Cholinesterase inhibitors to slow progression of visual hallucinations in Parkinson*s disease: a multi-center placebo-controlled trial (CHEVAL)

Published: 06-08-2013
Last updated: 24-04-2024

investigate whether early treatment with ChEI delays the progression of minor VH to major VH without insight or PDP. In addition, we will measure motor control, psychotic symptoms, cognitive impairment, mood disorders, adverse events and compliance...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Movement disorders (incl parkinsonism)
Study type	Interventional

Summary

ID

NL-OMON44866

Source
ToetsingOnline

Brief title
CHEVAL

Condition

- Movement disorders (incl parkinsonism)

Synonym
idiopathic Parkinson's disease, Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: ZonMw,Internationaal Parkinson Fonds (IPD) en Parkinson Patiënten Vereniging

Intervention

Keyword: cholinesterase inhibitors, Parkinson's disease, rivastigmine, visual hallucinations

Outcome measures

Primary outcome

The primary outcome measure is the median time until PD patients with minor VH progress to major VH without insight. The clinical endpoint is defined as the start with antipsychotic treatment.

Secondary outcome

Secondary outcome measures are changes in motor control, psychotic symptoms, cognitive impairment, mood disorders, daytime sleepiness, cholinergic deficiency, the number of adverse events, compliance, disability and caregiver burden. All relevant costs will be measured and valued.The median time until PD patients with minor VH progress to PD dementia is measured by means of changes in cognitive function. The secondary neurophysiological outcome measures are peak frequency, functional connectivity, topological network organisation and the direction of information flow. All relevant costs will be measured and valued.

Study description

Background summary

Visual hallucinations (VH) are the most common non-motor symptoms in Parkinson*s disease (PD). As an independent predictor for cognitive decline and nursing home placement they form an important disability milestone in the

course of PD. According to current clinical guidelines minor VH do not require treatment per se. But as minor VH precede the stage of major VH without insight and PD associated psychosis (PDP) they offer an opportunity for early intervention. Neuroleptic drugs delay the transition into PDP but are unsuitable for early treatment of VH due to their side effects. We hypothesize that cholinesterase inhibitors (ChEI) are a well-tolerated alternative for the early treatment of minor VH to delay the progression to PDP and that brain network analysis is suitable to predict treatment response.

Study objective

investigate whether early treatment with ChEI delays the progression of minor VH to major VH without insight or PDP. In addition, we will measure motor control, psychotic symptoms, cognitive impairment, mood disorders, adverse events and compliance, disability, caregiver burden and care use. We assess the cost-effectiveness of early chronic treatment of VH with ChEI. Finally, we analyse changes of functional brain networks before and during treatment.

Study design

a randomized, double blind, placebo-controlled, multi-center trial with an economic evaluation.

Intervention

rivastigmine capsule 6 mg BID or placebo BID for 24 months

Study burden and risks

The burden of participation consists of a total of 5 clinical visits (every 6 months), 4 telephone interviews on adverse events during the escalation phase and 9 internet questionnaires (every 3 months). Once12 ml blood will be drawn. In a subgroup 3 additional visits in the first year are needed for EEG recording. There is a risk for adverse reactions with rivastigmine treatment; the most common are nausea and vomiting.

Contacts

Public
Vrije Universiteit Medisch Centrum

De Boelelaan 1118
Amsterdam 1081 HZ
NL

Scientific
Vrije Universiteit Medisch Centrum

De Boelelaan 1118
Amsterdam 1081 HZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. idiopathic PD with bradykinesia and at least two of the following signs; resting tremor, rigidity, and asymmetry (in accordance with clinical diagnostic criteria of the UK PD Society Brain Bank);;2. the presence of minor visual hallucinations for at least 4 weeks, defined by a score of 1 or 2 on the hallucinations item of the Unified Parkinson*s Disease rating Scale (UPDRS)1-MDS;;3. age 40 years and over.

Exclusion criteria

1. Parkinson's disease associated psychosis, defined as the need for antipsychotic drug treatment in the opinion of the treating neurologist;;2. Parkinson's disease dementia, defined by a score of 26 or lower on the Mini Mental State Examination (MSSE);;3. current delirium (caused by infection or metabolic disturbance);;4. current treatment with drugs that have important central anticholinergic effects;5. current or recent (< 6 months) treatment with Cholinesterase inhibitors, such as rivastigmine (Exelon) or galantamine (Reminyl);;6. VH in response (<= 1 month) to increase of dopamingergic treatment;;7. history of psychosis, (known) sick sinus syndrome or other arrhythmia ;8. current severe ophtalmologic disease (defined as a visual acuity score of < 0.5 based on Snellen eye test';;9. permanent stay in a nursing home;;10. no informed consent.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-11-2013
Enrollment:	168
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Exelon
Generic name:	rivastigmine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	06-08-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-08-2013
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-05-2016
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2013-001722-25-NL
ClinicalTrials.gov	NCT01856738
CCMO	NL44622.029.13