In vitro COagulation Dynamics of conformational changes in ADAMTS13

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON25418

Source
NTR

Brief title
CODA13

Health condition

None

Sponsors and support

Primary sponsor: None
Source(s) of monetary or material Support: Amsterdam UMC, location AMC

Intervention

Outcome measures

Primary outcome

ROTEM lysis, EXTEM/FIBTEM/ABTEM (i.e. LT, LOT, Li (t), ML, CLR), measured on the day of the blood draw

Secondary outcome

ADAMTS13 plasma determinations (antigen, activity, conformation, degradation)
Plasma turbidity (time to onset, slope, degree)
Whole blood clot lysis, using HALO assay (time to onset, slope, degree),
Platelet activation (CD62P, PAC1), using flow cytometry
Platelet adhesion and aggregation, using flow model (Time to platelet adhesion, aggregation and breakdown of clots, measured using fluorescent live-cell imaging).

*There will be only one blood draw (and thus one timepoint) for the volunteer. All outcomes except the ADAMTS plasma determinations. will be measured on the day of thid blood draw. The ADAMTS13 plasma determinations will be performed on a later moment on frozen plasma obtained from the inital blood draw.

Study description

Background summary

Rationale:
Severely injured trauma patients present in 40% of cases with a trauma-induced coagulopathy, composed of severe platelet dysfunction, coagulation factor consumption and hyperfibrino(geno)lysis. ADAMTS13 is a cleaving enzyme of von Willebrand factor. Its role in coagulation during hyperfibrino(geno)lysis is poorly understood. Our hypothesis is that ADAMTS13 changes its conformation when it is cleaved by plasmin. This study on coagulation effects of conformation changes of ADAMTS13 will be performed in vitro after drawing blood from healthy volunteers.

Objectives:
1. To identify the role of conformational changes of ADAMTS13 in in vitro coagulation tests and flow models
2. To identify the role of plasmin on ADAMTS13 conformation on in vitro coagulation tests

Study design: healthy volunteer observational study

Study population: healthy human male volunteers, 18 - 35 yr old, n=24

Intervention (if applicable): Blood draw (1x)

Main study parameters/endpoints:
End-points are all measured in vitro using the whole blood obtained from healthy volunteers.
1. Amount of hyperfibrino(geno)lysis, conformation status of ADAMTS13, coagulation proteins, platelet surface markers and additionally in flow models endothelial activation markers

Study objective

tPA-induced lysis leads to cleaved ADAMTS13:

a. accelerating fibrin(ogen) breakdown in in vitro coagulation assays
b. leading to impaired platelet adhesion and aggregation in an in vitro flow model

Study design

Not applicable

Intervention

One time blood draw

Contacts

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Eligibility criteria

Inclusion criteria

- Male
- Age 18-35

Exclusion criteria

- Participation in a scientific intervention study in the last 3 months
- No informed consent
- History of coagulation disorders
- Active use of prescription medication
- Use of anticoagulant medication, including aspirin
- History of liver disease
- History of chronic transmittable disease

- History of alcohol, smoking or drug abuse

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	19-01-2021
Enrollment:	12
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	09-01-2021
Application type:	First submission

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
NTR-new	NL9193
Other	METC AMC : METC 2020_171

Study results