ISRCTN15878562 https://doi.org/10.1186/ISRCTN15878562

Determining the extent of liver scarring in patients with psoriasis using a non-invasive scan and assessing the relationship between liver scarring and other potential risk factors for liver damage including methotrexate

Submission date
06/04/2020

Recruitment status
No longer recruiting

Registration date
17/06/2020

Overall study status
Completed

Last Edited
20/05/2024

Condition category
Digestive System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Psoriasis is a skin condition that causes red, flaky, crusty patches of skin covered with silvery scales. Liver damage is thought to be more common in patients with psoriasis based on previous small studies. Several risk factors are associated with liver disease in this group of patients. This includes severity of psoriasis as inflammation has been linked to liver disease. Other risk factors include alcohol intake and obesity. When psoriasis is not controlled with creams, the first systemic medication of choice is methotrexate. There have been concerns that this medication can lead to liver damage or worsen the liver health of psoriasis patients, but currently there is no strong evidence to confirm this. Several tests are currently used by dermatologists to monitor the liver health of patients with psoriasis. These include blood tests to measure liver enzymes. However, these tests are not very accurate at detecting liver damage. Taking a sample directly from the liver is no longer routinely used to diagnose liver damage as it is invasive and has many risks. A non-invasive scan (Fibroscan) similar to an ultrasound can be used to measure how elastic or stiff the liver is. If the liver is stiff this indicates that some damage has occurred. This test is now increasingly used to diagnose liver damage. This study aims to evaluate the extent of liver scarring in patients with psoriasis and assess the relationship between liver scarring and other potential risk factors for liver damage including methotrexate. In addition, the relationship between the outcome of the Fibroscan and other simple tests such as blood tests and scoring systems currently used for monitoring of liver health will be assessed. The overall aim is to use the information gained from this study to determine the number of participants required for a larger study to investigate factors influencing liver damage in this group of patients and to determine whether or not methotrexate is an important contributor to liver damage. Ultimately a risk prediction model will be built to enable dermatologists to predict the risk of liver fibrosis in patients with psoriasis and more accurately assess which patients are suitable to commence and continue treatment with methotrexate.

Who can participate?
Patients aged 18 and over with chronic plaque psoriasis

What does the study involve?
Participants complete questionnaires, provide blood samples (as part of routine care), undergo measurements of weight, waist, height, blood pressure, and undergo an assessment of liver stiffness using a non-invasive test similar to an ultrasound (a Fibroscan).

What are the possible benefits and risks of participating?
It is known that many patients with psoriasis develop liver disease but it is not known why. Participants will have an assessment of their liver health and will contribute to improving the management of psoriatic liver disease in larger populations of psoriasis patients. Methotrexate is a highly effective, generally safe and highly cost-effective treatment option for psoriasis. In the NHS it is the first choice systemic drug for psoriasis. The ability to accurately predict which patients may be at risk from liver scarring would be advantageous. The outcome of this study will inform the design of the larger study to determine which factors can predict the risk of liver scarring and whether or not methotrexate is an important contributor to the risk of liver scarring. The most effective strategies for monitoring the development of liver scarring in this group of patients can then be determined and the result may help in stratification of treatment in this group of patients based on the risk of developing liver scarring.

Where is the study run from?
The Royal Victoria Infirmary (UK)

When is the study starting and how long is it expected to run for?
January 2019 to March 2023

Who is funding the study?
Psoriasis Association (UK)

Who is the main contact?
Dr Philip Hampton
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
265303

Protocol serial number
CPMS 44694, IRAS 265303

Study information

Scientific Title
Investigation of the prevalence of liver fibrosis in patients with psoriasis using transient elastography and evaluation of the relationship between liver fibrosis and risk factors for liver fibrosis including methotrexate

Study objectives
The prevalence of liver fibrosis in patients with psoriasis is high and unexplained. It is hypothesised that important risk factors such as obesity, alcohol and diabetes contribute to the risk of liver fibrosis more than methotrexate.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/03/2020, North East - Newcastle & North Tyneside 2 Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ; +44 (0) 207 104 8091, +44 (0)207 104 8222; newcastlenorthtyneside2.rec@hra.nhs.uk), REC ref: 20/NE /0039

Study design
Observational; Design type: Cross-sectional

Primary study design
Observational

Study type(s)
Screening

Health condition(s) or problem(s) studied
Liver fibrosis in psoriasis

Interventions

The study will be a cross-sectional design. Patients with chronic plaque psoriasis diagnosed by a dermatologist with a PASI score of at least 5 at any time will be invited to join the study. A patient information leaflet will be provided. Written consent will be obtained.

Data will be collected via questionnaires, from patient's medical and electronic records. The majority of the data that the researchers are interested in is recorded as part of standard clinical care and they do not want to repeat measurements unnecessarily. They will therefore accept values for blood tests and imaging that have been recorded within 6 months of recruitment to the study. For patient severity scores and assessments of clinical data such as BMI, these will be collected at the time of recruitment.

The following data will be recorded for each patient:
1. Patient demographics: age, gender, ethnicity socioeconomic status
2. Disease severity: duration of psoriasis, age of onset of psoriasis), year of diagnosis (best approximation), year first seen by a dermatologist, Psoriasis Area and Severity Index (PASI) at recruitment, worst ever PASI, Dermatology life Quality Index (DLQI) at recruitment, worst ever DLQI, family history of psoriasis (first degree relative such as parent, sibling or child)
3. Characteristics: height and weight, Body Mass Index (BMI), Waist circumference, smoking status, alcohol intake questionnaire and AUDIT score, blood pressure, skin type and skin cancer risk factors
4. Liver stiffness measurements: value, >7.9kPa (yes/no), > 7kPa (yes/no), > 9.5kPa (yes/no)
5. Alcohol-related questions: AUDIT score, average alcohol intake in the last year (units per day or units per week)*, a history of sustained excessive alcohol consumption of > 35 units/week for females or > 50 units per week for males for more than 1 year, a history of excessive alcohol consumption (>14 units/day for both) – document the average units/day or week and the duration of alcohol, a history of alcohol dependence
6. Comorbidities – has the patient ever had or required treatment for the following illnesses and year of onset of illness:
cardiac disease (heart failure, cardiac arrhythmias, stroke, coronary artery disorders, angina, myocardial infarction), vascular diseases (hypertension, peripheral vascular disorders, deep vein thrombosis, pulmonary embolism, disorders of metabolism and nutrition (diabetes mellitus, impaired glucose tolerance, dyslipidaemia, endocrine diseases (thyroid disease), nervous system disorders(demyelinating diseases, epilepsy), respiratory, thoracic and mediastinal disorders (asthma, COPD), renal and urinary tract diseases (chronic renal failure), hepatobiliary diseases (viral hepatitis infection, other liver disease), gastrointestinal diseases (peptic ulcer), gastrointestinal inflammatory conditions (Crohn's disease, ulcerative colitis), psychiatric diseases (depression, anxiety), infections and infestations (tuberculosis). immune system disorders, skin and soft tissue disorders (psoriatic arthritis (diagnosis of PSA by a rheumatologist? and year of diagnosis), other types of cancers: skin cancers (non-melanoma skin cancer, squamous cell, carcinoma, basal cell carcinoma) melanoma skin cancers and pre-cancerous skin lesions (melanoma skin cancer, melanoma in situ, Bowen disease, actinic keratosis, keratoacanthoma.
7. Duration on methotrexate in months, cumulative dose of methotrexate
8. UV Therapy– (yes/no), duration and type, response
9. Any current systemic drug, Oral PUVA or biologics for psoriasis, Small molecule immunomodulator therapy for psoriasis (apremilast or dimethyl fumarate) – dose, frequency and date started
10. All previous systemic or biologics or oral PUVA, small molecule immunomodulator therapy for psoriasis – start and stop dates and stop reason
11. Any other systemic drug or biologic drugs (dose and frequency) and durations with start dates and stop dates and duration
12. Current medications and start dates – including pimecrolimus or tacrolimus
13. Folic acid: duration and frequency

14. Blood tests: HbA1c, fasting glucose (if available), lipid profile including triglycerides, HDL cholesterol, AST, ALT, abnormal AST in the past year, abnormal ALT in the past year, worst ever AST/ALT, platelets, procollagen three peptide (PIIINP), albumin
15. Previous liver ultrasound report, previous liver biopsy report
16. NAFLD and FIB4 score will be calculated and metabolic syndrome will be assessed based on the IDF metabolic syndrome definition (modified version will be used when fasting results not available (fasting glucose will be replaced by HbAIc and HDL cholesterol and triglyceride will be replaced by non-fasting value)

Intervention Type
Other

Primary outcome(s)
1. Cumulative dose of methotrexate within 6 months of recruitment, calculated from data collected to identify weekly doses each patient received (mg) over time and adding these up to reach a total dose in gram for every patient
2. Liver stiffness measured using Fibroscan within 12 months of recruitment

Key secondary outcome(s))
1. Demographics, weight (kg), waist (cm), height (cm), blood pressure (mm/Hg) measured at baseline/within 6 months of recruitment
2. Risk factors for liver disease (HbA1c, triglycerides (mmol/L), HDL (mmol/L), LDL (mmol/L), cholesterol (mmol/L), platelets, liver function tests, ALT, worst ever ALT in the past year, AST, worst ever AST in the past year, ALT/AST ratio, albumin, procollagen three peptide (PIIINP) – worst value), measured using blood samples within 6 months of recruitment
3. Psoriasis severity measured using Psoriasis Area Severity Index (PASI) (score ranges: 0-72) at baseline and worst ever
4. Impact of skin disease on the quality of life measured using Dermatology Life Quality Index (DLQI) (score ranges: 0-30) at baseline and worst ever
5. Alcohol use measured using AUDIT Score at baseline and within 6 months of recruitment
6. Metabolic syndrome, defined as waist ≥94 cm (men) or ≥80 cm (women), and ≥2 of:
6.1. ≥5.6 mmol/L (100 mg/dL) or diagnosed diabetes
6.2. <1.0 mmol/L (40 mg/dL) (men); <1.3 mmol/L (50 mg/dL) (women) or drug treatment for low HDL cholesterol
6.3. ≥1.7 mmol/L (150 mg/dL) or drug treatment for high triglycerides
6.4. ≥130/85 mmHg or drug treatment for hypertension
Measured within 6 months of recruitment
7. Liver fibrosis/scarring measured using FIB 4 score within 6 months of recruitment
8. Fatty liver measured using NAFLD score within 6 months of recruitment

Completion date
30/03/2023

Eligibility

Key inclusion criteria
1. Adults > = 18 years of age
2. Ability to consent
3. Chronic plaque psoriasis diagnosed by a dermatologist with a PASI > = 5 at anytime

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Pregnancy
2. Potential participants who may have difficulties in adequately understanding written or verbal information in English

Date of first enrolment
08/06/2020

Date of final enrolment
31/03/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Victoria Infirmary
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Charity

Funder Name
Psoriasis Association

Alternative Name(s)
The Psoriasis Association

Funding Body Type
Government organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be included in the subsequent results publication. The elements to be public will be in the papers, e.g. as supplementary data.

(added 20/05/2024)
Type of data stored and name of repository:
- Investigator site File containing participants signed and dated study consent forms are archived at DATATRON Document Image Archiving Ltd. Contact Datatron for scanning and records management
- Identifiable data ie: recruitment log and non-identifiable link anonymised data ie: study clinical database, is held on a secure, password protected, Dermatology Research Drive on an NHS computer, with access only to authorized dermatology research personnel.
- Paper clinical research forms(CRF's) are stored in files within NuTH Dermatology Research Office, Dermatology Outpatients Department. The Dermatology unit out of hours is only accessed by authorized personnel with swipe ID passes.

The process for requesting access, timing for availability:
- Email request to DATATRON, return of archived boxes will be within 24 - 48hrs.
- Regulatory Access to NuTH computers - IT will need 5 days’ notice for new accounts.

Whether consent from participants was obtained:
- Yes, Data will be held for 5yrs as stated in Patient Information Sheet / Consent Form.

Comments on data anonymisation, any ethical or legal restrictions:
- Participants clinical data collected on paper CRF's and clinical database are link anonymised with a study code.

IPD sharing plan summary

Stored in publicly available repository, Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		17/02/2024	07/05/2024	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version v1.2	26/02/2020	17/06/2020	No	Yes
Protocol file	version v1.02	21/08/2019	17/06/2020	No	No