Mechanisms of Remote Ischaemic PreConditioning in humans

Published: 23-02-2012
Last updated: 30-04-2024

To further investigate the application in a clinical setting we aim to set up a model in which we can investigate the protective effects in an in vitro model, where subjects blood serum is used to transfer the protective effect of RIPC onto cells...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON37484

Source
ToetsingOnline

Brief title
Me-RIPC in vitro

Condition

- Coronary artery disorders
- Vascular injuries

Synonym
organprotection

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Conditioning, Heart, Ischemia, organprotection

Outcome measures

Primary outcome

The primary endpoint of this study will be apoptosis, caspase 3/8/9 activity

and LDH release measured at different time points in our in vitro models.

Secondary outcome

The secondary endpoints will be targets that will be analyzed from the

Reperfusion Injury Salvage Kinase (RISK) pathway.

Study description

Background summary

Cardiovascular events such as acute myocardial infarction and stroke are the main cause for morbidity and mortality in western countries. Although early reperfusion strategies improved the outcome for patients undergoing surgery, most patients suffer from significant tissue damage due to the burden of ischaemia/reperfusion (I/R).

The phenomenon of ischaemic preconditioning (IPC), an experimental treatment for producing resistance to the loss of sufficient oxygen to the tissue, is one of the most potent innate protective mechanisms against ischaemia/reperfusion injury.
Remote ischaemic preconditioning (RIPC), brief periods of induced peripheral ischaemia, was first described in 1993 by K. Przyklenk Data implied that preconditioning may be mediated by factor(s) activated, produced, or transported throughout the heart during brief I/R. The exact mechanism is not clear.

Conversely, in spite of protective effects verifiable in several experimental models, the practical hitches in the implementation of IPC had limited the clinical applications.
From a clinical perspective, RIPC application by repeated short periods of limb ischaemia using a tourniquet is a feasible practical approach. Clinical trials in healthy volunteers using inflation of a blood cuff for three times five

minutes show promising effects.

Study objective

To further investigate the application in a clinical setting we aim to set up a model in which we can investigate the protective effects in an in vitro model, where subjects blood serum is used to transfer the protective effect of RIPC onto cells grown in culture. Subsequently, the underlying mechanisms can be studied up-close.

Primary Objective: The primary objective of this study is to investigate if we can set-up an in vitro model to study RIPC up-close, by studying if remote ischaemic preconditioning can reduce apoptosis, caspase 3/8/9 activity and the leakage of lactate dehydrogenase (LDH), often used as a marker of tissue breakdown and a harbinger of future cell death.

Secondary Objective(s): The secondary objective of this study is to investigate possible mechanisms inducing RIPC by studying changes in the Reperfusion Injury Salvage Kinase (RISK)-Pathway, including prosurvival kinases, such as Akt and Erk1/2.

Study design

The study will be designed as a researcher blinded study. The PhD student executing the in vitro protocols in our laboratory will not give the subject the investigational intervention, or do the blood sampling.

The investigational intervention is a remote ischaemic conditioning stimulus.

Intervention

The investigational intervention is a remote ischaemic conditioning stimulus. Hereto, a pressure cuff will be placed on the upper arm and inflated to 200 mmHg for five minutes. Then, pressure will be released during five minutes allowing reperfusion, after which the cycle will be repeated three more times for a total of four cycles.

Blood will be sampled on three time points (figure 1); one baseline sample and two samples after RIPC. Each blood withdrawal will be taken by a separate venous puncture performed by a physician with extensive experience in this field, such as an anesthesiologist.

Blood withdrawal will take place at three time points, per time point 22cc blood will be sampled, after centrifugation (to separate cells from the serum) approximately 12cc serum will be left to do the in vitro experiments. In total,

the volunteer gives 66cc blood.

Study burden and risks

The investigational treatment, remote ischaemic conditioning, is in itself a safe intervention. Subjects can experience slight discomfort during inflation of the tourniquet around their upper arm.

Blood withdrawal can also give a slight discomfort. This will take place at three timepoints, per timepoint 22cc blood will be sampled, after centrifugation (to separate cells from the serum) approximately 12cc blood serum will be left to do the in vitro experiments.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1100 DD Amsterdam Zuid-Oost
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1100 DD Amsterdam Zuid-Oost
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Healthy, male volunteers aged 18-45 years.

Exclusion criteria

Cardiovascular diseases, Alcohol or drug abuse, Fibrinolytic treatment in the previous 30 days, Usage of the anti-diabetic drug glibenclamide (this drug is known to block any conditioning effect).
Doing any kind of sports on the night before the experimental day in the AMC

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-06-2012
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	23-02-2012
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
CCMO	NL38188.018.11