Thrombin Generation after Abrupt Cessation versus Weaning over 8 hours of Continuous Infusion of Unfractionated Heparin in ICU-patients after Discontinuation of Continuous Venovenous Hemofiltration (CVVH).

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The objective op this study is to answer the following questions:-Is thrombin generation increased after abrupt cessation of intravenous unfractionated heparin after discontinuation of CVVH?-Is there a difference in increase in thrombin generation...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON29772

Source
ToetsingOnline

Brief title
Heparin Rebound

Condition

- Other condition

Synonym
prevention of thrombosis, thrombosis prophylaxis

Health condition

preventie van thrombose

Research involving
Human

Sponsors and support

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

Intervention

Keyword: coagulation, fibrinolysis, heparin-rebound

Outcome measures

Primary outcome

Markers of coagulation and fibrinolysis:

aPTT, anti-Xa, factor VII/VIIa, TF, TFPI-antigen, TFPI activity, protein C /

activated protein C, prothrombine fragment 1.2, TATc, ETP (Endogenous Thrombin

Potential), Fibrin monomers, soluble thrombomodulin, PAPc, PAI.

Secondary outcome

-

Study description

Background summary

The F1K-MC-EVBR-trial (Xigris and Prophylactic hEparin in Severe Sepsis: XPRESS) study demonstrated that adult patients with severe sepsis receiving drotrecogin alfa (activated) with concomitant heparin treatment had an absolute 28 day mortality reduction of 3.6% compared to treatment with drotrecogin alfa (activated) combined with placebo. Evaluation of subgroups showed that patients receiving heparin at baseline who are assigned to treatment with placebo have a higher 28-day mortality (35.6%) and a higher incidence of venous thromboembolism (VTE) and other serious (thrombotic) adverse events than patients receiving heparin at baseline assigned to study treatment with heparin (26.9%). Patients who did not receive heparin previous to study enrollment

performed similar to the latter group (placebo 28.9%, study-heparin 29.5%) [unpublished data]. A possible explanation for this difference in mortality and (thrombotic) adverse events could be that thrombin generation is increased as a result of discontinuing heparin treatment.

Our hypothesis is that rebound thrombin generation occurs in ICU-patients after abrupt cessation of heparin treatment in terms of elevation of coagulation-markers and reduction fibrinolysis-markers. IV weaning of heparin reduces this rebound thrombin generation.

Study objective

The objective op this study is to answer the following questions:
-Is thrombin generation increased after abrupt cessation of intravenous unfractionated heparin after discontinuation of CVVH?
-Is there a difference in increase in thrombin generation after abrupt cessation of heparin versus intravenous weaning over a period of 8 hours?

Study design

Prospective, randomized study.

Intervention

In one group of patients Heparin infusion will be stopped simultaneous to stopping of CVVH.
In the other group of patients UFH infusion will be reduced to 50% from the previous infusion rate. After 4 hours the infusion rate will be reduced again by 50% (25% of original infusion rate) and discontinued 4 hours later. Blood samples will be taken at specific intervals to evaluate thrombin generation.

Study burden and risks

The risks associated with participation are minimal. Bloodsamples (7 x 10 ml) will be taken from an already present arterial catheter and IV administration of heparine will be either stopped or continued for 8 hours in a medical-surgical ICU setting in an academic hospital. This prolonged administration of heparin increases bleeding risk.
No direct benefit for the individual patient is to be expected from participation however extending the knowledge of the effects of heparin on ICU patients could benefit the entire patient group.

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 scheduled to stop treatment with CVVH because they no longer require it (physicians discretion / local protocol)
Age >18 years
At least 48 hours of CVVH treatment with concomitant continuous infusion of UFH
At least 36 hours of continuous UFH infusion in the last 48 hours prior to inclusion

Exclusion criteria

Patients with known coagulation disorders
Patients receiving any anti-coagulant treatment for reasons other than CVVH

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2006
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Heparin
Generic name:	Unfractionated Heparin
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	22-08-2006
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
EudraCT	EUCTR2006-003128-12-NL
CCMO	NL12899.018.06