Cortical inhibition by Retigabine. Assesment by transcranial magnetic stimulation in epilepsy patients.

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The study aims to answer the following questions: 1) What is the effect of Retigabine on cortical excitability measured by TMS ? (primary). 2) To what extent are changes in excitabilty meausred with TMS related to seizure control ? (secondary).

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

Summary

ID

NL-OMON37062

Source
ToetsingOnline

Brief title
Corticale inhibition by Retigabine.

Condition

- Seizures (incl subtypes)

Synonym
focal epilepsy, partial epilepsy

Research involving
Human

Sponsors and support

Primary sponsor: Epilepsiecentrum Kempenhaeghe
Source(s) of monetary or material Support: GlaxoSmithKline

Intervention

Keyword: focal epilepsy, motor cortex, retigabine, TMS

Outcome measures

Primary outcome

Primairy outcome is the change of intracortical facilitation and silent period

by 900 mg/day (or maximum dose) Retigabine.

Secondary outcome

Relation between long interval cortical inhibition and clinical effect (>50%

seizure reduction).

Study description

Background summary

Transcranial magnetic stimulation (TMS) has opened the possibility to asses cortical excitability noninvasively, both in controls and patients. Its application in epilepsy is a major area of research, since excitability changes are at the heart of the disease . TMS has been used to investigate the mechanism of action of several drugs. Sodium-channel blocking drugs elevate the threshold, while drugs that act on GABAergic transmission improve intracortical inhibition or prolong the silent period. In patients, TMS shortly after the application of an antiepileptic drug can predict long-term seizure control. Retigabine is a first-in-class antiepileptic drug that acts on potassium channels. Indirectly, changes in GABAergic synaptic transmission contribute to its efficacy. In-vivo studies of the physiological effect of Retigabine on motor cortex in normal humans could deepen our understanding of mechanisms. Our hypothesis is that Retigabine will shorten the silent period and diminish intracortical facilitation on account of its action by potentiation of inhibitory postsynaptic currents mediated by GABA receptors.

Study objective

The study aims to answer the following questions:
1) What is the effect of Retigabine on cortical excitability measured by TMS ? (primary).
2) To what extent are changes in excitabilty meausred with TMS related to

seizure control ? (secondary).

Study design

Observational neurophysiological/neuropharmacological study.
Patients with partial epilepsy, with or without secondary generalization that have an indication to initiate adjuvant treatment with Retigabine. The responsibility to start treatment remains within the responsibility of the treating neurologist.
Doses of concurrent medication are kept constant during the study.
Patients with any implanted electronic device are excluded.
Patients with clinical or radiological evidence of major structural abnormality of the motor cortex or the pyramidal tract are excluded.
TMS is performed before starting Retigabin, on 600 mg/day (post1), on 900/dag (post2) or after any other different maintenance dose is reached (post3).
In each session resting motor threshold, short interval (2 and 5 ms) intracortical inhibition, intracortical facilitation (10 and 15 ms), long interval intracortical inhibition (250 and 300 ms) en silent period are measured.

Study burden and risks

Magnetic stimulation is applied to the motor cortex. The motor response is measured with surface electrodes on small hand muscles. TMS is not painful, but feels unpleasant at high intensities. The present protocol focuses on responses close to threshold. These intensities are well tolerated.
The total number of stimuli and their intensity and frequency is far from the dose considered relevant for provocing seizures. A seizure that occurs coincidentally during the measurement can not be excluded.
Blood samples will be taken for serum levels of retiabine and other drugs.

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

Partial onset epilepsy (with or without secondary generalization) that is not sufficiently controlled by the current medication. There is an indication to initiate adjuvant treatment with Retigabine. The decision to start Retigabine is in taken by the patients neurologist. After that decision the patient may participate in the current study.

Exclusion criteria

- implanted electronic or magnetic devices (safety)
- clinical or radiological evidence of major structural abnormality of the motor cortex or the pyramidal tract

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2013
Enrollment:	15
Type:	Anticipated

Ethics review

Approved WMO

Date:	12-03-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL40735.091.12