ISRCTN94347640 https://doi.org/10.1186/ISRCTN94347640

Effect of systemic blood pressure change produced by noradrenaline on brain blood flow and oxygenation in Neuro-ICU patients

Submission date
03/12/2021

Recruitment status
No longer recruiting

Registration date
06/12/2021

Overall study status
Completed

Last Edited
06/12/2021

Condition category
Other

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

Plain English summary of protocol

Background and study aims
In patients with acute brain damage, irrespective of the cause, there is a tendency for reduced blood flow to the brain which can result in worsening of brain damage. This can manifest as weakness in the limbs, decreased level of consciousness, and not responding to stimulus. One way to increase the blood supply to the brain is by increasing blood pressure with the help of medicines injected through a vein. It is not known whether this increase in blood pressure always results in increased brain blood supply. On the contrary, there is a possibility that the medicines given to increase blood pressure can lead to decreased blood supply due to their direct action on the blood vessels.
The aim of this study is to look at the blood flow to the brain and its oxygen level when medicines are administered to patients to increase their blood pressure. The findings of this study will help the researchers to understand in which group of patients does this increased blood pressure translate to increased blood flow to the brain.

Who can participate?
Adult patients with aneurysmal subarachnoid haemorrhage (anterior circulation) (i.e. bleeding in the space between the brain and the tissue covering the brain) and traumatic brain injury (operated patients) who are admitted to the intensive care units and who require noradrenaline drug infusion to increase their blood pressure

What does the study involve?
To study the blood flow to the brain a Doppler machine will be used. A probe will be placed over the participant's forehead after applying a gel. They might feel some cold sensation when the gel is applied. This examination will not produce any pain or discomfort to the skin. One recording will take about 10 minutes and during this period other treatment and nursing care will continue uninterrupted. Once the recording is done, the neck blood vessels will be compressed for around 6
seconds and the changes in the brain’s blood flow will be recorded. During neck compression, participants might feel some discomfort. Their heart rate and blood pressure will be continuously monitored during the study period. When the dose of the administered drug is

changed during the ICU stay, this examination will be repeated. The repetition will be for a maximum of six times. To study the oxygen levels in the brain, two stickers like sensors will be placed on either side of the forehead and the values will be recorded. This recording will be done whenever the blood flow to the brain is being measured with the Doppler machine. The stickers will be removed once the measurement is done.

What are the possible benefits and risks of participating?
The findings might not benefit the participants at present, but the findings may be beneficial in making clinical decisions in the future. There are no risks involved in participating in the study.

Where is the study run from?
National Institute of Mental Health and Neurosciences (NIMHANS) (India)

When is the study starting and how long is it expected to run for?
October 2019 to March 2022

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Mouleeswaran Sundaram
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Contact information

Type(s)
Scientific

Contact name
Dr Mouleeswaran Sundaram

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Additional identifiers

Protocol serial number
NIMH/DO/IEC(BS&NS DIV)/2018-19

Study information

Scientific Title

Effect of noradrenaline on cerebral hemodynamics and oxygenation in Neuro-ICU patients - an observational study

Study objectives
Noradrenaline is a commonly used drug in neuro ICU for blood pressure augmentation. Literature shows no direct effect on cerebral vasculature following nor-adrenaline infusion. It cannot be presumed to act in the same manner in brain-injured patients. Hence, it is prudent to study the effect of noradrenaline on cerebral hemodynamics and oxygenation in brain-injured patients for its judicious use in the neuro ICU.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/01/2020, Institutional Ethics Committee, National Institute of Mental Health and Neurosciences (NIMHANS, Hosur Road, Bengaluru - 560029, India; Tel: not applicable; deannimhans@yahoo.com), ref: not applicable

Primary study design
Observational

Study design
Single-centre prospective observational longitudinal cohort study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Aneurysmal subarachnoid hemorrhage (aSAH) and traumatic brain injury (TBI)

Interventions
This prospective observational study will be initiated after obtaining clearance from the institute ethics committee. Written informed consent will be taken from all patients. For patients with altered mental status, consent will be taken from near relatives before their enrolment into the study. The study will be conducted in the neurointensive care unit (NICU) of NIMHANS Bangalore from March 2020 to March 2022.

Measurement techniques:
1. Transcranial Doppler measurements:
1.1. The middle cerebral artery (MCA) will be insonated bilaterally through the transtemporal window using a 2 MHz transcranial Doppler probe (Multi-Dop T2 Digital, DWL, Singen, Germany). A surface gel will be used for better skin contact. Flow towards the probe at depths 40 to 55 mm indicates flow through MCA of the same side. The average value of five cardiac cycles will be taken for the measurements. The values recorded will be peak flow velocity (PFV), end diastolic velocity (EDV), MFV (mean flow velocity), and pulsatility index (PI).
1.2. ZFP (Zero flow pressure) will be calculated using the following formula: ZFP = mean arterial blood pressure (MABP) – eCPP, where eCPP is the estimated cerebral perfusion pressure and calculated as follows: eCPP = {MABP× (EDV/MFV)} + 14
1.3. Cerebral autoregulation will be assessed using the transient hyperaemic response test (THRT). Before performing this test, carotid ultrasound will be performed in the neck bilaterally

to rule out atheromas. The test will be performed by compressing the common carotid artery for a brief period of 6-10 seconds. The PFV of MCA will be recorded for three cardiac cycles before compression and after compression release. The average value will be used for the calculation of the transient hyperaemic response ratio (THRR). THRR will be calculated by the following formula: THRR = F3/F1, where F1 = the waveforms preceding the compression and F3 = the waveform following the release of compression
2. Carotid ultrasound examination:
Patients will be placed supine with the neck extended and the head rotated in the opposite direction to the site under examination. Both internal carotid arteries (ICA) will be insonated in the neck using a 4-10 MHz high-frequency ultrasound transducer (FUJIFILM Sonosite, Bothell, USA). The carotid bifurcation, the internal carotid artery and external carotid arteries will be identified. With B-mode imaging, pulse wave Doppler will be placed across the ICA 1cm distal to the carotid bulb, and peak and mean flow velocity recorded.
3. NIRS measurements:
The NIRS sensors (Masimo Corporation, Irvine, CA) will be placed over the forehead on either side after cleaning the skin. The values displayed on the monitor will be taken at the time of measurement of TCD values. The rSO_2 values will be recorded for 1 minute, and the average of five values will be noted and corrected for the fraction of inspired oxygen.

Data collection:
TCD: PFV, MFV, EDV, in cm/sec, PI, Transient hyperaemic response ratio (THRR).
NIRS: values in percentage
Systemic parameters: mean arterial pressure (MABP), heart rate (HR), end-tidal carbon dioxide ($EtCO_2$), haemoglobin (Hb), peripheral oxygen saturation (SpO_2), temperature, Glasgow coma scale (GCS), serum urea, and creatinine.

Timepoints of measurements:
T0: Before starting the noradrenaline infusion
T1: If the patient is admitted to the NICU with ongoing noradrenaline infusion, then at the time of admission.
T2: when the infusion increase achieved a 10% increase in MABP from T0/T1.
T3: when the infusion increase achieved a 20% increase in MABP from T0/T1.
T4: when the infusion was decreased by 25% after stabilization of systemic haemodynamics.
T5: when the infusion was decreased by 50% after stabilization of systemic haemodynamics.
T6: after stopping the infusion.
The recordings will be done 10-15 minutes after dose/MABP change.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Noradrenaline

Primary outcome(s)
Middle cerebral artery (MCA) blood flow velocity and cerebral autoregulation measured using transcranial doppler at baseline, 10% increase and 20% increase in mean arterial blood pressure

Key secondary outcome(s)

Regional frontal cerebral oxygenation measured using near infra-red spectroscopy (NIRS) at baseline, 10% increase and 20% increase in mean arterial blood pressure

Completion date
31/03/2022

Eligibility

Key inclusion criteria
1. Adult anterior circulation aneurysmal subarachnoid patients following surgical clipping/coiling and requiring a continuous infusion of noradrenaline in the NICU
2. Adult traumatic brain injury patients following surgery requiring a continuous infusion of noradrenaline in the NICU

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Refusal to provide informed consent
2. Pregnant patients
3. Patients with a poor acoustic window on TCD
4. Patients with carotid atheroma
5. Patient with bradycardia and arrhythmia
6. Patients with contraindications to nor-adrenaline infusion, including pre-existing acute renal failure (serum creatinine >2 mg/dl) and ischemia of the digits
7. Patients who underwent decompressive craniectomy
8. Patients receiving more than one vasopressor

Date of first enrolment
01/03/2020

Date of final enrolment
31/03/2022

Locations

Countries of recruitment
India

Study participating centre
National Institute of Mental Health and Neurosciences
Neurointensive Care Unit
Hosur Road
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560029

Sponsor information

Organisation
National Institute of Mental Health and Neurosciences

ROR
https://ror.org/0405n5e57

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study are/will be available upon request from the primary investigator Dr Mouleeswaran Sundaram (moulee.mmc@gmail.com) provided the participant/guardian agrees and gives consent for the same. The data will be provided in a spreadsheet. Individual participant data that underlie the results reported in the publication (text, tables, figures, and appendices) will be made available after deidentification 3 months after the publication of results for researchers with a sound methodology for achieving the aims of the proposal.

IPD sharing plan summary
Available on request