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.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21886

Source
NTR

Brief title
Heparin Rebound

Health condition

Aburpt cessation of continuous intravenous treatment with Unfractionated Heparin.

Sponsors and support

Primary sponsor: none
Source(s) of monetary or material Support: Academic Medical Centre Intensive Care

Intervention

Outcome measures

Primary outcome

Thrombin-Antithrombin complexes (TATc).

Secondary outcome

aPTT, anti-Xa, factor VII/VIIa, TF, TFPI-antigen, TFPI activity, protein C / activated protein C, aPC-sr, prothrombine fragment 1.2, ETP (Endogenous Thrombin Potential), Fibrin monomers, soluble thrombomodulin, PAPc, PAI.

Study description

Background summary

Background:

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heparin previous to study enrollment performed similar to the latter group (placebo 28.9%, study-heparin 29.5%) [unpublished data].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.

Objective:

The objective op this study is to investigate whether thrombin generation is increased after

abrupt cessation of intravenous unfractionated heparin (UFH) after discontinuation of CVVH. We further want to establish if there is a difference in thrombin generation after abrupt cessation of heparin versus intravenous weaning over a period of 8 hours.

Study design:

Prospective, randomized placebo-controlled, double blind study.

Study polulation:

Patients scheduled to stop treatment with CVVH because they no longer require it. (physicians discretion/local protocol).

Intervention:

One group of patients will start treatment with placebo simultaneous to stopping of CVVH at infusion rate similar to previous UFH infusion. Placebo will be stopped after 8 hours.

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 parameters:

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.

Study objective

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 design

N/A

Intervention

Therapeutic protocol:

Prophylactic LMWH will not be given within 24 hours of discontinuation of CVVH. Patients are treated with help of standard guidelines effective in our units. The full medical treatment will be under the discretion of the supervising staff-intensivists who are not directly involved in the study.

Study protocol:

Randomization will take place using sealed envelopes:

1. In 10 patients UFH infusion will be stopped simultaneous to stopping of CVVH.

2. In 10 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 (see below) to evaluate thrombin generation.

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Eligibility criteria

Inclusion criteria

1. Patients scheduled to stop treatment with CVVH because they no longer require it (physicians discretion/local protocol);

2. Age >18 years;

3. At least 48 hours of CVVH treatment with concomitant continuous infusion of UFH;

4. At least 36 hours of continuous UFH infusion in the last 48 hours prior to inclusion.

Exclusion criteria

1. Patients with known coagulation disorders;

2. 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)
Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2006
Enrollment:	20
Type:	Actual

Ethics review

Positive opinion Date:	02-08-2006
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	NL732
NTR-old	NTR742
Other	: 0001
ISRCTN	ISRCTN33216118

Study results

Summary results
N/A