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Assessment of itch symptoms in primary sclerosing cholangitis and other chronic liver diseases

Submission date
09/02/2023

Recruitment status
No longer recruiting

Registration date
20/02/2023

Overall study status
Completed

Last Edited
17/01/2024

Condition category
Digestive System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Primary sclerosing cholangitis (PSC) is a disease that causes inflammation and scarring of the bile ducts. There are no medicines that have been shown to slow down the rate of liver damage, and liver transplantation is the only life-saving treatment for people with the disease.
Whilst many clinical trials are underway, few address the symptoms of the disease. In a survey led by the international charity PSC Support, itching (pruritus) was named as one of the symptoms that impacted quality of life the most. However, there is no published study so far which indicates how this symptom varies according to the natural history of the disease, or according to currently available anti-itch medicines.
The aim of this study is to obtain detailed information on the presence and impact of itch symptoms in people who have the liver condition primary sclerosing cholangitis and compare this with itch symptoms in other chronic liver diseases, in those with inflammatory bowel disease (IBD) alone and in healthy participants. The researchers will investigate if there are any links between itch symptoms and the severity of the liver disease and blood test results. The variability of itch symptoms over a 48-week period will also be observed, along with the impact itch has on quality of life.

Who can participate?
Essentially any person with the liver condition known as primary sclerosing cholangitis can participate in the PSC group. The comparison group will be those with certain other chronic liver diseases, IBD alone and healthy participants. All participants should be aged over 16 years.

What does the study involve?
Participation involves completing four or five health-related questionnaires; two exploring itch symptoms and two exploring quality of life. For the PSC group an additional specific health-related questionnaire will be completed). If blood testing is required as per routine care, there will be additional testing to measure certain biomarkers that may be linked to itch. This data will be collected 2-4 times over a 48-week period.

What are the possible benefits and risks of participating?
Results from this study may help us to better understand why those with liver disease experience itch symptoms. This may therefore result in improved treatments and management of this in the future. The only real disadvantage of taking part in this study will be the extra time it will take to complete the surveys. The researchers have tried to make the questionnaires; relevant, simple and easy to complete. They estimate it should take about 10 minutes in total to complete.

Where is the study run from?
The University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
July 2021 to April 2025

Who is funding the study?
GlaxoSmithKline (UK)

Who is the main contact?
Dr Nasir Hussain, nxh100@student.bham.ac.uk

Contact information

Type(s)
Principal Investigator

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
305983

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

IRAS 305983

Study information

Scientific Title
Characterising the burden and clinical trajectory of pruritus in primary sclerosing cholangitis and non-cholestatic chronic liver disease

Study objectives
To quantify the severity and variability of itch symptoms in people living with the disease primary sclerosing cholangitis (PSC) and evaluate how this compares with non cholestatic chronic liver disease, inflammatory bowel disease (IBD) alone and healthy participants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/10/2021, North of Scotland Research Ethics Committee (Summerfield House, 2 Eday Road, Aberdeen, AB15 6RE, UK; +44 (0)1224 558458; gram.norses@nhs.scot), ref: RG_21-051

Study design
Mulit-centre observational cohort study with cross-sectional and prospective elements

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Quality of life

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Pruritus in primary sclerosing cholangitis, non-cholestatic chronic liver disease, inflammatory bowel disease

Interventions
There will be data collection in the form of health-related questionnaires. These will include questionnaires exploring pruritus and quality of life. Participants' medical record data will also be collected to assess for any correlations between their disease and pruritus. Routine blood test results will be collected as well as particular blood markers that may be associated with pruritus. This data will be collected at different time points over a 48-week period.

Intervention Type
Other

Primary outcome measure
Exploratory primary outcome:
The prevalence and long-term variability of pruritus over 48 weeks in patients with primary sclerosing cholangitis. Pruritus is measured using the numerical rating scale (NRS), 5d itch scale and the Simple Cholestatic Complaints Score at baseline, 12, 24, 36 and 48 weeks.

Secondary outcome measures
1. The variability and intensity of pruritus in PSC, compared with pruritus in non-cholestatic liver diseases, IBD alone and healthy participants. Pruritus is measured using the NRS and 5d itch tool at baseline, 12, 24, 36 and 48 weeks for PSC and measured at baseline and 48 weeks for non-cholestatic liver disease, and measured at baseline only for those with IBD alone and healthy participants.
2. Severity and extent of the liver disease, collected from medical records at baseline and up until 48 weeks
3. Routinely collected laboratory blood tests (full blood count, renal function, liver function tests, HbA1C and INR test results) collected during routine clinic visits from baseline up until 48 weeks
4. Exploratory biomarkers (serum bile acid levels and autotaxin activity results) collected during routine clinic visits from baseline and up until 48 weeks
5. Current use of anti-pruritic therapies and their effectiveness, collected from medical records at baseline up until 48 weeks
6. Quality of life measures measured using the Chronic Liver Disease Questionnaire CLDQ and the EQ-5D-5L tools, taken at baseline, 12, 24, 36 and 48 weeks for those with PSC, baseline and 48 weeks for those with non-cholestatic liver disease, and at baseline for those with IBD alone and healthy controls.

Overall study start date
01/07/2021

Completion date
01/04/2025

Eligibility

Key inclusion criteria
For the PSC group:
1. Must have a diagnosis of PSC
2. Either, subjects attending liver medicine clinic; or registered participants within the nationwide UK-PSC study

Non PSC group:
1. Subjects attending the liver or gastroenterology medicine clinic or healthy participants (no present or previous diagnosis of liver disease or IBD)
2. Diagnosis of following liver diseases; metabolic/non-alcoholic fatty liver disease, alcohol induced liver disease, chronic viral hepatitis, drug-induced liver disease, autoimmune hepatitis, genetic disorders of cholestasis
3. Diagnosis of IBD

4. Healthy participants who have no present or previous diagnosis of liver disease or inflammatory bowel disease

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
800

Key exclusion criteria
PSC group:
1. Age <16 years
2. Women who are pregnant or lactating
3. Lack of capacity (as deemed by the investigator) to provide an accurate medical history
4. Not able to communicate in English and no translator available
5. Small duct PSC without concomitant inflammatory bowel disease (IBD)
6. Other causes of chronic liver disease including
6.1. IgG4-related disease
6.2. Primary biliary cholangitis (PBC)
6.3. Secondary sclerosing cholangitis
6.4. Fatty liver disease
6.5. Habitual alcohol consumption greater than 21 oz/week for men or 14 ox/week for women
6.6. HIV infection
6.7. Drug-induced liver disease
6.8. Genetic disorders of cholestasis
6.9. Wilson disease
6.10. Alpha-1-antitrypsin deficiency
6.11. Hepatic veno-occlusive disease, including portal vein thrombosis or Budd-Chiari syndrome
7. History of liver transplantation
8. Current or prior history of cholangiocarcinoma, pancreatic or hepatocellular cancer
9. Gallbladder cancer in the previous 12 months
10. Colorectal cancer (or evidence of active metastatic disease) in the previous twelve months
11. Chemo- or radiotherapy in the previous twelve months
12. Chronic kidney disease, defined by the use of renal replacement therapy or a urea >20 mmol/l

Non PSC Group:
1. Age <16 years
2. Women who are pregnant or lactating
3. Lack of capacity (as deemed by the investigator) to provide an accurate medical history
4. Not able to communicate in English and no translator available
5. Radiological evidence of cholangiography including secondary sclerosing cholangitis
6. Histological evidence of inflammatory bile duct lesions or periductal fibrosis

7. Mixed aetiology of liver disease
8. Other causes of chronic liver disease:
8.1. Primary biliary cholangitis (PBC)
8.2. Primary sclerosing cholangitis (PSC)
8.3. HIV infection
8.4. Wilson disease
8.5. Alpha-1-antitrypsin deficiency
8.6. Hepatic veno-occlusive disease, including portal vein thrombosis or Budd-Chiari syndrome
9. History of liver transplantation
10. Current or prior history of cholangiocarcinoma, pancreatic or hepatocellular cancer
11. Gallbladder cancer in the previous 12 months
12. Colorectal cancer (or evidence of active metastatic disease) in the previous twelve months
13. Chemo- or radiotherapy in the previous twelve months
14. Chronic kidney disease, defined by the use of renal replacement therapy or a urea >20 mmol/l
15. Other known dermatological, haematological or extrahepatic disorder, including iatrogenic causes (e.g. excessive opioid use) associated with pruritus; investigator discretion

Date of first enrolment
18/10/2021

Date of final enrolment
01/04/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
John Radcliffe Hospital
Headley Way
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OX3 9DU

Study participating centre
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SE5 8AB

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
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Study participating centre
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Sponsor type
University/education

Website

http://www.birmingham.ac.uk/index.aspx

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
18/10/2025

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 3.0	01/09/2022	13/02/2023	No	No