A randomized, double-blind, placebo-controlled, cross-over study to assess the effects of fampridine on eye movements and nerve conduction and function in patients with multiple sclerosis (MS) and a unilateral or bilateral internuclear ophthalmoplegia (INO)

Published: 26-01-2015
Last updated: 14-04-2024

Primary objective: - to evaluate the effects of fampridine on eye movements in MS patients with a unilateral or bilateral INO. Secondary objectives:- to determine whether there is an association between MRI signal of the medial longitudinal…

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

Summary

ID

NL-OMON42310

Source
ToetsingOnline

Brief title
Fampridine in MS patients with INO

Condition

- Demyelinating disorders

Synonym
multiple sclerosis, nerve disease

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Biogen Idec

Intervention

Keyword: fampridine, Internuclear Ophthalmoplegia, Multiple Sclerosis, nerve conduction

Outcome measures

Primary outcome

Eye movements at each day and time point. Variables will include (but not limit

to):

- eye position and velocity at the abducting/adducting eye

-Versional disconjugacy index: the inter-ocular ratio of the peak velocity and

peak acceleration of the abducting and adducting eye.

-first-pass amplitude: the ratio of the position of the abducting eye to the

adducting eye when both eyes reached their final position of ocular

displacement with respect to the target position.

- peak velocity ratio for each saccade

- saccade pulse in the 2 eyes

Secondary outcome

A MRI-scan brain:

- signal intensity MLF

- length of MLF

Nerve conduction speed as determined by lag time of the adducting eye divided

by the length of the MLF

Cognitive function test items from NeuroCart:

- Adaptive tracking (motor-coordination)

- Body sway (postural stability)

- Rapid visual information processing (RVIP)

- Simple reaction time task

- Symbol Digit Substitution Test (SDST, cognitive processing speed)

- Pharmaco-EEG

Pharmacokinetic endpoints: Tmax, Cmax, AUCinf, t1/2, Vd/f, CL/F

Safety endpoints: Pulse, diastolic blood pressure, systolic blood pressure.

Study description

Background summary

Fampridine is a potassium channel blocker which leads to inhibition of leakage of potassium ions causing a prolongation of repolarisation and hence improvement of formation of action potentials in demyelinated nerve fibres. Fampridine has been shown to enhance neurological functioning in patients with relapsing remitting MS (an improvement of approximately 25% was observed on walking speed), but there is very limited evidence about fampridine use in MS patients with internuclear ophtalmoplegia (INO).
Methods to quantify de- and remyelination and methods to quantify nerve conduction of demyelinated nerves are needed to investigate pharmacological effects of new compounds that are aimed at improving remyelination or improving nerve function of demyelinated nerve fibres, which are currently being developed for the treatment of MS.
This study will be performed in MS patients with slowing of eye adduction consistent with subclinical or clinically overt unilateral or bilateral INO, to

determine whether a change of nerve conduction and function can be observed after administration fampridine.

Study objective

Primary objective:
- to evaluate the effects of fampridine on eye movements in MS patients with a unilateral or bilateral INO.

Secondary objectives:
- to determine whether there is an association between MRI signal of the medial longitudinal fasciculus (MLF) and the nerve conduction velocity in MS patients with INO.
-to evaluate the efficacy of fampridine on neurophysiology as measured using NeuroCart test battery.
-to establish a pharmacokinetic-pharmacodynamic model for the effect of fampridine on eye movement in MS patients with INO.

Study design

This will be a randomized, double-blind, placebo-controlled, cross-over study with fampridine in patients with MS and a unilateral or bilateral INO.

Intervention

Fampridine 20 mg, once during the study.

Study burden and risks

There is no direct benefit for the subjects taking part in this study. The results of the study may provide valuable information for future research.

Incidentally, subjects participating this study will get a headache. This can be caused by not eating for a certain period of time or drinking no coffee. Placement of a canula can cause a bruise.

In therapy with fampridine sometimes also adverse events can occur, such as: urinary tract infections, anxiety, dizziness, headache, paresthesia, tremor, laryngeal pain and gastrointestinal disorders such as nausea, vomiting and dyspepsia.

Contacts

Public

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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 patients 18 years or more of age;
2. Diagnosis of multiple sclerosis according to the revised McDonald (2005) criteria;
3. A disease duration > 1 year as defined by a diagnosis of MS at least one year prior to inclusion in the study;
4. Clinically stable disease > 30 days;
5. Subject shows evidence of INO by quantitative neuro-ophthalmological criteria;
6. Subject is able to understand the demands of the protocol, has had any questions answered and has voluntarily signed the informed consent prior to any study procedures; and
7. Subject is otherwise in good health, based on complete medical history and physical examination, including blood pressure and pulse rate measurement, 12-lead ECG, and clinical laboratory tests.

Exclusion criteria

1. Subject is a pregnant female (as determined by a urine pregnancy test), a lactating

female, or a female of child-bearing potential, not sterilized and not using one of the following methods of birth control: oral or injectable contraceptive agent, implantable contraceptive device, or barrier method;
2. The neuro-ophthalmological examination demonstrates significant impairment of eye-movements due to cerebellar or other pathology which may infer with reliable testing of an INO;
3. Inability of a subject to maintain good visual fixation;
4. Subject has a prior history or current presentation of seizure;
5. Subject has a creatinine clearance less than 80 mL/min, calculated by Cockroft-Gault equation;
6. Subject has known allergy to fampridine;
7. Subject has any contraindication of MRI;
8. The subject has any medical condition, including psychiatric disease that might interfere with the interpretation of the results or with the conduct of the study;
9. Subject has a history of drug or ethanol abuse within the past year;
10. A positive urine drug screen;
11. Subject has a history of ischemic heart disease;
12. Concomitant use of fampridine with medicinal products that are inhibitors or substrates of organic cation transporter 2 (OCT2) such as cimetidine, carvedilol, propanolol and metformin;
13. Treatment with another investigational drug within 3 months prior to screening or having participated in more than 4 investigational drug studies within 1 year prior to screening; and/or
14. The subject has abnormal clinical laboratory values or an abnormal ECG, without approval of the study investigator.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Diagnostic

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	28-04-2015
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Fampyra
Generic name:	fampridine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	26-01-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-02-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-04-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-05-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-07-2015
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2015-000182-31-NL
CCMO	NL52195.056.15