ISRCTN10334895 https://doi.org/10.1186/ISRCTN10334895

Cannabidiol for the treatment of patients at a high-risk of psychosis

Submission date
01/08/2018

Recruitment status
No longer recruiting

Registration date
31/08/2018

Overall study status
Completed

Last Edited
21/02/2022

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Psychotic disorders such as schizophrenia typically affect young people and rank as one of the most disabling conditions worldwide. They pose an enormous burden on those affected and their families. They also cost society a great deal. In England alone, the total cost to society for services caring for people with schizophrenia and from lost employment is estimated to be £11.8 billion per year. Estimates suggest that in England alone, around 15,763 people every year have early symptoms of psychosis. Around a third of such people who are clinically at high risk (CHR) of developing psychosis will do so over the next 3 years. CHR patients commonly experience low level anxiety and psychotic symptoms such as delusions (e.g. false beliefs) and hallucinations (e. g. hearing voices that are not there). Typically these experiences are short-lasting or less severe compared to when they develop frank psychosis. We would like to prevent young people from developing psychotic illnesses. However, this is not easy, as it is not possible to accurately predict which CHR person will later develop psychosis. Also, current treatments do not always work. The medications (such as antipsychotic drugs) that we have available were originally developed for those with frank psychosis, and only have a modest benefit and are not tolerated very well. As treatments have to be offered to all CHR patients and not just those who will later develop frank psychosis, this also raises ethical concerns. Hence, at the moment, most CHR patients typically receive practical help and support (e.g. for housing or vocational support) and help from clinicians to address current issues.
Cannabidiol (CBD), a naturally available chemical found in the extract of cannabis plant, has emerged as a promising candidate as it displays anti-anxiety and anti-psychotic like properties in animals and humans. It has also been tolerated very well in human studies. We have recently tested this in a small number of CHR patients by giving them a 600 mg capsule of CBD daily for a short period (3 weeks) and comparing it with a group of CHR patients who were given an inactive drug. Results from these small studies suggest that CBD may be useful in treating symptoms in CHR patients. CBD was also safe and tolerated well by CHR patients. However, we do not know whether CBD treatment will actually be useful in providing symptom relief in CHR patients. A large clinical trial comparing CBD to placebo is needed to test this. Therefore, we aim to test whether CBD treatment will actually be useful in providing symptom relief in CHR patients in a large clinical trial.

Who can participate?
People aged 18-35 who have a diagnosis of a clinical high-risk state for psychosis with 'attenuated psychotic symptoms'

What does the study involve?
Patients will be randomly allocated to receive one of two treatments. Half of them will receive the same dose of CBD (600 mg once a day) given in capsule form and the other half will receive placebo capsule. In this study, patients will receive the treatment for 6 months. Neither the researchers nor patients will know what they have been treated with during the study. At the end of treatment, we will compare whether those who received CBD were significantly better off in terms of the symptoms that they were experiencing before they started treatment compared to those who received placebo. We will also study a subgroup of people (50 of those receiving CBD and 50 of those receiving placebo) to study brain chemistry and function using brain scanning (MRI scanners) to understand how CBD may work.

What are the possible benefits and risks of participating?
Patients taking part in the study may or may not receive any benefits from taking CBD as part of the study. CBD treatment might improve some of the psychological problems that patients may be experiencing. However, this is by no means certain, which is why we are conducting this study. Previous research has shown that the effects of CBD are very subtle. Apart from some mild sleepiness, mild diarrhea and nausea no adverse effects have been reported. Nevertheless, any unpleasant effects associated with taking part in the trial will be recorded throughout the study. The MRI scan procedure that will be employed is painless and safe and there are no known health risks. The MRI scanner makes loud noises while it is operating and participants will provide participants with headphones or earplugs to reduce the noise to safe levels. Some people find that being in an MRI scanner makes them feel anxious and/or claustrophobic, even if they have not experienced claustrophobia before. A member of staff will be in constant contact with participants via an intercom, and if they feel uncomfortable in any way the scanning can be stopped.
Further, the information we obtain from this study may help us to treat patients with mental health problems more effectively in the future.

Where is the study run from?
Institute of Psychiatry, Psychology & Neuroscience of Kings College London (UK)

When is the study starting and how long is it expected to run for?
July 2017 to May 2023

Who is funding the study?
National Institute for Health Research Efficacy and Mechanism Evaluation Programme (EME) (UK)

Who is the main contact?
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Contact information

Type(s)
Public

Contact name

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CANTOP-RCT

Study information

Scientific Title
CANnabidiol as a Treatment fOr clinical high-risk state Psychosis - a Randomised Clinical Trial (CANTOP-RCT)

Acronym
CANTOP-RCT

Study objectives
Efficacy/tolerability hypotheses:
1. CBD treatment will reduce the severity of attenuated psychotic symptoms in CHR patients as measured using established criteria compared to placebo
2. Greater proportion of patients treated with CBD will not meet the criteria for 'attenuated psychosis syndrome' compared to placebo
3. CBD will reduce distress associated with attenuated psychotic symptoms in CHR patients as measured using established criteria compared to placebo
4. CBD will reduce the severity of anxiety symptoms in CHR patients as measured using established rating scales compared to placebo
5. CBD will improve social and role functioning in CHR patients as measured using established rating scales compared to placebo
6. CBD will not be associated with greater incidence of side-effects compared to placebo

Mechanistic hypotheses:
7. CBD will modulate brain activation in the medial temporal cortex and basal ganglia as measured using fMRI while performing verbal paired memory and emotional (fear) processing tasks in CHR patients compared to placebo

8. CBD will modulate brain activation in the medial temporal cortex and basal ganglia as measured using arterial spin labeling in CHR patients compared to placebo
9. Cannabidiol will attenuate glutamate levels in the hippocampus as measured using proton magnetic resonance spectroscopy in CHR patients compared to placebo

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval pending with intention to submit by November 2018

Study design
Interventional pragmatic randomised placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Clinical high-risk for psychosis (CHR)

Interventions
Participants will be randomised into either the intervention or control group using block randomisation. Randomisation will be double-blind and stratified by site.
Participants both groups will receive treatment as usual (TAU), which is the standard clinical care provided to CHR psychosis patients in NHS early intervention services.
The intervention group will receive TAU and a single daily dose of cannabidiol (CBD) in capsule form for 6 months.
The control group will receive TAU and a placebo capsule to take daily for 6 months.
Both CBD and the placebo will be given as matched capsules.
Patients will be followed up for a period of 6 months.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Cannabidiol (CBD)

Primary outcome measure
Change in the severity of psychotic symptoms, assessed using the Comprehensive Assessment of At-Risk Mental States (CAARMS) questionnaire at the baseline and at the end of the study (day 182)

Secondary outcome measures
The following will be assessed at the baseline and at the end of the study (day 182):
1. Changes in the distress associated with psychotic symptoms, assessed using the Comprehensive Assessment of At-Risk Mental States (CAARMS) questionnaire
2. Changes in the severity of anxiety symptoms assessed using the Hospital Anxiety and Depression Scale (HADS) and in the level of global functioning (assessed using the social and role functioning scale)
3. Clinical remission, as defined as no longer meeting the criteria for a diagnosis of clinical high-risk: attenuated psychosis syndrome using the CAARMS questionnaire

Overall study start date
12/07/2017

Completion date
31/05/2023

Eligibility

Key inclusion criteria
1. Aged 18-35
2. Diagnosed with a clinical high-risk state for psychosis (CHR)
3. 'Attenuated psychotic symptoms' sub-group (CHR-APS) as defined using the CAARMS (Comprehensive Assessment of At-Risk Mental States) criteria

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
35 Years

Sex
Both

Target number of participants
300

Key exclusion criteria

1. History of a previous psychotic or manic episode lasting 7 days or more
2. Neurological disorders (e.g. epilepsy) or severe intercurrent illness
3. Current treatment with psychotropic medication or previous treatment with antipsychotic medication for more than 7 days
4. IQ of less than 70
5. Females who are pregnant, lactating or not using contraception

Date of first enrolment
01/09/2022

Date of final enrolment
30/09/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Institute of Psychiatry, Psychology & Neuroscience (IoPPN), KCL
London
United Kingdom
SE5 8AF

Study participating centre
University of Manchester
Manchester
United Kingdom
M13 9PL

Study participating centre
University of Birmingham
United Kingdom
B4 7BD

Study participating centre
University of Newcastle
United Kingdom
NE1 7RU

Study participating centre
Cambridgeshire & Peterborough NHS Foundation trust/ University of Cambridge
United Kingdom
CB4 1PR

Sponsor information

Organisation
King’s College London and South London and Maudsley NHS Foundation Trust

Sponsor details
16 De Crespigny Park
London
England
United Kingdom
SE5 8AF

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/015803449

Funder(s)

Funder type
Not defined

Funder Name
Efficacy and Mechanism Evaluation Programme

Alternative Name(s)
NIHR Efficacy and Mechanism Evaluation Programme, EME

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Manuscripts from the study will be submitted for publication in peer-reviewed high impact journals and published in brief format on the IoPPN website. Dissemination of these findings to other professionals in the field will also be facilitated through existing close links with clinical services, some of which in turn have extensive links with organisations for young people (schools, universities, hostels, etc.). Press releases on the findings will be delivered to encourage public feedback/involvement and links to published manuscripts will be disseminated through the IoPPN Press Office, harnessing existing links of the Investigators with media outlets. Arrangements will be also be made to disseminate these results to the wider user community through links with websites of charities such as MIND and RETHINK that are accessed by service-users.

Intention to publish date

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Not provided at time of registration