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Cannabidiol in patients with treatment-resistant epilepsy

We read with interest the results reported by Orrin Devinsky and colleagues[1] of an open-label trial of cannabidiol in people with refractory epilepsy. This is a sensitive topic for many as there are high expectations for cannabidiol as a potential therapy for epilepsy. Some of these expectations have been fuelled by the media. Unlike other compounds, which are conventionally trialled away from the public eye, cannabidiol is already legally available in some countries. Promising case reports **[A: references?]** have encouraged demand for cannabidiol to be made available at the earliest opportunity. However, little is known about its safety and efficacy of the compound, making the study by Devinsky and colleagues timely.

An overall seizure reduction of almost 50% compared with baseline is reported in this study. Figure 3 of the Article suggests that about a third of participants had an increased seizure frequency during the treatment period and another third had less than 50% seizure reduction. Patients often start or switch anti-epileptic drugs at times of an exacerbation of seizure frequency. Figure 3 seems to show a regression to the mean that can partly be attributed to the natural course of the condition, and which is inadequately controlled for by the short baseline period of this study. A baseline period of 4 weeks is too short, especially as the lowest seizure frequency was 11 motor seizures per month. A natural variation in seizure frequency of one or two seizures per month could explain a 10–20% change either way.

Adverse events are reported in 78% and serious adverse events in 30% of the participants in the 12-week treatment period. The authors conclude that "cannabidiol has an adequate safety profile". Compared with other anti-epileptic drugs in refractory epilepsy, the number of serious adverse events reported seems high.[2] This might be explained by epilepsy severity in this population, but this cannot be assessed with the design of this study.

What this study does show is that, contrary to what many hope, cannabidiol is probably not the magic treatment for severe childhood epilepsy. Properly randomised and controlled trials are urgently needed to assess whether the efficacy and safety profile of cannabidiol is similar to other anti-epileptic drugs, or worse.

[A: do you have any competing interests to declare? If so, please include here.]

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1 Devinsky O, Marsh E, Friedman D, et al. Cannabidiol in patients with treatment-resistant epilepsy: an open-label interventional trial. *Lancet Neurol* 2015; published online Dec 23. http://dx.doi.org/10.1016/S1474-4422(15)00379-8.

2 Brodie MJ, Lerche H, Gil-Nagel A, et al; RESTORE 2 Study Group. Efficacy and safety of adjunctive ezogabine (retigabine) in refractory partial epilepsy. *Neurology* 2010; **75:** 1817–24.