# The association between loss of gut wall integrity as measured by ZOnulin and hepatic ischaemia as measured by NIRS and Biliary Atresia development

Published: 28-10-2014 Last updated: 20-04-2024

To confirm that loss of gut wall integrity is associated with the development of biliary atresia and to investigate possible hypoxia in the liver/bile ducts in children with biliary atresia using NIRS

Ethical review	Approved WMO
Status	Will not start
Health condition type	Hepatic and hepatobiliary disorders
Study type	Observational non invasive

# Summary

### ID

NL-OMON41086

**Source** ToetsingOnline

**Brief title** ZOBANIRS

## Condition

• Hepatic and hepatobiliary disorders

**Synonym** bile duct atresia, biliary atresia

**Research involving** Human

### **Sponsors and support**

#### Primary sponsor: Universitair Medisch Centrum Groningen

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#### Source(s) of monetary or material Support: Ministerie van OC&W

### Intervention

Keyword: biliary atresia, gut wall integrity, near infrared spectroscopy, zonulin

### **Outcome measures**

#### **Primary outcome**

Serum Zonulin levels and liver NIRS

#### Secondary outcome

Other serum tight junction and translocation markers (e.g. Claudin 3 and/or LBP)

Histologic assessment of the tight junction complex in the small bowel, VEGF-A

expression in the liver

# **Study description**

#### **Background summary**

The aetiology of perinatal biliary atresia is unknown, but the cause is probably multifactorial. The end result seems an (auto) immunological event aimed at the cholangiocytes, leading to destruction of the biliary tree during early infancy. Recent studies demonstrated an association between loss of gut wall integrity due to a loss of tight junctions between the enterocytes in early infancy with the development of auto-immune disorders such as type I diabetes.

Zonulin is a small protein that (partly) regulates tight junction functioning. Zonulin leads to the release of ZO1, a component of the tight junction complex, and in that way opens the paracellular pathway. Zonulin can be measured in blood. As such it is considered a marker for tight junction function. In patients and in animal experiments a raise in serum Zonulin was associated with the development of Diabetes Mellitus Type 1 (DM1) later in life. Zonulin levels were also associated with the development and activity of Celiac Disease (CD). In animal models, blocking Zonulin could reverse CD symptoms and CD/DM development. This suggests an association between loss of gut wall integrity and the development of auto-immune disease. Furthermore, previous studies showed higher VEGF levels, as an expression of hypoxia/ischemia, in infants with biliary atresia, which suggest that ischaemia might be involved in the development of the obstructive cholangiopathy. A method that can reliable measure tissue oxygenation and hypoxia of an organ is Near-Infrared Spectroscopy (NIRS). NIRS is a non-invasive method to assess end-organ perfusion. With NIRS one measures regional tissue oxygen saturation (rSO2), as surrogate for tissue perfusion. Combined with the arterial oxygen saturation the fractional tissue oxygen extraction (FTOE) can be calculated (FTOE = [SpO2-rSO2]/SpO2). FTOE reflects the balance between tissue oxygen supply (perfusion) and tissue oxygen consumption. Both rSO2 and FTOE thus serve as an indicator of tissue ischemic hypoxia.

#### **Study objective**

To confirm that loss of gut wall integrity is associated with the development of biliary atresia and to investigate possible hypoxia in the liver/bile ducts in children with biliary atresia using NIRS

#### Study design

Prospective single center explorative study

#### Study burden and risks

There will be no risk or burden for the children, who will not have to undergo extra procedures for this research. As biliary atresia is a disease of the young children, this study can only be performed in this patient group. A small piece of small bowel will be sampled during the Kasai procedure. This consists of the most distal part towards the staple line, which is resected anyway prior to performing the anastomosis. The control group also routinely undergoes venapuncture for assessment of blood pH and electrolytes, therefore also in the control group there will not be extra burden.

# Contacts

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# **Trial sites**

### **Listed location countries**

Netherlands

# **Eligibility criteria**

Age Children (2-11 years)

### **Inclusion criteria**

Suspected biliary atresia, as controls patients with pyloric stenosis (same age group but without liver disease)

### **Exclusion criteria**

No biliary atresia during surgery, other gastro-intestinal diseases (except pyloric hypertrophy)

# Study design

### Design

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Masking:	Open (masking not used)
Allocation:	Non-randomized controlled trial
Intervention model:	Other
Study type:	Observational non invasive

Primary purpose: Basic science

### Recruitment

NL	
Recruitment status:	Will not start
Enrollment:	20
Туре:	Anticipated

# **Ethics review**

Approved WMO	
Date:	28-10-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

# **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** CCMO Other **ID** NL48591.042.14 volgt