Functional sympatholysis in heart failure: role of reactive oxygen species

Published: 01-10-2013
Last updated: 24-04-2024

The primary aim of this project is to examine the impact of heart failure on functional sympatholysis. The second aim of this study is to examine whether nitrate supplementation can improve the effects of functional sympatholysis in heart failure.

Ethical review	Not approved
Status	Will not start
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON38976

Source
ToetsingOnline

Brief title
Functional sympatholysis in heart failure

Condition

- Heart failures

Synonym
decompensatio cordis, heart decompensation, heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Beetroot juice, Functional sympatholysis, Heart failure, Reactive oxygen species

Outcome measures

Primary outcome

magnitude of decline in the combined oxygenated hemoglobin (HbO2) and myoglobin (MbO2) signal from the near-infrared spectroscopy during the cold pressor test at rest and during handgrip exercise at 10 and 30% MVC combined with the cold pressor test.

Secondary outcome

- Brachial artery blood flow (using non-invasive ultrasound as a secondary measure of exercise-induced blood flow during handgrip and performance of the cold pressor test)
- Mean arterial blood pressure (Nexfin, contra-lateral arm) (to control for potential differences in the blood pressure response between the subsequent tests)
- Forearm blood flow using plethysmography (contra-lateral arm)

Study description

Background summary

Heart failure is associated with poor prognosis and high levels of morbidity and mortality. Despite of improvements in pharmacological therapy, the prognosis in heart failure patients remains poor. Exercise training significantly improves symptoms and prognosis in heart failure. However, heart failure is associated with poor exercise tolerance, characterized with an imbalance between matching blood supply to oxygen demand. This importantly limits the benefits of exercise training in subjects with heart failure.
The sympathetic nervous system importantly contributes to successful

redistribution of blood during exercise by causing a strong vasoconstriction in the inactive areas. Simultaneously, the constriction in the active areas is attenuated, leading to an increased blood flow to the active muscles. This process is commonly referred to as functional sympatholysis and contributes to successful matching of the oxygen supply to demand of blood. Altered functional sympatholysis may leads to an impaired redistribution of blood during exercise, consequently contributing to poor exercise tolerance. Whilst previous studies reported an impaired functional sympatholysis in subjects with cardiovascular risk (e.g. hypertension), no previous study in humans examined the impact of heart failure on functional sympatholysis.
Previous data provided evidence that an increased production of reactive oxygen species contributes to the impaired functional sympatholysis in animals with heart failure. To study this hypothesis in humans, we will examine whether dietary nitrate supplementation using beetroot juice (a successful intervention to lower oxidative stress) can alter functional sympatholysis in humans with heart failure.

Study objective

The primary aim of this project is to examine the impact of heart failure on functional sympatholysis. The second aim of this study is to examine whether nitrate supplementation can improve the effects of functional sympatholysis in heart failure.

Study design

Cross-over intervention trial

Day 1 (1h)
• Medical screening

Day 2/3 (3h, beetroot juice or placebo ingested 2.5h before the test)
• Determination of MVC
• Venous blood sampling
• 10-minute forearm occlusion, measurement of maximal tissue desaturation/oxygen consumption
• Resting period of >20 minutes in the supine position
• 5-minute baseline measurement of blood pressure, forearm muscle oxygenation and brachial artery diameter and red blood cell velocity
• 6-minute period of continuous assessment of blood pressure, forearm muscle oxygenation and brachial artery diameter and red blood cell velocity + cold pressor test at minutes 4 and 5.
• Resting period of >20 minutes in the supine position
• 5-minute baseline measurement of blood pressure, forearm muscle oxygenation and brachial artery diameter and red blood cell velocity
• 6-minute period of continuous assessment of blood pressure, forearm muscle

oxygenation and brachial artery diameter and red blood cell velocity during handgrip exercise (0.5 Hz, metronome-assisted) at 10% MVC + cold pressor test at minutes 4 and 5.
• After a resting period of >20 minutes, the above 2 steps are repeated with handgrip exercise at 20 or 30% MVC. The order of handgrip exercise performance (10, 20 and 30% MVC) will be randomised between subjects.

Intervention

For the second aim, we will administer dietary nitrate through beetroot juice.

Study burden and risks

Performance of handgrip exercise in healthy individuals or in those with heart failure is not associated with a health risk. Also, our non-invasive techniques (NIRS, ultrasound) and interventions (cold pressor test, beetroot juice) are not associated with a health risk.
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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

Patients:
- Patients diagnosed with heart failure NYHA class II/III
- >= 18 years of age
- Mentally able/allowed to give informed consent;Controls:
- Subjects free of cardiovascular disease and/or cardiovascular medication
- >= 18 years of age
- Mentally able/allowed to give informed consent

Exclusion criteria

Controls:
Cardiovascular disease
The use of cardiovascular medication

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	24
Type:	Anticipated

Ethics review

Not approved

Date:	01-10-2013
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	NL45869.091.13