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Developing a new test for liver injury after taking too much paracetamol

Submission date
02/02/2023

Recruitment status
No longer recruiting

Registration date
15/09/2023

Overall study status
Completed

Last Edited
15/09/2023

Condition category
Injury, Occupational Diseases, Poisoning

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

Plain English summary of protocol

Background and study aims
Paracetamol overdose (POD) is common, with about 100,000 cases per year, and around 50,000 of these are treated and around 5,000 develop liver injury. The most common treatment used is called N-acetylcysteine (NAC). The sooner treatment with NAC is started after POD the greater the likelihood that drug-induced liver injury (DILI) will be prevented.
The current biomarker (a molecule in the blood) that shows us the extent of DILI is called ALT and it is a reliable gold standard for established liver injury. However, ALT increases too slowly after POD for the diagnosis of liver injury to occur so that treatment with NAC can have the best possible outcome. There is a need for an assay (a quick test) capable of telling us quicker that patients are likely to develop liver injury after POD to improve treatment knowledge and hopefully a better outcome.
K18 is another biomarker that is seen in liver injury earlier on than ALT. To try and improve patient care researchers have created a capillary blood (taken from a fingerpick), quantitative (can be measured), K18 Lateral Flow Assay/test (K18-LFA) that is low-cost, rapid and reliable. These look the same as the COVID-19 tests and can be read by the naked eye. The researchers also plan to test a device that uses a low-powered laser to read the strip and give a value (called a Raman Reader).

Who can participate?
Patients aged 16 years or older who have presented to the emergency department with a suspected deliberate or accidental paracetamol overdose

What does the study involve?
Participants will be asked to provide a tiny amount of blood with a blood sampling device which takes blood from the finger or thumb tip using a small lance. This will be carried out by a doctor or nurse. They will be asked for this soon after they have consented, 2 hours later and then on days 2-5 if they are in hospital. A small amount of any blood sample by the team looking after them whilst they are in hospital on days 1 and 2 will be requested - only if there is excess taken after the routine tests have been run.

What are the possible benefits and risks of participating?
There are no expected benefits for the participant. This is a very low-risk study. The results of

the research tests will not be used to impact the clinical care of the participant. There is a small risk of bruising from the blood sampling device.

Where is the study run from?
1. Royal Infirmary of Edinburgh (UK)
2. St John's Hospital Livingston (UK)

When is the study starting and how long is it expected to run for?
July 2021 to May 2024

Who is funding the study?
The Medical Research Council (MRC)

Who is the main contact?
THT-clinical@ed.ac.uk

Contact information

Type(s)
Public

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
317414

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
AC22112, IRAS 317414

Study information

Scientific Title

Point-of-care assessment of drug-induced liver injury (POC-DILI)

Acronym
POC-DILI

Study objectives
The novel medical devices will be able to identify liver injury post paracetamol overdose before the standard care test using a specific biomarker present in the blood.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Single-site observational prospective cohort study.

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Diagnosis of liver injury in patients presenting with paracetamol overdose

Interventions
Once consented:
1. Data will be collected on each patient including age, sex, gender, ethnicity, time of overdose, amount ingested, pattern of overdose, co-ingested medicines, blood results and treatment required.
2. At time 0, 2 hours (+/-1) and on days 2-5 (if admitted to hospital) approximately 25 µl of blood (could be a margin of 10-30 µl) will be taken using a standard finger prick lance will be mixed with 75 µl of buffer. The 100 µl of diluted blood will be added to the K18-LFA cassette at the bedside and a visual reading taken at between 10 and 30 minutes. An image of the cassette will be taken and uploaded to the database. The Handheld Raman Reader will then be used on the K18 LFA to quantify the assay in a separate area of the hospital and the results noted on the CRF /SDW. This will be performed in a timely manner (after 20 and before 120 minutes).
3. On days 1 and 2 (if the participant is admitted to the hospital) surplus blood (between 300 µl and 1 ml) (for serum) will be requested from the biochemistry labs at the recruiting hospital sites.
4. At Day 30 (+ 7 days) blood results and all clinical data required (treatment and health outcomes) will be recorded

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

Keratin 18 Lateral Flow Assay (K18-LFA), Raman Spectroscopy Reader (Raman Reader)

Primary outcome(s)
1. ALT measured as part of routine clinical care and recorded on the patient's electronic medical record (daily blood results will be recorded up until day 30)
2. K18 in finger prick capillary blood measured using the Point of Care DILI Diagnostic (lateral flow assay combined with handheld Raman Spectrometer) at baseline, +2 hours then daily for up to 5 days whilst the participant is in hospital

Key secondary outcome(s))
1. ALT, INR and bilirubin measured as part of routine clinical care and recorded on the patient's electronic medical record (daily blood results will be recorded up until day 30)
2. K18 from surplus blood serum measured by ELISA using the M65 Classic ELISA on days 1 and 2 if the participant is admitted and is in hospital on those days

Completion date
31/05/2024

Eligibility

Key inclusion criteria
1. Presentation at hospital within 5 days after suspected or confirmed paracetamol overdose (all patterns of overdose are eligible – including single and staggered overdoses whether accidental or deliberate)
2. Aged 16 years or older
3. Capacity to provide informed consent
4. Deemed suitable for study procedures by attending/treating clinician

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Deemed unfit by the Investigator or treating clinician to participate
2. Detained under the Mental Health (Care and Treatment) (Scotland) Act 2003

Date of first enrolment
01/05/2023

Date of final enrolment
26/05/2024

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Sponsor information

Organisation
Accord (United Kingdom)

ROR
https://ror.org/01x6s1m65

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Consent will be sought from participants to permit sharing of anonymised data with funders, commercial and non-commercial collaborators or published on publicly available resources as appropriate. 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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes