

Clinical Endocannabinoid Deficiency

ISSUE BRIEF ON CLINICAL ENDOCANNABINOID DEFICIENCY

Introduction

Briefings such as this one are prepared in response to petitions to add new conditions to the list of qualifying conditions for the Minnesota medical cannabis program. The intention of these briefings is to present to the Commissioner of Health, to members of the Medical Cannabis Review Panel, and to interested members of the public scientific studies of cannabis products as therapy for the petitioned condition. Brief information on the condition and its current treatment is provided to help give context to the studies. The primary focus is on clinical trials and observational studies, but for many conditions there are few of these. A selection of articles on pre-clinical studies (typically laboratory and animal model studies) will be included, especially if there are few clinical trials or observational studies. Though interpretation of surveys is usually difficult because it is unclear whether responders represent the population of interest and because of unknown validity of responses, when published in peer-reviewed journals surveys will be included for completeness. When found, published recommendations or opinions of national organizations medical organizations will be included.

Searches for published clinical trials and observational studies are performed using the National Library of Medicine's MEDLINE database using key words appropriate for the petitioned condition. Articles that appeared to be results of clinical trials, observational studies, or review articles of such studies, were accessed for examination. References in the articles were studied to identify additional articles that were not found on the initial search. This continued in an iterative fashion until no additional relevant articles were found. Finally, the federal government-maintained web site of clinical trials, clinicaltrials.gov, was searched to learn about trials currently under way or under development and to check whether additional articles on completed trials could be found.

Definition

Clinical endocannabinoid deficiency (CED) has been proposed as a cause of several conditions, but at this point it remains a theory; no criteria have been proposed for making a diagnosis of CED. The idea of CED was presented in 2001 in two publications by Russo and more thoroughly explored in a 2004 article (Russo 2004) that has been cited frequently in the literature. The theory of CED was based on the concept that many brain disorders are associated with neurotransmitter deficiencies – for example dopamine deficiency in parkinsonian diseases – and that a comparable deficiency in endocannabinoid levels might be manifest similarly in certain disorders that display predictable clinical features as sequelae of this deficiency (Russo 2016). In his 2004 article, Russo described similarities in clinicopathological features and overlap in occurrence for three disorders as suggestive evidence of CED: migraine, fibromyalgia, and irritable bowel syndrome. The similarities cited

included hyperalgesic states that must be clinically diagnosed based on subjective criteria; lack of characteristic tissue pathology or laboratory findings; each is a diagnosis of exclusion that often generates extensive negative diagnostic work-ups; each has an increased incidence of anxiety and depression; and each has been labeled as psychosomatic in origin or a wastebasket diagnosis by skeptical clinicians (Russo 2004). Since 2004 many other disorders have been cited as possibly falling under the CED rubric (Russo 2014).

Identification of the parts of the endocannabinoid system (ECS) and how they interact with each other and with other body systems remains an active area of investigation. Much remains unknown. The ECS consists of cannabinoids made by the body (endocannabinoids), enzymes that break down those cannabinoids, receptors that interact with endocannabinoids, and receptors and other cell structures that appear to be activated independently of endocannabinoids. Due to this complexity, the causes of an underperforming ECS could be many and could be different for different disorders. Simplistically, correcting CED could be approached in three ways, 1) increase the body's production of endocannabinoids (or administer plant-derived cannabinoids), 2) decrease endocannabinoid breakdown, and 3) increase or decrease receptor density or function (McPartland 2014). A recent review discusses a variety of approaches to enhancing the endocannabinoid system (McPartland 2014), including impact of over-the-counter and prescription drugs, dietary supplements and herbal remedies, chronic stress reduction practices, lifestyle modifications, and use of cannabis. The review outlines evidence of different effects of plant cannabinoids from acute versus chronic exposure and different impacts of THC, CBD, and other cannabis constituents. McPartland and Guy proposed that the many constituents of cannabis work, in part, by "jump-starting" the ECS system (McPartland 2004).

Prevalence

Migraine, fibromyalgia, and irritable bowel syndrome – as well as some of the other disorders suggested as results of ECD – are relatively common. However, the proportion of these disorders that might be primarily caused by an endocannabinoid deficiency is unclear.

Current Therapies

The recent review by McPartland et al (McPartland 2014) suggests a variety of strategies for enhancing the functions of the ECS, as described above.

Pre-Clinical Research

Numerous pre-clinical studies describe involvement of parts of the ECS in disorders suggested as resulting from CED. For a review, see Russo 2014.

Clinical Trials

Few or no clinical trials of cannabis or cannabinoids have been carried out for disorders suggested as resulting from CED. See Russo 2014.

Observational Studies

Few or no observational studies of cannabis or cannabinoids have been carried out for disorders suggested as resulting from CED. See Russo 2014.

National Medical Organization Recommendations

No guidance documents or recommendations from national medical organizations for the therapeutic use of cannabis or cannabinoids in the management of endocannabinoid deficiency were found.

References

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Minnesota Department of Health
PO Box 64882
St. Paul, MN 55164-0882
651-201-5598
health.cannabis@state.mn.us
<http://www.health.state.mn.us/topics/cannabis>

09/2017

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