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

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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23370

Bron
NTR

Verkorte titel
N/A

Aandoening

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

Ondersteuning

Primaire sponsor: See scientific contact
Zie contact wetenschappelijk
Overige ondersteuning: Centre for Human Drug Research

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

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’.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd

Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	13-12-2007
Aantal proefpersonen:	24
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	18-03-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1634
NTR-old	NTR1731
Ander register	: 2007-000140-27/P07.186
ISRCTN	ISRCTN wordt niet meer aangevraagd

Resultaten

Samenvatting resultaten
N/A