Effect of Transjugular Intrahepatic Portosystemic Shunt on pharmacokinetics

No registrations found.

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

Summary

ID

NL-OMON24097

Source
NTR

Brief title
TIPS and PK

Health condition

Cirrhosis, portal hypertension.
Levercirrose, portale hypertensie.

Sponsors and support

Primary sponsor: Academic Medical Center (AMC), Amsterdam
Source(s) of monetary or material Support: Academic Medical Center (AMC), Amsterdam

Intervention

Outcome measures

Primary outcome

1. To assess the effect of TIPS placement on drug metabolism of different drugs, metabolized

by different metabolic pathways in patients with cirrhosis using the drug cocktail approach after oral administration. Drug exposure is quantified by assessment of the area under the plasma concentration versus time curve (AUC) for each drug.

Secondary outcome

2. To assess the effect of TIPS placement on pharmacokinetic parameters as clearance, volume of distribution, absorption rate, mean residence time and elimination half-life.

3. To assess the effect of TIPS placement on the postprandial bile acid, glucose, lipid and energy metabolism.

Study description

Background summary

Rationale: Liver cirrhosis is the end stage of chronic liver injury, and is associated with portal hypertension and a decreased function of the liver. Drug dosage in patients with cirrhosis is difficult due to this decreased function. Transjugular Intrahepatic Portosystemic Shunt (TIPS) is a highly effective intervention to reduce elevated portal pressure and reduce complication rates of portal hypertension. Hepatic biotransformation of endogenous toxins, hormones or the pharmacokinetics of drugs and bile acid metabolism may be affected by TIPS placement, but prospective controlled studies are lacking.

Objective: To assess the effect of TIPS on drug metabolism of different drugs, metabolized by different metabolic pathways in patients with an elective TIPS placement using a cocktail approach, and to assess the effect of TIPS on bile acid metabolism.

Study objective

We hypothesize that TIPS placement has an significant effect on drug metabolism and bile acid metabolism.

Study design

Drug cocktail administration and measurement will take place two weeks before TIPS placement, a day after TIPS placement and twelve weeks after TIPS placement.

PK samples will be collected at approximately t=0, t=0,5, t=1, t=1.5, t=2, t=3, t=4, t=6, t=9 hours, 24 hours
(day 1) and 72 hours (day 3) after drug cocktail administration.

Intervention

This study consists of three interventions per patient. Patients will receive a single oral administration of a drug cocktail two weeks before TIPS placement, a day after TIPS placement, and twelve weeks after TIPS placement. The oral drug cocktail consists of 50 mg caffeine, 5 mg warfarin, 20 mg omeprazole, 20 mg metoprolol and 0.015 mg/kg midazolam. In addition to the drug cocktail, patients undergo a mixed meal tests (MMT), using Nutridrink compact, and measurement of body expenditure and body composition.

Contacts

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Eligibility criteria

Inclusion criteria

- Liver cirrhosis as documented by liver biopsy or elastography (e.g. Fibroscan > 15 kPa) in combination with usual radiological and biochemical signs.

- Age > 18 years.

- Elective indication for TIPS (recurrent tense ascites, recurrent/refractory hepatic hydrothorax, or (recurrent) oesophageal or gastric bleeding treated with endoscopic band ligation (EBL) or endoscopic injection sclerotherapy (EIS) more than 2 weeks prior to screening.

- Signed informed consent

Exclusion criteria

- Age > 75 years.

- History of grade III or IV HE or chronic overt HE.

- Patients with (recurrent) oesophageal or gastric bleeding treated with endoscopic band ligation (EBL) or endoscopic injection sclerotherapy (EIS) within 2 weeks previous to screening.

- Patients who meet the criteria for emergency TIPS for uncontrolled bleeding.

- Spontaneous Bacterial Peritonitis (SBP) during the past 7 days.

- Child Pugh score ≥ 10.

- MELD score > 20.

- Serum bilirubin 51 > µmol/L.

- INR > 1.7.

- Serum creatinine > 185 µmol/L.

- Complete portal vein thrombosis.

- Hepatocellular Carcinoma

- Polycystic liver disease/ multiple large liver cysts.

- Concomitant active infection.

- Congestive heart failure.

- Pulmonary hypertension

- Bile duct obstruction with dilatation of the bile ducts.

- Overt neurologic diseases such as Alzheimer’s disease, Parkinson’s disease.

- Pregnant or breastfeeding women.

- Drug abuse or alcoholism (>3 units of alcohol per day).

- Use of alcohol for at least 3 days prior to each study day.

- Strenuous exercise for at least 3 days prior to each study day, defined as more than 1 hour of exercise per day.

- Use of prescription or non-prescription drugs and herbal or dietary supplements within 14 days prior to the first administration of the drug cocktail, that will not be taken after TIPS placement.
- Use of tobacco products (induction liver enzymes).

- Drinking of coffee/thee or caffeine containing beverages (caffeine) within 1 day prior to study (based on the half-life of caffeine: t1/2=5 hours).

- Eating/drinking of grapefruit and grapefruit-containing products or star fruit for at least 2 days prior to each study day.

- Allergy for the study medications

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Other
Start date (anticipated):	04-07-2018
Enrollment:	11
Type:	Unknown

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	08-01-2019
Application type:	First submission

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
NTR-new	NL7465
NTR-old	NTR7707
Other	MEC AMC : 2018_089

Study results