Evaluating the effect of zolpidem and suvorexant in healthy elderly volunteers on walking (adapt)ability.

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* To assess effect of zolpidem compared to placebo on walking (adapt)ability in healthy elderly as measured by the Interactive Walkway. * To assess effect of suvorexant compared to placebo on walking (adapt)ability in healthy elderly as measured by...

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

Summary

ID

NL-OMON50820

Source
ToetsingOnline

Brief title
Evaluating the effect of zolpidem and suvorexant on walking ability.

Condition

- Other condition

Synonym
risk of falling, walking (adapt)ability

Health condition

Biomarker . Methodology

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Non-profit research institute

Intervention

Keyword: interactive walkway, Suvorexant, Zolpidem

Outcome measures

Primary outcome

Pharmacodynamic endpoints

The Interactive Walkway takes approximately 15 minutes and includes the following tests:

* 8-meter walking test. Walking at a self-selected walking speed. The outcome measures are walking speed (cm/s), step length (cm), step width (cm), cadence (steps/min), and step time (s). The test has a duration of approximately 1-2 minutes.

* Obstacle avoidance. Avoiding suddenly appearing obstacles. The outcome measures are obstacle-avoidance margins (cm), success rate (%), and (normalized) walking speed (%). The test has a duration of approximately 4-5 minutes.

* Goal-directed stepping. Stepping as accurately as possible onto the shoe-size-matched steppingstones placed in an irregular pattern. The outcome measures are stepping accuracy (cm) and (normalized) walking speed (%). The test has a duration of approximately 1-2 minutes.

* Tandem walking. Walking on a line. The outcome measures are success rate (%), (normalized) walking speed (%), and mediolateral sway (cm). The test has a

duration of approximately 1-2 minutes.

* Timed Up-and-Go test. Rising from a standard armchair, walking to a line on the floor 3 meters away, turning, returning, and sitting down again. The outcome measures is time (s). The test has a duration of approximately 3-4 minutes.

The NeuroCart for this study includes the following tests:

* Body Sway. This test assesses postural stability. The outcome measure is sway (mm). The test has a duration of approximately 2 minutes.

* Adaptive Tracker. This test assesses pursuit-tracking. The outcome measure is success rate (%) The test has a duration of approximately 3 minutes.

The Withings Steel HR smartwatch includes the following tests:

* Step count

* Heart rate

* Sleep pattern (time it takes to fall asleep, sleep duration, sleep cycles and sleep interruptions)

* Physical activity duration

Pharmacokinetic endpoints

PK parameters of suvorexant and zolpidem by non-compartmental analysis of the plasma concentration-time data:

Maximum concentration (Cmax), Time to attain Cmax (Tmax), Area under the concentration * time curve (AUClast), Terminal Elimination Half-life (t1/2).

Tolerability and safety endpoints

Adverse events and vital signs measurements.

Secondary outcome

NA

Study description

Background summary

Dynamic assessments like walking adaptability may yield a stronger predictor for falls, as falls predominantly occur during walking and transfers that demand gait adjustment. Previous studies have shown most walking-related falls result from inadequate interactions with environmental context, leading to balance loss due to a trip, slip or misplaced step14. Walking adaptability thus seems to be an important determinant of fall risk.
The Interactive Walkway is an instrument developed to assess walking adaptability by augmenting a multi-Kinect-v2 10-m walkway with gait-dependent visual context (stepping targets, obstacles) using real-time processed markerless full-body kinematics15,16. Measurement of walking adaptability using the Interactive Walkway includes the ability to avoid obstacles, make sudden stops and starts and accurately place the feet to environmental context.

Study objective

* To assess effect of zolpidem compared to placebo on walking (adapt)ability in healthy elderly as measured by the Interactive Walkway.
* To assess effect of suvorexant compared to placebo on walking (adapt)ability in healthy elderly as measured by the Interactive Walkway.
* To compare the effect of suvorexant with the effect of zolpidem on walking (adapt)ability in the first three hours after drug administration.
* To explore the influence of smartwatch-based night-time sleep on Interactive Walkway and NeuroCart endpoints.
* To explore the validity of a smartwatch-based Timed Up and Go model.
* Optional. To establish the relationship between walking (adapt)ability parameters, Body Sway, and Adaptive Tracker.

Study design

This study is a randomized, double-blind, placebo-controlled, three-way crossover pilot study to evaluate the effect of suvorexant 10 mg and zolpidem 5

mg on walking (adapt)ability in 18 healthy elderly volunteers.

Intervention

Suvorexant 10 mg
Zolpidem 5 mg
Placebo

Study burden and risks

Participation in this trial is without any (therapeutic) benefit for healthy subjects. Their participation, however, is of importance for the understanding of the effects on walking (adapt)ability of orexin antagonists as a relatively new class of medication for insomnia in an elderly population. Both suvorexant and zolpidem are expected to have sleep inducing effects. Symptoms such as somnolence, fatigue, reduced vigilance, dizziness, etc., are therefore expected following administration. The burden for the subjects is expected to be minimal given the time input and none invasive measurements. Conducting this study with elderly subjects makes this study clinically more relevant due to the higher risk of falling with more severe complications as a result in this population, as well as the high number of prescriptions for sleep-inducing medications in elderly.

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

1. Male and female subjects aged between 65 years and 80 years (inclusive) at screening.
2. Body mass index (BMI) within the range of 18 to 30 kg/m2 (inclusive) at screening.
3. Systolic blood pressure 100-160 mmHg, diastolic blood pressure 50-95 mmHg, and pulse rate 45-100 bpm (inclusive), measured on either arm, after 5 min in the supine position at screening.
4. Estimated creatinine clearance (using the Cockcroft &Gault formula) *60 mL/min to allow for some reduced renal function in the elderly.
5. Subject has a regular sleep pattern (bedtime between 22:00 and 00:30 and sleep for at least 6 h).

Exclusion criteria

1. Hypersensitivity to benzodiazepines and/ or meeting contraindication criteria for zolpidem: myasthenia gravis, sleep apnea syndrome, liver failure, respiratory depression.
2. Hypersensitivity to orexin antagonist and/ or meeting contraindication criteria for suvorexant: narcolepsy.
3. Regular use of sedative/hypnotic drugs.
4. Regular use of walking aids.
5. Recurrent fallers defined as > 3 falls per year.
6. Neurological diseases and/or orthopedic problems interfering with gait function
7. Mini Mental State Examination score < 25 at Screening.
8. Current or previous diagnosis of insomnia-related disorder according to the Diagnostic and Statistical Manual of Mental Disorders version 5 (DSM-5) criteria.
9. Vaccination for SARS-CoV-2 within 4 days of screening and/or dosing with study drug.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-04-2021
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Belsomra
Generic name:	Suvorexant
Product type:	Medicine
Brand name:	Zolpidem
Generic name:	Zolpidem
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	24-02-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	01-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 25974
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2021-000322-10-NL
CCMO	NL76600.056.21
OMON	NL-OMON25974