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The effects on the body and processing by the body of biperiden injected into the blood in elderly subjects

Submission date
18/07/2022

Recruitment status
No longer recruiting

Registration date
02/08/2022

Overall study status
Completed

Last Edited
02/08/2022

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Brain cells use certain messengers to communicate which each other, which are called neurotransmitters. Acetylcholine (ACh) is such a neurotransmitter and plays a crucial role in processes such as memory and attention. Importantly, it might have a role in the origin of disorders such as Alzheimer's disease and/or psychiatric disorders such as schizophrenia. Affecting brain cell communication with certain drugs that target ACh can reliably brings on symptoms in healthy volunteers that are similar to patients suffering from Alzheimer's or schizophrenia. These so-called challenges could potentially be new tools to investigate new drugs that interact with ACh and that could improve the symptoms of Alzheimer's disease or schizophrenia. One of these potential challenge drugs is biperiden, as it induces deficits in memory and attention. In this study the aim is to investigate biperiden administered into a vein (IV) as a challenge drug, so it can later be applied to test new drugs that interact with ACh.

Who can participate?
Healthy volunteers aged between 65 and 80 (inclusive) years old

What does the study involve?
The treatment phase will consist of three identical visits to the clinic during which biperiden or placebo will be administered. These visits will be separated by a period of 7-14 days between administrations. Participants will receive IV biperiden Lactate 2.6 mg over 60 min, IV biperiden Lactate 1.3 mg over 60 min and IV placebo (glucose 5%). During the study safety measures such as measurement of blood pressure, heart rate, breathing rate and ECG will be done. Additionally, two computerized test batteries will be performed several times to test, for example, memory and coordination.

What are the possible benefits and risks of participating?
Biperiden is a registered drug that is prescribed to patients suffering from Parkinson's disease. In addition to cognitive effects, self-limiting and mild dizziness and drowsiness may be observed.

All effects will be closely monitored up to 24 hours following biperiden administration. There will be no benefit from participating in this study. However, participation will provide valuable information for future research into dementia.

Where is the study run from?
Centre for Human Drug Research (Netherlands)

When is the study starting and how long is it expected to run for?
January 2022 to August 2022

Who is funding the study?
1. Centre for Human Drug Research (Netherlands)
2. Acadia Pharmaceuticals (USA)

Who is the main contact?
G. Jacobs (Principal investigator), clintrials@chdr.nl

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Additional identifiers

Clinical Trials Information System (CTIS)

2021-006546-13

Protocol serial number
CHDR2139

Study information

Scientific Title
Randomized, double-blind, placebo-controlled, 3-way cross-over study to characterize the pharmacodynamics and pharmacokinetics of single-dose intravenously administered biperiden in healthy elderly male and female subjects

Study objectives
Intraveneously administered biperiden will induce transient impairment on cognitive domains such as working memory and sustained attention.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/01/2022, Stichting BEBO (Doctor Nassaulaan 10, 9401 HK Assen, The Netherlands; +31 592-405871; info@stbebo.nl), ref: NL80005.056.21

Primary study design
Interventional

Study design
Single centre randomized double-blind placebo-controlled single dose three-way cross-over study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Improving the cognitive impairment associated with dementia and other neurocognitive disorders

Interventions
The double-blind treatment phase will consist of three identical treatment periods separated by a washout period of 7-14 days between the biperiden/placebo administrations. Admission to the CRU is on the evening of Day -1, study drug administration is on Day 1, and discharge on Day 2.

Study treatments:
IV biperiden Lactate (5 mg/ml) 2.6 mg over 60 min (corresponds to biperiden base 2.0 mg)
IV biperiden Lactate (5 mg/ml) 1.3 mg over 60 min (corresponds to biperiden base 1.0 mg)
IV placebo (glucose 5%) for 60 min

The study will consist of three treatment arms for 12 subjects. Each subject will receive one dose of placebo (glucose 5%) and two doses of IV biperiden Lactate dissolved in glucose 5% (5 mg /ml). Once 2.6 mg biperiden and once 1.3 mg biperiden. The study drug will be administered as a 60-minute continuous IV infusion given on Day 1 of the treatment period.

Subjects will have three treatment occasions separated by 7 to 14 days and one follow-up visit 7 to 14 days after the third treatment visit. Subjects will enter the clinical unit on Day -1 and be discharged on Day 2.

Subjects will be randomized using a 1- or 2-digit subject number. They will be randomized in a consecutive order, starting with the lowest number, in blocks of 4. Subjects will be randomized in such a way that biperiden 2.6 mg will only be administered after the subjects have completed the study day with the 1.3 mg dose. In this way, the effects of the 2.6 mg dose may be tolerated better. The randomization code will be generated using SAS version 9.4 (or a more recent version) by a study-independent, Centre for Human Drug Research (CHDR) statistician. The randomization code will be unblinded/broken and made available for data analysis only after study closure, i.e., when the study has been completed, the protocol deviations determined, and the clinical database declared complete, accurate and locked. The randomization code will be kept strictly confidential. Sealed individual randomization codes, per subject and per treatment, will be placed in a sealed envelope with the label 'emergency decoding envelopes' in a safe cabinet at CHDR.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Biperiden

Primary outcome(s)
Sustained attention and visuomotor coordination using adaptive tracking at baseline, 20 minutes, 1h, 2.5 h, 4 h, 7 h and 24 h

Key secondary outcome(s)
1. Measuring drug effects, sedation, memory and coordination using the Neurocart test battery at baseline, 20 minutes, 1 h, 2.5 h, 4 h, 7 h and 24 h
2. Measuring memory, attention and psychomotor function using the Cogstate test battery at baseline, 2 h and 3.5 h
3. Measuring the pharmacokinetic profile of biperiden in plasma at baseline, 20 minutes, 1 h, 2 h, 3 h, 5 h, 7 h and 11 h
4. Measuring safety of biperiden using:
4.1. Treatment-emergent (serious) adverse events ([S]AEs) and concomitant medication throughout the study at every study visit
4.2. Vital signs, respiratory rate and ECG at baseline, 1.5 h, 3 h, 6 h and 24 h
4.3. Clinical laboratory tests (Hematology, blood chemistry and urinalysis) at baseline and 24 h

Completion date
01/08/2022

Eligibility

Key inclusion criteria
1. Elderly male or female subjects aged between 65 and 80 (inclusive) years old
2. Healthy subjects as defined by the absence of evidence of any clinically relevant active or chronic disease following detailed medical and surgical history review and a complete physical examination including vital signs,12-lead ECG, haematology, blood chemistry, and urinalysis
3. Absence of cognitive impairment evident by a score of 28 or higher on the Mini-Mental State Examination (MMSE)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Total final enrolment
12

Key exclusion criteria
1. Clinically relevant history of abnormal physical or mental health interfering with the study as determined from the medical history review and the physical examinations obtained during the screening visit and/or at the start of the first study day for each period as judged by the investigator (including (but not limited to), neurological (including myasthenia gravis, epilepsy and tardive dyskinesia), cardiovascular (including current hypertension, orthostatic hypotension and recent myocardial infarction), respiratory, gastrointestinal (including previous ileus or megacolon and past or current gastro-intestinal stenosis), hepatic, renal, urogenital (including urinary retention or prostate hypertrophy) disorder or presence of narrow-angle glaucoma).
2. Current or history of any clinically relevant psychiatric disorder as classified according to DSM-IV or DSM 5 (e.g. psychotic disorder e.g. schizophrenia/schizo-affective disorder, bipolar disorder Type I or Type II, personality disorder, major depressive disorder/persistent depressive disorder, obsessive-compulsive disorder, panic disorder, anorexia nervosa, bulimia nervosa, generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD), autism spectrum disorder (ASD) sleep disorders and previous delirium).
3. Any disease associated with cognitive impairment.
4. History of severe allergies, or history of an anaphylactic reaction to prescription or non-prescription drugs or food.
5. History of hypersensitivity to biperiden or to the excipients used in the biperiden formulation.
6. Positive test for Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening.
7. Positive urine drug screen (UDS), or alcohol breath test at screening and/or upon admission to the Clinical Research Unit (CRU).
8. Presence or history (within 3 months of screening) of alcohol abuse confirmed by medical history, or daily alcohol consumption exceeding 2 standard drinks per day on average for

females or exceeding 3 standard drinks per day on average for males (1 standard drink = 10 grams of alcohol), and the inability to refrain from alcohol during the visits until discharge from the CRU (alcohol consumption will be prohibited during study confinement).
9. Use of tobacco and/or nicotine-containing products within 90 days of dosing and throughout the study until follow-up.
10. Excessive caffeine consumption, defined as >800 mg per day from 7 days prior to the first dose of the study drug until 24 hours prior to dosing. Subjects will abstain from caffeine-containing products for 24 hours prior each dosing and whilst in the study unit until discharge from the study unit. At other times throughout the study, subjects should not consume more than 800 mg caffeine per day. Caffeine quantities defined as: one cup of coffee contains 100 mg of caffeine; one cup of tea, or one glass of cola, or potion of chocolate (dark: 100 g, milk 200 g) contains approximately 40 mg of caffeine; one bottle of Red Bull contains approximately 80 mg of caffeine.
11. Any other concurrent disease or condition that could interfere with, or for which the concomitant treatment might interfere with, the conduct of the study, or that would, in the opinion of the Investigator, pose an unacceptable risk to the subject in this study.
12. Participation in an investigational drug trial in the 3 months prior to administration of the initial dose of the study drug or more than 4 times per year.
13. Vulnerable subjects (e.g., a person kept in detention or a person under guardianship).
14. Subject is an employee of the investigator or study site, with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator.
15. Subject is unable to read and understand the consent forms, complete study-related procedures, and/or communicate with the study staff.
16. Donation or loss of blood of more than 500 ml within 3 months (males) or 4 months (females) prior to screening.
17. Use of concomitant medications within 14 days prior to study drug administration or within 5 half-lives (whichever is longer).
18. Positive for SARS-CoV-2 infection prior to first dosing.

Date of first enrolment
17/02/2022

Date of final enrolment
22/04/2022

Locations

Countries of recruitment
Netherlands

Study participating centre
Centre for Human Drug Research
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Sponsor information

Organisation
Centre for Human Drug Research

ROR
https://ror.org/044hshx49

Funder(s)

Funder type
Research organisation

Funder Name
Centre of Human Drug Research

Funder Name
ACADIA Pharmaceuticals

Alternative Name(s)
Acadia Pharmaceuticals Inc., ACADIA Pharm, Receptor Technologies, ACADIA

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date