Influence of *9-tetrahydrocannabinol (THC) on oxycodone induced ventilatory depression in healthy volunteers

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In this study we will measure the effect of Bedrocan which contains primarily *9-tetrahydrocannabinol (THC) and a minute quantity cannabidiol (CBD), on ventilation at 55 mmHg end-tidal PCO2 in 20 healthy volunteers and the combination of THC and 20...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON52028

Source
ToetsingOnline

Brief title
COXY study

Condition

- Other condition

Synonym
respiratory depression

Health condition

opiaat bijwerkingen

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Bedrocan

Intervention

Keyword: healthy volunteers, oxycodone, THC, ventilatory depression

Outcome measures

Primary outcome

Primary objective: To measure the effect of inhaled THC (100 mg Bedrocan) on ventilation at isohypercapnia (end-tidal PCO2 = 55 mmHg) without and with concomitant intake of 20 mg oxycodone immediate release (IR) tablet in healthy volunteers 90 min after oxycodone intake.

Secondary outcome

Secondary objective: To measure the effect of inhaled THC (100 mg Bedrocan) without and with concomitant intake of 20 mg oxycodone immediate release (IR) on

- occurrence of apneic events;
- occurrence of desaturation events;
- baseline ventilation;
- psychomimetic side effects as measured by Bowdle and Bond & Lader questionnaires;
- cognition (p-deletion test)
- pain pressure threshold
- plasma concentrations of THC and oxycodone;
- blood pressure and heart rate.

Study description

Background summary

Opioids are commonly prescribed for moderate to severe pain. While initially intended for acute and cancer pain, opioids are currently frequently considered and prescribed in chronic noncancer pain. A consequence of this behavior is the increase in opioid misuse and abuse. The rate of unintentional drug overdose is rapidly increasing, not only in the Unites States but also in the Netherlands. A potential lethal consequence of opioid overdose is opioid-induced respiratory depression. Additionally, it is well known that opioids are often used (and abused) in combination with other legal or illicit substances, for example alcohol, benzodiazepines or cannabis, including medicinal (i.e. doctor prescribed) cannabis. We previously showed that combining ethanol with oxycodone (20 mg) increases respiratory depression, indicative of a dangerous alcohol-opioid combination (van der Schrier et al. Anesthesiology 2017; 102: 115-122). There are no data on the interaction between oxycodone and cannabis on the ventilatory control system. In our opinion, there is the false premise that cannabis has no effect on breathing. Apart from a direct effect on receptors in the brainstem, the sedative effects of cannabis may compromise breathing. Because of this side effect and also due to the rising number of addicted chronic opioid users, there is an increasing imminent societal, political and medical interest in furthering research on opioids, opioid-drug interaction and alternatives for the treatment of various chronic illnesses and chronic pain. Additionally, we expect that many patients at home using oxycodone, also use (coffeeshop) cannabis.

Study objective

In this study we will measure the effect of Bedrocan which contains primarily *9-tetrahydrocannabinol (THC) and a minute quantity cannabidiol (CBD), on ventilation at 55 mmHg end-tidal PCO2 in 20 healthy volunteers and the combination of THC and 20 mg oral oxycodone immediate release tablets. Primary endpoint is the effect of inhaled THC on ventilation at end-tidal PCO2 = 55 mmHg without and with concomitant intake of 20 mg oxycodone immediate release (IR) tablet in healthy volunteers 120 min after oxycodone intake. In this study we will use the Volcano cannabis vaporizer to vaporize 100 mg Bedrocan into an 8 L balloon. Volunteers will inhale the cannabis vapor from the balloon.

Study design

The design of the study is randomized, placebo-controlled crossover. Each subject will be studied twice, on occasion 1 he or she will receive THC and a placebo opioid capsule, and on occasion 2 THC and an oxycodone capsule. The

visits to the lab will be randomized.

Intervention

inhalation Bedrocan (with THC) and intake oxycodone or placebo

On fixed timepoints:
- respiratory measurements by giving CO2
- experimental pain test
- questionnaires
- blood sampling

Study burden and risks

The burden/risks for the volunteers are the occurrence of side effects from cannabis or oxycodone. Oxycodone may induce opioid-typical side effects such as respiratory depression (research endpoint), nausea/vomiting and sedation, of which nausea and vomiting is most burdensome. Other side effects, which are also cannabis related, include drug high, euphoria/dysphoria, dizziness/lightheadedness. During the study, we will closely monitor the subjects and treat side effects, most importantly nausea by administration of an antiemetic.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthy volunteers of either sex with earlier experience with cannabis (>2 lifetime exposures and <2x/week in the last 12 months).
- aged 18-45 years,
- body mass index < 30 kg.m-2,
- able to understand the written informed consent form,
- able to communicate with the staff,
- able and willing to complete the study procedures,
- signed the informed consent form,
- deemed suitable by the investigators.

Exclusion criteria

- Presence or history of any medical or psychiatric disease (incl. a history of substance abuse, anxiety, or the presence of a painful syndrome such as fibromyalgia);
- Use of any medication in the three months prior to the study (incl. paracetamol or other pain killers); except oral contraceptives (females)
- Use of more than 21 alcohol units per week;
- Use of cannabis in the 4 weeks prior to the study;
- A positive urinary drug test or a breath alcohol test at screening or on the morning of the experiment;
- Pregnancy, lactating or a positive pregnancy test on the morning of the experiment;
- Participation in another drug trial in the 60 days prior to dosing.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-11-2021
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bedrocan
Generic name:	Bedrocan cannabis flos
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Oxycodone
Generic name:	Oxycodone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	31-03-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	13-07-2021

Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	04-05-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2021-000083-29-NL
ClinicalTrials.gov	NCT05235503
CCMO	NL76443.058.21

Study results

Date completed:	29-06-2022
Actual enrolment:	32