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A study to investigate the prevalence of pituitary gland dysfunction and it's risk factors following traumatic brain injuries (TBI)

Submission date
28/08/2017

Recruitment status
No longer recruiting

Registration date
14/09/2017

Overall study status
Completed

Last Edited
20/05/2021

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
The number of patients that are hospitalised or that die as a result of traumatic brain injury (TBI) is between 150 to 250 patients per 100,000 population per year. In Scotland this equates to 7,500 patients per year. Up to one third of these patients have long-term problems with their pituitary gland (a gland that regulations vital body function and hormones) function (also known as post TBI pituitary dysfunction or PTPD). This would make PTPD by far the commonest cause of hypopituitarism (when the pituitary gland fails to produce enough hormones). The pituitary gland sits at underneath the brain, where it is surrounded by bones of the skull base. It is therefore susceptible to damage during TBI as it may be injured by the surrounding bones. The pituitary gland is a key part of the endocrine system. The endocrine system is important for maintaining metabolism but also has key roles in regulating stress, energy, libido, bone and muscle strength. It also involved in regulating mental health and wellbeing. Pituitary hormone dysfunction is therefore a serious illness that can cause physical and neuropsychiatric disabilities that can affect the way people recover following TBI. PTPD can be reversed if diagnosed early treatment and an effective screening programme for diagnosing the patients most at risk could represent one of the most important interventions in the management of patient with TBI in the last few decades. The aim of this study is to investigate how common is pituitary dysfunction following traumatic brain injury (TBI).

Who can participate?
Patients aged 17 and older who have a primary TBI.

What does the study involve?
Participants undergo blood tests to assess their pituitary gland function one week, within the first month, between three and six months and between six and 12 months after TBI. Participants are checked for their hormones levels at the first stage of the study. During this first stage, 20 participatns receive an MRI (a scan using magnetics) or their brain. During the follow up stages, participants also have tests to assess their levels of growth hormone

deficiencies (GHD) and secondary hypoadrenaism (SH). During the third and fourth stages of follow up, participants are asked to fill out questionnaires to assess their recovery following a TBI.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
1. Western General Hospital (UK)
2. Royal Infirmary of Edinburgh (UK)

When is the study starting and how long is it expected to run for?
September 2016 to August 2020

Who is funding the study?
Edinburgh and Lothians Health Foundation (UK)

Who is the main contact?
Dr John Emelifeonwu

Contact information

Type(s)
Public

Contact name
Dr John Emelifeonwu

Contact details
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
2017/0146

Study information

Scientific Title

Pituitary gland deficiencies after traumatic brain injury: An Outcomes and Prevalence Study

Acronym
PitSTOP

Study objectives
Post- traumatic brain injury (anterior) pituitary gland dysfunction (PTPD) is common following traumatic brain injury and clinical and radiological factors at the time of trauma may predict the risk of developing long-term PTPD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South East Scotland Regional Ethics Committee 02, 18/07/2017, ref: 17/SS/0043

Study design
Multi-centre cross-sectional longitudinal cohort study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
See additional fiels

Health condition(s) or problem(s) studied
Traumatic brain injury

Interventions
After informed consent, recruited participants have blood tests to assess the function of their brain. These tests are all performed between 8am and 10am and the patients have to be 'fasted' (nothing to eat from midnight the night before) before the blood test. The blood tests are performed at four stages during follow up:

Stage 1. In the first week after Traumatic brain injury (TBI)
Stage 2. Within the first month after TBI
Stage 3. At six months after TBI
Stage 4. At 12 months after TBI

Baseline levels of the following hormones are checked at all 4 stages. These include tests for: cortisol, insulin-like growth factor 1 (IGF-1), growth hormone (GH), prolactin, sodium, thyroid-stimulation hormone (TSH) and free thyroxine (fT4), testosterone levels in men and oestrogen

levels in premenopausal women who do not have a regular menstrual cycle. All of these blood tests can be performed using 3.5mLs (approximately half a tablespoon) of blood.

Also, during the first stage, a subset of participants will also have an magnetic resonance imaging (MRI) of their brain. These scans will be done at every stage of follow-up and will be done on the same day that the patients have their blood test. The MRI scans will be done to check whether there are any structural changes in the pituitary gland that can help predict likelihood of developing long-term PTPD.

The MRI protocol lasts less than 30 minutes and will include the following sequences: T1-weighted 3-D volumetric sequences of the whole brain T2-weighted 2D sequences of the whole brain 3-D Susceptibility weighted imaging (SWI) sequences of the whole brain T1-weighted and T2-weighted fine slices (2mm) of pituitary gland 30 direction diffusion-tensor imaging (DTI) with axial and sagittal sequences

During the second, third and fourth stages of follow up, in addition to the baseline blood tests, participants also have stimulation tests for growth hormone deficiencies (GHD) and secondary hypoadrenaism (SH):

1. Stimulation test for GHD:
GHRH + Arginine test is used to test for GHD. During this test, a dose of a hormone called growth hormone release hormone (GHRH) (1 micrograms per Kg) is given with a protein called Arginine (30g in 100mLs) as an infusion over 30 minutes. Blood samples to check GH levels are then taken at 30 minutes and at 60 minutes after the start of the infusion.

2. Stimulation test for SH:
Short Synacthen test (SST) is used to test for SH. During this test, a sample of blood is taken and then an intramuscular injection (into muscle, usually the shoulder muscle) of Synacthen is given. Synacthen is a synthetic hormone that mimics one of the hormones of the pituitary gland called ACTH. After it has been injected, two further blood tests are done 30 minutes and 60 minutes after the injection to analyse whether the Synacthen has caused an appropriate rise in the level of a hormone called cortisol.

The injections that are given during the stimulation tests are either naturally occurring or synthetic versions of naturally occurring substances. They are tolerated by most patients but the tests are done under the supervision of an appropriate clinician, in case of any adverse reactions.

The patients selected to have an MRI scan at the first stage have the scan repeated at all follow ups stages. Finally, during the third and fourth stages, participants are asked to complete the extended Glasgow Outcome Score (GOSE) to assesses functional recovery following TBI.

This feasibility study is planned to test all aspects of the PitSTOP protocol prior to starting the main study. During this feasibility study, the first follow up stage will be omitted.

Intervention Type
Biological/Vaccine

Primary outcome measure
Prevalence of post TBI pituitary gland dysfunction (PTPD) is measured with pituitary function test (baseline measurements of serum thyroid stimulating hormone, free T4, testosterone, IGF-1

and cortisol) acutely (within 7 days), sub-acutely (within one month) and long-term (up to 6 months and up to 12 months) after TBI. Also a short synacthen test and GHRH + Arginine tests will be performed in the sub-acutely (within one month) and long-term (6 month and 12 months).

Secondary outcome measures
1. Clinical and radiological markers are measured using the clinical information available at the time of presentation to hospital and serial MRI of the pituitary gland performed acutely, within one month and long-term (6 to 12 months) in a subset of patients to try to predict the occurrence of PTPD
2. Optimal timing for surveillance for PTPD using the clinical and radiological information detailed above
3. Functional recovery of patients with PTPD using Glasgow Outcome Score (eGOS) at end of study period (six to 12 months)

Overall study start date
01/09/2016

Completion date
01/08/2020

Eligibility

Key inclusion criteria
1. Primary traumatic Brain Injury (TBI) including multi trauma
2. Patients aged 17 years at the time of TBI
3. Informed consent obtained from participant

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
100

Key exclusion criteria
1. Patients with a pre-existing endocrine diagnosis
2. Morbidly obese patients with BMI > 35
3. Unlikely to survive for the next 24 hours in the opinion of the Intensive care or Neurosurgical team treating the patient
4. Patients with known epilepsy
5. Patients on medications that are known to affect the hypothalamic-pituitary axis
6. Patients who are not able to consent

Date of first enrolment
01/12/2017

Date of final enrolment
01/12/2019

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
United Kingdom
EH4 2XU

Study participating centre
Royal Infirmary of Edinburgh
51 Little France Crescent
Old Dalkeith Road
Edinburgh
United Kingdom
EH16 4SA

Sponsor information

Organisation
University of Edinburgh

Sponsor details
Academic and Central Clinical Office for Research and Development
College of Medicine & Veterinary Medicine
University of Edinburgh
The Queen's Medical Research Institute
47 Little France Crescent
Edinburgh
Scotland
United Kingdom
EH16 4TJ

Sponsor type
University/education

Website
http://www.accord.scot/

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Charity

Funder Name
Edinburgh and Lothians Health Foundation

Alternative Name(s)
ELHF

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
We intend to publish the results of this study by February 2020.

Intention to publish date
01/02/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from John Emelifeonwu johnemelifeonwu@gmail.com), Investigator

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