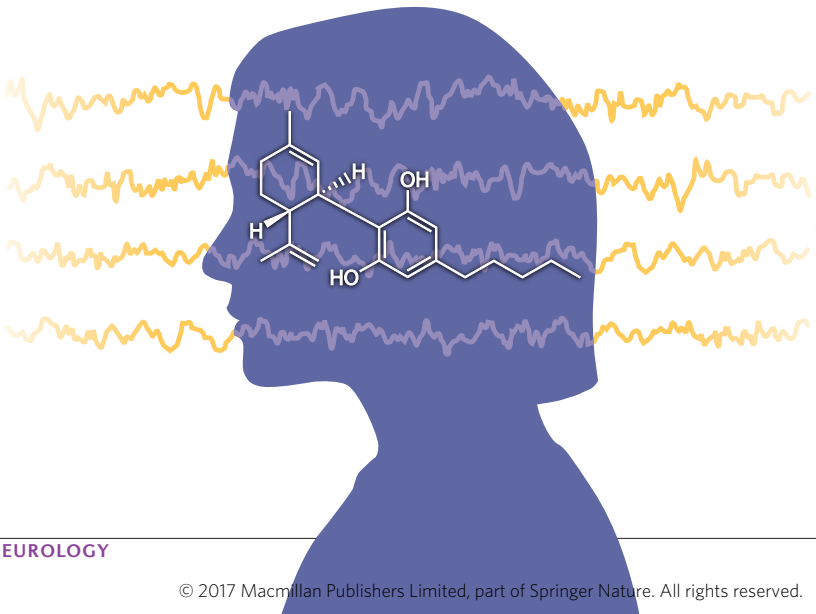
Among patients who received cannabidiol, the median seizure frequency reduced from 12.4 to 5.9 seizures per month, whereas among patients who received placebo, median seizure frequency only decreased from 14.9 to 14.1 seizures per month. In addition, seizure frequency was halved in 43% of those who received cannabidiol, compared with only 27% of the patients who received placebo. Importantly, 5% of cannabidiol-treated patients became completely seizure free, but no patients who were given placebo achieved freedom from seizures.

Several adverse effects were associated with cannabidiol treatment, including somnolence, loss of appetite, vomiting and diarrhoea, which resulted in a higher dropout rate in the treatment group than in the placebo group (eight of 61 versus one of 59 patients). "But, overall, the drug was well tolerated and the side effect profile was favourable compared with other approved antiepileptic drugs," argues Devinsky.

"This trial represents the beginning of solid evidence for the use of cannabinoids in epilepsy," comments Berkovic. However, he notes that the study requires replication.

The trial investigators are now also looking into the effects of cannabidiol in other forms of epilepsy. "We hope to see this medication approved for both Dravet and Lennox–Gastaut syndromes — two other studies in Lennox–Gastaut syndrome were positive but are not yet published," explains Devinsky, "We also hope that cannabidiol will be assessed in other epilepsy syndromes."

Charlotte Ridler



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ORIGINAL ARTICLE Devinsky, O. *et al.* Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. *N. Engl. J. Med.* **376**, 2011–2020 (2017)