A randomized, double-blind, placebo-controlled clinical trial assessing the efficacy of combining pasireotide with aspiration sclerotherapy to improve volume reduction of dominant hepatic cysts

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary disorders congenital
Study type	Interventional

Summary

ID

NL-OMON40608

Source
ToetsingOnline

Brief title
Sclerocyst

Condition

- Hepatobiliary disorders congenital

Synonym
dominant or simple liver cyst, Hepatic cyst, liver cyst

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W,Novartis

Intervention

Keyword: Aspiration, Cyst, Pasireotide, Sclerotherapy

Outcome measures

Primary outcome

The primary endpoint of this study is the proportional change (%) in cyst diameter measured by ultrasound after 4 weeks of follow-up.

Secondary outcome

Secondary endpoints are the absolute reduction in centimetres after 4 weeks, the proportional and absolute reduction after 2, 12 and 24 weeks, the proportion of patients having cyst recurrence (i.e. > 80% of its original diameter) at follow-up, change of symptoms and health-related quality of life (HRQL) and any complications or adverse events reported during procedure or follow-up.

Study description

Background summary

Liver cysts are fluid filled cavities located in the liver. They are present in 2-11% of the general population, typically not causing any symptoms or complications. However, in a small subset of patients complaints of pain, abdominal fullness and distension, dyspnea and nausea occur. Currently, aspiration and sclerotherapy is the treatment of choice in symptomatic patients with a large dominant liver cyst. However, studies reported early fluid reaccumulation and relative high recurrence rates of cyst growth after

aspiration sclerotherapy ultimately leading to re-interventions.

In this respect, somatostatin analogues are promising agents known for its volume reducing effect in patients with polycystic liver disease. In this study we want to evaluate the effect of combining aspiration sclerotherapy with the multi-receptor binding, long-acting somatostatin analogue pasireotide. We hypothesize that administrating pasireotide before and after aspiration sclerotherapy could prevent early fluid reaccumulation and thereby result in a greater reduction of cyst diameter. Moreover, we expect a lower rate of cyst recurrence and subsequently lower need for re-interventions.

Study objective

The primary objective is to minimize fluid reaccumulation in the hepatic cyst after aspiration sclerotherapy in order to reduce cyst size. The secondary objectives are to reduce symptoms, improve health-related quality of life (HRQL), and reduce cyst recurrence to prevent re-interventions.

Study design

Randomized, double-blind, placebo-controlled intervention study.

Intervention

The subjects will be randomized (1:1) into two groups. Both groups will undergo aspiration sclerotherapy following the standard procedure. The intervention group will additionally receive two injections of 60 mg pasireotide long-acting release (LAR) intramuscularly: the first injection 14 days before and the second injection 14 days after the intervention. Patients in the placebo arm will receive two injections of saline solution corresponding to the scheme of the intervention group.

Study burden and risks

Aspiration sclerotherapy and the accompanying physical examination, ultrasonography and blood samples prior to the procedure are regarded as the indicated standard procedure of dominant symptomatic liver cysts. When compared to aspiration sclerotherapy alone, the burden and risks associated with participation of this study are:
- Possible side effects or adverse events related to the administration of long-acting pasireotide.
- Two to three additional site visits in comparison to standard care after aspiration sclerotherapy
- Electrocardiogram (ECG)
- Three questionnaires (gastro-intestinal and HRQL) are assessed at baseline, 4, 12 and 24 weeks after aspiration sclerotherapy. Importantly, these

questionnaires are relatively short and are not considered having emotional impact on the patient.

The potential benefit of participation is that combining pasireotide with aspiration sclerotherapy might reduce the cyst diameter more effectively than the conventional aspiration sclerotherapy. We expect that this will subsequently reduce symptoms and improve HRQL. Moreover, the rate of cyst recurrence is expected to be lower in the treatment arm and thereby re-treatment can be postponed or even avoided.

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

All patients who are diagnosed with a dominant liver cyst with an indication for aspiration and

sclerotherapy are suitable for inclusion in this study;In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Age 18 - 70 years
- Indication for aspiration and sclerotherapy
- Providing informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study;ASPIRATION SCLEROTHERAPY RELATED EXCLUSION CRITERIA
1. Signs of cyst bleeding on ultrasound
2. Signs of cyst infection (elevated CRP and/or leukocytes or temperature exceeding 38 degrees with the exclusion of a different focus)
3. Cyst < 5 cm
4. Coagulopathy (INR > 2 or platelets < 80 x 10^9)
5. Severe co-morbidity contraindicating anesthesia (i.e. ASA 4 classification);SOMATOSTATIN TREATMENT RELATED EXCLUSION CRITERIA
6. Patients with a known hypersensitivity to SST analogues or any component of the pasireotide LAR or SQ formulations
7. Pregnant or nursing women
8. Symptomatic cholecystolithiasis
9. QT interval related exclusion criteria
9.1 Known (congenital) long QT syndrome or QTcF at screening 470 msec
9.2 Family history of long QT syndrome or idiopathic sudden death
9.3 Uncontrolled or significant cardiac disease including recent myocardial infarction, congestive heart failure, unstable angina or sustained and/or clinically significant cardiac arrhythmias (e.g. bradycardia)
9.4 Risk factors for torsades de pointes: hypokalemia, hypomagnesemia, hypocalcaemia, cardiac failure, clinically significant/symptomatic bradycardia, or high grade AV block
9.5 Patients with concomitant disease(s) that could prolong QT such as autonomic neuropathy (caused by diabetes, or Parkinson's disease), HIV, cirrhosis, uncontrolled hypothyroidism or cardiac failure
9.6 Taking anti-arrhythmic medicinal products or other substances that are known to lead to QT prolongation
10. Uncontrolled diabetes as defined by HbA1C > 64 mmol/ml despite adequate therapy
12. History of pancreatitis
13. Non-malignant medical illnesses that are uncontrolled or whose control may be jeopardized by the treatment with this study treatment;FURTHERMORE
14. Use of oral contraception or estrogen supplementation
15. Intervention (i.e. aspiration with or without sclerotherapy or surgical intervention) within six months before baseline
16. Treatment with somatostatin analogues within six months before baseline
17. Any current or prior medical condition that may interfere with the conduct of the study or the evaluation of its results in the opinion of the investigator

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-04-2014
Enrollment:	34
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pasireotide LAR
Generic name:	Pasireotide LAR

Ethics review

Approved WMO Date:	31-07-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-12-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	17-03-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-11-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-12-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2013-003168-29-NL
CCMO	NL45115.091.13