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A programme to develop a skin patch containing two medicines (physostigmine and hyoscine), Study 7: Assessment of effects of an armband covering the skin patch on the blood levels of the two medicines and any associated symptoms in healthy male participants

Submission date
17/12/2020

Recruitment status
No longer recruiting

Registration date
11/01/2021

Overall study status
Completed

Last Edited
18/12/2020

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 was to measure the effect of an armband applied over the F11/21 transdermal patch (area 21 cm2) on the amount of physostigmine and hyoscine delivered to the blood at different times. The participants in the study were healthy male participants.

Who can participate?
Study participants were males aged between 18 and 40 years.

What does the study involve?
Each participant wore a F11/21 transdermal patch for 24 hours on four separate occasions. There was a 7-day gap between each patch application. On two of the four occasions the patch was worn with an armband covering the patch, and on the other two occasions it was worn without one.
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 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, electrical activity of the heart (ECG), tests of vison and cognitive function were also recorded at set times.

What are the possible benefits and risks of participating?
There were 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. Application of the F-11/21 patch with and without an armband was considered to be well-tolerated.

Where is the study run from?
The study was conducted at Simbec Research Limited (UK).

When is the study starting and how long is it expected to run for?
December 2007 to February 2011

Who is funding the study?
Ministry of Defence (UK)

Who is the main contact?
Defence Science and Technology Laboratory, Porton Down
centralenquiries@dstl.gov.uk

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2008-000503-28

Protocol serial number
RD 209/24679

Study information

Scientific Title

An investigation of the effects of an armband applied over the F11/21 physostigmine and hyoscine
transdermal patch on pharmacokinetic, pharmacodynamic and safety profiles in healthy male subjects

Study objectives
The aim of the study was to assess the effect of the armband on the pharmacokinetic (PK) and pharmacodynamic (PD) profiles of physostigmine and hyoscine during 24h transdermal administration in healthy male subjects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/03/2008, South East Wales Local Research Ethics Committees (LREC) (Churchill House, 17 Churchill Way, Cardiff, CF10 2TW, UK; +44 (0)2920 402402; no email provided), ref: 08 /WSE04/21

Primary study design
Interventional

Study design
Single centre open label randomized within-subject replicate crossover study

Study type(s)
Other

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 24-hour application of active 21cm² patch formulation F-11 (F21/21) administered on 4 separate occasions with a 7- day interval between applications.

Randomisation
Subjects were allocated to one of six treatment sequences according to a randomisation code produced by the CRO.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)

1. Physostigmine and hyoscine plasma measured at pre-dose and regular intervals up to 54 hours after patch application. Assay- by liquid chromatography-tandem mass spectrometry (LC-MS-MS) method
2. Acetylcholinesterase levels measured at baseline, pre-dose, and intervals up to 54 hours after patch application. The method was validated spectrophotometric method

Key secondary outcome(s)
Safety and tolerability of the F11/21 transdermal patch worn with and without an armband:
1. Vital signs and ECG were measured at screening, pre-dose, up to 54 hour after patch application and at follow up
2. Ocular function (near point and accomodation) was measured at screening, pre-dose, up to 54 hours after patch application
Patch application site assessment was made at screening, baseline, and up to 48 hours after each patch application
3. Self-reported symptoms of nausea (attributed to relative physostigmine excess) or blurred vision (attributed to relative hyoscine excess) up to 54 hours after patch application

Completion date
15/02/2011

Eligibility

Key inclusion criteria
1. Ability to give written informed consent prior to study participation
2. Healthy Caucasian male subjects aged between 18 and 40 years (inclusive)
3. Body Mass Index (BMI) within the range of ≥21 and ≤29 kg/m²
4. Vital signs within the following ranges:
4.1. Heart 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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Male

Total final enrolment

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 considered to be clinically significant i.e. baseline prolongation of QT /QTc interval >450 ms or history of additional risk factors for Torsade de Point (heart failure, hypokalemia, family history of Long QT Syndrome)
4. Known or suspected hypersensitivity or idiosyncratic reaction to any of the study products
5. A dibucaine number of less than 70
6. History of asthma (within the previous 10 years), exercise induced bronchospasm or relevant seasonal bronchospasm
7. Lung function of less than 80% of predicted FEV1 and FVC
8. Any history of contact dermatitis
9. Any skin disorder, broken skin, scars, tattoos at the sites of patch application (i.e. on both arms)
10. Glaucoma or a history of glaucoma in first-degree relatives (i.e. parents, siblings or offspring)
11. Presence of Anterior Chamber Narrow Angle (Van Herrick Grade 1 and 2)
12. Intra-ocular pressure exceeding 20 mmHg
13. Uncorrected vision in both eyes of worse than 6/9 on the Snellen Scale
14. Corrected vision of 6/9 or better on the Snellen Scale when wearing +2.25 dioptre reading glasses
15. Required glasses or contact lenses for distance vision
16. History or evidence of drug abuse (opiates, methadone, cocaine, amphetamines, cannabinoids or barbiturates)
17. Positive test for HIV, hepatitis B or hepatitis C
18. 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
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 (apart from paracetamol) within the last seven days that may have an impact on the safety and objectives of the study (at the Investigator's discretion)
23. Donation of blood or blood products within the last three months, or the intention to donate blood or blood products within three months after completion of the study

Baseline (all periods):
1. Development of any exclusion criteria since last visit
2. Positive urine test for alcohol
3. Positive drugs of abuse test
4. Use of any prescription medication since last visit (with the exception of hormonal contraception)
5. Use of non-prescription medication that may impact the safety aspects and objectives of the study, within the last seven days (apart from paracetamol)

Date of first enrolment

06/03/2008

Date of final enrolment
10/11/2008

Locations

Countries of recruitment
United Kingdom

Wales

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

Sponsor information

Organisation
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

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