Activation and apoptosis of peripheral T cells in relation to liver fibrosis

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Observational invasive

Summary

ID

NL-OMON36633

Source
ToetsingOnline

Brief title
Acatlife

Condition

- Hepatic and hepatobiliary disorders
- Viral infectious disorders

Synonym
liver fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Hoffmann-La Roche,industrie

Intervention

Keyword: hepatitis, liver fibrosis, T cells

Outcome measures

Primary outcome

a number of immunological markers will be evaluated on all subjects and controls. Markers to be investigated are T cell surface markers of proliferation, differentiation, activation, homing and apoptosis, intracellular markers of activation and cell death and serum markers of apoptosis.

Secondary outcome

The level of fibrosis and various underlying hepatic diseases are secundary study parameters, together with certain markers of T cell activation and apoptosis.

Study description

Background summary

Hepatic fibrosis or liver scarring is the final common pathway of chronic liver disease in which apoptotic hepatocytes activate fibrogenous stellate cells. Activated and apoptotic T cells are also involved in hepatic fibrogenesis, although their precise contribution remains unclear. Preliminary results from a phase 2b study of a caspase-inhibitor in chronic hepatitis C virus (HCV) patients in which our medical centre participated shows increased activation and apoptosis of both peripheral CD4+ and CD8+ T cells in HCV patients compared to healthy controls. It is unclear whether these findings are specific for HCV.

Study objective

The primary objective is to explore the association between peripheral T-cell activation and apoptosis and hepatic fibrosis in various underlying liver diseases. Secondary objectives are 1) to investigate whether level of T cell activation and apoptosis correlates with severity of fibrosis; 2) whether activation and apoptosis of T cells differ between chronic HCV monoinfected

patients and those coinfected with HIV for which they are adequately treated 3) to evaluate whether T cell activation and apoptosis differs between non-symptomatic HBV carriers, active HBV hepatitis patients and treated HBV patients.

Study design

markers of T cell activation and apoptosis are measured in peripheral blood of patients with various hepatic diseases (asymptomatic hepatitis B virus (HBV) carriers, active but untreated HBV, treated HBV, HCV, HIV-HCV, non-alcoholic fatty liver disease (NAFLD) and primary biliary cirrhosis (PBC)) and various stages of fibrosis (F0-F2 versus F3-F4; except for NAFLD-cases).
T cell activation and apoptosis rates are compared between patients with hepatic diseases (viral hepatitis, PBC, NAFLD) to healthy controls or, in the case of HIV-HCV co-infecten, to HIV mono-infected patients. Subsequently, in patients with viral hepatitis and PBC, T cell activation and apoptosis rates will be compared between those subjects with mild fibrosis (F0-F2) versus severe fibrosis (F3-F4).

Study burden and risks

50mL of blood will be obtained from subjects of our study, of which risks and complications are negligible. Participation in this study will not provide individual benefit, but group-related benefit will include a first understanding of the level of T cell apoptosis and activation in patients with liver fibrosis with various underlying liver diseases and potential improvement of diagnostics and therapy in long term.

Contacts

Public
Academisch Medisch Centrum

Heidelberglaan 100
3584 CX
NL
Scientific
Academisch Medisch Centrum

Heidelberglaan 100
3584 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

One of the following chronic liver diseases:
- chronic hepatitis B
- chronic hepatitis C with or without treated HIV
- Non-alcoholic fatty liver disease (NAFLD)
- Primary Biliary Cirrosis (PBC)
- HIV-positive
Age >16yrs <65 yrs

Exclusion criteria

-Pregnant
-Other chronic liverdisease
-Other disorder interfering with T cel activity or apoptosis
-Alcohol intake >30g/day; substance abuse of cocaine or intravenous drugs.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-09-2010
Enrollment:	140
Type:	Actual

Ethics review

Approved WMO Date:	21-05-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-09-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL30749.041.09