Investigation of psychomotor performance to evaluate clinical impairment and pharmacokinetic aspects of methadone and buprenorphine: a double-blind placebo-controlled randomized trial

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

Summary

ID

NL-OMON43288

Source
ToetsingOnline

Brief title
The acute effects of methadone and buprenorphine on driving

Condition

- Other condition

Synonym
not applicable

Health condition

cognitief functioneren

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: the Norwegian Institute of Public Health ,the Norwegian Ministry of transport and communication

Intervention

Keyword: buprenorphine, driving, impairment, methadone

Outcome measures

Primary outcome

The primary objective of this study is to compare the acute effects of single

doses of methadone (5 and 10 mg) and buprenorphine (0.2 and 0.4 mg) with

placebo on driving performance and cognition.

Secondary outcome

Secondary objective is to study the pharmacokinetics of methadone and

buprenorphine in blood and oral fluid.

Study description

Background summary

Methadone and buprenorphine are used in maintenance therapy of persons with heroin addiction, but are also widely used as analgesics. Both methadone and buprenorphine are known to have CNS (central nervous system) effects which may be deleterious to safe driving. However, it is known that tolerance may develop to these deleterious effects. Recent epidemiological studies suggest an increased risk of traffic accidents for methadone maintenance treatment patients (MMP) and buprenorphine maintenance treatment patients (BMP). Persons outside maintenance treatment are regularly observed among drivers suspected for drugged driving testing positive for methadone or buprenorphine. Few

studies on performance of healthy volunteers after administration of single dose of methadone or buprenorphine have been performed.

Study objective

The primary objective of this study is to compare the acute effects of single doses of methadone (5 and 10 mg) and buprenorphine (0.2 and 0.4 mg) with placebo on driving performance and cognition. Secondary objective is to study the pharmacokinetics of methadone and buprenorphine in blood and oral fluid.

Study design

A five-way, single-blind, randomized, placebo-controlled, double-dummy, cross-over design to compare the acute effects of two single doses of methadone (5 and 10 mg) and buprenorphine (0.2 and 0.4 mg) with placebo on actual driving performance and a range of cognitive tests.

Intervention

n.a.

Study burden and risks

Volunteers* health will be assessed before treatment during a screening visit (1 hour, including an ECG test and assessment of a medical history questionnaire). Eligible participants will visit the research unit on seven more occasions. The first 2 sessions includes familiarization and practice of the driving and performance tests (approximately 2 hours per session). Subsequently, they will visit five times for intervention and testing (approximately 7 hours for each condition). The treatments are single doses of methadone 5 mg, methadone 10 mg, buprenorphine 0.2 mg, buprenorphine 0.4 mg and placebo. At the end of intervention days participants will be transported home by taxi. Total time spent by the participants will be approximately 39 hours. A total of four blood samples will be collected during each test day. During the experiment participants must refrain from consuming caffeine on the test days and alcohol intake from 24 hours prior to test days.

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

- Healthy males or females, in the opinion of the medical supervisor, based on a physical examination, medical history, vital signs, electrocardiogram, and the results of blood chemistry and hematology tests, and urinalysis
- Aged between 23 and 50 years (inclusive)
- BMI between 19 and 29 m2/kg (inclusive)
- Possession of a valid driving license for 4 years or more
- Driving experience of at least 5000 km per year on average
- Good sleepers
- Subjects should sign an Informed Consent Form

Exclusion criteria

- Sleep disorders such as insomnia and narcolepsy
- History of or current drug or alcohol abuse
- Current use of psycho-active medication, and inability to stay abstinent during the study
- Excessive alcohol use, defined as drinking more than 21 glasses of alcohol per week
- Excessive caffeine use, defined as drinking 5 or more cups of coffee per day
- Smoking more than 10 cigarettes per day
- History or presence of drug/alcohol abuse, including experience with heroin, methadone and

buprenorphine
- Intake of any opioid within 3 months before the study
- Use of any drug that is considered to influence the test drugs, including trade herbal products
- History of severe allergic disease
- History of significant mental, cardiovascular, renal or hepatic disorder, or other significant disease as judged by the investigator
- Positive pre-session urine sample of any of the following substances: ethanol, benzodiazepines, tetrahydrocannabinol, cocaine, amphetamines or opioids
- Poor metabolism due to CYP2B6 polymorphism
- Prolonged QT-interval (history of or presence at screening)
- Use of any drug that is known to inhibit or induce CYP3A4 activity
- Women who are pregnant or breastfeeding
- No use of a reliable contraceptive

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):	25-11-2016
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dolophine
Generic name:	methadone
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Temgesic
Generic name:	buprenorphine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-09-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-10-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2016-001512-38-NL
CCMO	NL57504.068.16
Other	nog niet beschikbaar