Very short-course versus standard course antibiotic therapy in patients with acute ChOlangitis after adequate endoscopic BiliaRy drAinage (COBRA trial).

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The primary objective is to investigate if a very short-course of antibiotics for cholangitis after adequate drainage is non-inferior with respect to clinical cure in comparison with a standard course of antibiotics.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bile duct disorders
Study type	Interventional

Summary

ID

NL-OMON56128

Source
ToetsingOnline

Brief title
COBRA

Condition

- Bile duct disorders
- Bacterial infectious disorders

Synonym
bile duct infection, cholangitis

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Antibiotic therapy, Cholangitis, ERCP, RCT

Outcome measures

Primary outcome

The primary endpoint is clinical cure by day 14 after ERCP without relapse by day 30. Clinical cure is defined as the absence of both fever (>38°C) and/or shaking chills, and initial presenting symptoms.

Secondary outcome

Secondary endpoints are all-cause mortality, relapse of cholangitis, any other

subsequent infection requiring antibiotic therapy, subsequent infections with

multidrug resistant (MDR) bacteria or Clostridioides difficile, other adverse

drug events, length of intensive care and hospital stay for the initial episode

of cholangitis, quality of life and health utility, and societal costs.

Study description

Background summary

Acute cholangitis is an infection of the biliary tract which is managed with biliary drainage and antibiotic therapy (ABT). Currently the international Tokyo Guidelines 2018 (TG18) recommend 4 to 7 days of ABT after source control. The national SWAB guideline of 2020 suggests a course of one to 3 days after biliary drainage. There are no randomized studies to guide the duration of ABT for acute cholangitis. Our recent retrospective study in the Netherlands showed that a short course of ABT seems safe and more evidence is available showing that other bacterial infections, including abdominal and bloodstream infections, can be treated with a short antibiotic course than previously assumed. Hence, the hypothesis is that a very short-course of ABT for acute cholangitis is non-inferior to a course of 4 to 7 days after adequate biliary

drainage.

Study objective

The primary objective is to investigate if a very short-course of antibiotics for cholangitis after adequate drainage is non-inferior with respect to clinical cure in comparison with a standard course of antibiotics.

Study design

This study is designed as a multicenter non-inferiority randomized controlled trial. Patients will be randomly assigned to the intervention group (one day of antibiotic therapy after ERCP) or the comparator group (4 to 7 days of antibiotic therapy after ERCP).

Intervention

Patients will be randomized to receive one day or 4-7 days of ABT after ERCP.

Study burden and risks

The risks of shortened ABT consist of insufficient treatment of cholangitis potentially complicated by bacteraemia and recurrent infection. Although it is assumed recurrent infections are often due to inadequate biliary drainage and therefore may not be preventable with longer ABT. All patients will be consented for the study and asked to contact their physician in case of fever and/or shaking chills after hospital discharge.
The presumed benefits of a very short-course of ABT are a reduction in the length of hospital stay, a decrease in antibiotic consumption and subsequent antibiotic-related toxicity, and reduced development of antimicrobial resistance in gram-negative bacteria.
The burden for patients participating in this trial is small. Patients will be contacted by telephone at day 14, 30 and 90 after the ERCP to evaluate clinical cure and adverse events which is part of daily clinical practice. In addition they will be asked to answer questionnaires to assess quality of life, health utility and cost effectiveness at three points in time.

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

- Patients with acute cholangitis due to common bile duct stones, benign or malignant distal biliary obstruction or distal biliary stent dysfunction (only stents in situ for a minimum of 30 days)
- ERCP with adequate biliary drainage (all common bile duct stones are removed and/or there is adequate flow of bile with or without a biliary stent(s))
- Age >= 18 years
- Written informed consent

Exclusion criteria

- Other etiologies of acute cholangitis (e.g. primary sclerosing cholangitis, (sub)hilar and/or intrahepatic strictures or hilar stents)
- A recurrent cholangitis (within 3 months)
- Concomitant pancreatitis, cholecystitis or liver abscess
- Another additional infectious diagnosis
- Use of maintenance antimicrobial therapy
- Use of immunosuppressants
- Neutropenia

Study design

Design

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

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-03-2023
Enrollment:	440
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	Amikacin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	-
Generic name:	Ceftriaxone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	-
Generic name:	Cefuroxime
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	-
Generic name:	Ciprofloxacin
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	-
Generic name:	Gentamicin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-02-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-06-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-10-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2022-002624-12-NL
CCMO	NL80410.029.22