CHANGES IN THE COAGULATION CASCADE IN PATIENTS WITH PROGRESSIVE (METABOLIC) LIVERDISEASE

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Observational invasive

Summary

ID

NL-OMON36796

Source
ToetsingOnline

Brief title
TG-study

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Hepatic and hepatobiliary disorders

Synonym
liver cirrhosis, liver scarring

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: CAT (Calibrated Automated Thrombin generation), Cirrhosis, Coagulation, Thrombin Generation Curve (TGC)

Outcome measures

Primary outcome

Thrombin Generation Curve in PPP (platelet poor plasma) and PRP (platelet rich

plasma) using CAT

Thrombocyte function test using the Multiplate (aggregometer)

Measurement of the fibronolysis pathway by use of the Fibrinolysis ROTEM

Measurement of microparticles with influence on the haemostasis.

Secondary outcome

Coagulatie parameters

o Factor II

o Factor VIII

o Antitrombin

Study description

Background summary

In the Netherlands the prevalence of liver disease is just below 1%. When reaching the terminal stage, liver diseases can cause severe complications and life-threatening symptoms, such as ascites, variceal bleeding, icterus and encefalopathy. Severe disfunctions in brain function, general circulation, kidney function and coagulation can occur. Prognosis of patients with liver cirrhosis and symptomatic complications as described above is poor: 50% of patients die within a year.
During the progress of liver disease the production of coagulation factors decreases in relation with the decrease in functional liver tissue, this concerns both pro-coagulants as anti-coagulants. This decreased production involves alterations in coagulation and fibrinolysis activity leading to severe

bleeding- or trombotic tendency. At the moment it is not fully clear what influence the alternations in coagulationfactors have on patients with cirrhosis and their bleedingrisk, because no suitable tests are available which reflect the balance between pro-coagulant and anti-coagulant factors in vivo. Conventional coagulation tests (PT, APPT, AT) do not entirely make activation of all the factors in the coagulation cascade clear. In practice this leads to an incomplete and unreliable evaluation of bleeding- or trombotic tendency. Conventional coagulation tests are used in classifications such as the Child-Pugh classification and the MELD-score, leading to a incomplete and unrealistic reproduction of the reality. Using the Thrombin Generation Curve (TGC) seems to be a reliable evaluation of the possible bleeding- or trombotic risk. This because the endproduct from the (pro and anti-)coagulation cascade, thrombin, is measured in stead of distinct factors in the (pro-)coagulation cascade.

Study objective

The objective of this study is to investigate if the Thrombin Generation Curve has an additional, possible more accurate, value besides the conventional tests such as PT, APTT, INR, AT and the mearument of coagulationfactors for determining coagulationfactordefects or disorders in patients with chronic liver diseases.
Second objective of this study is to investigate, with the help of the Thrombin Generation Curve, the possible changes in a patient with an acute decompensated liver cirrhosis, according to the coagulationfactors and their metabolism, alterations in the bleeding- versus trombotic risks will be explicitly investigated.
Third objective is to follow the course of possible changes in coagulationfactors and coagulation metabolism in patients with chronic liver disease, using the Thrombin Generation Curve, alterations in the bleeding- versus trombotic risks will be explicitly investigated.

Study design

This concerns a hypothesis generating study. The first part of the study will be a cross-sectional observative comparative study.
A healty population A will be compared to population B, patients with chronic liver diseases. The severity of the liver disease will be determined according to the Child-Pugh score, during a regular check-up appointment at the Gastro-enterology clinic (MUMC). Calculating the Child-Pugh score is also done during regular check-up's to investigate severity of the disease.
Both populations will fill out a questionnaire (questions about comorbidity, medication, lifestyle).
Every participant will donate 50 ml of blood (venapuncture), this blood will be used to perform following tests: Thrombin Generation Curve, thrombocyte aggregation (Multiplate), measuring coagulation factors.

Outcomes of both populations will be compared.

The second part of the study concerns a longitudinal follow up of only population B (6, 12, 18 months) to investigate if, when the severity of the liver disease increases, the Thrombin Generation Curve and the conventional coagulation tests will yield different results.
Population B will also be asked (on forehand at the inclusion) to donate blood for coagulation-testing during the follow up, when there is a clinical admission because of a liver-related event (e.g. varicael bleeding).

Study burden and risks

For both populations the risk of the study are equal to the risk of regular venapuncture.

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

Healthy controls (population A):
- minimum age of 18-years old
- decision making capacity;Patients (group B) (minimum of 18 years old) with cirrhosis, as diagnosed by a GE-specialist, due to one of the following chronic liver diseases: Primary Biliairy Sclerosis (PBS), Primary Sclerosis Cholangitis (PSC), Hepatitis B, Hepatitis C, Non-Alcoholic Fatty Liver Disease (NAFLD), Alcoholic Liverdisease, Non-Alcoholic Steatosis Hepatitis (NASH), Haemochromatosis, Cryptogenic levercirrhosis.

Exclusion criteria

For both healthy controls (population A) as patients (population B):
- proven congenital diseases concerning primary hemostasis (e.g. M. von Willebrand), defects in fibrinolysis, coagulation factor deficiencies (e.g. hemophilia A and B), vasculair defects which leed to higher bleeding risk (e.g. M. Rendu-Osler-Weber).
Patients using medication interfering with primary hemostasis or coagulation. Coagulation factor deficiencies due to malignancies, sepsis or trauma.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-03-2010
Enrollment:	140

Type:	Actual

Ethics review

Approved WMO Date:	01-03-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-10-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-07-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-03-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

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	NL30724.068.09