Transfusion of fresh frozen plasma in non bleeding ICU patients

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With the aim to restrict inappropriate FFP transfusions to critically ill patients, a randomized clinical trial will be conducted in a subgoup of ICU patients undergoing an invasive procedure. The objective is to assess the effectiveness and costs...

Ethical review	-
Status	Recruitment stopped
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON38043

Source
ToetsingOnline

Brief title
TOPIC trial

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Lower respiratory tract disorders (excl obstruction and infection)
- Therapeutic procedures and supportive care NEC

Synonym
coagulopathy, impaired clotting

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Adverse effects, Coagulopathy, Fresh frozen plasma, Intensive care

Outcome measures

Primary outcome

The primary outcome of this study will be a procedure-related relevant bleeding, occurring within 24 hours after the procedure.

Relevant bleeding will be defined using a validated tool for assessment of bleeding in the critically ill by: overt bleeding with anyone of the following:
-a decrease in haemoglobin by more then 20 g/l in the absence of another cause
-transfusion 2 or more units red cells without an increase in haemoglobin
-a decrease in systolic blood pressure by more then 20 mmHg
-an increase in heart rate of 20 beats/min,
-bleeding at a wound site requiring an intervention (for example, re-operation).

An assessment of bleeding will be standardized and performed by an independent research physician or intensivist blinded to the transfusion strategy 1 and 24 hours after the procedure and when clinically indicated. The assessment will consist of a physical examination, inspection of chest drain production. Also, haemoglobin will be measured at 1 and 24 hours after the procedure and when clinically indicated. A chest radiograph will be made to capture intra-thoracic bleeding. Hemodynamic parameters (blood pressure and heart rate) will be

recorded by an electronic patient data monitoring system.

Secondary outcome

Secondary outcomes:

- minor bleeding within 24 hours

- onset of acute lung injury within 48 hours.

- correction of INR to < 1.5, (after the transfusion and before the procedure,

only in intervention arm) and effect on other coagulation parameters

- length of ventilation days

- length of ICU stay

- ICU mortality

- serious adverse events

- costs

Study description

Background summary

Fresh frozen plasma (FFP) is an effective therapy to correct for a deficiency of multiple coagulation factors. International guidelines support its use in the case of bleeding in patients with such a deficiency. Use of FFP has grown steadily in the past years, in particular in the Intensive Care Unit (ICU). Nationally, approximately 90.000 FFP units are issued (personal communication with National Blood bank supply). In our ICU, 1.100 units of FFP are transfused annually, which accounts for 21% of our hospital FFP transfusions.
In the last decade, use of FFP has expanded to include prophylactic administration of FFP. However, there are concerns about the efficacy of FFP to prevent bleeding. Evidence from randomized controlled trials that support FFP transfusion to correct coagulopathy before an invasive procedure is limited, including commonly performed procedures on the ICU, such as insertion of a central venous catheter, a chest drain or a percutaneous tracheotomy. Retrospective studies suggest that the risk of bleeding after an invasive procedure is low. Relevant bleeding requiring blood transfusion or an intervention is less then 1 %.

Prophylactic FFP does not further reduce bleeding incidence, but carries the risk of development of acute lung injury, occurring in up to 30 % of transfused ICU patients, resulting in an increased length of mechanical ventilation and ICU stay. However, despite the absence of evidence, in our ICU patients, 33% of plasma is transfused in the absence of bleeding, which is in accordance with reports from ICU*s in Europe and the US. We performed a survey on national practice, revealing that approximately 50% of intensivists administer profylactic FFP to patients with a coagulopathy undergoing a percutaneous tracheotomy. This practice may add up to an estimated national number of 10.000 units of FFP for prophylactic use per year.
The use of prophylactic FFP may be explained by the fact that ICU patients are thought to have an increased bleeding tendency, reflected by prolonged coagulation screening tests. In ICU patients, the majority indeed has a prolonged INR. In addition, ICU patients frequently undergo invasive procedures, which carry the risk of bleeding. Studies on transfusion practice point to the assumption of ICU physicians that FFP corrects coagulopathy, thereby preventing bleeding.

Study objective

With the aim to restrict inappropriate FFP transfusions to critically ill patients, a randomized clinical trial will be conducted in a subgoup of ICU patients undergoing an invasive procedure. The objective is to assess the effectiveness and costs of omitting prophylactic FFP transfusion compared to current practice of prophylactic transfusion, in non-bleeding ICU patients with a coagulopathy.

Study design

Study design: prospective, multicentre, randomized, open-label, blinded end point evaluation (PROBE) design.

Intervention

Intervention: omitting prophylactic transfusion of a fixed dose of 12 ml/kg of FFP prior to an invasive procedure compared to transfusion of a fixed dose of FFP of 12 ml/kg.

Study burden and risks

Intervention group:
No transfusion related morbidity. Possible increased risk of bleeding after the intervention, but retrospective studies suggest that the risk of bleeding after an invasive procedure is low. Relevant bleeding requiring blood transfusion or an intervention is less then 1%.

Burden:
-patients are already admitted to the intensive care and monitored, registration of hemodynamic parameters will not result in an extra burden for the patient
-4 bloodsamples will be collected after the transfusion, the blood will be aspirated from an arterial catheter, there is no extra burden from venapunctures
-chest x-ray is performed standard after the insertion of a chest tube or central venous catheter in the subclavian or jugular vein, it is no extra burden for the patient. After other procedures which do not standardly require a x-ray, it is a minimal extra burden.
-physical examination: will be performed 2 times after the procedure, the examination will focus on the location of intervention, internal rectal or vaginal examination won't be included in this physical examination

When participating in substudy to determine lung injury (one of secondary end points) the additive burden consists of:
-One non directed broncho-alveolar minilavage in all patients (n=40) participating in this substudy. This is part of routine care in all intubated and mechanically ventilated patients in our department and performed by nurses 4 times per day. The only difference with routine care is that the amount of saline used is now more standardized, and fluids are collected for research (while otherwise the obtained fluid is discarded)
-20 patients, receiving FFP transfusion will undergo PLI measurement to determine capillary leakage of fluid in the lung. The PLI measurement has a radiation load of 1.0 mSv. With a yearly radiation load out of the universe of 2.5 mSv, the radiation load during the PLI measurement can be considered low. In total an extra of 32 ml of blood will be drawn for PLI measurements, this will be done using an arterial catheter which is allready in place.

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

-18 years and older
-INR >1.5 and <3.0
-undergoing invasive procedure (insertion of a central venous catheter, a chest drain, percutaneous tracheostomy)

Exclusion criteria

- clinically overt bleeding at the time of the procedure (excludes minor epistaxis, minor gum bleeding, microscopic hematuria, superficial bruises, or normal menses)
- thrombocytopenia of < 30 x 109/L.
- use of aspirin, clopidogrel, abciximab, tirofiban, ticlopidine or activated protein C
- use of heparin < 1 hour prior to the procedure, or low molecular weight heparin in therapeutic doses < 12 hours prior to procedure
- history of congenital or acquired coagulation factor deficiency or bleeding diathesis
- no informed consent

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-05-2010
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO

Date:	06-06-2012
Application type:	Amendment
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
CCMO	NL30808.018.10