ISRCTN11735871 https://doi.org/10.1186/ISRCTN11735871

Optical coherence tomography in cerebral malaria

Submission date
25/10/2022

Recruitment status
No longer recruiting

Registration date
09/12/2022

Overall study status
Ongoing

Last Edited
09/12/2022

Condition category
Infections and Infestations

[_] 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
This study aims to show whether changes in the eye can be used to predict changes in the brain in children in a coma caused by malaria. The optic nerve is the 'electrical cable' which connects the eye to the brain. When the brain is swollen, the optic nerve can become swollen. We hope to show that swelling in the optic nerve, detected with a hi-tech camera, can be used to predict swelling in the brain. This is useful because the current way to detect brain swelling is using MRI scans, which are expensive and are often not available in sub-Saharan Africa, where malaria is most problematic. We will also check the eyes of children with coma from causes other than malaria. The retina is the part of the eye that senses light. We will use the same camera to detect areas in the retina which have a reduced blood supply. This could help to predict whether parts of the brain also have reduced blood supply, which may result in a developmental delay in affected children.

Who can participate?
Children aged 16 years old and under with a coma caused by malaria, with a coma caused by other diseases and healthy children

What does the study involve?
The hi-tech camera is called an optical coherence tomography (OCT) machine. For children in comas, we use a handheld OCT camera. Currently, handheld OCT cameras are available from medical suppliers, but they are expensive. Working with a team from the University of Liverpool Department of Electrical Engineering we hope to produce a new machine which performs just as well as the machines available on the market but costs much less.

All included children will have their eyes examined and photographs of their eyes taken with the camera. They will also have tests to assess their development. Those that are in a coma will also have an MRI scan.

What are the possible benefits and risks of participating?
The benefits to all participants are that they will get a scan of their eyes which will be looked at

by an eye doctor. This may help identify eye diseases that the patient didn't know about. The study will not interfere with the usual care for children with coma, so the risks of participating are very small.

Where is the study run from?
The Paediatric Research Ward at Queen Elizabeth Central Hospital, Blantyre (Malawi)

When is the study starting and how long is it expected to run for?
July 2021 and will run until April 2026

Who is funding the study?
Wellcome Trust (UK)

Who is the main contact?
Dr Nicholas Beare, nbeare@liverpool.ac.uk

Contact information

Type(s)
Principal Investigator

Contact name
Dr Nicholas Beare

ORCID ID
http://orcid.org/0000-0001-8086-990X

Contact details
Department of Eye & Vision Science
Institute of Life Course and Medical Sciences
University of Liverpool
William Henry Duncan Building
6 West Derby Street
Liverpool
United Kingdom
L7 8TX
+44 (0) 151 794 2064
nbeare@liverpool.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

Nil known

Study information

Scientific Title
Predicting acute and post-recovery outcomes in cerebral malaria and other comas by optical coherence tomography

Acronym
OCT in CM

Study objectives
Predicting brain swelling
Optical coherence tomography (OCT) scans of the optic nerve can be used to predict clinically significant brain swelling in cerebral malaria (CM). Enumeration of retinal haemorrhages can be used to predict clinically significant brain swelling.

Predicting neurodevelopmental deficits
OCT scans of the macula can be used to predict neurodevelopmental deficits post-recovery from CM.

Development of a low-cost handheld OCT
A robust, low-cost, handheld OCT can be produced for significantly less than commercially available machines, with similar usability and effectiveness.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 27/10/2022, Research Ethics Committee for the University of Liverpool (University of Liverpool, Liverpool, L69 3BX, UK; +44 (0)151 794 8290; ethics@liverpool.ac.uk), ref: UOL001660
2. Approved 28/03/2022, Michigan State University Institutional Review Board (4000 Collins Rd., Suite 136 (IRB) or Suite 137 (Compliance), Lansing, MI 48910; +1 517 355 2180; irb@ora.msu.edu), ref: STUDY00007131
3. Approved 02/06/2022, University of Malawi College of Medicine Research and Ethics Committee (Private Bag 360, Chichiri Blantyre 3 Malawi; +265 1 874 377; comrec@medcol.mw), ref: P.11/21/3460

Study design
Observational single-site cohort study with an acute phase and 1- to 2-year follow-up

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

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
Prediction of acute and post-recovery outcomes in paediatric cerebral malaria

Interventions
This is a cohort study to determine if an imaging device can differentiate different groups within the cohort (severe brain swelling versus no/mild/moderate brain swelling; and in follow-up, neurodevelopmental deficit versus none). There is no randomisation or intervention. Some controls are being recruited in order to determine normal child development in this population in order to aid the identification of neurodevelopmental deficits in the cohort.
We will be evaluating OCT of the optic nerve head (ONH) as a test to identify severe brain swelling in paediatric patients with cerebral malaria (CM), against a gold standard of graded brain MRI images. We will prospectively evaluate a number of ONH parameters measurable by OCT to determine which has the best AUC to detect severe brain swelling versus no/mild /moderate brain swelling. Paediatric patients with other comas will also be recruited for a similar analysis.
The same CM patients will also be studied to evaluate macula ischaemia as a predictor of neurological deficit in CM. Macular ischaemia is detectable as hyper-reflectivity on OCT scans of the macula which will be done along with ONH scans on admission. In order to detect all neurological deficits including subtle developmental abnormalities, participants will be seen at 1, 12 and 24 months (except those recruited in the final year) for neurodevelopmental assessment. This will consist of Malawi Developmental Assessment Tool (MDAT) for those under 5 years, the Kaufmann Assessment Battery for Children (ABC) for those 5 years of age and older, and the Liverpool Neurological Outcome Score. From the results, we will create an age-adjusted measure of global development and cognition. Healthy age-matched controls will be recruited and added to existing data to determine the normal age-specific range for child development in this population.
A novel OCT which is robust and low-cost will be developed in Liverpool in collaboration with the University of Liverpool Department of Electrical Engineering. The University of Liverpool OCT will be evaluated in Malawi in comparison to a commercially available handheld OCT. The operator will record ease of use on a 5-point scale, the time taken to acquire OCT scans and any factors affecting scan quality. At image analysis, a quality assessment of the images will be made (good, acceptable, unacceptable/ungradable). Measured parameters from the optic nerve head and extracted data on hyper-reflectivity and other parameters in the macula will be compared between the two devices using intraclass correlation coefficients

Intervention Type
Other

Primary outcome measure
Optic nerve head (ONH) swelling measured using optical coherence tomography (OCT) at admission, then daily during admission

Secondary outcome measures

1. Macular ischaemia measured using OCT at admission, then daily during admission
2. Acceptability of novel OCT measured using a 5-point scale at each use
3. Effectiveness of novel OCT measured using intraclass correlation coefficients during data analysis

Overall study start date
06/07/2021

Completion date
01/04/2026

Eligibility

Key inclusion criteria
1. Parent or guardian gives informed consent for their child's participation
2. Cerebral malaria: under 16 years of age, BCS≤2, Plasmodium falciparum parasitaemia on a blood film, no other cause of coma evident
3. Other comas: under 16 years of age, BCS≤3 with acute presentation.
4. Healthy controls age-matched under 16 years

Participant type(s)
Mixed

Age group
Child

Upper age limit
16 Years

Sex
Both

Target number of participants
270

Key exclusion criteria
1. Hypoglycaemia, post-ictal, or other transient state accounting for coma
2. Contraindication to MRI
3. History or evidence of pre-existing hydrocephalus, significant neurological disease, gross neurological disability or learning difficulties
4. History or evidence of pre-existing significant ocular disease
5. History or evidence of severe life-limiting or chronic disease including but not limited to advanced HIV/AIDS (Stage 4), disseminated TB and malignancy

Date of first enrolment
10/11/2022

Date of final enrolment
01/04/2025

Locations

Countries of recruitment
Malawi

Study participating centre
Malawi-Liverpool-Wellcome Trust and Queen Elizabeth Central Hospital
Queen Elizabeth Central Hospital
College of Medicine
P.O. Box 30096
Chichiri
Blantyre 3
Malawi
P.O. Box 30096

Sponsor information

Organisation
University of Liverpool

Sponsor details
-
Liverpool
England
United Kingdom
L69 3BX
+44 (0) 151 794 2000
sponsor@liverpool.ac.uk

Sponsor type
University/education

Website
http://www.liverpool.ac.uk/

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Research council

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The findings of the study will be shared and disseminated through presentation at relevant national and international meetings and publication in peer review journals. In Malawi this will include the KUHeS Research Dissemination Day and Malawi-Liverpool-Wellcome Annual Scientific Meeting. Results will be presented at relevant international meetings particularly those with a focus on malaria. Publications will be open access as required by the funder.

Intention to publish date
01/09/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository at the University of Liverpool and the Malawi-Liverpool-Wellcome Trust. Imaging data will be available for sharing with research teams after discussion by prospective users of the data with senior researchers within our team and after dissemination of the results of the project. Only anonymised data will be shared.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 4.0	13/10/2022	21/11/2022	No	No