A double-blind, randomized, placebo-controlled, five-way cross-over interaction trial to investigate the inhibitory effect of olanzapine on a THC-induced increase on the Positive and Negative Syndrome Scale

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- To investigate whether olanzapine influences the (psychomimetic) effects of THC, in particular on the Positive and Negative Syndrome Scale (PANSS) - To further explore the pharmacologic basis of the THC model - To investigate the effects of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Schizophrenia and other psychotic disorders
Study type	Interventional

Summary

ID

NL-OMON33219

Source
ToetsingOnline

Brief title
The effect of olanzapine on a THC-induced increase on the PANSS

Condition

- Schizophrenia and other psychotic disorders

Synonym
Psychosis, Psychotic disorder

Research involving

Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Grotendeels betaald door het Centre for Human Drug Research (CHDR). Tevens subsidie van het programma Assuring Safety without Animal Testing (ASAT);uitgevoerd door SenterNovum in opdracht van de Minister van Volksgezondheid;Welzijn en Sport

Intervention

Keyword: challenge-test, olanzapine, PANSS, THC

Outcome measures

Primary outcome

- the PANSS (Positive and Negative Syndrome Scale - a widely used, clinical

questionnaire based on a semi-structured interview)

- Visual Analogue Scales (VAS - Bond & Lader, Bowdle - validated scales to

objectify subjective parameters)

Secondary outcome

- other parameters for the functioning of the central nervous systems (see

protocol chapter 7)

Study description

Background summary

Background of the study:
There is a large amount of evidence suggesting a relation between cannabis and psychosis and the possible increase in dopamine in the prefrontal cortex by THC. THC-induced psychomimetic effects could be used as a practical 'psychosis'-model to investigate the therapeutical effects of a (novel) antipsychotic. The current study is designed to investigate the 'THC-psychosis-model' for the second time. The hypothesis is that olanzapine will lead, in a similar manner as haloperidol (previous study), to less

'psychomimetic' effects in reaction to the THC-challenge.

Study objective

- To investigate whether olanzapine influences the (psychomimetic) effects of THC, in particular on the Positive and Negative Syndrome Scale (PANSS)
- To further explore the pharmacologic basis of the THC model
- To investigate the effects of olanzapine on the central nervous system
- To further investigate the effects of THC on the central nervous system
- To investigate the genetic influence on THC sensitivity

Study design

Double-blind, randomised, placebo-controlled, 5-way cross-over interaction study in healthy volunteers.

Intervention

The drugs used in the study are olanzapine 10 mg orally, diphenhydramine 2x15 mg orally and/or THC intrapulmonary (2, 4, and 6 mg with intervals of 90 minutes) or placebo of any of these drugs.

Study burden and risks

Screening: medical history taking, physical examination, venapuntion (haematology, chemistry, virology), saliva sampling (determination of specified haplotypes), drugs screening, personality questionnaires
5 occasions: repeated performance of several tests, insertion of intravenous catheter for repeated blood sampling, ECG, three inhalations of THC (or placebo).
Follow-up: physical examination, ECG

Restrictions: during the study period, restriction will be applied to living pattern and the use of alcohol, tobacco, cafeine, recreational drugs and medication.

Side-effects: all study drugs can lead to drowsiness, dizziness, nausea and a light increase in heart rate. THC can cause a 'high' sensation and perceptions may change. A rare side-effect of olanzapine are muscle spasms/stiffness, which can be easily treated with biperiden.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Male sex
• Age between 18 and 45 (extremes included)
• Body Mass Index (BMI) between 18 and 30 kg/m2 (extremes included)
• Mild cannabis user for at least one year, defined as use of cannabis no more than once a week (as an average in the last year)
• Ability to refrain from using cannabinoids (other than the THC used in the study) from at least two weeks prior to the first treatment period till the end of the follow-up periods
• Willing to give written informed consent to participate in the study and to comply with the study procedures

Exclusion criteria

• Clinically significant (history of) psychiatric illness (including substance abuse)
• Clinically significant cardiac, pulmonary, gastrointestinal, hepatic, renal, haematological, endocrine or neurological disease as determined by medical history, physical examination,

ECG or laboratory test results
• Family history (first-degree relatives) of relevant psychiatric disorders and/or family history (second-degree relatives) of psychotic disorders
• Participation in a clinical study within the past three months
• Participation in four or more clinical studies in the past twelve months
• Positive urine screen for recreational drugs, i.e. cocaine, opioids, benzodiazepines, amphetamines, metamphetamines, or MDMA. THC will be tested as well; since volunteers are cannabis users, subjects with a positive THC urine test will be tested again and have to be found THC-negative before the first study day. Subjects with a positive drug test on a study day, including THC, will be excluded
• Exposure to any medication, including over-the-counter medication and herbal agents, 14 days prior to randomization (except paracetamol)
• Exposure to prescription medication within 30 days prior to screening
• Positive testing for Hepatitis B or C, or HIV-1 or HIV-2
• Smokes more than four cigarettes per day
• Unable or unwilling to refrain from alcohol, starting 24 hours before each study day until the end of the study day
• Unable or unwilling to refrain from smoking on study days
• Unable or unwilling to refrain from xanthine (i.e. caffeine) intake on study days
• Unable or unwilling to refrain from quinine (bitter drinks in general, i.e. tonic, grapefruit juice) from 14 days before dosing until discharge
• Unable or unwilling to refrain from heavy physical exercise 24 hours before study days
• Unable or unwilling to maintain a regular day/night rhythm during the study
• Donation (or loss) of more blood, including this study, than allowed by the regulations of the Dutch blood bank (Sanquin)
• Relevant (history of) drug allergy or hypersensitivity to drugs
• Subject is the investigator or any sub-investigator, or a subordinate of the investigator or any sub-investigator

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-04-2009
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Betadorm / Nytol
Generic name:	diphenhydramine
Product type:	Medicine
Brand name:	Zyprexa
Generic name:	olanzapine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-03-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	20-04-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	12-05-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	10-06-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2008-008520-33-NL
CCMO	NL26986.058.09