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Kelly Garcia, Interim Director
Iowa Department of Public Health
Lucas Office Building
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Re: 2021 Report on Use of Medical Cannabidiol

Dear Members of the Iowa General Assembly and Interim Director Garcia:

Pursuant to the 2014 Iowa Acts Ch 1125, §10h, enclosed is the 2021 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

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Attachments
cc:
Legislative Liaisons
Legislative Log

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June 14th, 2021
University of Iowa

Jennifer Harbison
Director Health Policy | Office of the Vice President for Medical Affairs

Re: **2021 Report to the Department of Public Health and the Iowa General Assembly**

Recent Publications and additions since the last review submitted July 2020:

There have only been seven randomized placebo-controlled trials published since the last review. One looks at the use of cannabidiol (CBD) to help with withdrawal symptoms from stopping chronic cannabis use, another looks at medical cannabis effects on obsessive-convulsive disorder, one on anti-nausea effects during cancer treatment, one on spasticity in children with cerebral palsy. Then there are three studies that look at different aspects of treatment of pain.

- The first was published by Freeman and coworkers [1] in 2020 in the journal *Lancet Psychiatry*. In this randomized, double-blind, placebo-controlled study (n = 48) patients in London with diagnosed cannabis use disorder (addiction) and who desired to quit smoking cannabis were given a placebo or 200 or 400 or 800 mg of oral cannabidiol to try to help the subjects stop smoking cannabis. After 4 weeks of treatment, the results showed a statistically significant reduction in abstinence (days not smoking in a week) from 3 to 2.5 in the oral CBD groups compared to placebo. A published commentary about this article says that is a start, but the goal should be complete abstinence. The authors reported no serious adverse events, but fairly common mild events and some moderate events. They did not specify what these adverse events were. The 400 and 800 mg doses reduced the number of cannabis cigarettes smoked. The 400 mg dose demonstrated improved sleep quality and the 800 mg helped relieve withdrawal symptoms. Note: these are much higher doses than are available in the Iowa dispensaries (usually only 20 or 25 mg of CBD per capsule or dropperful).
- The second study by Kayser and colleagues [2] in 2020 in the journal *Depression and Anxiety* looked at whether or not medical cannabis could be a cause of obsessive-compulsive disorder (OCD). Fourteen adults with OCD entered in to this randomized, placebo-controlled study to compare the effects of OCD symptoms when exposed to a placebo (0% THC, 0% CBD), THC (7% THC, 0.18% CBD) or CBD (0.4% THC, 10.4%CBD) each delivered in a smoked cigarette. It was a cross-over design so all subjects received each treatment with an appropriate washout between each treatment so there was no carryover effect. Only 12 of the 14 completed all 3 treatments. The research subjects reported euphoria (high) when they received the THC and an elevated heart rate and blood pressure, but they did not experience these with the placebo or the CBD dosage form. Self-reported symptoms of OCD and anxiety decreased over time with all 3 of the treatments. Third, neither THC or CBD significantly affected OCD symptoms compared to placebo. The authors would like to suggest that the THC and CBD do not affect OCD symptoms. However, the authors do acknowledge that their pilot study was small with only 12 subjects and a larger trial needs to be conducted. Also, the cannabis used was smoked and the authors acknowledge that the habit of smoking can affect anxiety and indicate that alternative dosage forms (oral or sprays) might produce different results.

- The third study was published by Grimson and colleagues [3] in 2020 in the journal *Annals of Oncology*. In this double-blind, placebo-controlled crossover study in 80 patients with chemotherapy induced nausea and vomiting the authors were evaluating effectiveness of capsules containing 2.5 mg of THC and 2.5 mg of CBD given 3 times a day starting the day before chemotherapy and going through all 5 days of treatment. The goal was to detect a 20% reduction in in nausea and vomiting compared to placebo. Complete response (absence of emesis) was improved from 14% when they received placebo to 25% when they received the medical cannabis. This was a statistically significant improvement, but not the 20% improvement they were hoping for. Thirty-one percent experienced moderate or severe cannabinoid-related adverse events such as sedation, dizziness, or disorientation, but 83% of participants preferred cannabis to placebo. No serious adverse events were attributed to THC:CBD. This was the first published study that used the medical cannabis in addition to standard anti-nausea treatment protocols and the authors concluded that addition of oral THC:CBD to standard antiemetics was associated with less nausea and vomiting but there were additional side-effects. Most participants preferred THC:CBD to placebo. Based on those promising results, they plan to recruit an additional 170 participants to complete accrual for the definitive, phase III, parallel group analysis.
- The fourth study was published by Fairhurst and colleagues [4] in 2020 in the journal *Developmental Medicine & Child Neurology*. Nabiximols is an oral-mucosal spray that for every 0.1 ml actuation delivers 2.7 mg of THC and 2.5 mg of CBD and was used in this study to assess the efficacy, safety, and tolerability of oromucosal nabiximols as adjunct therapy for children with spasticity due to cerebral palsy/traumatic central nervous system injury with inadequate response to existing treatments. Children 12-18 years old (n=70) were randomly assigned to receive placebo or nabiximols (up to a max of 12 sprays a day) for 12 weeks. The authors looked for a change in spasticity from baseline using a numerical rating score. The authors found no change in the spasticity score after 12 weeks and no change in additional measures for sleep quality, pain, health-related quality of life, comfort, or depression. Adverse events were mild or moderate, but there were three cases of hallucinations. The authors concluded that oromucosal nabiximols was generally well tolerated in children, except for 3 patients who had hallucinations, however, there was no reduction in spasticity.
- The fifth study by Chaves and coworkers [5] appeared in the journal of *Pain Medicine*. This study was a double-blind, randomized, placebo-controlled clinical trial to determine the benefit of a THC-rich cannabis oil (24.44 mg/mL of THC and 0.51 mg/mL of cannabidiol [CBD]) on symptoms and quality of life of 17 women with fibromyalgia, residents of a neighborhood with a low socioeconomic profile and a high incidence of violence in Brazil. The subjects placed 1 drop (1.2 mg THC and 0.02 mg of CBD) of the oil under the tongue each day and they were followed for 8 weeks. They were allowed to increase the numbers of drops if they felt necessary. By the end of the study subjects were using an average of 4 drops (4.4 mg of THC and 0.08 mg CBD). Every 10 days the subjects completed a questionnaire to assess the outcome of the treatment. It is not clear if this assessment tool has been validated outside of Brazil. Also, the dose used to treat fibromyalgia in other studies has been considerably higher. Based upon improvement in the outcome score compared to placebo they suggest that this was an effective treatment. However, they admit that larger and longer studies are needed and also it would be important to evaluate other ratios of THC to CBD. This preliminary study indicates there may be some potential for the treatment of fibromyalgia, but more information is needed to be able to promote this use.
- The sixth study by Abrams and coworkers [6] was published in the journal of *JAMA Open Network*. This small pilot study used 23 patients to compare inhaled (vaporized) placebo to cannabis (4.4% THC and 4.9%CBD) for effectiveness in treating chronic pain associated with sickle cell disease. In this randomized, placebo-controlled crossover design there was no significant difference in pain rating from day 1 to day 5 of treatment for the placebo and the cannabis treatment. The same was true for measurement of interference with daily activities, walking, sleep and enjoyment. However, there was significant difference in mood. There was also no difference in the occurrence of adverse effects (most common being sedation) between the two treatments. The authors concluded that vaporized cannabis did not improve pain control but did improve mood in patients with chronic pain associated with sickle

cell disease. It is important to note that this pilot study had a small sample size and a larger study would be warranted.

- The seventh study by Bebee and colleagues [7] in 2021 in the *Medical Journal of Australia* looked at whether or not a single dose of oral CBD as an add on to standard care in the emergency room was effective in helping to relieve acute low back pain. This randomized placebo-controlled trial was conducted in Melbourne Australia. There were 100 patients who presented with non-traumatic low back pain and were then randomized to receive 400 mg of oral CBD (with no THC) or placebo in addition to standard emergency department analgesic medications. The main outcome was an assessment of pain two hours after administration of the medication. There was no significant difference in the pain assessment between the placebo and the CBD. This was not a surprising finding since studies on pain relief with a mixture of THC and CBD seem to indicate that the higher the THC, the better the analgesic relief.

Research to evaluate new treatments always begins with small studies (pilot) to suggest that there is potential benefit. Those results are then used to identify funding sources so that large conclusive studies can be conducted to provide clear recommendations. Several of these studies fit in this category and in each case the authors suggest that larger studies need to be conducted based on the promising results.

Bottom line from these studies:

- There may be a role for CBD alone to help with individuals who want to withdraw from smoking cannabis.
- THC and CBD are not likely to make OCD symptoms worse.
- A balanced THC:CBD mixture given with standard anti-nausea treatments might have some added benefit.
- An oral-mucosal spray of THC and CBD does not reduce spasticity in children with cerebral palsy.
- A small study with some concerns about its design, but there may be a role for THC:CBD for treatment of fibromyalgia.
- A vaporized balanced mixture of THC/CBD did not improve pain in patients with chronic sickle cell disease, but more study is needed.
- CBD alone in a single dose is not effective in relieving acute low back pain.

References

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Sincerely,

Ronald A. Herman

Dr. Ron Herman PhD
Clinical Professor, University of Iowa
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I would suggest there is no new significant data that is relevant in regards to medical marijuana and epilepsy form my standpoint. I frankly am rarely using medical marijuana anymore. The University of Iowa Carver College of Medicine and the University of Iowa College of Pharmacy recommends that based on the approval of oral cannabidiol solution for the treatment of these two epileptic seizure disorders that this prescription product be used instead of the oral cannabidiol/medical marijuana products produced by the State of Iowa for the treatment of epilepsy. The new prescription product should be covered by Medicare and most private insurance programs; whereas the state products are costly and not covered by Medicare or private insurance.

Sincerely,

Michael Ciliberto, MD
Assistant Professor
Division of Pediatric Neurology
Stead Family Department of Pediatrics
University of Iowa Children's Hospital