The influence of Perampanel on Cortical Inhibition in People with Epilepsy: Assessment with Transcranial Magnetic Stimulation

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Main Objectives: To assess the effect of perampanel on cortical excitability in people with medically refractory epilepsy.Secondary Objectives; To investigate the predictive value of TMS-EMG/EEG for long-term seizure control after starting...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Seizures (incl subtypes)
Study type	Observational non invasive

Summary

ID

NL-OMON47007

Source
ToetsingOnline

Brief title
Perampanel and Cortical Excitability

Condition

- Seizures (incl subtypes)

Synonym
Epilepsy, Fits

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Epilepsie Instellingen Nederland

Source(s) of monetary or material Support: EISAI,EISEI groep

Intervention

Keyword: Anti-Epileptic Drug, Cortical Excitability, Perampanel, Transcranial Magnetic Stimulation

Outcome measures

Primary outcome

Main Study Parameters:

- Change in cortical excitability parameters (motor threshold, MEP (motor evoked potential) amplitude, cortical silent period, recovery curve, short and long intra-cortical inhibition, intra-cortical facilitation).

- Seizure reduction: seizure free intervals, number of seizures, seizure type

Primary Study Endpoint:

- Change in long interval intracortical inhibition (interval 250 ms) at maximum tolerated dosage of perampanel (T2) compared to baseline (T0).

Secondary outcome

- Change in rMT at maximum tolerated dosage of perampanel (T2) compared to baseline (T0).

- Intolerance for research Methods (TMS,EEG,EMG)

- Change in long interval intracortical inhibition (interval 250 ms) at 4mg/day dosage of perampanel (T1) compared to baseline (T0)

- Predictability of long-term effectiveness of perampanel, using the change in cortical excitability parameters at 4mg/day dosage of Perampanel (T1) measurement to predict AED effectiveness at maximum dosage

Other Study Parameters:

- EEG (TMS-evoked potential, latency, amplitude, phase coherence: pathologic

EEG changes)

- QOLIE-10 and Sensory Profiling correlation analysis with the cortical

excitability parameters

Study description

Background summary

A biomarker to predict long-term seizure control shortly after initiation of antiepileptic drug treatment (AED) could speed up the process of finding the AED appropriate for that person with epilepsy. A prospective study in newly diagnosed people with epilepsy demonstrated that transcranial magnetic stimulation (TMS) responses measured shortly after the start of AED treatment can predict long-term seizure control. Perampanel is a newly licensed AED for people with localization-related epilepsy, with or without secondary generalization. Perampanel selectively blocks AMPA receptor-mediated synaptic transmission, reducing neuronal excitation. This proposed study aims to investigate the effect of perampanel on cortical excitability in people with medically refractory epilepsy.

Study objective

Main Objectives:

To assess the effect of perampanel on cortical excitability in people with medically refractory epilepsy.

Secondary Objectives;

To investigate the predictive value of TMS-EMG/EEG for long-term seizure control after starting perampanel therapy.

Study design

We aim to conduct a within-subject controlled longitudinal study to investigate the effect of perampanel on cortical excitability measured by TMS-EMG/EEG. To assess the effect of perampanel on cortical excitability, people with refractory localization-related epilepsy will be recruited. Doses of concurrent

medication are kept constant for at least 6 weeks before the baseline measurement and during the study, if possible. Participants will be asked to keep a seizure diary starting 6 weeks before the baseline measurement of the study and during the study. If such data is available retrospectively and reliable, participants can start immediately with the baseline T0 measurement. In the case of low seizure frequency (<1 seizure per month), seizure frequency will be determined anamnestically. Titration of perampanel will follow the baseline measurement according to standard clinical practice and is at the discretion of the person*s neurologist. A normal titration schedule would start with a dosage of 2mg daily with increases of 2 mg per two weeks up to 8-12 mg daily, but deviations from the scheme are allowed. Phase II studies showed that once-daily doses of perampanel at 8 and 12 mg were effective, safe, and tolerability was acceptable.7,8 TMS measurements will performed before starting titration (T0), at 4 mg dose (T1), and after reaching the maximum effective but tolerated dose (T2). The participants will be asked to continue with their seizure diary for a follow-up of three months.

Study burden and risks

TMS is non-invasive and few seizures have been reported with single- or paired pulse TMS (much less than with repetitive TMS), and most occurred in patients with underlying brain pathology or taking neuro-active medication. In people with epilepsy, seizure occurrence due to TMS stimulation is about 0-3.6%. Seizures occurred most frequently (3.6%) in people with temporal lobe epilepsy who were undergoing pre-surgical evaluation. The setting however is different, as pre-surgical evaluation aims at inducing seizures for ictal measurements. Therefore, we expect seizures in relation to TMS to occur less frequently in our subject group.

With this study we investigate the changes induced by perampanel treatment on cortical excitability. A change in intracortical inhibition at the 250 ms interval can potentially be used to predict long-term seizure control for perampanel, thereby accelerating the process of finding the AED appropriate for individual person with refractory epilepsy and limiting exposure to non-effective AEDs and their side-effects.

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

People with refractory localization-bound epilepsy, with or without secundary generalisation with a minimum of 1 epileptic seizures per 2 months.

Exclusion criteria

- Previous head/skull surgery where metal is left in the head, with the exception of titanium plates and/or fragments
- Implanted with any electronic device, with the exception of nervus vagus stimulators and cardiac pacemakers
- Any major Neurological or Psychiatric condition

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-09-2016
Enrollment:	0
Type:	Actual

Ethics review

Approved WMO

Date:	13-04-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	15-03-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	27-09-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL53005.058.15

Study results

Date completed: 28-12-2018

Actual enrolment: 18

Summary results
Trial ended prematurely