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NeoCLEAR: optimising lumbar punctures in newborns

Submission date
30/05/2018

Recruitment status
No longer recruiting

Registration date
26/06/2018

Overall study status
Completed

Last Edited
28/12/2023

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Every year at least 15,000 newborns undergo a lumbar puncture to confirm suspected meningitis. Lumbar puncture technique varies in practice, and success rates are low (50-60%) meaning procedures need to be repeated, causing distress to the infants and their parents and extending treatment and hospital stay time. There is a pressing need for a large study to determine which lumbar puncture technique is the best approach. The aim of this study is to compare lumbar puncture techniques with the infant in a sitting position versus a lying position, and early versus late stylet removal.

Who can participate?
Newborns and infants in neonatal units and maternity wards who are having a lumbar puncture

What does the study involve?
The participants are randomly allocated to one of the following technique combinations:
1. Lying position and early stylet removal
2. Sitting position and early stylet removal
3. Lying position and late stylet removal
4. Sitting position and late stylet removal
The proportion of successful lumbar punctures is measured in the four groups.

What are the possible benefits and risks of participating?
The results of this trial will inform best practice, and ultimately, improved technique would result in fewer uninterpretable samples, fewer repeated procedures, reduced distress for infants and families, decreased antibiotic use and risk of antibiotic resistance, and reduced NHS costs due to fewer procedures, reduced length of stay, shorter antibiotic courses, and minimised antibiotic-associated complications. All of the methods used in the study are used routinely within UK hospitals. At the moment it is not known whether one method is better than others, so babies taking part could be given any of them.

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

When is the study starting and how long is it expected to run for?
September 2017 to February 2021

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

Who is the main contact?
Christina Cole
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Study website
https://www.npeu.ox.ac.uk/neoclear

Contact information

Type(s)
Scientific

Contact name
Ms Christina Cole

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
223737

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
35643

Study information

Scientific Title

NeoCLEAR: Neonatal Champagne Lumbar punctures Every time – An RCT. A multicentre, randomised controlled 2x2 factorial trial to investigate techniques to increase lumbar puncture success

Acronym
NeoCLEAR

Study objectives
Every year at least 15,000 newborns undergo a lumbar puncture to confirm suspected meningitis. Lumbar puncture technique varies in practice, and success rates are low (50-60%) meaning procedures need to be repeated, causing distress to the infants and their parents and extending treatment and hospital stay time. There is a pressing need for a large randomised controlled trial to determine which lumbar puncture technique is the best approach.

The trialists have designed a pragmatic (i.e a low level of trial-driven standards is enforced and sites work to their standard practices and processes for generalisability of the trial results), multi-centre, randomised controlled trial comparing two traditional lumbar puncture techniques:
1. The infant in sitting position versus lying position
2. Early versus late stylet removal

The aim is to determine the optimal technique for performing lumbar puncture in infants. The results of this trial will inform best practice, and ultimately, improved technique would result in:
1. Fewer uninterpretable samples
2. Fewer repeated procedures
3. Reduced distress for infants & families
4. Decreased antibiotic use and risk of antibiotic resistance
5. Reduced NHS costs due to fewer procedures, reduced length of stay, shorter antibiotic courses, and minimised antibiotic-associated complications

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central Hampshire-B, 12/06/2018, ref: 18/SC/0222

Study design
Randomised; Interventional; Design type: Diagnosis, Other

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet

https://www.npeu.ox.ac.uk/neoclear/parents

Health condition(s) or problem(s) studied
Meningitis

Interventions
Stratified block randomisation will be used to ensure balance between the groups with respect to the collaborating hospital and corrected gestational age at trial entry.

The interventions compare:
1. Sitting position, in which the infant is held in a sitting position compared to lying ('lateral decubitus') position
2. Early stylet removal, which is the removal of the stylet from the hollow lumbar puncture needle shaft once it has penetrated the subcutaneous tissue before advancing the needle into the cerebrospinal fluid, compared to late stylet removal, which is removal of the stylet once it has been inserted into the expected cerebrospinal fluid space

The participants will be randomly allocated (with equal chance i.e. 1:1:1:1) to one of the following technique combinations:
1. Lying position and early stylet removal
2. Sitting position and early stylet removal
3. Lying position and late stylet removal
4. Sitting position and late stylet removal

Infants will be followed up until they are discharged home.

Intervention Type
Procedure/Surgery

Primary outcome measure
Proportion of infants with successful lumbar punctures, measured by whether cerebrospinal fluid is obtained and red blood cell count <10,000/mm3 on the first lumbar puncture procedure

Secondary outcome measures
Current secondary outcome measures as of 24/04/2020:
The following short-term clinical, resource and safety outcomes have been defined as:
1. The proportion of infants with:
1.1. No cerebrospinal fluid (CSF) obtained, or pure blood/clotted, or blood-stained, or clear
1.2. CSF obtained and red blood cell (RBC) count <500, <5000, <10,000, or <25,000/mm3, or any RBC count
1.3. A CSF white blood cell (WBC) count not requiring a correction (whatever the RBC count)
2. Total number of procedures and attempts performed per infant
3. Proportion of infants diagnosed (by WBC count criteria, culture, Gram stain, and/or clinically) via CSF with:
3.1. Meningitis: WBC count 20 or more in CSF, or a true positive culture/polymerase chain reaction (PCR) (if RBC count is ≥500, the WBC count will be reduced by 1 for every 500 RBC counts to give a 'corrected' WBC count)
3.2. Equivocal: WBC count (or corrected WBC) <20, AND negative (or contaminated/incidental) culture and PCR with:
3.2.1. Polymorphonuclear leukocytes (PMN) >2 (and RBC count <500) OR
3.2.2. Organism found on Gram stain

3.3. Negative: WBC (or corrected WBC) count <20, PMN ≤2 (if RBC count <500), and negative (or contaminated/incidental) cultures, PCR, and Gram stain
3.4. Uninterpretable: No CSF obtained, or clotted, or CSF so bloody or insufficient that a cell count was impossible
4. CSF WBC, RBC, corrected WBC counts, PMNs and lymphocytes from the clearest sample
5. Time taken on first procedure from start of cleaning skin to removing needle at end of all attempts
6. Infant movement on first procedure using basic 4-point scale

Outcomes relating to cost and safety:
7. In all infants, according to CSF-defined and clinically-defined diagnostic criteria:
7.1. Duration of the antibiotic course
7.2. Length of stay in surviving infants
7.3. Immediate complications related to LP:
7.3.1. Cardiovascular instability including oxygen saturations and heart rate
7.3.2. Respiratory deterioration (escalating respiratory support) post-LP
8. For the pilot phase: parental anxiety assessed using the State Trait Anxiety Inventory - State Subscale (STAI-S) Questionnaire

Previous secondary outcome measures:
Short-term clinical outcomes are measured by assessing:
1. The proportion of infants with:
1.1. No cerebrospinal fluid (CSF) obtained, or Pure blood/Clotted, or blood-stained, or clear
1.2. CSF obtained and red blood cell (RBC) count <500, <5,000, <10000, or <25000 /mm3, or any RBC count
1.3. A CSF white cell count not requiring a correction (whatever the RBC count)
2. Total number of procedures, and attempts within procedures, performed per infant to obtain interpretable CSF (RBC counts at the above thresholds)
3. Proportion of infants diagnosed (by WBC count criteria, culture, gram stain, and/or clinically) via CSF with:
3.1. Meningitis: WBC count 20 or more in CSF, or more than 2 PMNs, or a positive culture or gram stain, or clinically diagnosed (if RBC count is >500, the WBC count will be reduced by 1 for every 500 RBC counts to give a 'corrected' WBC count)
3.2. Equivocal: borderline white blood cell (WBC) counts, or uncertain culture result or uncertain clinical diagnosis
3.3. Negative: <20 CSF WBC count and 0–2 PMNs and negative cultures and gram stain and no clinical diagnosis of meningitis
3.4. Uninterpretable: no CSF obtained, or CSF so bloody that a cell count was impossible
4. CSF WBC, RBC, corrected WBC counts, PMNs, and lymphocytes, for any of the above
5. Time taken from start of cleaning skin to removing needle at end of all attempts
6. Infant movement assessed using a basic 4-point scale at time of procedure
7. Parental anxiety, measured using short-version STAI at baseline and within 48 hours of the first lumbar puncture procedure
8. Cost measured by assessing the duration of the antibiotic course from trial entry to discharge home
9. Cost measured by assessing the length of stay in hospital from trial entry until discharge home
10. Safety measured by assessing cardiovascular instability, including oxygen saturations and heart rate during the lumbar puncture procedure
11. Safety measured by assessing respiratory deterioration based on the requirement for escalating respiratory support within 1 hour of the lumbar puncture procedure

Overall study start date

01/09/2017

Completion date
28/02/2021

Eligibility

Key inclusion criteria
1. Neonates and infants in neonatal units and their maternity wards who are having a lumbar puncture
2. Parent(s) willing and able to give informed consent
3. Infants of corrected gestational age from 27+0 weeks to 44+0 weeks, AND working weight of 1,000 g or more
4. First lumbar puncture for current indication

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
Planned Sample Size: 1,020; UK Sample Size: 1,020

Total final enrolment
1082

Key exclusion criteria
Current exclusion criteria as of 24/04/2020:
1. Unable to be held in sitting position (including infants intubated and mechanically-ventilated) or other clinical condition which is likely, in the opinion of the treating clinician, to make sitting difficult, or which is likely to be compromised by sitting (e.g.open gastroschisis)
2. Previously randomised to the trial

Previous exclusion criteria:
1. Unable to be held in sitting position (e.g. intubated and mechanically-ventilated) or other clinical condition which is likely to make sitting difficult, or which is likely to be compromised by sitting (e.g. open gastroschisis)
2. Previously randomised to the trial

Date of first enrolment
01/06/2018

Date of final enrolment
31/08/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
John Radcliffe Hospital (lead site)
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Birmingham Heartlands Hospital
Bordesley Green East
Birmingham
United Kingdom
B9 5SS

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Northampton General Hospital
Cliftonville
Northampton
United Kingdom
NN1 5BD

Study participating centre
Princess Anne Hospital
Coxford Road
Southampton
United Kingdom
SO16 5YA

Study participating centre
Royal Berkshire Hospital
London Road
Reading
United Kingdom
RG1 5AN

Study participating centre
Royal Hampshire County Hospital
Department of Paediatrics
Winchester
United Kingdom
SO22 5DG

Study participating centre
Southmead Hospital
Southmead road
Westbury-on-Trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
St Michael's Hospital
Southwell Street
Bristol
United Kingdom
BS2 8EG

Study participating centre
Bradford Royal Infirmary
Smith Lane
Bradford
United Kingdom
BD9 6DA

Study participating centre
Colchester General Hospital
Turner Rd

Mile End
Colchester
United Kingdom
CO4 5JL

Study participating centre
Derriford Hospital
Derriford Rd
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Gloucestershire Royal Hospital
Great Western Rd
Gloucester
United Kingdom
GL1 3NN

Study participating centre
Great Western Hospital
Marlborough Rd
Swindon
United Kingdom
SN3 6BB

Study participating centre
Medway Maritime Hospital
Windmill Road
Gillingham
United Kingdom
ME7 5NY

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
Royal Devon and Exeter Hospital
Barrack Rd
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United Kingdom
EX2 5DW

Study participating centre
Royal Oldham Hospital
Rochdale Rd
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OL1 2JH

Study participating centre
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KT16 0PZ

Study participating centre
Stoke Mandeville Hospital
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HP21 8AL

Study participating centre
Basingstoke and North Hampshire Hospital
Aldermaston Rd
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RG24 9NA

Sponsor information

Organisation

University of Oxford

Sponsor details
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ctrg@admin.ox.ac.uk

Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 15/188/106

Results and Publications

Publication and dissemination plan
The study protocol and other documentation will be made available on the trial website: https://www.npeu.ox.ac.uk/neoclear. Planned publication of the study results in a high-impact peer reviewed journal.

Intention to publish date
01/07/2022

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 article	protocol	15/04/2020	24/04/2020	Yes	No
Results article		29/11/2022	05/12/2022	Yes	No
HRA research summary			28/06/2023	No	No
Results article		01/12/2023	28/12/2023	Yes	No