Fixed versus variable dosing strategy of prothrombin complex concentrate for bleeding complications of vitamin K antagonists

Published: 09-07-2014
Last updated: 20-04-2024

To test whether the clinical outcome of lower fixed dose of PCC is superior to higher variable dose of PCC, for VKA related bleeding in a randomized setting. Secondary objectives include the comparison of INR after administration of PCC, time to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Haematological and lymphoid tissue therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON44764

Source
ToetsingOnline

Brief title
PROPER3

Condition

- Haematological and lymphoid tissue therapeutic procedures

Synonym
VKA related bleeding complication; bleeding

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Ministerie van OC&W,Sanquin

Intervention

Keyword: Bleeding, dosing strategy, Prothrombin complex concentrate, Vitamin K antagonists

Outcome measures

Primary outcome

The main study parameter is successful clinical outcome, defined as cessation of visual bleeding, stable haemoglobin, normalized blood pressure and no further transfusions of PCC or blood products, assessed over 24 hours from end of infusion.

Secondary outcome

- proportion of patients with excellent, good and poor/none haemostatic efficacy
- INR 15-60 minutes after end of infusion of PCC
- proportion of patients reaching INR * 2.0 15-60 min after end of infusion of PCC
- time between admission to emergency room and start of infusion of PCC
- repeated dosing of, total administered dose of PCC
- in-hospital all-cause mortality
- all-cause mortality at 30 days after initial PCC administration
- thrombotic complications (venous thrombosis, pulmonary embolism, myocardial infarction, ischemic stroke) during hospital stay and at 30 days
- duration of hospital stay, number of days in ICU

Study description

Background summary

There is no consensus on the optimal dosing strategy for PCC. In clinical practice, both fixed and variable protocols are used. In an observational, prospective, two-cohort comparison of dosing PCC in bleeding complications of vitamin K antagonists (VKA), we showed that a lower fixed dose was at least as successful from a clinical point of view as a higher variable dose. The lower fixed dose can be administered more quickly, is cheaper and might decrease the risk of thrombotic complications.

Study objective

To test whether the clinical outcome of lower fixed dose of PCC is superior to higher variable dose of PCC, for VKA related bleeding in a randomized setting. Secondary objectives include the comparison of INR after administration of PCC, time to administration, mortality, other complications and drivers of costs.

Study design

Randomized controlled trial in 8 large Dutch hospitals.

Intervention

Patients receive either a fixed dose of 40 cc of PCC, or a variable dose based on INR on presentation, body weight and target INR.

Study burden and risks

Both dosing strategies are used in routine clinical practice. There is no burden for the individual patient regarding the choice of strategy. The risks and/or benefits are related to clinical outcome: a lower fixed dose might be less effective, while the higher variable dose might have a higher risk of side-effects. Given the data already available, these risks are small.
A delayed consent procedure is used, as it is unacceptable to lose valuable time before the start of treatment. This makes it impossible for patients to decline randomization, and therefore poses a burden on patients. Patients can still refuse to participate in the study.
Most of the benefit from the study is applicable to future similar patients. However, patients who present with bleeding on VKA are at increased risk of rebleeding, so a proportion of participants might benefit themselves.

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

Indication for PCC, because of VKA related bleeding;Age * 18 years

Exclusion criteria

Intracranial bleeding
Indication for PCC not related to bleeding
Indication for PCC not related to VKA
Previous participation in the study

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-10-2015
Enrollment:	310
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cofact
Generic name:	prothrombin complex concentrate
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	09-07-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-06-2015
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-11-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-12-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-02-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-04-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-05-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-05-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-12-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-07-2017
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-09-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2014-000392-33-NL
CCMO	NL48407.042.14