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Study to demonstrate the clinical efficacy and effects on brain electrical activity of the special Ginkgo extract EGb 761 in patients suffering from dizziness with disturbance of balance and eye movements after attacks of reduced perfusion in the rear areas of the brain

Submission date
23/10/2020

Registration date
27/10/2020

Last Edited
26/10/2020

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Vertigo is when persons feels as if they or the objects around them are moving when they are not. It is a symptom of different diseases, it may occur during or after an event of impaired perfusion (blood flow) of certain parts of the brain. Vertigo may appear continuously or in intervals, it may affect the ability to stand firmly and the movement of the eyes. EGb 761® is a dry extract of Ginkgo biloba (maidenhair tree) which may be used for treatment of vertigo. Previous studies suggest that EGb 761® could improve the various symptoms of vertigo. Therefore the aim of this study is to test whether EGb 761® improves the patients' overall perception of the severity of vertigo symptoms more than capsules without any active ingredient. Further aims are to find out whether EGb 761® improves the frequency, duration and severity of vertigo, the ability to stand firmly and eye movements.

Who can participate?
Adults aged 30 to 75 with a diagnosis of vertigo due to impaired perfusion of certain parts of the brain.

What does the trial involve?
After a screening period (at most 14 consecutive days), participants are divided into two groups to receive either capsules containing EGb 761® or capsules without active ingredient for about 180 consecutive days (about 6 months). Participants take two capsules per day (one in the morning and one in the evening) regardless of mealtimes. They do not know which kind of capsules they are taking. In addition, participants are asked to regularly carry out exercises that may improve balance. Throughout the study side effects from the medication are monitored by the patient and care team. After 2, 4 and 6 months, participants answer questions about the

severity, duration and frequency of their symptoms of vertigo, and stand on a platform and sit on a rotating chair in order to find out if the medication has helped reduce their symptoms and improve their ability to stand firmly and their eye movements.

What are the possible benefits and risks of participating?
All participants are taught how to do special exercises that are expected to better control symptoms of vertigo and to improve balance. Half of the patients receive EGb 761® treatment in addition, which is also expected to reduce or eliminate symptoms of vertigo. Therefore, participants may benefit from an improvement in their quality of life. They may also benefit from detailed and extensive diagnostic tests. Blood tests may cause mild pain and can provoke bruises or tenderness in the extraction area. As part of the vertigo assessment, patients undergo several diagnostic examinations some of which can cause slight discomfort (e.g. applying warm water to the ear, sitting on a rotating chair). As EGb 761® is well tolerated according to the data gathered so far, there is no major risk in taking EGb 761®. The adverse events potentially associated with EGb 761®, such as upset stomach, headache and allergic skin reactions, are usually mild in nature. Bleeding may also occur during treatment with EGb 761®.

Where is the study run from?
Medical University of Luebeck (Germany)

When is the study starting and how long is it expected to run for?
October 1991 to April 1994

Who is funding the trial?
Dr Willmar Schwabe GmbH & Co. KG (Germany)

Who is the main contact?
Dr Robert Hoerr
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
523001.01.001

Study information

Scientific Title
Randomized, placebo-controlled, double-blind trial to demonstrate the clinical efficacy of EGb 761 in patients with central vertigo, impaired state regulation and oculomotor function, due to vertebrobasilar ischaemic events

Study objectives
The study hypothesis is that the clinical efficacy of EGb 761®, in terms of patients' global impression of change in symptom severity, is superior to that of placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/02/1992, Ethics Committee at the Medical University of Luebeck (Medical University of Luebeck, Ratzeburger Allee 160, Luebeck, 23562, Germany; +49 (0)451 3101 1008 or +49 (0)451 3101 1025; ethikkommission@uni-luebeck.de), ref: 143 Pu/La

Study design
Interventional randomized placebo-controlled double-blind monocentric phase IV clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Vertigo due to vertebrobasilar ischemic events

Interventions
Treatments (EGb 761® or placebo) were assigned to patient numbers by a computer program. EGb 761® and placebo capsules were indistinguishable by appearance, packed and labelled with patient numbers in an otherwise indistinguishable manner. By allocating patient numbers in ascending order to the patients enrolled, treatments were allocated strictly at random to the patients, while concealment was upheld.

After a screening period (at most 14 consecutive days), participants are divided into two groups to receive either capsules containing EGb 761® or capsules without active ingredient, for about 180 consecutive days (about 6 months). Participants take two capsules per day (one in the morning and one in the evening, 120 mg every day) regardless of mealtimes. They do not know which kind of capsules they are taking. In addition, participants are asked to regularly carry out exercises that may improve balance. Throughout the study side effects from the medication are monitored by the patient and care team. After 2, 4 and 6 months, participants answer questions about the severity, duration and frequency of their symptoms of vertigo, stand on a platform and sit on a rotating chair, in order to find out if the medication has helped reduce their symptoms and improve their ability to stand firmly and their eye movements.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
EGb 761® (Ginkgo biloba extract)

Primary outcome(s)
1. Improvement of vertigo, assessed by the difference in changes in patient's global impression of vertigo severity (0-100 analogue scale) from Day 0 visit to Day 120 visit
2. Improvement of vertigo, assessed by the difference at Day 120 visit in the physician's global impression of change in vertigo severity

Key secondary outcome(s))
1. Improvement of vertigo, assessed by the difference in changes in patient's global impression of vertigo severity (0-100 analogue scale) from Day 0 to Day 60 and from Day 0 to Day 180
2. Improvement of vertigo, assessed by the differences in the physician's global impression of change in vertigo severity at Day 60 and Day 180
3. Improvement of vertigo, assessed by the difference in changes in the vertigo score, which is derived from frequency, duration and severity of vertigo, from Day 0 to Day 60, Day 120 and Day 180, respectively
4. Improvement of balance, assessed by the difference in changes in the lateral sway amplitude in posturography from Day 0 to Day 60, Day 120 and Day 180, respectively
5. Improvement in oculomotor disturbances, assessed by the difference in changes in oculomotor test parameters from Day 0 to Day 120 and Day 180, respectively
6. Improvement in cognition, assessed by the difference in changes in neuropsychological test scores (only in patients who had abnormal scores at baseline) from Day 0 to Day 120
7. Serious (SAEs) and non-serious adverse events (AEs), spontaneously reported by the patient or observed by the investigator continuously throughout the trial
8. Safety laboratory results (hematology, clinical chemistry) measured via blood samples at screening and Day 180

Completion date
28/04/1994

Eligibility

Key inclusion criteria
1. Informed consent in accordance with applicable laws
2. Age at least 30 years, no older than 75 years
3. Patients who had experienced an ischemic event (transient or insult type) in the vertebrobasilar supply area. Unambiguous localization of the ischemia based on clinical symptoms or computed tomography or magnetic resonance tomography
4. Vertigo and/or imbalance still present permanently or in form of recurrent attacks
5. Vertigo score (derived from frequency, duration an severity) at least 5
6. Additional criterion for patients to be diagnosed with cognitive impairment: abnormally low performance in at least one of three cognitive tests (Short Test of General Intelligence, KAI, at least 10% loss; Auditory Verbal Learning Test, AVLT, less than 8 points in the 5th cycle; Mosaic Test, less than 15 raw points

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
40

Key exclusion criteria
1. Participation in another experimental drug trial at the same time or within the past 4 weeks before the baseline visit
2. Pregnancy or breastfeeding
3. Age below 30 years
4. Peripheral vestibular vertigo, as assessed by the caloric labyrinth test (if the difference of maximal velocity of slow nystagmus phases is more than 25% of the sum of the means under cold and hot stimuli) or head-shaking nystagmus (if provokable) or vestibulo-ocular reflex, VOR (if gain at high-frequency stimulation (e.g. Halmagy test) not bilaterally normal)
5. Vertigo/dizziness of cardio-vascular origin (clinical signs of decompensated cardiac failure or signs of recurrent periods of tachycardia or bradycardia in EEG which are supposed to affect hemodynamics)
6. Dementia or severe organic brain syndrome which would render the vertigo-related medical history as provided by the patient unreliable
7. Brainstem or cerebellar lesions of a non-vascular origin or impaired brain function due to non-vascular (e.g. metabolic, toxic, inflammatory) causes or intracranial mass
8. Severe vision disorder (visual acuity less than 0.5 on both eyes)
9. Oculomotor dysfunction due to a disorder not covered by the inclusion criteria
10. Chronic alcohol abuse or alcohol dependency
11. Severe cardio-circulatory failure, severe liver or renal failure, severe respiratory failure, advanced neoplasia
12. Gait impairment due to Parkinson syndrome
13. Severe hemiparesis or aphasia

14. Spinal lesion or severe polyneuropathy with impairment of deep sensibility (vibration sensibility at the knees less than 3/8)
15. Continued treatment with rheologically active or perfusion-enhancing drugs, phenytoin, carbamazepine, neuroleptics, benzodiazepines, nootropics, or ant-vertigo agents (e.g. dimenhydrinate, metoclopramide, scopolamine, cinnarizine, flunarizine, diphenhydramine, alizapride, betahistine)
16. Hypersensitivity to Ginkgo biloba extracts

Date of first enrolment
08/04/1992

Date of final enrolment
12/10/1993

Locations

Countries of recruitment
Germany

Study participating centre
Medical University of Luebeck
Department of Neurology
Ratzeburger Allee 160
Luebeck
Germany
23562

Sponsor information

Organisation
Dr Willmar Schwabe (Germany)

ROR
https://ror.org/043rrkc78

Funder(s)

Funder type
Industry

Funder Name
Dr Willmar Schwabe (Germany)

Results and Publications

Individual participant data (IPD) sharing plan
When the trial was conducted, making datasets publicly available was uncommon. Hence, no wording related to this topic was incorporated in the patient information and consent form or the application to the ethics committee. Making data publicly available, even in completely anonymized form, was therefore not covered by patients' consent and ethics committee approval.

IPD sharing plan summary
Not expected to be made available