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A programme to develop a skin patch containing two medicines (physostigmine and hyoscine), study 4: Assessment of blood levels of the two medicines and any associated symptoms in healthy male participants with Fitzpatrick Grade 5 skin pigmentation.

Submission date
31/10/2019

Registration date
05/11/2019

Last Edited
01/11/2019

Recruitment status
No longer recruiting

Overall study status
Completed

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 was to measure the amount of physostigmine and hyoscine in the blood at different times, and assess any associated symptoms. The participants in the study were healthy male subjects with specific skin pigmentation

Who can participate?
Study participants were healthy males aged between 18 and 45 years with specific skin pigmentation

What does the study involve?
Each participant wore a transdermal patch for 72 hours on two different occasions separated by at least a week. On one occasion they wore a patch containing physostigmine and hyoscine, while on the other occasion they wore a placebo patch. Blood samples were 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) was measured in these blood samples. The condition of the skin under the patch was recorded at set times and any symptoms experienced while it was worn were noted. Heart rate, blood pressure, the electrical activity of the heart (ECG), tests of vision and cognitive function were also recorded at set times

What are the possible benefits and risks of participating?
There were no direct individual benefits for the participants participating. However, the

information collected from these individuals added to the scientific knowledge about the physostigmine and hyoscine patch. All medicinal products have a risk of causing 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 was considered to be well tolerated

Where is the study run from?
The study was conducted at Simbec Research Limited

When is the study starting and how long is it expected to run for?
February 2006 to April 2007

Who is funding the study?
The study was funded by UK MoD

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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2005-005492-15

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
RD 209/24241

Study information

Scientific Title
A Randomised, Double-Blind, Placebo-Controlled, Crossover Study to Investigate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of a Single Application of a Transdermal Patch Formulation of Hyoscine and Physostigmine in Healthy Male Subjects with Pigmented Skin of Grade 5 on the Fitzpatrick Skin Scale

Study objectives
The aim of this study was to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple applications of a transdermal patch (21cm² area) in healthy male subjects with Fitzpatrick Grade 5 skin pigmentation

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/02/2006, South East Wales Local Research Ethics Committees (LREC) (Churchill House, 17 Churchill Way, Cardiff, CF10 2TW; +44 (0)2920402402), ref: 06/WSE/04/13

Study design
Single centre randomized double-blind placebo-controlled 2-part crossover 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: a single active or placebo 21cm2 patch formulation F-11.
Method and frequency of administration: a single dose of either active or placebo patch formulation F-11 was worn for 72 hours.
Randomisation: a sequential three-digit subject (randomisation) number was assigned once eligibility for the study was confirmed. Subjects were randomised to receive one of the two IMPs in Period 1 and the alternative in Period 2. Treatment was allocated according to the randomisation schedule produced by the CRO.

Intervention Type

Drug

Phase
Phase I

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

Primary outcome measure
The safety and tolerability of a single application of physostigmine/hyoscine transdermal patch formulation was assessed by monitoring vital signs, ECG, ocular function (near point), patch application site assessment, using digital photography. These parameters were measured at baseline and at pre-determined intervals up to 96 hours after patch application and at follow up

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

Overall study start date
20/09/2005

Completion date
23/04/2007

Eligibility

Key inclusion criteria
Screening:
1. Ability to give written informed consent prior to study participation
2. Healthy male subjects with pigmented skin of Grade 5 on the Fitzpatrick skin scale
3. Aged between 18 and 45 years (inclusive)
4. Body Mass Index (BMI) within the range of 21and 30 kg/m2
5. Vital signs within the following ranges:
5.1. Pulse rate 40-90 bpm
5.2. Systolic blood pressure 90- 150 mmHg
5.3. Diastolic blood pressure 50- 95 mmHg
6. Ability to communicate well with the Investigator and to comply with the requirements of the study

Baseline Period 2:
1. Successful completion of Period 1
2. Willingness to continue in the study

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
6

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 have significantly altered 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 (sinus bradycardia and respiratory sinus arrhythmia are considered to be normal findings in healthy young adults)
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. Skin disorders, broken skin, scars or tattoos that were extensive enough to obscure the patch application sites 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. Required glasses or contact lenses for distance vision
13. History of asthma (within the previous 10 years), exercise induced bronchospasm or relevant seasonal bronchospasm
14. Lung function of less than 80% of predicted FEV1 and FVC values.
15. History or evidence of drug abuse (opiates, methadone, cocaine, amphetamines, methamphetamines, cannabinoids, barbiturates)
16. Positive test for HIV, Hepatitis B or Hepatitis C
17. History or evidence of alcohol abuse defined as an intake of more than 28 units per week (4 units per day), where 1 unit corresponds to 250 ml beer, 20 ml spirits/liqueur or one glass (100 ml) of wine
18. Positive urine test for alcohol
19. Participation in another clinical study within the previous three months
20. Use of any prescription medication within the previous 14 days
21. Use of non-prescription medication within the previous seven days (apart from paracetamol)
22. Donation of blood or blood products within the previous three months, or the intention to donate blood or blood products within three months after completion of the study

Date of first enrolment
14/02/2006

Date of final enrolment
07/06/2006

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec Research Limited
Merthyr Tydfil
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Sponsor information

Organisation
Defence Science Technology Laboratory (Dstl)

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Sponsor type
Other

ROR
https://ror.org/04jswqb94

Funder(s)

Funder type
Government

Funder Name
Study conducted on behalf of UK Ministry of Defence

Results and Publications

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
31/12/2020

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