Treatment With Cannabis Oil Containing Canabidiol (CBD) Only or 20:1 CBD:THC vs. Placebo of Persons Diagnosed With ADHD After Failure of Conventional Treatment

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Version 4

Background

ADHD is the most frequent neuro-developmental disorder in childhood affecting around 8% of children and continues into adolescence and adulthood for some 70% of them. In some cases, ADHD appears in adulthood.

There are 3 subtypes for this disorder:

Mainly inattentive, mainly hyperactive-impulsive and combined type.

Indicated drug treatments for ADHD fall into 2 categories: stimulants (such as

methylphenidate and amphetamines) and non-stimulants (such as atomoxetine, guanfacine and clonidine) but some patients cannot tolerate their side effects (decreased appetite and weight, insomnia, irritability, headache, fatigue, etc) or serious side effects like psychosis onset and CV complications or find them non effective in some 50% of the cases.

In the last decade, medical cannabis products have been researched as possible treatment for neurological and mental diseases such as: PTD, ASD, epilepsy, FM and more.

Data on the effects of cannabidiol rich cannabis extract use for ADHD seems promising but is still limited.

The aim of this study is to investigate if oral cannabinoids given to adults with ADHD affect the symptoms of the disorder. At the same time, side effects and DDI will be assessed.

In this trial, 3 different types of cannabis oil will be compared to a placebo drug.

Participants will be randomized to any of the 4 arms.

Objectives

Primary

To assess the efficacy of the cannabis oil treatment containing different concentrations of CBD, THC, CBDV, CBG as per TOVA and Conners test results.

Secondary

To assess side effects of cannabis treatments and to compare them with those of conventional drugs prescribed for ADHD.

To assess the quality of life of participants with ADHD treated with the different cannabis oils.

Methods

Participants will undergo a prescreening interview (phone and mail) which includes: inclusion/exclusion criteria, medical history and concomitant medications, previous treatments for ADHD. After assuring the eligibility to the study, the will be invited to take part in the study.

Each participant will attend three visits in the clinic and will be contacted by phone twice.

Visit 1: randomization**,** day 1

Actions and procedures:

- Consent process, including signing ICF
- inclusion/exclusion criteria
- Review of medical history and concomitant medications
- TOVA test
- Vital signs and physical examination
- Urine and blood test
- Questionnaires filling (eat, sleep, behavior)
- Randomization
- Drug dispense and instructions for use

Follow up: day 14 (±3 days)

- Adverse events, change in concomitant medications ,blinding questionnaire

Visit 2: end of treatment, day 26 (±2 days)

Actions and procedures:

- Adverse events, change in concomitant medications
- TOVA test
- Vital signs and physical examination
- Urine and blood test
- Questionnaires filling (eat, sleep, behavior)

Visit 3: follow up, day 42 (±2 days)

- Adverse events, change in concomitant medications
- Questionnaires filling (eat, sleep, behavior)

- Return of study drug

Dose regimen

Days 1-2: 10 drops/day (total 0.3 ml/day)*

Days 3-7: 20 drops/day (total 0.6 ml/day)

Days 8-21: 40 drops/day (total 1.2 ml/day)

Days 22-28: 60 drops/day (total 1.8 ml/day)

After day 28, dose will be tapered: 40 drops at day 29, 20 drops at day 30, 10 drops at days 31-32. Day 32 will be the last day of treatment.

*The volume of one drop is approx.0.03 ml.

Main inclusion criteria:

- Participants aged at least 18 years old diagnosed with ADHD by DSM

-Participants with a smaller than 0 TOVA score or with a greater than 0 score that as per investigator opinion suffer from ADHD

-Participants who experienced treatment failure with more than one ADHD conventional drug

- Participants willing to attend all the visits in the trial.

Main exclusion criteria:

- Participants who were treated with benzodiazepines or antihistamines in the week that preceded the trial start.

-Participants suffering from neurologic or psychiatric diseases

-Participants suffering from malignant diseases

-Participants suffering from syndromes or metabolic diseases

-Participants with significant clinical diagnosis that can damage the trial unfolding. The investigator may include them after the end of the situation which prevented their previous inclusion.

-Participants breastfeeding, pregnant or not willing to use contraceptives.

-Participants that will not follow the protocol as per investigator opinion.

-Participants who weight less than 45 kg or more than 120kg or with BMI greater than 30

-Participants participating in another clinical trial which includes drug treatment

-Participants receiving any treatment for ADHD

-Participants using drugs

-Participants using cannabis or products containing cannabinoids, including medical cannabis.

Sample size calculation

In order to detect differences at p=0.05 with 80 % power, 53 participants in each arm (total of 212 participants) will be needed. With an estimation of 15% drop-out, 244 participants will be recruited.

Statistical analysis plan

Paired T-tests to assess longitudinal changes in scores before and under treatment will be performed for each participant.

In addition, results from the 4 arms will be compared.

Trial products

If possible the trial drugs will be dispensed with a syringe instead of a dropper. Dosage will stay identical and will be measured by volume.

table 1. Max. daily dose in mg of each cannabinoid in the different trial products

arm	CBG (mg/day)	CBDV (mg/day)	THC (mg/day)	CBD (mg/day)
Placebo	0	0	0	0
Arm1	0	27	9	171
Arm 2	171	0	4.5	0
Arm 3	171	27	9	171

In arm 3 that contains higher dosages, a person weighing 45 kg (minimum for participating) and receiving the max dosage of 60 drops will get 3.8 mg/kg/day CBD and 0.2 mg/kg/day THC.

In special cases (for ex. extreme BMI) investigator will consider changing the dosage program from the standard in the trial in order to adapt them better to the participant.

Participants will keep a diary (hard copy or electronic) and fill in actual treatment ingestion.

In any case, daily dose will not exceed 400 mg CBD and 20 mg THC.

Placebo will have same package, color and taste as trial product.

Treatment cessation

Treatment cessation because of early termination will be done as described in dose regimen or as per researcher decision.

Bibliography

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