Characterization of intrahepatic immune responses and gene expression profiles in patients with chronic hepatitis Delta

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To characterize the phenotype, function and gene expression profiles of immune cells and hepatocytes in blood and liver of patients with chronic hepatitis D.

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

Summary

ID

NL-OMON56721

Source
ToetsingOnline

Brief title
RAPID

Condition

- Hepatic and hepatobiliary disorders
- Viral infectious disorders

Synonym
Chronic hepatitis Delta, viral liver inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Stichting Lever en Maag-Darm Onderzoek

Intervention

Keyword: Chronic hepatits D, Fine-Needle Aspiration Biopsy, Gene expression profile, immuno-phenotype

Outcome measures

Primary outcome

The immuno-phenotype of CD4+ T cells, CD8+ T cells, monocytes/macrophages,

neutrophils, NK cells, NKT cells, MAIT cells, and B cells will be assessed in

blood and liver of patients chronic HBV-HDV.

The function of CD4+ T cells, CD8+ T cells, monocytes/macrophages, neutrophils,

NK cells, NKT cells, MAIT cells, and B cells will be assessed in blood.

Gene expression profiles of immune cells and hepatocytes in blood and liver of

patients will be assessed.

Secondary outcome

not applicable

Study description

Background summary

Hepatitis delta virus (HDV) is a defective RNA virus that requires presence of hepatitis B virus (HBV) to complete virion assembly and secretion. HDV infection can occur as an acute co-infection with HBV and HDV, which evolves to chronicity in only 2% of patients, or as an HDV superinfection in patients with a chronic HBV infection resulting in a chronic HBV-HDV co-infection in 70-90% of patients. HBV-HDV coinfection (*hepatitis delta*) has been associated with severe liver injury that may result in rapid progression to cirrhosis and hepatic decompensation, as well as a higher risk of liver cancer when compared to patients with HBV mono-infection. In a recent long-term follow-up study, 30%

of hepatitis delta patients had cirrhosis at the time of diagnosis, and 31% of non-cirrhotic patients developed cirrhosis during a median follow-up of 8 years. These rates are similar to those reported in a cohort from the 1990*s.

At this time, therapeutic options for hepatitis delta are limited.
Peginterferon alfa (PEG-IFN) treatment may result in HDV RNA undetectability in a small subset of patients, but relapse rates are high. Treatment with nucleo(s)tide analogues (NUCs) does not directly influence HDV RNA levels, but is effective in suppressing HBV replication and is therefore recommended in patients with advanced liver disease and detectable HBV DNA.
There is limited information of the immune status of chronic HBV-HDV patients off and on therapy which may provide important information that may help in decision-making on the design and selection of novel antivirals that are in the pipeline. The aim of this study is to perform longitudinal sampling of chronically infected HBV-HDV patients to describe the immunological and transcriptomic intrahepatic processes.

Sampling of the liver for research purposes is possible by the collection of Fine Needle Aspirates (FNA). Complications like hemorrhage limit the frequent performance of diagnostic core-needle biopsies (TB), and the cells of peripheral blood have to be used as surrogate markers instead. The collection of fine-needle-aspirates of the liver represents a safe and minimally traumatic method that allows frequent cytological sampling. During this procedure a small needle (25 Gauge or 0.5 mm) is used to aspirate hepatocytes and intrahepatic leukocytes from the liver. The low rate of complications associated with a FNA and the absence of anesthetic measures or observation nominates this method for the follow up of liver immunology in a research setting.

Study objective

To characterize the phenotype, function and gene expression profiles of immune cells and hepatocytes in blood and liver of patients with chronic hepatitis D.

Study design

prospective observational single center study

Study burden and risks

The current study does not pose any significant risk to the patients, and the only burden is collection of blood and fine-needle aspirates. Both the blood collection and FNA can cause pain and bruising. In rare cases, FNA can cause a bleeding in the liver. The study has no direct benefit for the included subjects.

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

- Active hepatitis delta based on a positive anti-HDV and a positive HDV-RNA test
- Patients must be >=18 years and <= 70 years.
- Non-cirrhotic or cirrhotic compensated liver disease
- Patients must be able to provie a written informed consent

Exclusion criteria

• Clinical decompensated cirrhosis (Child-Pugh Grade B or C).
• Hepatic imaging (ultrasound, CT or MRI) with evidence of hepatocellular carcinoma.

• Females who are pregnant or breast-feeding.
• History or other evidence of severe illness, malignancy or any other condition which would make the patient, in the opinion of the investigators, unsuitable for the study.
• Received prolonged therapy with immunomodulatory agents (e.g. corticosteroids) or biologics (e.g. monoclonal antibody, interferon) within 6 months of screening.
• Thrombocytes < 60x109/L
• Inability to provide written informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-05-2024
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	17-04-2024
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL85638.078.23