Efficacy of amantadine on behavioural and emotional problems and impairment of executive functioning due to acquired brain injury to the frontal lobes: a series of single case experimental design studies.

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Objective: The objective of this study is to establish the effectiveness and safety of amantadine on emotional lability/irritability, aggression, apathy and impaired executive functioning due to frontal lobe brain injury.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON45205

Source
ToetsingOnline

Brief title
Efficacy of amantadine in acquired brain injury.

Condition

- Neurological disorders NEC
- Psychiatric and behavioural symptoms NEC

Synonym
acquired brain injury

Research involving
Human

Sponsors and support

Primary sponsor: GGZ Oost Brabant (Rosmalen)
Source(s) of monetary or material Support: Fonds van de Commissie Onderzoek en Innovatie van GGZ Oost Brabant

Intervention

Keyword: amantadine, behavioural problems, brain injury, emotional problems

Outcome measures

Primary outcome

Main study parameters/endpoints:

* The behavioural problems: emotional lability/irritability, aggression, and

apathy will be measured by the Neuro Psychiatric Inventory (NPI).

* Individual target behaviour will be established and measured by a Visual

Analogue Scale (VAS (1-100)).

* The impairment of executive functioning is measured by the Behaviour Rating

Inventory of Executive Function-A (BRIEF-A)

Secondary outcome

Cognitive impairments as measured by the Mine Mental State Examination (MMSE)

Study description

Background summary

Rationale: Brain injury due to different causes is common and can have severe functional impact. Frontal lesions often lead to cognitive impairments, but also to behavioural consequences, e.g. apathy, agitation, aggression, and emotional lability.
Amantadine may be effective in the treatment of these cognitive and behavioural

consequences. Anatomical and neurochemical theory support these findings and amantadine is clinically used albeit without the support of scientific evidence.

Study objective

Objective: The objective of this study is to establish the effectiveness and safety of amantadine on emotional lability/irritability, aggression, apathy and impaired executive functioning due to frontal lobe brain injury.

Study design

Study design:
This study is a series of Single Case Experimental Design (SCED) studies. Each study has an A-A1-B-A, or A-B-A1-A double blind, randomized, placebo-controlled, and multiple baseline design. (A=baseline/withdrawal; A1=placebo; B=amantadine)

Intervention

Intervention : Amantadine is the pharmaceutical intervention in each Single Case experiment in this series.
Dosage schedule amantadine in the B phase:
Day 1-7, 100 mgs od
Day 8-28, 100 mgs bd
Day 29-35 100 mgs od
During baseline and withdrawal no amantadine is given. In the treatment phase (amantadine or placebo) the subject takes two pills per day. Depending on the randomisation schedule these will contain amantadine or placebo.

Study burden and risks

Amantadine has no major side effects and low risk of adverse events. Amantadine's undesirable effects are often mild and transient, usually appearing within the first 2 to 4 days of treatment and promptly disappearing 24 to 48 hours after discontinuation.
Although amantadine has been widely used in clinical practice for other indications and was found safe, in the current study every precaution is taken, on the one hand to monitor side effects constantly and on the other hand to react immediately if side effects are forming a health risk for the patient.
Before treatment starts, risk factors are carefully established and if risk factors emerge subjects will be excluded.
Side effects will be monitored weekly.
The subject can withdraw at any moment in time without any restriction if side effects are too cumbersome for the patient.

So far the only adverse event reported in the literature is the association of acute withdrawal from amantadine and a Malignant Neuroleptic Syndrome. The study design does not include instant withdrawal. Subjects and significant others will be warned explicitly against instant withdrawal.
Of the questionnaires only the MMSE and the side effect monitor will involve the subject directly.
So the burden of medication and measurements to the patient is negligible.

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

* Subjects have suffered acquired brain damage due to various aetiologies as verified by CT or MRI
* Subjects suffer from emotional lability/irritability, aggressiveness, apathy as established

through clinical observation and/or impairment of executive functioning as established by clinical judgement or on the basis of neuropsychological assesment.
* Subjects are >3 months post injury
* Subjects are 18 years or older
* Written informed consent is given

Exclusion criteria

* Current drug addiction
* Current psychoses
* The current use of incompatible medications: methylphenidate, typical or atypical antipsychotics, combination diuretics (hydrochlorthiazide + potassium sparing diuretics) or Levodopa.
* Pregnancy and lactation
* Cardiac disease. Inclusion only after the consulting cardiologists consent
* Refractory epilepsy
* Kidney failure (eGFR<10 ml/min)
* A history of gastric ulceration
* Current glaucoma
* Hypersensitivity to amantadine or any of the excipients
. Suicidality

Study design

Design

Study type: Interventional

Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-10-2015
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	symmetrel
Generic name:	amantadine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	01-10-2014
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-03-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-07-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-08-2017
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	EUCTR2012-005723-33-NL
CCMO	NL50088.068.14