Examining the pharmacokinetic and pharmacodynamic profile of biperiden

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We will examine the cognitive performance of healthy young participants at different time points after a single administration of biperiden. The behavioural outcomes and electrophysiological correlates will be linked with the serum levels of…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON47428

Source
ToetsingOnline

Brief title
PK/PD biperiden

Condition

- Other condition
- Cognitive and attention disorders and disturbances

Synonym
memory impairment; MCI

Health condition

aandachtstekorten

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Biperiden, cognition, pharmacodynamic, pharmacokinetic

Outcome measures

Primary outcome

the main endpoints for the cognitive tasks are the behavioural scores on the immediate and delayed recall of the VLT. This includes the number of words recalled immediately and after a 20-minute delay.

Amendment:

The main endpoints for the attention tasks are the behavioral score on Alerting, Orienting and Executive Network (ANT), endogenous and exogenous attention (VCT), and recognition of deep encoded, shallowly encoded and novel stimuli (BUNM).

Secondary outcome

To establish the pharmacokinetic and pharmacodynamic profile of biperiden, the primary endpoints will be the blood serum values and physiological measures (body temperature, blood pressure, heart rate and pupil size). Furthermore the behavioural outcomes of the n-back, DAT, and simple and choice reaction tasks will be used for analysis, as well as the score on the B&L and complaints questionnaire. Next to this, the event-related potentials during the behavioural tasks will be analysed. Another important measure is the brain

response to the novelty oddball task, which will give an indication of the role

of acetylcholine in novelty processing.

Amendment:

We will analyze the scores on general attention (VCT) the B&L and complaints

questionnaire. Next to this, the event-related potentials during the

behavioural tasks will be analyzed.

Study description

Background summary

Since current treatments for Alzheimer*s Disease are only show minimal effects, it is of vital importance to search for drugs that are more successful. A way to investigate possible drug therapies in young adults is to use pharmacological deficit models to induce memory impairments that can mimic age- and dementia-related memory impairments. The *golden standard* scopolamine is known to cause side-effects (e.g., attention) that indirectly affect the cognitive performance of participants. Therefore a more selective drug with less peripheral side effects may be more preferable. Biperiden is a muscarinic antagonist that, when administered to healthy subjects, produces memory impairments without impairing attention or motor functions. So far, little research was done to investigate the pharmacokinetics and - dynamics of biperiden. In the current study, we will examine the pharmacokinetic and pharmacodynamic profile of biperiden.

Amendment:
During an interim analysis of the current study, we found that the effects on memory were much larger after 4 mg than after 2 mg. To exclude mediating effects of attention to the memory impairment, we will only provide the 4 mg dose to healthy volunteers and measure their attention. This is not necessary for the 2 mg dose, as we did not find any significant effects on attention in a previous study examining a 2 mg dose.

Study objective

We will examine the cognitive performance of healthy young participants at different time points after a single administration of biperiden. The behavioural outcomes and electrophysiological correlates will be linked with the serum levels of biperiden to establish the pharmacodynamic and kinetic properties. This will provide a better understanding of the time dependent effects on physiological, brain activity, and cognitive functions in relation to plasma levels. This is essential to characterize biperiden as a possible pharmacological model for cognitive dysfunction in Alzheimer's Disease.

Amendment:
In this study, we examine cognitive performance on attention tasks. in the same participants at one timepoint after biperiden administration. This is essential to determine if biperiden is a good deficit-model for memory impairment, or whether it impairs attention at higher doses and thus is not an appropriate memory model.

Study design

The study will be conducted according to a double-blind, placebo controlled, three-way cross-over design.

Amendment:
The study will be conducted according to a double-blind, placebo controlled, two-way cross-over design.

Intervention

Subjects will participate in 3 treatment conditions: i.e. placebo and biperiden 2 mg and biperiden 4 mg. All medications will be administered orally. Order of treatments will be balanced over three test sessions, which will be separated by a washout period of at least 7 days.

Amendment:
Subjects will participate in 2 treatment conditions: i.e. placebo and biperiden 2 mg. All medications will be administered orally. Order of treatments will be balanced over two test sessions, which will be separated by a washout period of at least 7 days.

Study burden and risks

The time investment for the participants will be around 29 hours (or 1740 min), which is comprised of 1) medical screening (60 min), 2) training session of cognitive tasks (60 min), and 3) three test sessions of around 540 min. The day before each test day, the participants are not allowed to drink any alcohol. During each test session multiple blood samples bill be taken. The treatment are single doses of biperiden 2.0 mg or 4.0 mg, and placebo.

Amendment:
The time investment for the participants will be around 8 hours (480 minutes), which is comprised of 1) medical screening (60 min), 2) training session of cognitive tasks (60 min), and 3) two test sessions of around 180 min. The day before each test day, the participants are not allowed to drink any alcohol.
The treatments are single doses of biperiden 2.0 mg and placebo.

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

• In the opinion of the investigator, the participant is capable of understanding and complying with protocol requirements.
• The participant has a body mass index of 18.5-30 kg/m2, inclusive, at medical screening.
• The participant is aged 18 to 35 years, inclusive, at the time of informed consent.

• The volunteer is healthy, i.e. absence of all exclusion criteria and had normal or corrected to normal static binocular acuity with or without correction.
• The participant signs and dates a written informed consent form before the start of the experiments.
• The participant has sufficient knowledge of the English language.

Exclusion criteria

• The subject has uncontrolled, clinically significant neurologic, cardiovascular, pulmonary, hepatic, renal, metabolic, gastrointestinal, or endocrine disease or other abnormality which may impact the ability of the subject to participate or potentially confound the study results.
• The volunteer has uncontrolled existing major psychiatric symptoms.
• The participant has known hypersensitivity to any component of the formulation or biperiden or related compounds.
• The subject has a history of drug abuse (defined as any illicit drug use) or a history of alcohol abuse within 1 year prior to the first visit or is unwilling to agree to abstain from alcohol from 24 hours prior to each test day and/or drugs throughout the study.
• The participant has any sensory or motor deficits which could reasonably be expected to affect test performance.
• Other exclusion criteria are smoking, excessive drinking (>20 glasses of alcohol containing beverages a week), pregnancy or lactation, use of medication other than oral contraceptives.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-03-2017
Enrollment:	42

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Akineton
Generic name:	Biperiden
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-09-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-12-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-01-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-02-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-11-2018
Application type:	Amendment
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	EUCTR2016-003357-14-NL
CCMO	NL58970.068.16