BLO2D Unlimited
The effect of repeated exercise at high altitude on blood coagulation

Published: 01-06-2017
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To investigate the effect of monitored strenuous exercise at high altitude on blood coagulation, more specifically on thrombin generation, platelet function and fibrinolysis.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON45638

Source
ToetsingOnline

Brief title
BLO2D Unlimited

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Embolism and thrombosis

Synonym
blood coagulation disorders, hypercoagulability

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W,Synapse Research Institute

Intervention

Keyword: Blood coagulation, High altitude, Physical exercise, Thrombosis

Outcome measures

Primary outcome

Thrombin generation in platelet poor plasma (PPP), platelet rich plasma (PRP)

and whole blood (WB).

Secondary outcome

- Plasmin generation

- Platelet function test

- Thromboelastometry

- Blood count

- Fibrinolysis (clot lysis time)

- Coagulation factor analysis: von Willebrand factor (vWF), factor 8 (FVIII),

D-dimers

- Biochemical markers: lactate, creatinine, urea, albumin

Other outcome parameters:

- Age

- Vital signs (heart rate and SpO2)

- Blood pressure

- Questionnaire (AMS)

Study description

Background summary

In The Netherlands, 2.9 per 1000 men and 1.7 per 1000 women per year suffer from acute coronary syndrome (ACS), and in 4-10% of ACS cases, the patient had exercised vigorously within 1 hour before onset. Strenuous exercise activates blood coagulation, mostly due to elevated platelet count, platelet hyperreactivity, increased thrombin generation and increased activity of several coagulation factors, especially factor 8 (FVIII) and von Willebrand factor (vWF). We corroborated these findings recently when testing healthy subjects during an amateur bike race. The hypercoagulability may cause the formation of coronary thrombi, provoking ACS.
Mountaineering also appears to pose a risk for developing thrombosis. Healthy lowlanders moving to high altitude for a mean duration of 10 months were found to have a 30 times increased risk of developing a venous thromboembolism (VTE). Similarly, healthy soldiers stationed at high altitude were characterized by an almost 25-fold increased risk of developing deep calf vein thrombosis. There are little reports on the prevalence of coronary thrombosis or cerebrovascular ischemia at high altitude. Our group recently investigated the effect of hypobaric hypoxia on coagulation, by ascending from 50m to 3900m above sea level. One group climbed actively and one group ascended passively by bus, train and cable car. Blood samples were taken at different altitudes. Thrombin generation measured in whole blood proved to rise with increasing altitude. This indicates that hypobaric hypoxia at high altitude causes hypercoagulability, irrespective of the exercise, and may contribute to the occurrence of thrombosis.
Mountaineering usually involves repeated strenuous exercise, when walking, climbing, skiing or cycling. Because hypoxia and exercise both cause procoagulant changes, one might expect that exercise will amplify the altitude-induced hypercoagulability. This would put susceptible individuals at more risk of developing ACS. However, in a small study in 2004 it was found that hypoxia actually attenuates the exercise-induced procoagulant changes. More specifically, an augmented fibrinolytic response, measured by absence of plasmin activator inhibitor (PAI-1) elevation was found. Additionally, recently our group performed a pilot study, subjecting healthy volunteers to strenuous exercise during 3 consecutive days. We found that exercise indeed induces procoagulant changes, but that these were attenuated during the repeated exposure [not published]. These findings prompt further research.
Our group is specialized in measuring markers of coagulation in unusual circumstances, for instance during high altitude expeditions or during cycling competitions. Furthermore, we have recently developed an assay for measuring plasmin generation [not published]. Plasmin is responsible for breaking down the fibrin network (fibrinolysis). Using the specific knowledge and know-how of our lab, we will further unravel the effect of hypoxia combined with repeated strenuous exercise on blood coagulation.

Study objective

To investigate the effect of monitored strenuous exercise at high altitude on blood coagulation, more specifically on thrombin generation, platelet function and fibrinolysis.

Study design

6 healthy male volunteers, 18 - 50 years old, will exert strenuous exercise (measured by a heart rate reserve of 60-85%) during 2 hours on an exercise bike, both at sea level (normoxia) and at 3,883 m above sea level (hypobaric hypoxia), which will be repeated on 3 consecutive days. Blood samples will be drawn just before and immediately after the exercise.
Between the baseline exercise test at sea level and the hypoxic exercise tests, volunteers will acclimatise to the altitude for 5 days according to a fixed schedule.

Intervention

Strenuous physical exercise during 2 hours on an exercise bicycle at 4,000 m above sea level. The heart rate will be monitored during the exercise and targeted at a heart rate reserve of 60 to 85%. The exercise test will be repeated on 3 consecutive days.

As a control, participants will undergo the same exercise test at sea level once.

Study burden and risks

- All volunteers will undergo an exercise stress test by a cardiologist prior to the start of the study, to ensure that all participants are physically healthy.
- Eight blood samples of 27 ml each will be drawn, which poses a risk of developing a local bruise or hematoma.
- Mountaineering poses a risk of developing acute mountain sickness (AMS), a clinical syndrome ranging from dizziness, nausea and lethargy to ataxia, vomiting and unconsciousness. Participants will be accompanied by at least 1 medical doctor at high altitude and emergency care will be delivered if necessary. Symptoms of AMS will be screened for daily by using the Lake Louise AMS questionnaire. An experienced mountain guide will be present. Participants will be escorted back to sea level immediately if AMS symptoms are present.

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

- Healthy male volunteer
- Age between 18 and 50 years old

Exclusion criteria

- Previous history of cardiovascular disease, pulmonary disease, bleeding disorder or venous thromboembolism
- Medication interfering with blood coagulation (low molecular weight heparins, vitamin K antagonists, direct oral anticoagulants, non-steroidal anti-inflammatory drugs)
- Impaired mobility
- Active smoking
- Not passing medical assessment
- Disapproval of contacting general practitioner in case of abnormalities found during medical assessment or during the study.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-06-2017
Enrollment:	7
Type:	Actual

Ethics review

Approved WMO

Date:	01-06-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 29315
Source: NTR
Title:

In other registers

Register	ID
Other	Nederlands Trial Register: NTR6279
CCMO	NL61217.068.17
OMON	NL-OMON29315

Study results

Date completed: 28-06-2017

Actual enrolment: 6

Summary results
Trial is onging in other countries