Study of the interaction of haloperidol and THC (cannabis) in healthy volunteers.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23370

Source
Nationaal Trial Register

Brief title
N/A

Health condition

English: THC, haloperidol, psychosis, model, healthy volunteers, schizophrenia
Dutch: THC, haloperidol, psychose, model, gezonde vrijwilligers, schizofrenie

Sponsors and support

Primary sponsor: See scientific contact
Zie contact wetenschappelijk
Source(s) of monetary or material Support: Centre for Human Drug Research

Intervention

Outcome measures

Primary outcome

Positive And Negative Symptoms Scale (PANSS): scores (negative, positive, and total scores).

Secondary outcome

1. Visual Analogue Scales from Bowdle for external effects (mm);

2. Visual Analogue Scales from Bond & Lader for subjective effects, and Bowdle for psychedelic effects (mm);

3. Saccadic eye movements: peak saccadic velocity (deg/s), saccadic latency (sec) and saccadic inaccuracy (%);

4. Smooth pursuit eye movements: average percentage of smooth pursuit for all stimulus frequencies the target (%);

5. Alpha Fz-Cz lead, Alpha Pz-Oz lead, Beta Fz-Cz lead, Beta Pz-Oz lead, Delta Fz-Cz lead, Delta Pz-Oz lead, Theta Fz-Cz lead, Theta Pz-Oz lead;

6. Body sway: antero-posteral sway (mm/2min);

7. Stroop: number correct and reaction time for correct answer both in basic and conflict situation;

8. VVLT: immediate word recall number correct (1st trial, 2nd trial, 3rd trial and average of 1st, 2nd, and 3rd trial), delayed word recall number correct, delayed word recognition (number correct and average reaction time correct);

9. LH, FSH, and cortisol concentrations;

10. Graphs and summary measures per treatment and time point for THC and metabolites and compartmental PK for THC.

Study description

Background summary

Background:

In this study the hypothesis that haloperidol would lead to an amelioration of delta-9-tetrahydrocannabinol (THC)-induced ‘psychotomimetic’ effects was investigated.

Methods:

In a double-blind, placebo-controlled, partial 3-way crossover ascending dose study the effects of THC, haloperidol and their combination were investigated in 35 healthy male mild

cannabis users, measuring Positive and Negative Syndrome Scale (PANSS), Visual Analogue Scales (VAS) for alertness, mood, calmness and psychedelic effects, saccadic and smooth pursuit eye measurements, EEG, body sway, Stroop test, Visual and Verbal Learning Task, hormone levels and pharmacokinetics.

Results:

Compared to placebo, THC significantly decreased smooth pursuit, VAS alertness, Stroop test performance, immediate and delayed word recall and prolactin concentrations and significantly increased positive and general PANSS score, VAS feeling high, body sway and EEG alpha. Haloperidol reversed the THC-induced positive PANSS increase to levels observed with haloperidol alone. However, haloperidol did not have any effects on the 'high' feelings induced by THC.
Compared to placebo, haloperidol significantly decreased saccadic peak velocity, smooth pursuit, VAS mood and immediate and delayed word recall and significantly increased body sway, EEG theta and prolactin levels.

Conclusions:

THC-induced increases in positive PANSS but not in VAS feeling high were reversed by haloperidol. This indicates that psychotic-like effects induced by THC are mediated by dopaminergic systems, but that other systems are involved in 'feeling high'. In addition, the clear reductions of psychotic-like symptoms by a clinically relevant dose of haloperidol suggest that THC administration may be a useful pharmacological cannabinoid model for psychotic effects in healthy volunteers.

Study objective

As there is a large amount of evidence for the relation between cannabis and psychosis and the possible increase of forebrain dopamine by THC, THC-induced psychotomimetic effects could be used as a pharmacological challenge test to study the involvement of cannabinoid systems in psychosis, or even a practical 'psychosis'-model to assess therapeutic effects of antipsychotic agents. The current study is designed as an exploration of this model. As haloperidol is a well-known typical antipsychotic with high central dopamine receptor blockade selectivity, our hypothesis was that haloperidol would lead to an amelioration of the psychotic-like effects of the THC-challenge. At the same time, it was expected that the antidopaminergic effects of haloperidol would cause a reduction of the pleasurable subjective effects of THC.

Study design

Frequency depends on the endpoint (from 1.5 hours before and 24 hours after haloperidol administration).

Intervention

All subjects received the treatment combinations ‘THC + placebo’ and ‘THC + haloperidol’ and half of the subjects received ‘haloperidol + placebo’ and the other half ‘placebo + placebo’.

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Eligibility criteria

Inclusion criteria

1. Healthy male volunteers between 18 and 45 years of age;

2. Body Mass Index between 18 and 28.5 kg/m² inclusive;

3. Mild cannabis user for at least one year: cannabis use of no more than once a week (as an average in the last year), and able to refrain from using cannabinoids from at least 2 weeks prior to the first treatment period to the end of the follow-up period;

4. Volunteers are willing to give written informed consent to participate in the study and to comply with the study procedures.

Exclusion criteria

1. Clinically significant (history of) major psychiatric illness or substance abuse;

2. Clinically significant cardiac, pulmonary, gastrointestinal, hepatic, renal, hematological, endocrine, neurological and psychiatric disease as determined by medical history, physical examination, ECG or laboratory test results;

3. Congenital long QT syndrome in medical history;

4. Participation in a clinical study within 3 months preceding study, or participation in 4 or more trials in the past 12 months;

5. Positive urine screen for recreational drugs, i.e. cocaine, opioids, benzodiazepines, MDMA, metamphetamines, or amphetamines. THC will be tested as well. Since the volunteers are cannabis users and THC can be detected in the urine up to two weeks after cannabis use, subjects with a positive THC test at screening will be tested again and have to be found negative before the first study day. Subjects with a positive drug test, including THC, on a study day will be excluded;

6. Exposure to any medication, including over-the counter medications, 14 days prior to randomization (except paracetamol);

7. Exposure to prescription medications or to drugs known to interfere with metabolism of drugs within 30 days prior to screening;

8. Positive testing for Hepatitis B or C, or HIV 1-2;

9. Subject not able to refrain from alcohol from 24 hours before each study day until the end of the second study day;

10. Subject not able to refrain from smoking on study days;

11. Subject smokes more than 5 cigarettes per day;

12. Subject not able to refrain from xanthine intake on study days;

13. Subject not able to refrain from products containing quinine (bitter drinks in general) or grapefruit from 14 days prior to dosing until discharge;

14. Subject not able to refrain from exerting heavy physical exertion 24 hours before the study days;

15. Volunteers cannot participate if they have donated, including this study, more blood than allowed according to the regulations of the Dutch blood bank (Sanquin). Men are allowed to donate 500 ml of blood every three months;

16. Relevant (history of) drug allergy, history of hypersensitivity to drugs with a similar chemical structure as haloperidol;

17. Subject is the investigator or any sub investigator, research assistant, pharmacist, study coordinator, other staff or relative thereof directly involved in the conduct of the protocol.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-12-2007
Enrollment:	24
Type:	Actual

Ethics review

Positive opinion

Date:	18-03-2009
Application type:	First submission

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
NTR-new	NL1634
NTR-old	NTR1731
Other	: 2007-000140-27/P07.186
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A