Danaparoid dosing during continuous venovenous hemofiltration - a randomized controlled pilot study investigating two danaparoid dosing schemes with a standard heparin dosing scheme

Published: 18-10-2007
Last updated: 08-05-2024

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Ethical review	Approved WMO
Status	Pending
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON30497

Source
ToetsingOnline

Brief title
Danaparoid CVVH trial

Condition

- Renal disorders (excl nephropathies)

Synonym
acute kindey failure, Acute renal failure

Research involving

Human

Sponsors and support

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

Intervention

Keyword: CRRT, Danapaoid, dosing, ICU-patients

Outcome measures

Primary outcome

*Area under the curve of serial anti-Xa measurements

*Circuit survival time

*Occurrence and severity of bleeding events

Secondary outcome

markers of thrombin generation (e.g. thrombin-antithrombin complexes,

prothrombin fragment F1+2 and endogenous thrombin potential)

Study description

Background summary

Critically ill patients often suffer from low platelet counts or platelet dysfunction. However, this does not obviate the need for systemic anticoagulant treatment in some of these patients. Therefore, anticoagulants with little effect on platelet function are needed in the intensive care unit.
Although extensive experience with danaparoid has been gained in the clinical setting, there is little evidence on its use in patients with acute renal failure, especially in those patients dependent on continuous renal replacement therapy (CRRT). The elimination of danaparoid is predominantly renal and an antidote is lacking. Dosing of danaparoid is based on the guideline of the Dutch Society of Intensive Care Medicine, recommending an intravenous (iv) loading dose ranging from 750 to 2250 U and a dose for continuous infusion ranging from 1- 3 U/kg/h (5). In a small retrospective study however, the

authors conclude that a loading dose of 750 U iv, followed by a maintenance dose of 50-150 U/h iv might be sufficient to maintain an effective and safe level of anticoagulation.

Study objective

The aims of the current study are
1. to investigate the efficacy and safety of a continuous infusion of 'low dose' danaparoid in patients with acute renal failure needing CRRT
2. to investigate whether repeated measurements of anti-Xa levels are necessary for adequate dosing of a continuous infusion of danaparoid used as an anticoagulant in patents with acute renal failure needing CRRT
3. to study a continuous infusion of 'low dose' danaparoid, danaparoid titrated by anti-Xa levels and unfractionated heparin in patients with acute renal failure needing CRRT

Study design

Prospective randomized pilot study

Intervention

After having obtained informed consent, eighteen critically ill patients with acute renal failure needing CRRT will be randomized into 3 groups receiving either danaparoid or unfractionated heparin iv in different dosing schemes:
Group 1: 'Low dose' danaparoid: continuous infusion of 0.6 U/kg/h without a loading dose
Group 2: 'Titrated dose danaparoid': continuous infusion of danaparoid titrated on anti-Xa levels after a loading dose of 9 U/kg, aiming at an anti-Xa level of 0.3-0.7 anti-Xa U/ml
Group 3: 'Heparin control': continuous infusion of 6 U/kg/h unfractionated heparin after a loading dose of 30 U/kg
Anti-Xa levels and markers of thrombin generation (thrombin-antithrombin complexes, prothrombin fragment F1+2 and endogenous thrombin potential) will be measured at the following timepoints: t=0, 5, 15, 30 min, 2, 4, 6, 12, 24, 48 and 72h after the loading dose.

Study burden and risks

The anticoagulant strategies in group 2 and 3 are presently considered standard regimens, whereas the strategy in group 1 is not. However, since group 1 uses a lower danaparoid dose than group 2, less bleeding complications are expected.

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

Critically ill patients with acute renal failure, needing CRRT.

Exclusion criteria

-No informed consent
-Use of unfractionated heparin or low molecular weight heparin in therapeutic doses within 24 hours before enrollment
-Extreme coagulation disorders, such as platelet count < 30 x 109/l, PT > 20 sec or APTT > 80 sec.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2007
Enrollment:	18
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Heparine LEO
Generic name:	Heparin LEO
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Orgaran
Generic name:	Danaparoid
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

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	EUCTR2006-006998-24-NL
CCMO	NL15916.018.07