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The formation of carbamazepine metabolites and carbamazepine-protein conjugates in epilepsy patients

Submission date
18/02/2015

Recruitment status
No longer recruiting

Registration date
19/02/2015

Overall study status
Completed

Last Edited
21/09/2021

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Carbamazepine is an effective drug that is used in the treatment of epilepsy, neuralgia and psychiatric disorders. Although generally well tolerated, it can cause hypersensitivity reactions such as a skin rash in up to 10% of patients. These reactions can result in hospital admission, long-term complications such as blindness, and can cause death in up to 30% of patients. These reactions are caused by the immune system. Recent research has identified that patients with specific genes are at a higher risk of developing this hypersensitivity. Carbamazepine is converted by the liver to other chemical products called metabolites. It is believed that one or more of these metabolites activate the immune system. However, it is not known how this happens. This aim of this study is to assess the stable and toxic products formed in the blood and urine of patients receiving carbamazepine.

Who can participate?
Adults aged at least 18 who have either just been prescribed carbamazepine or have received the treatment at the same dose for at least 4 weeks

What does the study involve?
Participants provide blood and urine samples in order to identify the chemicals responsible for triggering the immune system in susceptible people. Genetic variations are also analysed to determine their effects on carbamazepine.

What are the possible benefits and risks of participating?
These results may help to explain the variation in carbamazepine hypersensitivity between patients. Lessons learned from this research will provide valuable information for other drugs that cause similar hypersensitivity reactions (e.g. penicillins). Improved understanding of the mechanism of carbamazepine hypersensitivity will enable safer drug design in future and the development of predictive tests that can diagnose and identify patients susceptible to adverse reactions.

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

When is the study starting and how long is it expected to run for?
November 2013 to April 2015

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Dr Vincent Yip

Contact information

Type(s)
Scientific

Contact name
Dr Vincent Yip

Contact details
University of Liverpool
Wolfson Centre for Personalised Medicine
Department of Pharmacology
Block A: Waterhouse Buildings
1–5 Brownlow Street
Liverpool
United Kingdom
L69 3GL

Additional identifiers

EudraCT/CTIS number
2013-002743-28

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
15543

Study information

Scientific Title
A pharmacokinetic investigation into the formation of carbamazepine metabolites and carbamazepine-protein conjugates in epilepsy patients

Acronym
PICME II

Study objectives
This study aims to improve our mechanistic understanding of carbamazepine hypersensitivity by using high sensitivity mass spectrometry to characterise and quantify the stable and toxic products formed in the blood and urine of patients receiving carbamazepine therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
13/NW/0503

Study design
Non-randomised; Both; Treatment

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Topic: Neurological; Subtopic: Neurological (all Subtopics); Disease: Epilepsy

Interventions
Patients in the auto-induction group will be newly prescribed carbamazepine. All other subjects in the study will have been prescribed carbamazepine by their neurologist as part of clinical care for patient for at least 4 weeks.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Pharmacokinetic analyses; Timepoint(s): Time points dependent on time of presentation to clinic

Secondary outcome measures

N/A

Overall study start date
05/11/2013

Completion date
30/04/2015

Eligibility

Key inclusion criteria
Autoinduction group:
1. Subject is willing and able to give written informed consent
2. Subject is aged 18 or over
3.Subject is newly prescribed carbamazepine by their attending physician

Maintenance group:
1. Subject is willing and able to give written informed consent
2. Subject is aged 18 or over
3. Subject has received CBZ therapy at the same dosage for at least 4 weeks

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 158; UK Sample Size: 158

Key exclusion criteria
Autoinduction group:
1. Subject is not willing to take part or unable to give written informed consent
2. Subject has in the past 4 weeks received other medication that is a CYP3A4 inducer or inhibitor (see medications below)
3. Subject has taken part on another research study within 90 days of commencement
4. Subject has any condition which in the opinion of the investigator will interfere with the study

Excluded medications:
Rifampicin, Amiodarone, Fluvoxamine, Saquinavir, Rifampin, Amprenavir, Indinavir, SVerapamil, Isoniazid, Atazanavir, Lopinavir, Verapamil, Phenytoin, Azithromycin, Mifepristone, Phenobarbital, Grapefruit juice, Nelfinavir, Omeprazole, Clarithromycin, Norverapamil,

Clotrimazole, Cyclosporine A, Ritonavir, HMGCoA reductase inhibitors, Delavirdine, Ndesmethylerythromycin, Cyclophosphamide, Erythromycin, Roxithromycin, Spironolactone, Fluoxetine, RVerapamil

Maintenance group:
1. Subject is not willing to take part or unable to give written informed consent
2. Subject has any condition which in the opinion of the investigator will interfere with the study

Date of first enrolment
05/11/2013

Date of final enrolment
30/04/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Liverpool
Wolfson Centre for Personalised Medicine
Department of Pharmacology
Block A: Waterhouse Buildings
1–5 Brownlow Street
Liverpool
United Kingdom
L69 3GL

Sponsor information

Organisation
University of Liverpool

Sponsor details
Head of Division of Primary Care
Whelan Building
Quadrangle
Brownlow Hill
Liverpool
England
United Kingdom
L69 3GB

Sponsor type
University/education

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

2016 thesis in https://core.ac.uk/download/pdf/80777101.pdf (added 24/07/2020)

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/06/2021	21/09/2021	Yes	No
HRA research summary			28/06/2023	No	No