
Is medicinal cannabis effective for drug-resistant seizures in Dravet syndrome?

Source: Devinsky, O et al. *Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome*. *New England Journal of Medicine*. 2017; 376: 2011 – 20.

Plain Language Summary

Research findings have just been published from the first randomised, double-blind, placebo controlled trial using medicinal cannabis for the treatment of a form of epilepsy in the prestigious medical journal the *New England Journal of Medicine*. The trial looked at whether cannabidiol (medicinal marijuana) was effective for treating drug-resistant seizures in Dravet syndrome as an add-on treatment to current anti-epileptic drug routines.

This clinical trial involved a large collaboration (known as the Cannabidiol in Dravet Syndrome Study Group) from several countries around the world. One of the members was Professor Ingrid Scheffer, an epileptologist (specialist neurologist) from the Florey Institute at Austin Health in Melbourne.

Multiple anecdotal reports have shown that medicinal cannabis is effective and beneficial for the treatment of seizures in epilepsy. However, there is a lack of high quality (well-controlled), scientific, evidence-based studies to support these findings.

To date there have only been 4 small trials using medicinal cannabis (cannabidiol) for the treatment of epilepsy but the findings have not been clear. Findings from an open-label trial – a trial where both the researchers and participants know which treatment is being provided - was published last year in the *Lancet* medical journal but this was not a double-blind randomised clinical trial. Therefore, it was important to know if cannabidiol was effective for drug-resistant types of epilepsy such as Dravet syndrome using high-quality scientific methods.

What were the findings of the trial?

- 120 children and young adults ranging in ages from 2 years to 18 years were involved. The frequency of convulsive seizures ranged from 4 to 1717 a month (on average 13 seizures a month). Most patients had tried on average 4 anti-epileptic drugs to control convulsive seizures, with the most common being clobazam and valproate.
- Following consent, patients were randomised to receive 20mg per kg per day of cannabidiol solution or an equal volume of placebo solution for a total of 14 weeks.
- Treatment with cannabidiol (medicinal cannabis) was found to be effective – it significantly reduced the rate of convulsive seizures, but not non-convulsive seizures.
- Furthermore 43% of patients treated with cannabidiol had at least a 50% reduction in convulsive seizures. In patients who had placebo treatment, 27% had at least a 50% reduction in seizures.
- An improvement was also shown in the overall condition (behaviour and quality of life) of most patients taking cannabidiol (62%), compared to 34% of patients taking placebo.

- 5% of all patients who took cannabidiol were seizure-free, whereas no patients in the placebo group were found to be seizure-free.
- Higher rates of adverse events and more withdrawals from the trial were also reported following treatment with cannabidiol.

Although the results of this randomised clinical trial are very promising, some caution should be applied. In other words, cannabidiol should not be used as a stand-alone treatment for drug-resistant Dravet syndrome. Also, cannabidiol is a treatment but not a cure for Dravet syndrome which is a rare genetic form of epilepsy.

Future research studies should look at the effectiveness of cannabidiol over a longer period of treatment and to see what adverse effects may be present.

What is Dravet Syndrome?

Dravet syndrome is a type of epilepsy which starts in childhood (around 6 months of age) and is caused by a rare genetic mutation in the SCN1A gene. Seizures are triggered by hot temperature or fever, also called febrile seizures, and get progressively worse with age, developing into several other different types of seizures.

Seizures experienced in Dravet syndrome are difficult to control as they do not respond well to anti-epileptic drugs, this concept is referred to as being drug-resistant. Children with Dravet syndrome have severe developmental problems and there is also a high rate of death (mortality) which can occur.

What is cannabidiol?

Cannabidiol or CBD is a type of cannabinoid which is one of the main ingredients in the marijuana plant *Cannabis sativa*. There are approximately 100 different cannabinoids present in the plant. One of the most well-known cannabinoids is tetrahydrocannabinol or THC which produces hallucinogenic effects - the 'high' associated with marijuana.

Cannabidiol does not produce any hallucinogenic effects, however it is thought to respond to seizure activity, a key symptom of epilepsy.

Medicinal cannabis is mostly made up of cannabidiol with a relatively low amount of THC. Illegal marijuana on the other hand is mostly made up of THC and a low amount of cannabidiol.

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