Hypoperfusion and activated protein C after out of hospital cardiac arrest: triggers for hyperfibrinolysis

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON37362

Source
ToetsingOnline

Brief title
LYSIS-OHCA

Condition

- Heart failures

Synonym
cardiac arrest, cardiopulmonary arrest

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cardiopulmonary arrest, Hemostasis, Thromboelastometry, Tissue perfusion

Outcome measures

Primary outcome

Main study parameter/endpoint:

Hypoperfusion as reflected by cerebral tissue hemoglobin oxygenation and the

incidence and onset time of hyperfibrinolysis in OHCA patients

Secondary outcome

Secondary study parameters/endpoints

- Blood coagulation and fibrinolytic parameters.

- Patient demographics including age, gender, body mass index, smoking.

- Cause of out of hospital cardiac arrest.

- Medication use

- Time to cardiopulmonary resuscitation, duration of cardiopulmonary

resuscitation, body temperature upon arrival.

- Lowest temperature during post-resuscitation cooling, duration of cooling.

- Mortality.

Study description

Background summary

Out of hospital cardiac arrest (OHCA), also known as cardiopulmonary arrest, is the cessation of systemic blood flow due to cardiac failure. Previous studies

in animals and humans showed an increase in activation of coagulation after resuscitation in patients with out of hospital cardiac arrest.3,4 Hyperfibrinolysis is a state of enhanced fibrinolysis, frequently associated with a high rate of clot breakdown and bleeding. In particular, patients with signs of hypoperfusion due to cessation of systemic circulation more frequently show hyperfibrinolysis, probably due to hypoperfusion-induced activation of the protein-C pathway. We recently found that almost 50% of all OHCA patients develop hyperfibrinolysis, and this was associated with indirect markers of tissue hypoperfusion. The study was however limited by several factors and its retrospective nature.

This study will therefore prospectively investigate the relation between tissue hemoglobin oxygenation and the occurrence of hyperfibrinolysis in the context of altered levels of hyperfibrinolytic markers in patients with out of hospital cardiac arrest.

Study objective

Our research group recently found that almost 50% of all OHCA patients develop hyperfibrinolysis, and found an interesting association between the degree of hyperfibrinolysis and hypoperfusion. Hypoperfusion was determined by base excess (BE), arterial oxygen pressure (pO2), arterial carbon dioxide pressure (pCO2), lactate, pH and cardiopulmonary resuscitation (CPR) time. Moreover, data tended to show worse patient outcome in cases of severe hyperfibrinolysis. The study was however limited by several factors and its retrospective nature. In particular, as arterial blood gas analyses were static and not precise enough as indicators of tissue perfusion, studies using specific longitudinal tissue hemoglobin oxygenation measurements are warranted to determine the relation between hypoperfusion and hyperfibrinolysis. Furthermore, the relation between hypoperfusion and hyperfibrinolysis in the context of alterations in the levels of activated protein C, PAI-1 and TAFI has never been investigated in patients after OHCA.

In the present study we aim to investigate the relation between tissue hemoglobin oxygenation as indicator of tissue perfusion and the occurrence of hyperfibrinolysis in the context of altered levels of activated protein C, PAI-1 and TAFI in patients admitted to the emergency department of the VU University Medical Center with out of hospital cardiac arrest.

Primary objective:
- What is the correlation between hypoperfusion as measured by tissue hemoglobin oxygenation and the onset time and level of hyperfibrinolysis measured by ROTEM in patients with out of hospital cardiac arrest?

Secondary objectives:
- How are fibrinolytic markers, especially the activation of protein C, associated with the degree of hypoperfusion and hyperfibrinolysis in patients

with out of hospital cardiac arrest?
- What is the role of the lysis onset time in relation to the onset time of hypoperfusion?

Study design

This study is retrospective, single center, observational study.
The study will be performed in the departments of Anesthesiology, Emergency Medicine and Intensive Care Medicine of the VUmc in Amsterdam.

Study period:
- The study ends when the required sample size is reached.

Study procedure:
- Upon emergency department admission, patients receive a non-invasive cerebral oxymetry probe for tissue hemoglobin oxygenation measurements using Near Infrared Spectroscopy (NIRS).
- Blood sampling starts upon emergency department admission acording to routine clinical care. Subsequent blood samples will be drawn at 2, 4 and 24 hours following patient admission (3 x 20 ml). Blood samples will be used for routine coagulation measurements, ROTEM, platelet activation and the determination of hyperfibrinolytic markers.
- Patients with return of spontaneous circulation (ROSC) will be admitted tot the intensive care department, where they will be exposed to a cooling protocol for ischemic protection (routine procedure).

Study burden and risks

Blood sampling using a peripheral intravenous catheter is a standard procedure in all OHCA patients admitted to the shock room. The use of an intravenous catheter will therefore not add up to patient discomfort in the present study.
The volume of blood drawn for the present study does not increase the risk for anemia in the patients. OHCA are routinely admitted to a special or intensive care ward, and the intravenous catheter will in most patients not be removed until admission to a general ward (> 24 hours). The non-invasive cerebral tissue hemoglobin oxygenation measurements are performed with a probe that is integrated in a forehead patch. These measurements are already performed during cardiothoracic procedures in order to monitor cerebral tissue perfusion, and do not add up to patient discomfort.

There are no benefits for patients when they enter the study.

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

Adult patients
Admitted to shock room by paramedic ambulance (presence of registration files for cardiopulmonary resuscitation)
Return of spontaneous circulation (ROSC) after out of hospital cardiac arrest
Presence of hyperfibrinolysis

Exclusion criteria

Patients with hemostatic deficiencies or previous hemostatic problems
Deceased patients upon ED arrival
Absence of a peripheral intravenous catheter
Patients using vitamine K antagonists, clopidogrel or dabigatran

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-09-2012
Enrollment:	60
Type:	Actual

Medical products/devices used

Generic name:	Near-infrared spectroscopy (NIRS)
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	14-08-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-11-2012
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	NL39831.029.12