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.

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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21886

Bron
NTR

Verkorte titel
Heparin Rebound

Aandoening

Aburpt cessation of continuous intravenous treatment with Unfractionated Heparin.

Ondersteuning

Primaire sponsor: none
Overige ondersteuning: Academic Medical Centre Intensive Care

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Thrombin-Antithrombin complexes (TATc).

Toelichting onderzoek

Achtergrond van het onderzoek

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heparin previous to study enrollment performed similar to the latter group (placebo 28.9%, study-heparin 29.5%) [unpublished data].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

Doel van het onderzoek

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.

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

Academic Medical Center (AMC)
IC Unit,
P.O. Box 22660
J.J. Hofstra
Meibergdreef 9
IC Unit, C3-423
Amsterdam 1100 DD
The Netherlands
+31(0)20 5668224

Wetenschappelijk

Academic Medical Center (AMC)
IC Unit,
P.O. Box 22660
J.J. Hofstra
Meibergdreef 9
IC Unit, C3-423
Amsterdam 1100 DD
The Netherlands

+31(0)20 5668224

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Patients with known coagulation disorders;

2. Patients receiving any anti-coagulant treatment for reasons other than CVVH.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland
Status: Werving gestopt

(Verwachte) startdatum:	01-09-2006
Aantal proefpersonen:	20
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	02-08-2006
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL732
NTR-old	NTR742
Ander register	: 0001
ISRCTN	ISRCTN33216118

Resultaten

Samenvatting resultaten
N/A