International Study on Syncope of Uncertain Etiology 3
Pacemaker therapy for patients with asystolic neurally-mediated syncope

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To assess the effectiveness of pacing therapy for preventing syncope recurrence inpatients with a high probability of neurally-mediated syncope different from carotid sinus syndrome.

Ethical review	Approved WMO
Status	Pending
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON30422

Source
ToetsingOnline

Brief title
ISSUE 3

Condition

- Cardiac arrhythmias

Synonym
conscience loss, Dizziness

Research involving
Human

Sponsors and support

Primary sponsor: Vitatron
Source(s) of monetary or material Support: Medtronic

Intervention

Keyword: ISSUE 3, Pacemaker, Reveal Plus, Syncope

Outcome measures

Primary outcome

Primary end-point:

- The time to first syncope recurrence.

Secondary outcome

Secondary end-points:

· ILR findings at the time of syncopal recurrence in the control group

(reproducibility of responses), and

· predictive value of tilt testing.

Study description

Background summary

In asystolic neurally-mediated syncope (NMS) documented by Implantable Loop recorder (ILR), ISSUE-2, an observational trial, showed that pacemaker was effective in reducing the 1-year first syncope recurrence rate from 33% rate before implant (ILR phase 1) to 5% rate after implant (phase 2). Moreover, the control non-asystolic group still continued to have a 41% recurrence rate after the first recurrence of syncope, thus supporting the conclusion that the reduction with pacemaker was due to the beneficial effect of pacemaker itself and not to other factors. However a formal controlled trial is needed to confirm these findings.

Study objective

To assess the effectiveness of pacing therapy for preventing syncope recurrence in
patients with a high probability of neurally-mediated syncope different from carotid sinus syndrome.

Study design

ISSUE 3 is a multi-center, prospective, randomised, double-blind study evaluating the effectiveness of pacing therapy for preventing syncope recurrence in patients with documented spontaneous asystolic neurally-mediated syncope. The patients
undergoing randomisation are identified by ILR diagnostic observations among patients who met the ESC criteria for a diagnosis of suspected neurally-mediated syncope. The strategy requires early application of an ILR, irrespective of tilt testing results (phase 1), and delay of therapy until after ILR documentation of occurrence of an asystolic neurallymediated episode (phase 2)

Intervention

Implantation of Reveal Plus (insertable loop recorder) and possibly implantation of a pacemaker with first doucmented syncope.

Study burden and risks

No additional risks.
In phase I and in phase II the patient is expected to visit the hospital every 3 months, with a maximum duration of 2 years.
In phase I Reveal Plus will be implanted. In phase II the patient might be implanted with a pacemaker.
Both implantations are standard procedures.

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

- Suspected or certain neurally-mediated syncope.
- >3 Syncope episodes in the last 2 years
- Clinical presentation of syncope of sufficient severity requiring treatment initiation in the physician and patient's justment
- Age > 40 year
- Negative caroatid sinus massage

Exclusion criteria

- Carotid sinus hypersensitivity
· Suspected or certain heart disease and high likelihood of cardiac syncope:
- Syncope during exercise;
- Overt heart failure
- Ejection fraction > 40%;
- Old or recent myocardial infarction;
- Hypertrophic cardiomyopathy;
- Dilated cardiomyopathy;
- Significant valvular disease;
- Sinus bradycardia < 50 bpm or sino-atrial block;
- Mobitz I second degree atrioventricular block;
- Mobitz II 2nd or 3rd degree atrioventricular block;
- Bundle branch block;
- Rapid paroxysmal supraventricular tachycardia or ventricular tachycardia;
- Pre-excited QRS complexes
- Prolonged QT interval
- Right bundle branch block pattern with ST-elevation in leads V1-V3 (Brugada syndrome)

- Negative T waves in right precordial leads, epsilon waves and ventricular late potentials suggestive of arrhythmogenic right ventricular dysplasia.
· Symptomatic orthostatic hypotension diagnosed by standing blood pressure measurement;
· Loss of consciousness different from syncope (e.g. epilepsy, psychiatric, metabolic, drop-attack, TIA, intoxication, cataplexy);
· Subclavian steal syndrome;
· Psychologically or physically (due to any other illness) or cognitively unfit for participation in the study according to the opinion of the investigator;

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2006
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Generic name:	Reveal Plus;Implantable Loop Recorder(ILR) and Pacemaker
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Application type:	First submission

Review commission: METC Amsterdam UMC

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
ClinicalTrials.gov	NCT00120094
CCMO	NL14040.018.06