ISRCTN14018410 https://doi.org/10.1186/ISRCTN14018410

Endoscopic lavage after intraventricular haemorrhage in neonates in the UK: a national randomised controlled trial on the efficacy of neuro-endoscopic lavage

Submission date
15/11/2023

Recruitment status
Recruiting

Registration date
21/12/2023

Overall study status
Ongoing

Last Edited
10/06/2025

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Around one in thirteen infants is born preterm in the United Kingdom. Despite major advances in survival, intraventricular haemorrhage (IVH) remains one of the most serious complications of preterm birth. Intraventricular haemorrhage (IVH) is bleeding into the fluid spaces of the brain with severe Intraventricular Haemorrhage (IVH) and Post-haemorrhagic Ventricular Dilatation (PHVD) and is common in babies who are born premature. This results in a build-up of brain fluid, that may increase the pressure in the brain. Bleeding in the brain can cause a risk to life and also cause problems with vision, hearing, cognition (understanding) and motor function (movement). The current best treatment available involves implanting a temporary drainage device in a short operation. There is a new treatment called neuroendoscopic lavage (NEL), which involves the insertion of a small camera into the fluid spaces (ventricles) of the brain to wash out as much of the blood as possible before inserting the temporary drainage tube. This study will investigate whether the addition of NEL to the standard procedure of inserting a temporary cerebrospinal fluid (CSF) drainage device will improve children's development at 2 years of age

Who can participate?
Premature infants born before 37 weeks of gestational age with severe IVH and PHVD

What does the study involve?
Eligible participants will be randomly allocated into one of two groups:
1. Intervention group: neuroendoscopic lavage, or washout, and temporary drainage device.
2. Control group: continue with usual care.
After the operation all participants will be cared for in the usual way. Participants from both groups will undergo follow ups which will include regular neurosurgical and paediatric check-ups over a 2-year period. During study visits the participant’s parent/guardian(s) will be asked to complete questionnaires to collect information about their views of the participant’s development. They will also be asked about the participants’ and their own quality of life. At about 2 years of age, participants will also be required to attend an additional visit where they

will undergo specific assessments to see how well the participant is developing. This assessment will be done by a qualified healthcare professional with experience at performing developmental assessments for children and who does not know which group the participant is in.

What are the possible benefits and risks of participating?
The information from the trial will help to improve treatment for future patients with IVH.
All medical procedures involve the risk of harm, but this is usually low. The risks of taking part in the study are mostly associated with the side effects of the washout procedure and the temporary device insertion. These are listed below:
Risk of infection
Risk of causing further bleeding into the brain
Drainage tube blockage or dysfunction – If this occurs the participant's doctor will assess if they may need to have another operation to correct this or to insert a permanent VP shunt.
Seizure (seizures are caused by a sudden burst of electrical activity that temporarily affects how it works).
Leakage of fluid surrounding the brain
Electrolyte disturbance
Stroke (less than 1 %): Any procedure carried out on the brain carries a small risk of stroke.
For participants randomised to receive neuroendoscopic lavage (or washout) (Intervention Group), this is a more invasive procedure. It therefore increases the anaesthetic time by about 30 minutes, but this is not thought to be a significant risk. General anaesthetics have some risks and side effects, and the participant's anaesthetist will discuss these with the parent/guardian(s) before surgery.
Risks associated with the neuroendoscopic lavage (or washout) are listed here:
Risk of brain injury (less than 1%): The procedure involves the insertion of a small camera (neuroendoscope) into the fluid spaces of the brain to wash out as much of the blood as possible before inserting the temporary drainage tube. Because the camera (neuroendoscope) has a slightly larger diameter than the catheter used to inset the drainage device, there is the potential to cause damage to the brain at the point where the camera enters the fluid space.
Risk of further bleeding (less than 1 in 10): Washing the blood clot out from the ventricular system may also carry a risk of causing a further bleed within the brain. In a small pilot study the rate of rebleeding was found to be very low, but adding the washout procedure to the normal standard treatment may increase the risk.
Electrolyte disturbance: The use of a washout fluid may cause fluctuations in salt levels in the blood. This also increases the risk of seizure in babies that receive the washout.
Study doctors will be monitoring all participants in the study very carefully. Continuing to assess any risk related to this procedure is an important part of the study.

Where is the study run from?
UCL Comprehensive Clinical Trials Unit (CCTU) (UK)

When is the study starting and how long is it expected to run for?
March 2023 to February 2029

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
1. Chief Scientific Investigator: Kristian Aquilina: kristian.aquilina@gosh.nhs.uk
2. Trial Manager: Sue Massingham: cctu.enlivenuk@ucl.ac.uk

Contact information

Type(s)
Scientific, Principal Investigator

Contact name
Mr Kristian Aquilina

Contact details
Consultant paediatric neurosurgeon
Great Ormond Street Hospital
Department of Neurosurgery
Level 10 Old Nurses Home
Great Ormond Street
London
United Kingdom
WC1N 3JH
+44 (0)7791613155
kristian.aquilina@gosh.nhs.uk

Type(s)
Public

Contact name
Ms Sue Massingham

Contact details
Comprehensive Clinical Trials Unit at UCL
Floor 2, 90 High Holborn
London
United Kingdom
WC1V 6LJ
+44 (0)20 7679 9351
cctu.enlivenuk@ucl.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
322127

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 56647, NIHR151288, IRAS 322127

Study information

Scientific Title
Endoscopic lavage after intraventricular haemorrhage in neonates in the UK: a national randomised controlled trial on the efficacy of neuro-endoscopic lavage

Acronym
ENLIVEN-UK

Study objectives
It is hypothesised that the addition of Neuroendoscopic Lavage (NEL) will be safe and will improve neurodevelopmental outcomes at 2 years in children with severe Intraventricular Haemorrhage (IVH) and Post-haemorrhagic Ventricular Dilatation (PHVD).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/12/2023, South West - Central Bristol (2 Redman Place, London, E20 1JQ, United Kingdom; 0207 104 8197; centralbristol.rec@hra.nhs.uk), ref: 23/SW/0137

Study design
Phase III multi-centre assessor-blinded randomized controlled interventional trial, including an internal pilot study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment, Efficacy

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
Intraventricular Haemorrhage (IVH) and Post-haemorrhagic Ventricular Dilatation (PHVD) in premature infants born before 37 weeks of gestational age

Interventions
This is a phase III, multi-centre, randomised, assessor-blinded, controlled trial of NEL with temporising device (intervention Arm A) vs temporising device alone (standard treatment /Control Arm B).

Arm A (Intervention): NEL with the temporising device. NEL will be carried out within the same operative procedure as the insertion of a clinically indicated temporising device. NEL involves the irrigation of the blood and its breakdown products within the ventricular system and is carried out in a controlled procedure, within approximately 30 minutes, under direct vision.

Arm B (Control/Usual Care) - temporising device alone. Infants will undergo the standard surgical procedure to insert either a Ventricular access device (VAD) or Ventriculosubgaleal shunt (VSGS), at the discretion of the treating surgeon, in line with their standard current practice.

Both the intervention (Arm A) and control arm (Arm B) procedures will be performed by paediatric neurosurgeons who have experience in infant neuro-endoscopy. All infants in Arms A and B will be followed up until they reach 2 years corrected age (+/-2 months).

A computer-generated randomisation sequence, using the SealedEnvelope.com system, will be used to assign the participants to one of the two treatment arms using a 1:1 ratio.

Intervention Type
Procedure/Surgery

Primary outcome measure
Cognitive Quotient (CQ) measured by the Bayley Scales of Infant and Toddler Development Fourth Edition (Bayley IV) at 2 years' corrected age (+/- 2 months)

Secondary outcome measures
1. Developmental measures:
1.1. Motor quotient (MQ): Age equivalent motor score of the Bayley IV divided by corrected age at assessment, measured at 2 years' corrected age
1.2. Language quotient (LQ): Age equivalent language score of the Bayley IV divided by corrected age at assessment, measured at 2 years' corrected age
2. Other neurological and functional assessments conducted during the 2-year follow-up visit:
2.1. Presence of seizures during the first 2 years and use of anticonvulsant medication at 2 years
2.2. Presence of cerebral palsy (+ accompanying Gross Motor Function Classification System (GMFCS) grade and deficit distribution map using the Classification of SCPE
2.3. Assessment of hearing and vision (British Association of Perinatal Medicine classification) at 2 years' corrected age
2.4. Parent report at 2 years' corrected age:
2.4.1. Brief Infant Toddler Social Emotional Assessment (BITSEA)
2.4.2. Quantitative Checklist for Autism in Toddlers (Q-CHAT)
3. Mortality up to 2 years corrected age
4. NEL and VP shunt related outcomes:
4.1. Safety of NEL, measured by the number of Adverse Events reported until 2 years' corrected age
4.2. Number and type of further surgical procedures required until 2 years' corrected age
4.3. Requirement for permanent VP shunt insertion at 6 months' corrected age
5. Quality of life and health economic assessments:
5.1. Health-related quality of life (HRQoL) in children measured using the TNO-AZL Preschool Children's Quality of Life (TAPQOL) at 12 months and 2 years' corrected age
5.2. HRQoL in primary caregiver measured using the EuroQoL EQ-5D-5L at baseline, 6 months, 12 months and 2 years' corrected age
5.3. Healthcare resource use costs (CSRI (adapted) children version) at 3, 6, 12, 18 months and 2

years' corrected age
5.4. Subsequent cost-effectiveness analysis and cost-benefit analysis of impact on carers based on responses to the EQ-5D-5L

Overall study start date
01/03/2023

Completion date
28/02/2029

Eligibility

Key inclusion criteria
1. Premature infants born before 37 weeks of gestational age
2. IVH: Papile Grades II-IV on cranial ultrasound scan
3. PHVD: Ventricular index at or beyond the threshold point of the 97th centile for gestational age plus 4 mm on the Levene chart despite 2 attempted lumbar or ventricular punctures.

Participant type(s)
Patient

Age group
Neonate

Lower age limit
22 Weeks

Upper age limit
36.85 Weeks

Sex
Both

Target number of participants
Planned Sample Size: 100; UK Sample Size: 100

Key exclusion criteria
1. Infants with coagulopathy (INR > 1.6) or platelet disorders (platelet count under 80,000/mL) that persist on attempted correction. Clinical judgement will be made by the Investigator.
2. Infants deemed too unstable for neurosurgical intervention. This is a clinical judgement made by the responsible neurosurgeon, neonatologist and anaesthetic team.
3. Parents or carers unwilling to provide informed consent.

Date of first enrolment
09/05/2024

Date of final enrolment
31/08/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street
London
United Kingdom
WC1N 3JH

Study participating centre
Alder Hey Children's Hospital
Eaton Road
West Derby
Liverpool
United Kingdom
L12 2AP

Sponsor information

Organisation
University College London

Sponsor details
Comprehensive Clinical Trials Unit at UCL
Institute of Clinical Trials & Methodology
90 High Holborn
London
England
United Kingdom
WC1V 6LJ
+44 (0)20 7679 9351
cctu.enlivenuk@ucl.ac.uk

Sponsor type
University/education

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

ROR

https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The results of the trial will be disseminated regardless of the magnitude and interpretation of any effect of the intervention. The publication of the results will comply with the UCL CCTU Publication Policies.

A lay summary of the results will also be produced to be disseminated to those participants who took part who express an interest in the findings.

A summary of results will be submitted to the REC via the HRA and published through an open-access mechanism in a peer-reviewed journal within 12 months of the trial closure.

Intention to publish date
01/01/2030

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