ISRCTN88693704 https://doi.org/10.1186/ISRCTN88693704

The effect of Individual Shear Rate Therapy and treadmill running exercise on the activation of molecular markers (bradykinin receptors and downstream NO metabolites and telomerase activity) on circulating peripheral leukocytes

Submission date 17/02/2014	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 09/05/2014	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 02/02/2015	**Condition category** Circulatory System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims

Cardiovascular occlusive diseases (heart disease) are the most common cause of death and lasting disabilities. Physical exercise and passive training such as Individual Shear Rate Therapy (ISRT) are effective for prevention and treatment of cardiovascular diseases. Here, we are carrying out a study of 26 young healthy volunteers to compare passive training (ISRT) to active treadmill running (exercise). It is our aim to shed light on how ISRT and exercise positively affect physiological and blood parameters.

Who can participate?

This study aims on recruiting 26 subjects (men and women), age 18 - 35 years, enrolled at the University Medical Centre at the Charité Berlin, Germany. Subjects need to be healthy without any known disorder or current medication (except for oral contraceptives).

What does the study involve?

Volunteers will be randomly allocated to undergo ISRT treatment followed by treadmill running, or undergo the same procedures in the reverse sequence. ISRT treatment and treadmill running will be performed on two different dates within an interval of one week. In order to undergo ISRT the volunteers rest on a couch and pneumatic cuffs are applied to the lower and upper thighs. The device is connected to a monitor for evaluation of heart rate. Treadmill running is done with automatic adjustment of the heart rate to 120-130 bpm.

What are the possible benefits and risks of participating?

The results of the clinical examinations may aid in the diagnosis of heart disease. ISRT and treadmill running are suspected to be beneficial for patients' heart health. The results of this study may help improve our understanding of how ISRT improves heart health. ISRT has been shown to be safe. Side effects include skin redness and muscular pain. Therefore, trial

participants will be offered to wear protective pants underneath the cuffs. The Berlin ISRT centre has used these and successfully avoided the abovementioned side effects. Blood-taking will be carried out with the following well-known potential side-effects: bruising, bleeding, infection, tissue lesions, pain.

Where is the study run from?
Charité Universitätsmedizin Berlin, Campus Virchow together with the Experimental and Clinical Research Center (ECRC), Berlin, Germany.

When is the study starting and how long is it expected to run for?
The study will run from March to June 2014.

Who is funding the study?
Charité Universitätsmedizin Berlin (Germany).

Who is the main contact?
Dr. med. Eva-Elina Buschmann
eva_elina.buschmann@charite.de

Contact information

Type(s)
Scientific

Contact name
Dr EvaElina Buschmann

Contact details
Chartié - Campus Virchow Klinkum
Augustenburger Platz 1
Berlin
Germany
13353

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
A prospective controlled trial to evaluate the effect of Individual Shear Rate Therapy and treadmill exercise on leukocyte molecular marker expression on DNA, RNA and protein level

(bradykinin receptors, telomerase activity, NO metabolites) as well as on physiological parameters (relative Pulse Slope Index) to evaluate the efficiency of training

Acronym
ISRT I

Study objectives
It is hypothesised that treadmill running and an equivalent dose of individual shear rate therapy (ISRT) increases expression of molecular markers in leukocytes, in particular bradykinin receptor 1 (B1R) and bradykinin receptor 2 (B2R) expression and components of the kallikrein-kinin system, as well as downstream effects, such as NO plasma level increase and enhanced telomerase activity among others. ISRT and exercise triggers RNA expression adjustment in leukocytes and improves the relative Pulse Slope Index (rPSI) relevant for vascular remodelling (arteriogenesis). The null hypothesis is that there will be no difference in theses parameters when comparing samples taken prior or after treatment of the ISRT and the treadmill running.

On 02/02/2015 the trial record was updated to change all references to Personal Shear Rate Therapy (PSRT) to Individual Shear Rate Therapy (ISRT).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Charité University Medical Centre Berlin Ethics Committee, 15/08/2013, ref: EA2/108/13

Study design
Open comparative randomized controlled prospective clinical pilot study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Cardiovascular ischemia

Interventions
The study will involve 26 young healthy volunteers, 18-35 years of age, who are willing to be assigned to any of the study intervention schemes, recruited at the Charité - University Medical Center Berlin, CVK, Berlin, Germany. Participation will be over a one-week period (until last

intervention). Participants will be randomly assigned to undergo ISRT treatment followed by treadmill running, or undergo the same procedures in inverted sequence. ISRT treatment and treadmill running will be performed on two different dates within an interval of one week.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. Leukocyte bradykinin receptor expression patterns (B1R/B2R) measured by qRT-PCR
2. Leukocyte telomerase activity measured by telomeric repeat amplification protocol (TRAP)
3. Plasma NO levels measured by an assay using gries-reagent
4. Relative Pulse Slope Index (rPSI) measured by ultrasound
5. Electrical cardiometry ('Window to the heart' Osypka Medical GmbH)

Each outcome will be measured directly before and after exercise and ISRT. Likewise, for molecular analysis, volunteer blood samples are collected before and after exercise and ISRT.

Secondary outcome measures
1. Kallikrein-Kinin system molecule quantification Kininogen, Kallikrein, ACE
2. Molecular parameters such as protein expression analysis, DNA analysis, RNA expression quantification of leukocyte subpopulation markers (M1/M2 macrophage marker, Toll-like receptor TLR2/TLR4, shelterin components [TRF1, TRF2], TERT, G-CSF/GM-CSF receptor, endothelial progenitor cell marker CD133, CD34, and VEGFR-2 as well as CCR2 and ligand MCP-1), NO plasma levels, and plasma secretome analysis for endothelial monoculture, as well as endothelial cell and smooth muscle cell co-culture assays before and after ISRT vs control. Measured by qRT-PCR, western blot or ELISA, respectively

Each outcome will be measured directly before and after exercise and ISRT. Likewise, for molecular analysis, volunteer blood samples are collected before and after exercise and ISRT.

Overall study start date
01/03/2014

Completion date
01/06/2014

Eligibility

Key inclusion criteria
1. Age 18-35
2. Willing to be assigned to any of the study intervention schemes

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
35 Years

Sex
Both

Target number of participants
26

Key exclusion criteria
1. Smoking
2. Relevant cardiovascular, endocrine or psychological disease
2.1. Hearing defects
2.2. Cardiomyopathy
2.3. Thrombo-embolic events
2.4. Arterial hypertension
3. Metabolic disorders
3.1. BMI >30
3.2. Diabetes mellitus
3.3. Lipometabolic disorders
4. No current treatment (except for oral contraceptives)
5. Pregnancy

Date of first enrolment
01/03/2014

Date of final enrolment
01/06/2014

Locations

Countries of recruitment
Germany

Study participating centre
Chartié - Campus Virchow Klinkum
Berlin
Germany
13353

Sponsor information

Organisation
Charité Berlin Center for Cardiovascular Research (CCR) (Germany)

Sponsor details
c/o Dr. rer. nat. Philipp Hillmeister
Richard-Thoma-Laboratories for Arteriogenesis Research
AG Buschmann
Hessische Straße 3-4
Berlin
Germany
10115

Sponsor type
University/education

Website
http://www.ccr.charite.de/en/about_us/

ROR
https://ror.org/001w7jn25

Funder(s)

Funder type
University/education

Funder Name
Charité Universitätsmedizin Berlin (Germany)

Alternative Name(s)
Medical School - Charité - University Medicine Berlin

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration