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June 29, 2022

Mr. Charlie Smithson
Secretary of the Senate
State Capitol Building
Des Moines IA 50319

Ms. Meghan Nelson
Chief Clerk of the House
State Capitol Building
Des Moines IA 50319

Kelly Garcia, Director
Iowa Department of Health &
Human Services
Hoover State Office Bldg
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Re: 2024 Report on Use of Medical Cannabidiol

Dear Members of the Iowa General Assembly and Director Garcia:

Pursuant to the 2014 Iowa Acts Ch 1125, §10h, enclosed is the 2024 report on Report on Use of Medical Cannabidiol.

If you have any questions or need more information, please don't hesitate to contact this office.

Sincerely,



Mark J. Braun

Re: 2024 Report to the Department of Public Health and the Iowa General Assembly regarding Cannabidiol (CBD) and Epilepsy

Recent Publications and additions since the last review submitted July 2023:

In a PubMed.gov search with the search criteria of “cannabidiol,” “epilepsy,” and “randomized control trial” only three results were returned. However, two were reports on previously described trials and one was a study of adjunctive treatment with cannabidiol in “Acute Bipolar Depression” and not epilepsy.

A search utilizing the criteria of “cannabidiol,” “epilepsy,” and “clinical trial” resulted in five studies reported. Three were repeated from the previous search as described above.

A search utilizing the criteria of “cannabidiol” and “epilepsy” in humans resulted in 71 papers. Most were review papers or retrospective in nature.

Clinical trials:

Peters JM et al. reported on the co-administration of CBD and nasal diazepam (Valtoco). This was a post-hoc analysis of the phase 3 trials of Valtoco and so was not powered to determine the safety of these two medications together. However, 23 patients were on CBD (Epidiolex) and 21 received other “CBD” products and also received nasal diazepam. The analysis noted that patients taking pharmaceutical grade CBD (Epidiolex) had comparable to fewer treatment related adverse events compared to patients not taking CBD (13% vs. 18.5%) while patients taking “other CBD” products had more treatment related adverse events than patients not taking CBD products (23.8% vs. 18.5%). This trend occurred when concomitant clobazam was present. This medication is known to be affected by the presence of CBD products. Patients taking “other CBD” products + clobazam had more treatment related adverse events than patients not taking CBD products but taking clobazam (40% vs. 21%). The results were complicated by the fact that patients taking all CBD products were more likely to have more severe epilepsy.

Wray et al. described a phase 1 study of healthy volunteers in which they gave a single dose of everolimus (an mTOR inhibitor used in the treatment of diseases known as mTORopathies (specifically tuberous sclerosis complex)) with or without concomitant use of pharmaceutical grade CBD (Epidiolex). Everolimus levels showed a 2.5-fold increase when used with CBD than without.

Other Papers

Glatt et al. recruited 19 patients with to be treated with CBD-oil (a 260mg CBD/12mg THC product of unknown source) as adjunctive therapy to treat their epilepsy. Seven patients (43.75%) were responders (>50% seizure reduction) demonstrating an average *reduction* of 82.4% in seizures, however nine patients (56.25%) were non-responders with an average seizure *increase* of 30.1%. No difference could be appreciated in EEG findings between responders and non-responders. No difference in demographics or clinical characteristics could be found between responders and non-responders.

Patel et al. reported 16 patients with a statistically significant response to CBD (Epidiolex) in regards to their typical hemiplegic spells in a disease known as alternating hemiplegia of childhood. This disease does have associated seizures, but the primary manifestation that is most disabling are spells lasting hours-days of dystonia or paralysis of one or more limbs.

Desnoux et al. reported 46 patients with Rett syndrome. Patients were recruited from March 2020 to October 2022 and were treated with Epidiolex® (cannabidiol, CBD, 100 mg/mL oral solution). 26 patients

had associated epilepsy (26/46 [56%]), and 10/26 (38%) were treated with CBD, in combination with clobazam in 50% of cases. CBD reduced the incidence of seizures in seven out of 10 patients (70%) with one seizure-free patient, two patients with a reduction of seizures of more than 75%, and four patients with a decrease of more than 50%. No aggravation of symptoms or adverse effects were observed. Only one patient experienced a transitory drooling and somnolence episode at the CBD initiation. Half of the patients showed a reduction in agitation and/or anxiety attacks, and an improvement in spasticity was reported in 4/10 (40%) of patients. CBD appears to have potential therapeutic value for the treatment of drug-resistant epilepsy in Rett syndrome.

Summary

- Pharmaceutical grade CBD (Epidiolex) seems to be safe when nasal diazepam is used but use of “other” CBD products may increase the rate of treatment emergent side effects. The study was not powered to make definitive conclusions about this however.
- Everolimus levels may be higher when used with CBD than when used without.
- CBD oil with a CBD/THC mixture can help some patients, but the majority in the Glatt study were non-responders and, on average, had an increase in seizure frequency. No predictors of who will be a responder vs. a non-responder could be appreciated.
- Pharmaceutical grade CBD (Epidiolex) seems to be safe and effective in some patients with alternating hemiplegia of childhood for decreasing the occurrence of hemiplegic spells.
- Patients with Rett syndrome may benefit from Pharmaceutical grade CBD (Epidiolex) regarding seizure frequency and possibly other neurobehavioral aspects of the disease in an unblinded observational study

References

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Sincerely,

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