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Aggression following traumatic brain injury: Testing the effectiveness of risperidone

Submission date
15/12/2016

Recruitment status
No longer recruiting

Registration date
19/12/2016

Overall study status
Completed

Last Edited
15/09/2020

Condition category
Injury, Occupational Diseases, Poisoning

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

Plain English summary of protocol

Background and study aims
Traumatic brain injury (TBI) is an injury to the brain caused by a head injury (trauma to the head). Depending on the part of the brain that is injured, it can cause changes in behaviour, physical abilities or even personality. Many people who suffer a TBI experience long lasting emotional problems such as irritability and anger, which can lead to aggressive behaviour. This can be extremely distressing for people with TBI and their family. Both drug and non-drug treatments are used to manage aggression in people after a head injury. Although doctors use many drugs for this purpose, their use is often based on evidence of successful treatment of aggression in other conditions, such as autism or epilepsy. One drug that has shown promise in people with autism is an antipsychotic called risperidone. Risperidone is also used regularly to treat aggressive behaviour in people who have had a head injury. However, there is currently insufficient information to know how effective risperidone is for improving irritability and aggression after head injury. The aim of this study is to find out whether it is feasible to conduct a larger scale trial to determine if risperidone is a worthwhile treatment for people experiencing irritability and aggression following a head injury (TBI) when the possible benefits and possible side effects are weighed up.

Who can participate?
Adults with TBI who have been referred to a clinician for the management of aggression

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are treated with a placebo (dummy drug) for 12 weeks and those in the second group are treated with risperidone for 12 weeks. The starting dose of trial treatment will be 1 capsule per day, which is 1mg of risperidone, which may be increased up to a maximum of 4 capsules per day. Participants in both groups are followed up weekly for 12 weeks to assess aggression levels as well as a check of general health and wellbeing.

What are the possible benefits and risks of participating?
There are no direct benefits involved with participating. To reduce the risk of side effects for

those allocated to risperidone, all participants start on a low dose and increase the dose slowly. Therefore, major side effects are unlikely although this cannot be guaranteed. The most common side effects of risperidone are drowsiness and weight gain.

Where is the study run from?
1. St George's Hospital (UK)
2. Hammersmith Hospital (UK)
3. Neuropsychiatry (West Kent and Medway) (UK)
4. Wolfson Rehabilitation Service (UK)

When is the study starting and how long is it expected to run for?
November 2015 to October 2018

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

Who is the main contact?
Dr Verity Leeson
after@imperial.ac.uk

Study website
http://www.aftertrial.org/

Contact information

Type(s)
Scientific

Contact name
Dr Verity Leeson

Contact details
Trial Coordinating Office
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Additional identifiers

EudraCT/CTIS number
2015-000641-23

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
19575

Study information

Scientific Title
Aggression Following TBI: Effectiveness of Risperidone

Acronym
AFTER

Study objectives
The aim of this study is to assess the feasibility of conducting a substantive full scale definitive randomised controlled trial investigating the efficacy of risperidone versus placebo in the treatment of aggression in adults with Traumatic Brain Injury (TBI).

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Westminster Research Ethics Committee, 21/09/2015, ref: 15/LO/1181

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Specialty: Mental Health, Primary sub-specialty: Physical

Interventions
Eligible participants will be randomised to receive either risperidone or placebo at a ratio of 1:1, stratified by site. A flexible dosing regimen of risperdone will be used. Dosing will start with 1 mg once daily and be titrated in 1mg increments, not more than once every 7 days, to a

maximum of 4mg a day (2mg bd). The dose may also be reduced to a lower dose (minimum 1 mg once daily) at any time. The decision about whether to amend the dose will be based on the participant's response to the trial medication in terms of level of aggression, and whether any unacceptable side effects that may be due to the trial medication are reported. A lower dose may be maintained before the maximum dose is reached where substantial improvement occurs, or where side effects are reported. Equivalent numbers of placebo capsules will also be administered to the appropriate participants.
Participants are followed up weekly for a total of 12 weeks.

Intervention Type
Other

Phase
Phase IV

Primary outcome measure
Self-reported aggression is measured using the Modified Overt Aggression Scale (MOAS) at baseline and weekly for 12 weeks.

Secondary outcome measures
1. Irritability is assessed using the Irritability Questionnaire (IRQ) at baseline and 12 weeks
2. Social functioning is measured using the Extended Glasgow Outcome Scale (GOS-E) at baseline and 12 weeks
3. Health-related Quality of life (QoL) is measured using the EQ-5D-5L and SF-12 questionnaires at baseline and 12 weeks
4. Adverse events profile is assessed using the UKU scale at baseline and 12 weeks
5. Carer Wellbeing is assessed using the wellbeing section of the 'carer wellbeing and support questionnaire (CWS) at baseline and 12 weeks
6. Health economics are assessed using the Client Service Receipt Inventory (CSRI) at baseline and 12 weeks

Overall study start date
27/11/2015

Completion date
22/10/2018

Eligibility

Key inclusion criteria
1. Aged between 18 and 65 years
2. A confirmed clinical diagnosis of TBI which occurred at least six months prior to recruitment, evidenced as a rating of moderate/severe or mild (probable) based on Mayo Clinic criteria
3. Referred to the clinician for the management of aggression and for whom the clinician is considering a pharmacological intervention for this problem after investigating and addressing physical, psychological and social triggers
4. Competent and willing to provide written, informed consent
5. The patient or their carer is able to understand how to manage prescribed medication

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 50; UK Sample Size: 50

Total final enrolment
14

Key exclusion criteria
1. Suffering from Post-Traumatic Amnesia (PTA), which constitutes a sub-acute confusional state
2. Co-morbid severe mental illness such as schizophrenia and other psychoses, bipolar disorder, major depressive disorder, personality disorder, and dementia, and where the clinicians are treating primarily a psychiatric disorder rather than aggressive behaviour
3. Already prescribed an antipsychotic drug or any other drug that may interact with risperidone at the time of randomisation. A wash-out period of at least two weeks is required prior to randomisation.
4. Any other contraindication for using risperidone including a previous history of severe adverse events
5. Has no fixed abode or any other reason for which compliance with trial medication and monitoring could pose a major problem
6. Is pregnant or trying to conceive, breastfeeding, or a woman of childbearing potential not using a highly effective birth control
7. Lactose intolerance
8. Known cardiovascular disease (e.g., heart failure, myocardial infarction, conduction abnormalities including family history of QT prolongation, dehydration, hypovolaemia, bradycardia, or electrolyte disturbances (hypokalaemia, hypomagnesaemia), or cerebrovascular disease
9. A clinically significant low white blood cell count or a drug-induced leukopenia/neutropenia
10. A history of seizures

Date of first enrolment
09/01/2017

Date of final enrolment
16/01/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St George’s Hospital
Blackshaw Road
London
United Kingdom
SW17 0QT

Study participating centre
Hammersmith Hospital
Du Cane Road
White City
London
United Kingdom
W12 0HS

Study participating centre
Neuropsychiatry (West Kent and Medway)
Darent House
Hospital Road
Sevenoaks
United Kingdom
TN13 3PG

Study participating centre
Wolfson Rehabilitation Service
Queen Mary's Hospital
Roehampton Lane
London
United Kingdom
SW15 5PN

Sponsor information

Organisation
Central and North West London NHS Foundation Trust

Sponsor details

1st Floor, Bloomsbury Building
St Pancras Hospital
4, St Pancras Way
London
England
United Kingdom
NW1 0PE

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05drfg619

Funder(s)

Funder type
Government

Funder Name
National Institute for Health 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
One conference will be organised at the end of the project to disseminate findings. This event will be free of charge to attend and open to a wide range of delegates. A summary report will be produced and sent to a wide range of stakeholders. Papers will be prepared for publication in high impact peer-reviewed journals. Findings of the study will also be presented in local, national and international meetings and conferences. The results of the trial will be posted by the sponsor on EudraCT and made available to the public via the EU Clinical Trials Register. Care will be paid to disseminating to care staff and family carers via appropriate organisations.

Intention to publish date
22/10/2019

Individual participant data (IPD) sharing plan
The current 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	21/06/2018		Yes	No
Basic results			17/06/2020	No	No
Results article	results	10/09/2020	15/09/2020	Yes	No
HRA research summary			28/06/2023	No	No