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A programme to develop a skin patch containing two medicines (physostigmine and hyoscine), Study 8: Assessment of effects of consecutive 24-hour applications of patches for 21 days on the blood levels of the two medicines and any associated symptoms in healthy male and female participants

Submission date
15/04/2021

Recruitment status
No longer recruiting

Registration date
17/06/2021

Overall study status
Completed

Last Edited
10/06/2021

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 effect of daily application of the transdermal patch over 21 consecutive days on the amount of physostigmine and hyoscine delivered to the blood at different times.

Who can participate?
Healthy volunteers aged between 18 and 40 with either normal vision or requirements for glasses over a range of lens strengths.

What does the study involve?
Each participant wears a transdermal patch placed under an armband each day for 21 days. The patch is replaced each day. 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 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 was worn are noted. Heart rate, blood pressure, heart electrical activity, and vision and cognitive function tests are also recorded at set times.

What are the possible benefits and risks of participating?
There are no direct benefits for the participants. 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. Daily application of the transdermal patch for 21 consecutive days is considered to be well-tolerated.

Where is the study run from?
Simbec Research Limited (UK)

When is the study starting and how long is it expected to run for?
December 2007 to July 2012

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

Who is the main contact?
Defence Science and Technology Laboratory, Porton Down
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2008-005286-58

Protocol serial number
RD 209/24774

Study information

Scientific Title

A double-blind investigation of the effects of daily applications of the physostigmine and hyoscine transdermal patch (NAPS2 F11/21) with an armband on the pharmacokinetic (PK), pharmacodynamic (PD) and safety profiles over a 21-day period in healthy male and female Caucasian subjects

Study objectives
The study aim is to assess the effects of daily applications of the physostigmine and hyoscine F11 /21 patch on pharmacokinetic, pharmacokinetic and safety profiles over a 21-day period in healthy male and female subjects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/01/2009, South East Wales Local Research Ethics Committees (LREC, Business Services Centre, Churchill House, 17 Churchill Way, Cardiff, CF10 2TW, UK; +44 (0)2920376820; Wales.REC1@wales.nhs.uk), ref: 09/WSE04/2

Primary study design
Interventional

Study design
Single-centre parallel-group double-blind placebo-controlled randomized 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 daily (24 hour) application of active 21 cm^2 patch formulation F-11 (F11/21) or placebo, administered for 21 consecutive days.

Randomization method:
Stratified randomization took place, whereby subjects are randomized according to their equivalent spherical error in 1D (dioptre) bands. This is to ensure a full range of subjects were recruited with refractive errors throughout the range -1 to +4D.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)

1. Plasma concentrations of physostigmine/hyoscine measured using liquid chromatography-tandem mass spectrometry (LC-MS-MS) on blood samples collected 12 hourly during the first 20 days and more frequently up to 54 hours after the final patch was applied.
2. Plasma concentrations of AchE measured using spectrophotometry on blood samples collected 12 hourly during the first 20 days and more frequently up to 54 hours after the final patch was applied
3. Safety measurements recorded before dosing and at intervals throughout the 21-day period of patch application up until 49 hours after final patch application:
3.1. Vital signs (supine blood pressure and pulse rate) measured using Good Clinical Practice (GCP)-validated automated blood pressure machine and pulse oximeter
3.2. Heart rhythm and electrical activity assessed from 12-lead ECGs recorded using GCP-validated electrocardiogram machine
3.3. Cognitive function measured using Bond-Lader visual analogue scale (VAS) of mood and alertness
3.4. Patch adhesion measured using digital photography

Key secondary outcome(s)
Ocular function measured by an optometrist by testing eye performance including visual acuity, refractive error, accommodation, intraocular pressure according to the following schedule:
Baseline: on two consecutive days
Dosing period: post patch application on days 2, 5, 10, 15 and 20 and 24 h and 48 h after last patch application
Follow-up on two consecutive days

Completion date
17/07/2012

Eligibility

Key inclusion criteria
Screening:
1. Ability to give written informed consent prior to study participation
2. Healthy Caucasian male and female subjects aged between 18 and 40 years (inclusive)
3. Female subjects enrolled provided she:
3.1. Had a negative pregnancy test prior to entry into the study and:
Either
3.2. Had a documented record of surgical sterilisation
Or
3.3. Was of child-bearing potential and:
3.3.1. Agreed not to attempt to become pregnant during the study
3.3.2. Was routinely using an acceptable form of effective contraception (established use of oral, injected or implanted hormonal methods of contraception, intrauterine device (IUD) or intrauterine system (IUS), barrier method of contraception (condom or occlusive cap with spermicide), male sterilisation of sole partner; agreed to continue to do so during the study and for 28 days after study completion and agreed to use an additional barrier method for the duration of the study and for 28 days after study completion. (Hormonal contraception was not changed in the 3 months before the study).
3.3.3. Was not breastfeeding
4. Had a refractive error between -1 and +4 dioptres (D) spherical error and ≤1 D cylindrical error as measured by cycloplegic examination, habitually uncorrected
5. Had a spherical error between 1 D myopia and 4 D hyperopia.

6. Was able to read reduced Snellen type 6/9 at 35 cm (to exclude early presbyopia)
7. Had a best corrected visual acuity of 6/9 or better in each eye at 6 m
8. Had a near point stereopsis of 40 arc sec or better
9. Body Mass Index (BMI) within the range of ≥21 and ≤30 kg/m²
10. Vital signs with no clinically significant deviations outside the following ranges:
10.1. Heart rate 40-90 bpm
10.2. Systolic blood pressure 90-140 mmHg
10.3. Diastolic blood pressure 50-90 mmHg
11. Ability to communicate well with the Investigator and to comply with the requirements of the study (including contraception requirement)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
54

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 Torsades 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 mm Hg
13. Habitual wearers of spectacles or contact lenses, although if they had been prescribed them in the past and did not use them, they could still be included

14. Astigmatism greater than 1 D cyl
15. History or evidence of drug abuse (opiates, methadone, cocaine, amphetamines, cannabinoids or 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 21 units (females) or 28 units (males) per week 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 last three months
20. Use of any prescription medication within the last 14 days (with the exception of hormonal contraception)
21. Use of non-prescription medication (apart from paracetamol and ibuprofen) within the last 7 days that could have an impact on the safety and objectives of the study (at the Investigator's discretion).
22. 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 (all periods):
1. Development of any exclusion criteria since last visit
2. Positive urine test for alcohol
3. Positive drugs of abuse test
4. Positive pregnancy test
5. Use of any prescription medication since last visit (with the exception of hormonal contraception)
6. Use of non-prescription medication that may impact the safety aspects and objectives of the study, within the last 7 days (apart from paracetamol and ibuprofen)

Date of first enrolment
27/01/2009

Date of final enrolment
04/09/2009

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 a lack of participant consent being obtained at the time of the study.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No