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Tolerability of enhanced external counter pulsation to improve circulation in patients with vascular disease

Submission date	Recruitment status	[ ] Prospectively registered
13/11/2019	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
09/12/2019	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
09/12/2019	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Coronary heart disease is the term that describes what happens when the heart's blood supply is blocked or interrupted by a build-up of fatty substances in the coronary arteries. Numerous clinical studies have shown that external counterpulsation (EPT) relieves symptoms of coronary heart disease (angina pectoris and dyspnea) and reduces the incidence of cardiovascular events.

Who can participate?
Patients aged 18 years or older suffering from systemic atherosclerosis

What does the study involve?
In the lying position, three pairs of pneumatic cuffs are wrapped around the patient’s hip, thighs and lower leg with different pressure settings. Patients are treated with high-pressure counterpulsation for one hour a day for five days, and with low-pressure counterpulsation for one hour a day for five days

What are the possible benefits and risks of participating?
Patients benefit from the study therapy in particular by improvement of endothelial function and vascular regeneration. Possible risks are provided by cuff pressure on tissue (tissue damage) or discomfort

Where is the study run from?
Brandenburg Medical School (MHB)

When is the study starting and how long is it expected to run for?
October 2019 to March 2020

Who is funding the study?
Brandenburg Medical School (MHB)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
Version 1.5 06/08/2019

Study information

Scientific Title
Tolerability of external pulsation therapy by patients with existing symptomatic arterial vascular disease and its effect on microcirculation, kidney function and skeletal muscles at different therapeutic pressure levels

Acronym
EPT-Comfort

Study objectives
The aim of the study is to test how tolerable external pulsation therapy (EPT) is for patients with systemic atherosclerosis (CHD and manifest PAOD), and whether as a result of EPT any measurable change occurs to the microcirculation, as well as whether this effect is dependent on the pressure level.
In addition, the aim is to test whether the conventional treatment (see above) with high-pressure EPT is comparable with low-pressure L-EPT treatment.
A further aim is to clarify whether any possible influence occurs only for a short term or for a long term, and whether it activates the regeneration capacity of the vessels by increasing the shear stress in the leg arteries, and stimulates peripheral arteriogenesis to compensate for the PAOD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/09/2019, Ethics Committee Schleswig-Holstein, Germany - Ethikkommission bei der Ärztekammer Schleswig-Holstein, Deutschland (Ethikkommission II, Bismarkstraße 8-12, 23795 Bad Segeberg, Germany; +49 4551 803432; anne.hostmann@aeksh.de), ref: 063/19 II

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Coronary heart disease (CHD), sable angina pectoris with systemic atherosclerosis, constrictions and occlusions of the arterial vessels throughout the body, and therefore also peripheral
arterial occlusion disorder (PAOD), Fontaine stage II.

Interventions
Here we test the effect of low pressure external pulsation therapy (100 - 160 mmHg) in comparision to high pressure external pulsation therapy (250 - 280 mmHg) on 20 patients suffering from systemic atheroslerosis, coronary heart diseases and peripheral artery disease (Stadium II). In a randomized cross over trial patients are treated with high pressure counterpulsation for one hour a day for five days, and with low pressure counterpulsation each day for five days. Quality of life, microcirculation, hemolysis, myolysis, and kidney function parameters are analysed in the following. Both methods (high and low pressure pulsation therapy) are tested for compatibility, safety, and qualitiy of life.

Medicinal product (Renew, NCP-5):
External leg cuffs with ECG-controlled variable compressed air compression equipment (principle of external pulsation therapy).
Two therapeutic sequences (phases):
1. Low-pressure external pulsation therapy (EPT) with limited therapeutic pressure (corresponding to average arterial pressure) for 60 min on 5 successive days. n = 20
2. High-pressure EPT (EECP = enhanced EPT) with conventional therapeutic pressure (250–280 mmHg) for 60 min on 5 successive days. n = 20

Progression:
1. Visit 1 - Recruitment
2. Visit 2 - Baseline Analysis
3. Randomization (using an online randomization tool)
4. Start either high-pressure EECP or low-pressure EPT. Therapy 1. Total duration therapy: 5 days (one week) for 1h each day
5. 7 days break
6. Visit 3: Laboratory and Questionaire
7. Therapy 2: Start either low-pressure EPT or high-pressure EECP (cross-over design. Start with

the other possible therapy): total duration therapy: 5 days (one week) for 1h each day
8. 3 days break
9. Visit 4: Laboratory and Questionaire
10. End of study

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Renew, NCP-5

Primary outcome(s)
Quality of Life measured using German IGZ Quality of Life Standard Questionnaire at baseline (visit 2), visit 3, and visit 4

Key secondary outcome(s)
Measured at Visit 2 (baseline), 3rd and 5th days in the first therapy phase of the study, 1st 3rd and 5th day of the second therapy phase and Visit 4 (3 days post last intervention).
1. O2C measurement under external counterpulsation therapy treatment measured using LEA Medizintechnik Giesen (Units and % oxygen)
2. Changes to perfusion of tissue (blood flow verlocity, blood filling of micro vessels, capillary sinus oxygen saturation)
3. Serum:
3.1. Creatinine (mg/dl) using the enzymatic method
3.2. Urea (mg/dl) using photometry
3.3. LDH (U/l) using photometry
3.4. Myoglobin (µg/l) using Sandwich Immunoassay
3.5. Creatine Kinase (g/g) using the enzymatic method
3.6. Potassium(mmol/l) using ion-selective electrode (ISE)
3.7. Lactate (mmol/l) using photometry
4. Urine: sediment (mg/dl), protein (g/g), protein/creatinine ratio measured using the laboratory standard of City Clinic Husum, Germany or Dr. Limbach Laboratory Heidelberg, Germany, and the Clinic of Kiel, Germany

Completion date
31/03/2020

Eligibility

Key inclusion criteria
1. Age ≥ 18 years
2. Generalised atherosclerosis with at least one diseased vessel section
3. Coronary heart disease (CHD), stable angina pectoris with systemic atherosclerosis = PAOD Fontaine stages II–IVa
4. Already treated with ASA + statin therapy for at least 3 months

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Abdominal aortic aneurysm > 4.5 cm
2. Cardiac arrhythmias or atrial fibrillation
3. Acute deep vein thrombosis of the lower limbs or vein thrombosis <3 months
4. Cardiac insufficiency NYHA III + IV
5. LVEF <20 per cent
6. Dementia or severe cognitive function disturbances with inability to understand the meaning and context of the clinical study
7. Spastic paralyses, hemiplegia or any other neurological-orthopaedic disorder that makes adequate treadmill measurements impossible
8. Medium severe aortic valve insufficiency > II° + mitral valve insufficiency ≥ III°
9. Uncontrolled hypertension > 180/100 mmHg
10. FEV1 <1.5 L
11. Abnormal laboratory parameters at visit 1:
11.1. Glomerular filtration rate (GFR) <30 ml/min/1.73 m2
11.2. Haemoglobin <10 g/dl
11.3. Serum liver enzymes (ASAT, ALAT, GGT) > 3x normal value
12. Severe drug addiction, excepting stable nicotine abuse in the past six months
13. Simultaneous participation in another clinical study, excepting non-interventional studies
14. PAOD in stages 1 and IVb

Date of first enrolment
01/10/2019

Date of final enrolment
01/01/2020

Locations

Countries of recruitment
Germany

Study participating centre
Interdisziplinäres Gefäßzentrum Nord (Interdisciplinary Vascular Center)
Erichsenweg 16

Husum
Germany
25813

Sponsor information

Organisation
Interdisziplinäre Gefäßzentrum Nord

ROR
https://ror.org/02rppq041

Funder(s)

Funder type
Government

Funder Name
Brandenburg Medical School (MHB)

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date