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Cortisol profiles in the critically ill after traumatic brain injury

Submission date
22/08/2019

Recruitment status
Suspended

Registration date
04/09/2019

Overall study status
Completed

Last Edited
04/08/2020

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
Traumatic brain injury (TBI) is responsible for 160,000 hospital admissions in the UK every year and trauma is the leading cause of death in people under the age of 44. TBI has two components: the injury itself, as well as 'secondary injury' – damage to brain that occurs as a result of inflammation. One of the hormones that protects against inflammation is the hormone cortisol produced by the adrenal glands. It has been shown that cortisol in health is produced in pulses lasting around an hour and that these pulse patterns impact on the genes that cortisol activates and the effects that it has. No one has examined whether these pulses of cortisol exist after head injury and if so, what the patterns are and how they might relate to the patients' final outcome. Doctors on the Intensive Care Unit (ICU) frequently test cortisol as they think that some people after head injury may not produce enough because of damage to the pituitary gland in the head, as well as changes in the way the adrenal gland is controlled. Currently used tests of pituitary and adrenal gland function on the ICU do not take into account the pulses and patterns of cortisol. In patients who are critically ill after heart surgery, researchers have seen a different pattern of cortisol secretion in patients who die compared to those who survive. Patients who die produce very high levels of cortisol with no pulses. Patients who survive produce pulses of cortisol, but with a different pattern to when they are healthy. The researchers would like to see if this is the case after TBI. Pituitary and adrenal function in patients who are critically ill and those who have suffered a head injury specifically has not been fully elucidated. There have been recent consensus statements from national bodies calling for greater understanding of the changes in function of both the pituitary and adrenal glands and their implications for patients. This is a preliminary project to inform a larger study which can truly establish the mechanisms behind any changes and find out whether the changes in pattern have any effect on the patient's final clinical outcome. The aim of this study is to describe the 24-hour profiles of tissue cortisol that occur following TBI to find out whether tissue concentrations of cortisol are pulsatile in critically ill patients with TBI. If cortisol concentrations are pulsatile, then the methods currently used to test the amount of cortisol produced after a head injury will be inaccurate and therefore obsolete. There may also be differences in the patterns of cortisol between patients who do well and those who do not. This could potentially be used for helping to predict outcomes for patients.

Who can participate?
Critically ill patients aged 18 and over with isolated moderate TBI, isolated severe TBI or non-head trauma

What does the study involve?
Participants' cortisol is collected every 20 minutes for 24 hours using a technique called microdialysis in which a tiny catheter sits just under the skin. Other hormones of the cortisol secretion system are also profiled as well as markers of inflammation. The images of the patient's pituitary gland on the brain scan when they first arrive at hospital will be correlated to the patient's cortisol profile.

What are the possible benefits and risks of participating?
There is no direct benefit to study participants but the information collected should help to improve the treatment of other critically unwell on the intensive care unit. This study has been assessed as being low risk. The only potential risk is infection at the site of catheter insertion. This risk is extremely low as the researchers will take all possible measures to prevent this. The small volume of blood taken as part of the extra research samples is safe to lose and will not affected participants' condition in any way. There will be no change to the clinical care of the participants.

Where is the study run from?
The study is being run on the Intensive Care Unit at North Bristol NHS Trust in collaboration with the Henry Wellcome Laboratories for Integrative Neuroscience and the Clinical Trials and Evaluation Unit (both part of the University of Bristol) (UK)

When is the study starting and how long is it expected to run for?
January 2019 to December 2020

Who is funding the study?
British Society for Neuroendocrinology and the David Telling Charitable Trust

Who is the main contact?
Dr Ben Gibbison
ben.gibbison@bristol.ac.uk

Contact information

Type(s)
Public

Contact name
Dr Ben Gibbison

ORCID ID
http://orcid.org/0000-0003-3635-6212

Contact details
Level 7
Bristol Royal Infirmary
Marlborough Street
Bristol

United Kingdom
BS2 8HW
+44 (0)7932059594
ben.gibbison@bristol.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
74039

Study information

Scientific Title
Cortisol profiles in the critically ill after traumatic brain injury

Study objectives
The study is designed to describe the changes in ultradian cortisol rhythms in critically ill patients following TBI. It aims to test the following original hypotheses:
1. Tissue concentrations of cortisol are pulsatile in brain-injured patients, but the frequency and amplitude of these pulses are different in those with moderate as compared to severe brain injury
2. Tissue concentrations of free cortisol are related to but not the same as plasma total concentrations after traumatic brain injury

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/04/2019, London - Camden & Kings Cross Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ; Tel: +44 (0)207 972 2561; Email: nrescommittee.london-camdenandkingscross@nhs.net), REC ref: 19/LO/0304

Study design
Single-centre observational study

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
Traumatic brain injury (TBI) - moderate and severe, major trauma without traumatic brain injury

Interventions
The 24-hour tissue cortisol profile will be mapped using subcutaneous microdialysis. This involves a small probe being inserted into the subcutaneous tissue overlying the abdomen, and attachment to a pump and sampling device that obtains samples every 20 minutes to generate a 72-point 24-hour profile.
Concomitant blood samples will be taken every 4 hours for cortisol, ACTH and inflammatory mediators.
Clinical outcome data will be collected to correlate any patterns seen.

Intervention Type
Other

Primary outcome measure
Tissue cortisol level measured by subcutaneous microdialysis every 20 minutes for 24 hours, generating a 24-hour hormone profile

Secondary outcome measures
Measured using ICU observation charts, medical notes and ICNARC audit data (collected for every patient routinely during an ICU stay):
1. Acute hospital mortality: inpatient mortality during acute hospital stay
2. Cardiac arrest during inpatient stay
3. Duration of renal replacement therapy in hours (during ICU stay)
4. Duration of mechanical ventilation in hours (during ICU stay)
5. Total number of spikes in intracranial pressure (ICP) during ICU stay and max level recorded
6. Amount of time in hours spent with ICP greater than 20 mmHg
7. Maximum therapy intensity level whilst on ICU (relates to degree of therapy for raised ICP)
8. Number of days of ICP targeted therapy whilst on ICU
9. Total dose and duration (in hours) or inotrope and vasopressor therapy whilst on ICU
10. Length of ICU stay in days
11. Length of hospital stay in days
12. Level of care at ICU discharge using ICNARC (Intensive Care National Audit and Research Centre) scale
13. Expected dependency post-acute hospital discharge using ICNARC scale
14. Residence post-discharge from acute hospital using ICNARC data

Overall study start date
01/01/2019

Completion date

31/12/2021

Eligibility

Key inclusion criteria
Inclusion criteria for the TBI groups:
1. Adults aged at least 18 years of age
2. Intensive Care Unit admission
3. Traumatic brain injury:
3.1. 10 patients with moderate TBI (Glasgow Coma Score 9-12 after resuscitation or prior to intubation)
3.2. 10 patients with severe TBI (Glasgow Coma Score ≤8 after resuscitation or prior to intubation)

Inclusion criteria for the non-TBI group:
1. Adults aged at least 18 years of age
2. Bodily injuries sustained as a result of trauma but without significant head injury
3. Intensive Care Unit admission

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
10 patients with moderate TBI, 10 patients with severe TBI, 10 patients with major trauma without TBI

Key exclusion criteria
Exclusion criteria for the TBI groups:
1. Life or limb-threatening extra-cranial injury (in the opinion of the treating intensivist)
2. Patients with known pre-existing HPA axis disease
3. Untreated thyroid disease
4. Current or prior steroid therapy within the last 3 months
5. Patients less than 18 years of age
6. Patients who are pregnant
7. Prisoners
8. Widespread burns/skin breakdown creating inability to place microdialysis catheter
9. Admission with perceived devastating brain injury for purposes of prognostication or organ donation
10. Refusal of consent or assent
11. More than 48 hours after injury
12. Severe metabolic acidosis (pH <7.20)

Exclusion criteria for the non-TBI group:
1. Significant head injury (GCS <13 or abnormal admission brain imaging)
2. Patients with known pre-existing HPA axis disease
3. Untreated thyroid disease
4. Current or prior steroid therapy within the last 3 months
5. Patients less than 18 years of age
6. Patients who are pregnant
7. Prisoners
8. Widespread burns/skin breakdown creating inability to place microdialysis catheter
9. Admission with devastating brain injury for purposes of prognostication or organ donation
10. Refusal of consent or assent
11. More than 48 hours after injury
12. Severe metabolic acidosis (pH <7.20)

Date of first enrolment
02/09/2019

Date of final enrolment
01/08/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
North Bristol NHS Trust
Southmead Hospital
Southmead Road
Bristol
United Kingdom
BS10 5NB

Sponsor information

Organisation
University of Bristol

Sponsor details
RED
University of Bristol
One Cathedral Square
Bristol
England

United Kingdom
BS1 5DD
+44 (0)117 428 3065
research-governance@bristol.ac.uk

Sponsor type
University/education

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Charity

Funder Name
British Society for Neuroendocrinology

Alternative Name(s)
The British Society for Neuroendocrinology, British Neuroendocrine Group, BSN

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Funder Name
David Telling Charitable Trust

Results and Publications

Publication and dissemination plan
1. The protocol is not published or available online. An example of a statistical analysis method that will be used has been published here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2662594/
2. Study results may be presented at national or international conferences after full analyses

have been undertaken in late 2020 or early 2021
3. Formal publication of results will be undertaken at the end of analyses in a peer-reviewed journal in late 2020 or early 2021

Intention to publish date
30/04/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Ben Gibbison (ben.gibbison@bristol.ac.uk). All data would be anonymised.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No