ISRCTN79173829 https://doi.org/10.1186/ISRCTN79173829

A programme to develop a skin patch containing two medicines (physostigmine and hyoscine), study 5: Assessment of blood levels of the two medicines and any associated symptoms in healthy male participants

Submission date
09/01/2020

Recruitment status
No longer recruiting

Registration date
10/01/2020

Overall study status
Completed

Last Edited
10/01/2020

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
A skin patch containing two medicines (physostigmine and hyoscine) has been developed. The skin patch releases these medicines enabling them to cross the skin into the bloodstream. The aim of this study is to measure the amount of physostigmine and hyoscine in the blood at different times, and assess any associated symptoms with a slightly larger size (25cm² as compared to 21cm²) patch than studied in previous trials. The participants in the study are healthy male participants.

Who can participate?
Study participants are healthy males aged between 18 and 45 years.

What does the study involve?
Each participant in period 1 of the study wore an active transdermal patch for 72 hours. Each participant in period 2 will wear an active or placebo patch for 3 consecutive periods of 72 hours over 9 days (each individual received 3 patches).
Blood samples are taken before and after patch application to measure the amounts of the two medicines (physostigmine and hyoscine). In addition the activity of the enzyme acetylcholinesterase (AchE) is measured in these blood samples. The condition of the skin under the patch is recorded at set times and any symptoms experienced while it is worn are noted. Heart rate, blood pressure, electrical activity of the heart (ECG), tests of vision and cognitive function are also recorded at set times.

What are the possible benefits and risks of participating?
There are no direct benefits for the individuals participating in this study. However, the information collected from the study will add to the scientific knowledge about the physostigmine and hyoscine patch. All medicinal products may cause side effects. The most

common side effects known about the medicines in the patch are nausea and vomiting due to physostigmine and blurred vision and dry mouth due to hyoscine. Overall the patch used is considered to be well tolerated in participants in this study.

Where is the study run from?
Simbec Research Limited, UK.

When is the study starting and how long is it expected to run for?
October 2006 to April 2008

Who is funding the study?
UK Ministry of Defence

Who is the main contact?
centralenquiries@dstl.gov.uk

Contact information

Type(s)
Scientific

Contact name
Dr Medical Advisor

Contact details
Defence Science and Technology Laboratory
Porton Down
Salisbury
United Kingdom
SP4 0JQ
-
centralenquiries@dstl.gov.uk

Additional identifiers

EudraCT/CTIS number
2006-004352-20

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
RD 209/24425

Study information

Scientific Title

A two-part study to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple applications of the F11/25 transdermal patch formulation of hyoscine and physostigmine in healthy male participants

Study objectives
The aim of this study was to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of single and three consecutive applications of a transdermal patch (25cm2 area) in healthy male participants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/10/2006, South East Wales Local Research Ethics Committees (LREC) (Churchill House, 17 Churchill Way, Cardiff, CF10 2TW, UK; +44 (0)2920402402; no email provided), ref: 06 /WSE04/110

Study design
Single centre randomized double-blind placebo-controlled 2-part study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Potential risk of poisoning by nerve agent

Interventions
Generic drug name- physostigmine and hyoscine (transdermal patch)
Dosage - period 1: a single 72 hour application of active 25cm2 patch formulation F-11.
Dosage – period 2: three consecutive 72 hour applications of active or placebo 25cm2 patch formulation F-11.

The safety and tolerability of single application of physostigmine/hyoscine transdermal patches was assessed by monitoring vital signs, ECG, ocular function (near point), patch application site assessment, using digital photography. Tests were performed at intervals for up to Day 14 in period 1 and Day 20 in period 2.

Intervention Type

Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Physostigmine and hyoscine

Primary outcome measure
Safety and tolerability of the drug assessed by monitoring vital signs, ECG, ocular function (near point), patch application site assessment, using digital photography. Tests were performed at intervals for up to Day 14 in period 1 and Day 20 in period 2

Secondary outcome measures
1. Pharmacokinetic (PK) and pharmacodynamic (PD) profiles measured at regular time points at pre-dose and up to 96 hours after patch application
1.1. Physostigmine and hyoscine plasma measured by liquid chromatography-tandem mass spectrometry (LC-MS-MS) method
1.2. Acetylcholinesterase levels measured at baseline, pre-dose, and intervals up to 96 hours after patch application. The method was validated spectrophotometric method

Overall study start date
23/05/2005

Completion date
22/04/2008

Eligibility

Key inclusion criteria
1. Ability to give written informed consent prior to study participation
2. Healthy Caucasian male participants aged between 18 and 45 years (inclusive)
3. Body Mass Index (BMI) within the range of ≥ 21 and ≤ 30 kg/m2
4. Vital signs within the following ranges:
4.1. Pulse rate 40-90 bpm
4.2. Systolic blood pressure 90-140 mmHg
4.3. Diastolic blood pressure 50-90 mmHg
5. Ability to communicate well with the Investigator and to comply with the requirements of the study.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex

Male

Target number of participants
30

Total final enrolment
30

Key exclusion criteria
Screening:
1. Presence of any clinically-significant medical condition as determined by the investigator
2. Any surgical or medical condition which might significantly alter the absorption, distribution, metabolism or excretion of any drug (e.g. renal or liver disease, respiratory, immunological, endocrine or neurological disorders)
3. Any ECG abnormality other than sinus bradycardia or respiratory sinus arrhythmia
4. Known or suspected hypersensitivity or idiosyncratic reaction related to any of the study products
5. Any history of contact dermatitis
6. A dibucaine number of less than 70
7. Any skin disorder, broken skin, scars, tattoos at the sites of patch application (i.e. on both arms)
8. Glaucoma or a history of glaucoma in first-degree relatives (i.e. parents, siblings or offspring)
9. Presence of Anterior Chamber Narrow Angle (Van Herrick Grade 1 and 2)
10. Intra-ocular pressure exceeding 20 mm Hg
11. Uncorrected vision in both eyes of worse than 6/9 on the Snellen Scale
12. Corrected vision of 6/9 or better on the Snellen Scale when wearing +2.25 dioptre reading glasses
13. Requires glasses or contact lenses for distance vision
14. History of asthma (within the previous 10 years), exercise-induced bronchospasm or relevant seasonal bronchospasm
15. Lung function of less than 80% of predicted FEV1 and FVC values
16. History or evidence of drug abuse (opiates, methadone, cocaine, amphetamines, methamphetamines, cannabinoids, barbiturates)
17. Positive test for HIV, Hepatitis B surface antigen or Hepatitis C antibody
18. History or evidence of alcohol abuse defined as an intake of more than 28 units per week (where 1 unit corresponds to 250 ml beer, 20 ml spirits/liqueur or one glass (100 ml) of wine)
19. Positive urine test for alcohol
20. Participation in another clinical study within the last three months
21. Use of any prescription medication within the last 14 days
22. Use of non-prescription medication within the last 7 days (apart from paracetamol)
23. Donation of blood or blood products within the last 3 months, or the intention to donate blood or blood products within 3 months after completion of the study

Baseline:
1. Development of any exclusion criteria since screening
2. Positive urine test for alcohol
3. Positive drugs of abuse test
4. Use of any prescription medication since screening
5. Use of non-prescription medication may impact the safety aspects and objectives of the study, within the last 7 days (apart from paracetamol)

Date of first enrolment
16/10/2006

Date of final enrolment
22/12/2006

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec Research Limited
Merthyr Tydfil
Merthyr Tydfil
United Kingdom
CF48 4DR

Sponsor information

Organisation
Defence Science and Technology Laboratory

Sponsor details
Porton Down
Salisbury
United Kingdom
SP4 0JQ
-
centralenquiries@dstl.gov.uk

Sponsor type
Research organisation

Website
https://www.gov.uk/government/organisations/defence-science-and-technology-laboratory

ROR
https://ror.org/04jswqb94

Funder(s)

Funder type
Government

Funder Name
Ministry of Defence

Alternative Name(s)
MOD

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Publication and dissemination plan
Our intention is to submit the results of this study for publication in an academic journal later in the development programme.

Intention to publish date
09/01/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to confidentiality.

IPD sharing plan summary
Not expected to be made available