Blood outgrowth endothelial cells as a patient-derived ex vivo model system to study degranulation mechanisms in storage pool disease

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1. To study the mechanisms that control endothelial and platelet secretion using blood outgrowth endothelial cells (BOECs) as an ex vivo model of endothelial and platelet secretion, in order to identify new regulators of and further unravel their…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Platelet disorders
Study type	Observational invasive

Summary

ID

NL-OMON42746

Source
ToetsingOnline

Brief title
secREtion mechanisms in storage pooL disEASE (RELEASE study)

Condition

- Platelet disorders
- Blood and lymphatic system disorders congenital

Synonym
platelet function disorder, storage pool disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Sanquin ,Sanquin Bloedbank

Intervention

Keyword: blood outgrowth endothelial cells, degranulation mechanisms, mepacrine staining, storage pool disease

Outcome measures

Primary outcome

Secretory responses of SPD platelets and BOECs as compared to healthy platelets

and BOECs.

Defects or abnormalities in Weibel-Palade bodies (WPB) biogenesis of SPD BOECs

as compared to healthy BOECs.

Alterations of SPD whole platelet and BOEC proteomes as compared to already

established healthy platelet and BOEC proteomes

Secondary outcome

Mepacrine uptake and release of platelets of patients with storage pool disease

as compared to healthy platelets

Diagnostic utility of mepacrine uptake and release as compared to ATP/ADP

ratio, electron microscopy, fluorescence microscopy and measurement of dense

granule markers after activation using flow cytometry

Study description

Background summary

Despite the fact that platelet secretion defects are the most common amongst inherited platelet function disorders, little is known about the mechanisms

responsible for platelet exocytosis. We hypothesize that individuals suffering from congenital disorders that result in defective platelet secretory mechanisms, such as presented in storage pool disease (SPD), (also) have aberrant endothelial secretory responses.

Furthermore, there is no consensus about the best laboratory practice for detecting platelet secretion defects and the current available tests have several major limitations.

Study objective

1. To study the mechanisms that control endothelial and platelet secretion using blood outgrowth endothelial cells (BOECs) as an ex vivo model of endothelial and platelet secretion, in order to identify new regulators of and further unravel their secretory mechanisms

2. To investigate if mepacrine staining of platelets can be a robust and accurate laboratory test for diagnosing δ-storage pool disease

Study design

Cross-sectional descriptive study coordinated at the Van Creveldkliniek (VCK) of the University Medical Center Utrecht (UMCU) in collaboration with Sanquin Research, Amsterdam.

Study burden and risks

This study will contribute to the knowledge on the mechanisms that control endothelial and platelet secretion, which will have fundamental importance for our understanding of secretory processes in these but also in other (blood) cell types. Furthermore, we will evaluate a new methodology for detection of platelet secretion defects. The participating patients will not benefit directly from participation. However, the results of this study can lead to new diagnostic tools and/or therapeutic strategies for hemostatic and immunological disorders that are caused by secretory defects. The study consists of one visit to the VCK for venipuncture. Risks imposed by participation are considered negligible.

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

- Age >= 18 years
- Diagnosed with storage pool disease using standard luminoaggregometry

Exclusion criteria

- Inability to give informed consent
- Received a bone marrow or stem cell transplantation

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-05-2016
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	24-02-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL56264.041.15