Motor function optimization in advanced Parkinson*s disease patients, combined with galantamine to prevent visual hallucinations.

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To investigate the effects of galantamine on cognitive impairment and visual hallucinations in Parkinson`s disease, both therapeutic (direct effect) and preventive (protection against an acute increase of dopaminergic medication used by the patient...

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

Summary

ID

NL-OMON32454

Source
ToetsingOnline

Brief title
Motor function and visual hallucinations in advanced PD.

Condition

- Movement disorders (incl parkinsonism)
- Disturbances in thinking and perception

Synonym
Parkinson`s disease, visual hallucinations

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: unrestricted grant farmacie

Intervention

Keyword: galantamine, L-dopa, Parkinson`s disease, visual hallucinations

Outcome measures

Primary outcome

Cognition and existence of neuropsychiatric symptoms, for which the following tests will be used: -University of Miami Parkinson*s disease Hallucinations Questionnaire (UM-PDHQ).

Secondary outcome

- SCales for Outcome of PArkinson`s disease (SCOPA) - part cognition (SCOPA-Cog), this is a questionnaire focussing on executive, visuospatial and (working)memory functions.

- Motorfunction: Unified Parkinson`s Disease Rating Scale (UPDRS) - part 3 (motorfunction).

- Mood: BDI (questionnaire depressive complaints)

- Adverse events

Study description

Background summary

Parkinson*s disease (PD) is frequently accompanied by cognitive disturbances, mainly consisting of a dysexecutive syndrome, visuospatial and attentional impairments and memory deficits (Cummings JL 1988). If this cognitive decline reaches a certain severity, the diagnosis Parkinson*s disease dementia (PDD) can be made. Recent studies show prevalence data of PDD varying from 20-40% of

the total population with PD (Chaudhuri 2006, Mayeux R 1992). Visual hallucinations (VH) are often experienced by PD patients and are associated with a decline in cognitive function (Fenelon G 2000).
Although the exact pathophysiology of VH in PD is unknown, both dopaminergic and cholinergic neurotransmitter systems seem to play an important role. Until recently VH in PD were considered to be provoked only by overstimulation of the dopaminergic receptor system by dopaminomimetic therapy. However, recent publications suggest that an additional cholinergic defect is needed for VH in PD to occur (Francis 2007). In line with this, cholinergic enhancement, by administration of cholinesterase inhibitors (ChEI), in PDD patients has a positive effect on cognition and reduces the frequency of VH (Emre M 2004).
The ChEi rivastigmine and galantamine both have a moderate effect in the treatment of cognitive disturbances in Alzheimer*s disease (Kaduszkiewicz 05). Both substances have comparable side effects. In a double-blind placebo-controlled trial, rivastigmine has been proven to be effective to treat cognitive deficits in PD as well (Emre 04). The effectiveness of rivastigmine in PD was similar to the effectiveness reported in trials of rivastigmine for Alzheimer's disease (Emre 04). In addition, the occurrence of VH predicted a larger effect of rivastigmine on cognition and improved VH (Burn 06). A smaller study has shown that galantamine improved cognitive dysfunction in PD and improved VH as well (Aarsland 03). ChEI generally do not worsen motor performance in PD, as is known from the typical antipsychotics.
When PD advances, motor symptoms worsen, resulting in decreased mobility. If the decreased mobility is accompanied by cognitive deterioration, dopaminergic suppletion may result in an increase of VH. The addition of a CHEI, for instance galantamine, seems to result in fewer psychotic symptoms, compared to patients not receiving ChEI*s (own observations). We hypothesize that galantamine has both a therapeutic and a preventive effect on psychotic symptoms, especially the occurrence of VH. Therefore galantamine might even be able to prevent an increase of VH after the increase of dopaminergic treatment.

Study objective

To investigate the effects of galantamine on cognitive impairment and visual hallucinations in Parkinson`s disease, both therapeutic (direct effect) and preventive (protection against an acute increase of dopaminergic medication used by the patient).

Study design

This study is an open label trial investigating the effect of galantamine on visual hallucinations (VH) and cognitive decline in patients with PDD. The therapeutic effect of galantamine will be determined by investigating patients` score on several tests before medication and when on a stable dose of galantamine. Also, the possible preventive effect of galantamine will be investigated, by testing if it protects patients against a dose increase of

L-dopa medication.

Intervention

The intervention is the administration of the drug galantamine

Study burden and risks

For the subjects participating in this study, 2 extra visits (regarding a normal control frequency of 1x per 3 months) to the outpatient clinic neurology. During these 2 extra and the 2 regular visits, the UM-PDHQ and SCOPA-cog will be assesed in addition to regular tests (UPDRS-III). The first 3 visits last approximately 45 minutes.
The risc of the optimization of L-dopa therapy is the appearance of adverse events like VH. After L-dopa is reduced to the original level, galantamine will be titrated. The risc in this phase is the occurence of adverse events related to galantamine use, like gastro-intestinal complaints and sleepiness. When these occur, the dose will be reduced.
After 2,5 months, when patients receive an optimal dose of galantamine, L-dopa therapy will be increased. It is known that this often leads to VH in patients with advanced PD. It is expected that galantamine will prevent the emergence or increase of VH after increase of L-dopa. If galantamine does not have this expected effect, patients might experience VH.

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

- PD according to the UK Brain Bank Criteria
- At least weakly visual hallucinations
- Patients must be able to understand the procedures
- Stable medication for at least 1 month

Exclusion criteria

- Unstable internal disease
- Major depression
- Use of anticholinergics, amantadine or selegiline (washout at least 2 weeks)
- Tricyclic antidepressants (washout al least 1 month)
- Use of cholinesterase inhibitors

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-07-2019
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Reminyl retard
Generic name:	galantamine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Sinemet
Generic name:	levodopa/carbidopa
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	31-03-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2008-006278-13-NL
CCMO	NL24092.042.08