Effect of bile drainage and rifampicin on recovery of obstructive cholestatic patients.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24804

Source
NTR

Brief title
BIDRIP trial

Health condition

Obstructive cholestasis
Jaundice
Rifampicin therapy
Bile Flow
Bilirubin
Pruritus

Sponsors and support

Primary sponsor: Academic Medical Centre Amsterdam
Source(s) of monetary or material Support: This work was supported by a grant “Primary sclerosing cholangitis” from the “Deutsche Crohn and Colitis Vereinigung”

Intervention

Outcome measures

Primary outcome

Serum total bilirubin reduction in % after one week of biliary drainage with or without short-term rifampicin treatment.

Secondary outcome

1. Intensity of pruritus (VAS);

2. Quality of life (Short form 36 and Liver Disease Symptom Index 2.0);

3. Serum: Biliary bile salt profiles, gamma-glutamyltransferase, alkaline phosphatase, Asat, Alat, autotaxin, lysofosfatidic acid, fibroblast growth factor 19 and HCO3-;

4. Bile: Lysofosfatidic acid, autotaxin, fibroblast growth factor 19 and bicarbonate.

Study description

Background summary

The antibiotic rifampicin is identified as an activator of the nuclear receptor pregnane X receptor (PXR). In vitro and in vivo studies have shown that rifampicin, by being a PXR-ligand, has several possible pharmacological targets for the treatment of cholestasis and thereby improves liver cell secretion and cholestasis-induced pruritus. In a pilot study eleven patients with progressive hepatocellular secretory failure (serum bilirubin >255µmol/L) were successfully treated with rifampicin, resulting in amelioration of bilirubin levels, and pruritus also improved rapidly (article under submission). Rifampicin is effective in cholestasis associated pruritus. It is shown that short-term treatment with PXR agonists such as rifampicin is highly effective and safe. Rifampicin for short duration, not longer than two weeks, is associated with a low risk of hepatotoxicity, Rifampicin-induced hepatitis is only seen after 2-3 months of treatment.

We would like to study the effect of alleviation of obstructive cholestasis by biliary drainage with or without rifampicin on serum bilirubin levels. On the other hand we also study want to study the effect on cholestatis-induced pruritus. Various cholestatic disorders are associated with pruritus. Recent results of our group suggest that lysophosphatidic acid (LPA) and autotaxin (ATX) play a critical role in cholestatic pruritus. However, the source of increased serum ATX levels remains to be elucidated. Certain substances in bile may induce gene expression of autotaxin. It is our aim to reveal the nature of these substances. Without adequate therapy chronic cholestatic diseases can progress through stages of inflammation and fibrosis to cirrhosis. The function of bile salts during cholestasis is ambiguous: they act as pro-inflammatory agents on the one hand and as signaling ligands via membrane bound and

nuclear receptors on the other hand. It is not known how hepatocytes and cholangiocytes gain resistance against these noxious compounds in bile. Our group hypothesized an import role for HCO3- secretion in the biliary tract as a defense mechanism against noxious compounds in bile.

Study objective

We postulate that:

1. Restoration of bile flow by means of bile drainage during obstructive cholestasis affects the composition of bile and serum including total bilirubin concentrations and thereby improves jaundice and cholestasis;

2. Restoration of bile flow by means of bile drainage during obstructive cholestasis affects the composition of bile and serum including serum LPA and ATX concentrations, and, thereby, relieving pruritus and improving quality of life in the cholestatic patient;

3 The potent PXR agonist and antipruritogen, rifampicin, does not only beneficially affect pruritus in addition to biliary drainage, but also enhances impaired hepatocellular secretory capacity thereby accelerating clinical and biochemical recovery and, thereby, quality of life of the cholestatic patient;

4. Biliary HCO3- secretion as a protective mechanism against bile acid-induced cholangiocyte damage is impaired more severely in preexistent bile duct disease, than under conditions of local bile duct obstruction and recovers more effectively after drainage and rifampicin treatment.

Study design

1. At baseline (T=0);

2. Day 1;

3. One week after baseline;

4. Four weeks after baseline.

Intervention

Treatment with rifampicin 150 mg bd for seven days and blood sampling and questionairres.

Controls will not receive additional rifampicin.

Contacts

Public
Tytgat Instituut, AMC
Meibergdreef 69
R. Dijk, van
Amsterdam
The Netherlands
+31 (0)20 5668701
Scientific
Tytgat Instituut, AMC
Meibergdreef 69
R. Dijk, van
Amsterdam
The Netherlands
+31 (0)20 5668701

Eligibility criteria

Inclusion criteria

1. Male or female with severe obstructive cholestasis for whom biliary drainage by PTC or nasobiliary drainage by ERCP is clinically indicated;

2. An established diagnosis of obstructive cholestasis by ultrasound-scan (US-scan), magnetic resonance cholangiopancreatography (MRCP) and/or endoscopic retrograde cholangiopancreatography (ERCP);

3. Age 18-90 years;

4. Able to understand and give fully informed written consent;

5. Hyperbilirubinemia > 170 µmol/L;

6. Cholestatic serum enzyme pattern.

Exclusion criteria

1. Patients with purely hepatocellular, non-obstructive cholestasis in whom biliary drainage by PTC or ERCP is not clinically indicated;

2. Patients with known allergy to rifampicin;

3. Patients who are pregnant.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2012
Enrollment:	50
Type:	Anticipated

Ethics review

Positive opinion

Date:	27-01-2012
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 36732
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL3113
NTR-old	NTR3262
CCMO	NL34567.018.11
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON36732

Study results

Summary results
N/A